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Journal of Clinical Epidemiology ■ (2017) ■

Journal of Clinical Epidemiology

COMMENTARY

Fostering responsible research practices is a shared responsibility of multiple stakeholders

Lex M. Bouter*

Department of Epidemiology and Biostatistics, VU University Medical Center, P.O. Box 7057, 1007 MB Amsterdam, The Netherlands

Accepted 20 December 2017; Published online xxxx

1. Introduction

In their commentary, Wallach et al. explain that breaches of research integrity will typically do damage to the reliability and validity of biomedical research [1]. This may harm regulatory and clinical decision-making. Consequently health care and public health may suffer. They point out that prevalent questionable research practices like poor study design, low power and selective reporting probably do substantially more damage than the rare occurrence of the classical ''deadly sins'' of fabrication, falsification, and plagiarism. Wallace et al. do not dwell much on the causes of the shortcomings listed in their table 1 and take the view that the remedy should come from better guidelines, more transparency, and mandatory training [1].

While I agree with all this, I would like to strengthen the argumentation by first analyzing the replicability crisis and the need for more transparency a bit further. Second, I shall explore what biomedical research can learn about fostering responsible research practices from other disciplines, social sciences first and foremost. Finally, the putative determinants of research misconduct and questionable research practices will be discussed, and the actions different stakeholders can take shall be explored.

2. Replicability crisis

A 2012 Nature publication showed the reproducibility of oncological animal studies to be embarrassingly low [2]. Also for other types of research, reproducibility rates between 10% and 40% are reported [3]. This is no surprise for methodologists, as some of the background was already pointed out in the classical article ''Why most research findings are false'' [4]. Next to low power and flawed study design, especially, selective reporting of positive results may be the most important driver of the replicability crisis.

We do not yet have a clear view on what we exactly mean when we say that a study is replicated [5]. We also do not know how common the problem is and what would be the most effective ways to deal with it. A common prejudice seems to be that replication is a second rate activity for investigators not bright enough to do innovative work. But that might not be true given the abundance of good quality applications for the research program on replication studies of the Netherlands Organisation for Scientific Research [6]. Interestingly, the field of clinical trials may be an exception in the sense that large prospectively registered well-designed multicentre trials may be quite reproducible. In this arena, even redundant replication may be an issue as can be illustrated in cumulative meta-analyses [7].

Wallace et al. point correctly out that there is still substantial room for improving the reliability and validity of clinical trials as the fundament of regulatory and clinical decision-making [1]. My point is that the situation is probably much worse in observational etiologic, diagnostic, and prognostic research. And also that these fields can learn a lot from the decades of experience in making randomized clinical trials more reliable and more valid.

3. Need for more transparency

Although the compliance should be improved further, prospective trial registration is the example that can most likely help other fields to fight selective reporting and to improve replicability. In its full version, the idea is that complete study protocols need to be deposited before the start of data collection [8,9]. Later changes are possible, but will leave traces and might be considered data-driven.

Funding: No financial support was received for this work.

Conflict of interest: L.M.B. chairs the World Conferences on Research Integrity Foundation, the Netherlands Research Integrity Network, and the program committee Replication Studies of the Netherlands Organisation for Scientific Research. L.M.B. organized and co-chaired the 5th World Conference on Research Integrity in Amsterdam, May 2017. L.M.B. is also a member of the steering committee of the REWARD (REduce research Waste And Reward Diligence) Alliance.

* Corresponding author. Tel.: +31 20 4441285.
E-mail address: lm.bouter@vumc.nl

https://doi.org/10.1016/j.jclinepi.2017.12.016

Also, the data analysis plan must be uploaded before the statistical analyses start. And after the study, the archive needs to be completed by adding the log of data collection, the syntaxes of the analyses, the full data set and its code book, and all results. It is debatable if and when the elements of this archive must be publicly accessible. And if not under which conditions and to whom access will be granted. To be able to practice transparency, a number of conditions have to be met, such as having the essential skills and facilities, and the means to adequately protect the identity of study participants. And there may be negative side effects of making data public, like *mala fide* misuse of data sets. For a fuller discussion, I refer to the ten commentaries on transparency that appeared in the February 2016 issue of this journal [10].

