Journal of Psychosomatic Research 79 (2015) 1–12

Contents lists available at ScienceDirect

Journal of Psychosomatic Research

Transparency of outcome reporting and trial registration of randomized controlled trials in top psychosomatic and behavioral health journals: A 5-year follow-up

Kira E Riehm [a,b], Marleine Azar [a,b], Brett D Thombs [a,b,c,d,e,f,g,*]

[a] Lady Davis Institute for Medical Research, Jewish General Hospital, Montréal, Québec, Canada
[b] Department of Psychology, McGill University, Montréal, Québec, Canada
[c] Department of Psychiatry, McGill University, Montréal, Québec, Canada
[d] Department of Epidemiology, Biostatistics, and Occupational Health, McGill University, Montréal, Québec, Canada
[e] Department of Educational and Counselling Psychology, McGill University, Montréal, Québec, Canada
[f] Department of Medicine, McGill University, Montréal, Québec, Canada
[g] School of Nursing, McGill University, Montréal, Québec, Canada

ARTICLE INFO

Article history:
Received 18 February 2015
Received in revised form 17 April 2015
Accepted 22 April 2015

Keywords:
Behavioral medicine
Bias
Randomized controlled trials
Selective outcome reporting
Trial registration

ABSTRACT

Objective: The extent that randomized controlled trials (RCTs) accurately reflect intervention effectiveness depends on the completeness and accuracy of published results. A previous study found that only 40% of 63 RCTs published in top behavioral health journals in 2008–2009 clearly declared primary and secondary outcomes and only 21% were registered. The objective of this study was to conduct a five-year follow-up to assess outcome reporting clarity, proportion of registered trials, and adequacy of outcome registration in RCTs in top behavioral health journals.
Method: Eligible studies were RCTs published in *Annals of Behavioral Medicine*, *Health Psychology*, *Journal of Psychosomatic Research*, and *Psychosomatic Medicine* from January 2013 to October 2014.
Results: Of 76 RCT publications reviewed, only 25 (32.9%) adequately declared primary or secondary outcomes, whereas 51 (67.1%) had multiple primary outcomes or did not define outcomes. Of the 76 trials, 40 (52.6%) had been registered. Only 3 studies registered a single primary outcome and time point of assessment prior to enrolling patients, and registered and published outcomes were discrepant in 1 of the 3 studies. No studies were adequately registered as per Standard Protocol Items: Recommendation for Interventional Trials guidelines. Compared to 5 years prior, the proportion of published trials with adequate outcome declaration decreased from 39.7% to 32.9% ($p = 0.514$). The proportion of registered trials increased from 20.6% to 52.6% ($p < 0.001$).
Conclusion: The quality of published outcome declarations and trial registrations remains largely inadequate. Greater attention to trial registration and outcome definition in published reports is needed.

Introduction

Well-designed and conducted randomized controlled trials (RCTs) provide the highest quality evidence for evaluating the effectiveness of health care interventions [1]. The degree to which published reports of RCTs reflect accurate, realistic estimates of intervention effectiveness, however, depends on how outcomes are defined and reported [2–4].

Most RCTs assess multiple outcomes, but ideally a single primary outcome variable is identified to answer the main question the trial is designed to address. Other outcome variables are designated as secondary [3–5]. The failure to designate a primary outcome complicates interpretation of results, particularly when different outcome variables give contradictory results [3]. Furthermore, without statistical adjustment, multiple outcomes generate a potentially large number of hypothesis tests, which increases the likelihood of false-positive claims of effectiveness [3,6].

Not designating primary outcomes and analysis methods *a priori* can also lead to selective outcome reporting [3,7], which occurs when statistically significant or outcomes from a study are published, whereas negative outcomes from the same study are not [8]. Even when a single primary outcome variable is identified, selective reporting biases may occur if multiple analyses methods are undertaken, if outcomes are assessed at multiple time points, or if outcome variables are compared using different metrics (e.g., change from baseline, final value) or methods of aggregation (e.g., mean, median) without specification of the primary method prior to enrolling patients [9,10]. The existence of selective reporting biases in published trial reports is well-documented. One review evaluated 16 studies that compared trial protocols or trial

* Corresponding author at: Jewish General Hospital; 4333 Cote Ste Catherine Road; Montreal, Quebec H3T 1E4; Tel.: +1 514 340 8222x5112.
E-mail address: brett.thombs@mcgill.ca (B.D. Thombs).

http://dx.doi.org/10.1016/j.jpsychores.2015.04.010
0022-3999/

registry entries to published results in a median of 54 RCTs (range 2–362) and found that at least one primary outcome had been changed, introduced, or omitted post hoc in 2–50% of the trials examined in the 16 studies [8].

Two initiatives have been introduced to increase transparency in trial reporting. First, the Consolidated Standards of Reporting Trials (CONSORT) statement [11] was developed to improve reporting of trials and to guide readers, peer reviewers, and editors in critical evaluations of RCT reports. CONSORT provides authors with a checklist of critical items that should be included in trial reports. A recent review found that RCTs published in medical journals that endorse the CONSORT statement are more completely reported than RCTs published in journals that have not formally endorsed CONSORT [12].

Second, in September 2004, the International Committee of Medical Journal Editors (ICMJE) implemented as policy the requirement that clinical trials must be registered in a public trial registry to be considered for publication in member journals [13]. Ongoing trials that began enrollment prior to July 1st, 2005, were required to register before September 13th, 2005. Trials beginning enrollment after July 1st, 2005, are required to register before beginning patient enrollment. Ongoing trials are defined as trials that are still collecting, cleaning, or analyzing data. Thus, currently, all newly published trials should be registered [13].

