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Knowledge dissemination in clinical trials: Exploring influences of institutional support and type of innovation on selective reporting

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ABSTRACT

This paper contributes to the ongoing debate on the reliability of published research. In particular, this study focuses on the selective reporting of research findings in clinical trials, defined as the publication of only part of the findings originally recorded during a research study, on the basis of the results. Selective reporting can lead to concerns ranging from publishing flawed scientific knowledge, to skewing medical evidence, to wasting time and resources invested in the conduct of research. Drawing upon a unique hand-collected dataset, this study investigates the contextual factors associated with selective reporting. Using 'risk of bias' ratings assessed based on expert judgment and presented in systematic reviews of clinical literature, this study explores whether selective reporting is associated with: (1) the source of *institutional support*; and, (2) the *type of innovation* evaluated. The results indicate that the odds of selective reporting are higher for industry-funded studies than for publicly-funded studies; however, this effect is restricted to studies where at least one author is industry-affiliated. In addition, the results suggest that selective reporting is more likely in projects exploring radical innovation, compared to those investigating incremental innovation.

1. Introduction

Although full disclosure of high-quality scientific knowledge is widely believed to support the advancement of science by allowing researchers to replicate prior works and to enhance opportunities for new investigations (Dasgupta and David, 1994; Merton, 1973), science is currently facing a 'reproducibility crisis' (Allison et al., 2016; Baker, 2016). In the field of management, among many others, scholars are voicing growing concerns about the prevalence of inconsistencies in publication (Goldfarb and King, 2016), the proliferation of questionable research practices (Necker, 2014; Fanelli, 2009, John et al., 2012) and the rise in the number of retractions, the majority of which appear to be the outcome of research misconduct (Fang et al., 2012; Van Noorden, 2011).

As a result of the systematic errors affecting the literature across fields, the scientific community is increasingly doubting the validity of published research (Byington and Felps, 2017). This debate raises questions, for example on the value of the knowledge that is produced, not only among the scientific community, but also for firms, investors and policymakers. Since scientific knowledge is a driver of social welfare and economic growth (Stephan, 1996; Stephan, 2012), flawed research can lead to substantial social and economic costs. In preclinical research, USD$28b are estimated to be spent every year in the US on studies that are irreproducible, leading to high costs and delays in the development of new drugs (Freedman et al., 2015). In clinical research, 85% of studies are believed to be avoidably wasted because of flaws in the design, conduct and reporting, leading to a substantial loss of public and private investment (Chalmers and Glasziou, 2009). Additional waste may be generated when research priorities are set by researchers and funders (Chalmers et al., 2014).

Despite the interest of researchers and research stakeholders in preserving the reliability of scientific literature, the current understanding of the drivers and consequences of flawed published research is limited. A recent review of evidence-based best practices for management research indicates that "Regardless of whether this lack of reproducibility is a more recent phenomenon, or one that has existed for a long time but has only recently gained prominence, it seems that we have reached a tipping point such that there is an urgency to understand this phenomenon and find solutions to address it" (Aguinis et al., 2017, p. 1–2).

Several studies have investigated the implications of defective science and errors in publication, focussing mostly on retractions (Lu et al., 2013; Furman et al., 2012, Azoulay et al., 2015; Azoulay et al., 2017). Financial interests (Bekelman et al., 2003) and other structural or individual incentives, including pressure to publish, organizational culture and the lack of policies on research integrity (Fanelli et al., 2015, Fanelli, 2010a; Fanelli et al., 2017; Davis et al., 2007), are often blamed for inducing questionable research behaviour. Lacetera and

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Zirulia (2011)'s model focuses on the incentives to falsify research, and on how frauds can be identified and prevented. Although some evidence comes from studies measuring publication bias, documented in various studies and disciplines within the biomedical and social sciences (Easterbrook et al., 1991; Franco et al., 2014), the drivers of poor reporting practices are not completely clear. Data sources are often restricted to surveys and ex-post reports of scientists who were found deceiving. Empirical tests are further complicated by challenges in detecting misconduct and in distinguishing the effects of outright misconduct from other influences.

Against this background, this study sets to explore selective reporting, defined as the publication of only part of the findings originally recorded during a research study, based on the results e.g., whether such findings are significant for the study investigators (Hutton and Williamson, 2000; Higgins and Green, 2011). The concern with selective reporting is that if results are selectively withheld based on their direction, then biases are introduced in the final research publication.[1]

This study examines selective reporting using data on clinical research projects. This is an apt setting for exploring selective reporting for a number of reasons. Firstly, the thorough revision of published studies is at the very heart of evidence-based medicine (e.g., Guyatt et al., 2008; Oxman and Group, 2004); thus, most extant research on publication bias has been conducted in the biomedical sciences (Easterbrook et al., 1991; Dwan et al., 2008; Dwan et al., 2013). Secondly, conversations on clinical trial data transparency have gained momentum in recent years, following several instances of large scale scientific mistakes or deliberate misconduct (e.g., Horton, 2004; Goldacre, 2014). Thirdly, the social and economic consequences of flawed reporting in clinical research can be substantial. Biased evidence can delay the introduction of potential life-saving treatments, and at worst, cause harm to patients and trial volunteers. Considering the high costs of clinical research, misreporting can waste substantial resources, as proved by the Tamiflu case (Smith, 2009) and as described in The Lancet's series of publications about reducing waste in biomedical research (e.g., Glasziou et al., 2014).