We should realize that the practice of transparency in the sense outlined previously concerns the tradition of hypothesis testing research. The essence of exploratory research is that the next steps in the project are data-driven; therefore, having a fixed study protocol is not useful. In exploratory research ''anything goes'', as long as it is clearly reported what has been done, and no conclusions are drawn on the emerging (*post hoc*) hypotheses.

Please note that the need to be transparent and to fight the lack of replicability and selective reporting are also the core elements in the Lancet REWARD Campaign that has many university medical centers and biomedical funding agencies as signatories [11]. The core idea is simple and started by an analysis that argued that 85% of clinical research may be wasted [12]. The reasons for that being avoidable were because the studies at issue have (1) irrelevant research questions, (2) poor research methods, (3) selective reporting, or (4) poor reporting quality. The last point links to the many ($N = 376$) useful reporting guidelines that are currently available for biomedical research and conveniently made accessible by the Enhancing the QUAlity and Transparency Of health Research (Equator) Network [13].

4. What can be learned from the neighbors?

Although biomedical research is important and may concern about half of the research volume worldwide, there exist other academic disciplines and their experiences with research misconduct, questionable research practices, and replication problems might be different. Biomedical research can learn from that and might consider adoption of effective solutions developed by its disciplinary neighbors. Although the evidence is thin, it seems that qualitative empirical research and hermeneutic and reflective approaches that are prevalent in the Humanities and in Law schools suffer from partly other threats to reliability and validity. Plagiarism, selective use of sources, and lack of transparency in the various steps of the argumentation seems to be relatively important in these domains. And in the natural sciences, replicability may be less a problem than elsewhere due to its tradition of internal replication, intense international collaboration, publishing preprints, and making available data sets to interested colleagues. For a comprehensive orientation, I recommend the recent report on *Fostering Integrity of Research* by the US National Academies of Science [14] and the European Commission briefing article on *Research Integrity: What it Means, Why it Is Important, and How we Might Protect it* [15].

A lot of inspiring work has been done in the Social Sciences. In a way it started with the case of data fabrication by Diederik Stapel that deeply shocked both the general public and scientists. An excellent investigation report appeared [16], and Tilburg University and the social sciences at large responded with important improvements and preventive measures. Recently, Klaas Sijtsma, who succeeded Stapel as dean of the School of Social and Behavioral Sciences at Tilburg University, presented a keynote lecture on the 5th World Conference on Research Integrity (WCRI) with the telling title ''Never waste a good crisis'' [17].

Another game changer in social science was the 2015 Science publication on ''Estimating the reproducibility of psychological science'' [18]. That made clear that on replication, the effect size of 100 ''cornerstone publications'' were only half of the initial magnitude, and the proportion of significant studies deceased from 97% to 36%. This lead to intensive soul searching and gave substantial momentum to the Center of Open Science [19] that introduced a number of highly relevant improvements like the Open Science Framework [20], the Transparency and Openness Promotion guidelines [21,22], and Registered Reports [23,24]. Recently, the ''Manifesto for Reproducible Science'' was published, highlighting the practical measures that most likely would help in solving the issues [25]. These developments could inspire further improvements in biomedical research. Also, the concept of ''researcher degrees of freedom'' and the need to restrict these as much as possible seems very relevant for biomedical research [26].

5. Determinants of research misbehavior

Ideally, interventions to prevent, diagnose, or treat the various forms of research misbehavior should be based on evidence on its most important determinants. Unfortunately, so far the evidence is scarce, and the field of ''meta-research'' is still in its infancy. The good news is that this seems to change fast, with increasing funds for research (e.g., in the European Union Horizon 2020 program [27] and programs on Fostering Responsible Research Practices [28] and Replication Studies [6] in the Netherlands). Also, research institutes are emerging, similar to the Collaboration for Research Integrity and Transparency [29], were Wallace et al. are based, the