Trial registration may reduce publication bias, which occurs when entire trials go unpublished due to unfavorable results, because registration generates a public record of a trial, even if the results are not published [14]. However, trial registration can only reduce selective reporting of some results and not others to the extent that investigators adequately define primary and secondary outcomes in pre-trial registration. ICMJE policy states that, minimally, investigators must define a single primary outcome with a time point of assessment, as well as key secondary outcomes, at the time of registration [15].

In 2011, Milette et al. [16] examined the extent to which RCTs published in 4 top psychosomatic and behavioral medicine journals (*Annals of Behavioral Medicine, Health Psychology, Journal of Psychosomatic Research,* and *Psychosomatic Medicine*) between January 2008 and October 2009 had clearly defined primary and secondary outcomes in the published trial reports and had adequately registered trial outcomes pre-trial. Of 63 published RCTs, only 40% clearly declared primary and secondary outcomes and only 21% were registered. Only 1 trial registered primary outcomes with enough information for comparison to published outcomes, and registered and published outcomes were discrepant. Of the 4 journals reviewed, *Annals of Behavioral Medicine* [17], *Health Psychology* [18], and *Psychosomatic Medicine* [19] began requiring adherence to CONSORT in 2002 or 2003, and the *Journal of Psychosomatic Research* implemented CONSORT following publication of the Milette et al. study in 2011 [20]. Trial registration policies were implemented by *Annals of Behavioral Medicine* in 2010 [21] and by *Psychosomatic Medicine* [22] and the *Journal of Psychosomatic Research* [20] in 2011. *Health Psychology* does not require clinical trial registration.

In 2013, the Standard Protocol Items: Recommendation for Interventional Trials (SPIRIT) statement [23] was published for clinical trial protocols. The SPIRIT guidelines require that for each primary and secondary outcome trial protocols specify: (1) the specific measurement variable (e.g., Beck Depression Inventory score); (2) the participant-level analysis metric (e.g., change from baseline, final value, time to event); (3) the method of aggregation (e.g., mean, proportion above or below a cutoff threshold); and (4) the primary time point of interest for analysis.

The aim of the present study was to provide a five-year update on outcome reporting and trial registration practices for RCTs testing interventions designed to improve health published in *Annals of Behavioral Medicine, Health Psychology, Journal of Psychosomatic Research,* and *Psychosomatic Medicine*. Specific objectives were to (1) determine the proportion of RCT publications that clearly defined primary and secondary trial outcomes; (2) assess the proportion of adequately registered RCTs according to the methods used in Milette et al. [16] and the SPIRIT 2013 guidelines; (3) evaluate whether published primary outcomes were consistent with registered primary outcomes; and (4) compare the proportion of published RCTs with clearly defined outcomes and adequate pre-trial registration to results obtained by Milette et al. [16] 5 years ago.

Methods

Article selection

Milette et al. [16] reviewed articles published between January 2008 and October 2009 in 4 journals that had been identified previously as "leading psychosomatic and behavioral medicine journals" (p. 206) (*Annals of Behavioural Medicine, Health Psychology, Journal of Psychosomatic Research,* and *Psychosomatic Medicine*) [24]. In the present study, we sought RCTs published in the same 4 journals 5 years later, from January 2013 through October 2014. Titles and abstracts for all articles published in these journals during this period were uploaded into the citation management database RefWorks then into the systematic review manager DistillerSR. DistillerSR was used for all coding procedures and for tracking results of the review process.

Two reviewers independently reviewed titles and abstracts for eligibility. If either reviewer determined that a study was potentially eligible, full-text review was conducted by two reviewers, with disagreement resolved by consensus, including a third investigator as necessary.

Based on the ICMJE definition of clinical trials [13], which has been used in previous studies of RCT registrations [16,25], articles were included if they reported data from any RCT that randomly assigned participants to intervention and comparison groups to study the cause-and-effect relationship between an intervention and a health outcome. Articles that reported analyses of secondary trial outcomes, including subgroup analyses, were included. Studies that randomized participants into experimental conditions not intended to improve health (e.g., laughter versus mental stress conditions to assess arterial stiffness) or that primarily assessed intervention feasibility were excluded. Articles that reported only mediation or moderation analyses without reporting previously unpublished trial outcomes, used RCT data for cross-sectional analyses only, reported on longitudinal outcomes for all participants in a trial regardless of group assignment, assessed cost-effectiveness, or analyzed only control or treatment group data were excluded.

Data extraction and classification

Two investigators independently extracted and entered data into an online database using DistillerSR software. Discrepancies were resolved by consensus.

Objective 1 – clearly and adequately declared outcomes in published articles

Published articles were classified as reporting: (1) *primary*, (2) *multiple primary (same report)*, (3) *multiple primary (different report)*, (4) *multiple primary (with statistical adjustment)*, (5) *secondary*, or (6) *undefined* outcomes.

An article was classified as reporting a *primary* outcome if a single outcome was clearly and consistently defined as primary throughout the article or, alternatively, if a single primary outcome could be determined from the power analysis. Articles that measured a primary outcome variable at multiple time points in the context of a single repeated measures assessment with only one hypothesis test were classified as reporting a single *primary* outcome. Studies that identified more than one variable as the primary outcome variable or that identified a single variable, but analyzed multiple time points without specification of primacy, were classified as reporting *multiple primary (same report)* outcomes with one exception. If these studies made appropriate