Despite ample empirical confirmation of the widespread occurrence of selective reporting, the evidence on the correlates of selective reporting is scarce (e.g., Dwan et al., 2013). Although some suggestions are provided by the analysis of prominent cases, such cases are likely to capture only the tip of the iceberg and may be of limited value for policy and prevention. Additional complications are introduced by the lack of standardised methodologies for assessing bias (e.g., Dechartres et al., 2011).

Starting from the above evidence, this study attempts to generate insights into the factors associated with selective reporting. Specifically, focussing on contextual factors, this paper sets to explore whether selective reporting correlates with two salient characteristics of the clinical research project: (1) *the source of institutional support*; and, (2) the *type of innovation* evaluated. The exploration of the relationship between the source of institutional support and selective reporting is important in view of growing concerns regarding the links between the commercialisation of research and publication bias (Bekelman et al., 2003). More generally, although private institutions are involved in publishing and have many reasons to so do (Polidoro and Theeke, 2012; Azoulay, 2002; Hicks, 1995), the logics of industrial science may differ from those of academic science, creating conflicting incentives (Aghion et al., 2008; Gittelman and Kogut, 2003; Murray, 2010). With regard to the association between the nature of research and selective reporting, empirical evidence so far is limited. In particular, we do not know much about the influences on publication bias that may arise from the type of innovation explored in a project (e.g., drugs in clinical trials). This is interesting considering that incremental and radical research projects may be more or less likely to be fraudulent and more or less liable to be discovered as fraudulent (Lacetera and Zirulia, 2011). A better understanding of this issue is also important given recent recommendations that quality control measures could prioritise innovative studies, such as publications about drugs that have high therapeutic potential (Ioannidis et al., 2017).

To tackle these issues, this study employs a unique hand–collected sample using 'risk of bias' ratings presented in the reviews compiled by the Cochrane Collaboration, the leading organisation in the field of provision of informed medical decisions.[2] Cochrane reviews use rigorous expert judgment and are distinctively placed to assess bias in clinical research papers.

The results of the present study show that the receipt of industry funding correlates positively with selective reporting; however, this effect is restricted to studies where at least one author is affiliated to industry. In addition, the analysis of the relationship between the type of innovation and selective reporting indicates that the chances of selective reporting are higher for projects exploring radical innovation, compared to projects investigating incremental innovation.

Although causality cannot be proved, these results contribute to a better understanding of the drivers of publication bias, adding to prior literature on scientific misconduct (Fanelli et al., 2015; Lacetera and Zirulia, 2011), on publication bias (e.g., Franco et al., 2014; Fanelli et al., 2017), on errors in publication leading to retractions (Furman et al., 2012; Van Noorden, 2011; Azoulay et al., 2017; Azoulay et al., 2015) and on lack of replication (Aguinis et al., 2017; Baker, 2016).

Besides indicating specific correlates of selective reporting, this analysis speaks to the ongoing debate regarding the quality of published research, with repercussions for important matters, such as tackling research waste. Specifically, the findings support the view that prevention and quality control measures should be tailored or prioritised based on studies' characteristics, such as the subject of investigation and the field.

2. The debate on transparency and selective reporting in clinical research

Clinical trials are central to the functioning of evidence-based medicine, a system aimed at grounding clinical decision-making in prior medical knowledge (Sackett et al., 1996; Guyatt et al., 2004). Although the evidence-based system has gained remarkable support over time, and in 2007 readers of the British Medical Journal chose it as one of '15 milestones of medicine' (Godlee, 2007), recent developments have drawn attention to the possible flaws within this system. To name a few, concerns were raised following the case of the nonsteroidal anti-inflammatory drug Vioxx, withdrawn from the market in 2004, while unacceptable cardiovascular risks of the drug were evident as early as 2000 (Horton, 2004; Krumholz et al., 2007). In the UK, public attention to the issues surrounding trial transparency amplified as a result of the government decision to stock the influenza vaccine Tamiflu at great cost, notwithstanding concerns about the drug's efficacy (Smith, 2009).

Against this background, the issues of transparency and trial data release have been given increased attention by academics and consumer groups. In particular, although trials need to be registered and their results have to be published in trial registries, enforcing such legislation has proved difficult (Zarin et al., 2011; Devito et al., 2018; Tang et al., 2015; Prayle et al., 2012). The AllTrials campaign, launched in 2013 to advocate for greater trial data disclosure (Chalmers et al., 2013), has been credited for highlighting the issue and for helping shape legislation.[3]

Although trial data can be disclosed in several ways (e.g., trial registries), the peer-review system still holds its original function to

[1] In the context of this study, the term bias is used to identify "a systematic error, or deviation from the truth, in results or inferences." (Higgins and Green, 2011).

[2] http://www.cochrane.org/ Accessed in March 2018.

[3] http://www.alltrials.net Accessed in March 2018.