Research Policy xxx (xxxx) xxx–xxx

Contents lists available at ScienceDirect

Research Policy

journal homepage: www.elsevier.com/locate/respol

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

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ARTICLE INFO

Keywords:
Reliability of research
Reproducibility crisis
Science policy
Scientific misconduct

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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https://doi.org/10.1016/j.respol.2018.04.005
Received 29 April 2016; Received in revised form 1 April 2018; Accepted 3 April 2018

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.

certify research results (Merton, 1973) and writing manuscripts for publication remains a fundamental component of clinical research. As far as publication in academic journals is concerned, a profusion of statistically significant, 'good' results have long been acknowledged by the scientific community. Far from giving any optimistic interpretation e.g., on the efficacy of research, scholars have identified several publication practices that directly contribute to the skewness of printed results.

First, researchers may simply decide against the publication of entire studies, based on whether the results are 'positive'. This practice, concerning the entire suppression of a research paper, has been discussed in many studies, with recent estimates indicating that the results of half of clinical trials are never published (Lexchin et al., 2003; Bekelman et al., 2003; Dwan et al., 2008; Mcgauran et al., 2010; Song et al., 2010; Lee et al., 2008; Riveros et al., 2013).

In addition, even for those studies that reach publication, only part of the original research findings may be included in the published paper, a practice that is referred to as selective reporting. More specifically, the term selective reporting has been used to indicate the selection of a subset of research findings on the basis of their direction for publication in academic journals (Hutton and Williamson, 2000; Higgins and Green, 2011). The most recent systematic review of the evidence on selective reporting discusses the increasing proportion of studies in which at least one outcome is changed or omitted, with some analyses concluding that up to 62% of the investigated trials had major discrepancies in the outcomes (Dwan et al., 2013).

Selective reporting has received a lot of attention in clinical research (Dwan et al., 2008; Chan et al., 2004; Chan and Altman, 2005; Dwan et al., 2013; Dechartres et al., 2017; Smyth et al., 2011). Two main themes emerge from these studies: (1) selective reporting is a potential threat to the reliability of research; and, (2) bias can be introduced in many ways and it is difficult to detect.

The central point to note in the definition of selective reporting is that the publication of a study's findings or, rather, the lack thereof, is influenced by the direction and statistical significance of these findings. In other words, 'negative' or 'null' outcomes have lower chances of being reported. Accordingly, it has been argued that selective reporting can present the scientific enterprise with greater threats than those caused by high profile fraud cases (Martinson et al., 2005). The implications of selective reporting are particularly serious in clinical research: efficacy of a treatment may be overestimated or, even more concerning, adverse effects may be underestimated (Ioannidis, 2009).

Trial publications may be subject to different types of selective reporting. The effects of a drug on certain outcome variables may be recorded, but then entirely excluded from publication. Additionally, papers may discuss only one of the several different ways in which an outcome can be gathered or operationalised (e.g., continuous or binary). More subtly, the descriptions of outcomes as 'primary' or 'secondary' can be altered retrospectively in light of findings (e.g., Chan et al., 2004). Selective reporting may also refer to the inadequate reporting of a drug's adverse events (e.g., Tang et al., 2015) or to the misreporting of statistical methods.

Compared to other disciplines, the acknowledgement of selective reporting is somehow less problematic in clinical research, because distinctive procedures are in place. Detailed descriptions of study objectives and intended outcomes may be available in trial protocols or trial registries, official catalogues for recording clinical studies. Thus, selective reporting can be detected by comparing the published report against the research protocol and/or the clinical trial registry record.[4]

[4] When these are not available, selective reporting can be assessed by comparing a study to grey literature or even with the examination of one sole publication. For example, selective reporting can be identified when some measurements are expected to appear together, such as systolic and diastolic blood pressure, but only one is reported (Higgins and Green, 2011).

3. Emerging evidence on the correlates of selective reporting

In this study, I ask the following question about selective reporting: *Are specific factors systematically associated with (the incidence) of selective reporting?* Although the pervasiveness and importance of selective reporting have been widely discussed, the evidence on the factors associated to selective reporting is limited. Past works largely rely on self-reported data from surveys of researchers, which may be subject to bias and not provide suitable foundations for prevention or policy. Few empirical studies describe the reasons why research outcomes are not reported: these include lack of clinical importance and lack of statistical significance (Chan and Altman, 2005, Chan et al., 2004, Smyth et al., 2011, Dechartres et al., 2017).

In seeking to explore the correlates of selective reporting, this study focuses on contextual factors, and specifically on project-level characteristics. These may be more or less important than other factors (e.g., individual-level characteristics); nevertheless, the observation of structural factors should represent a good starting point to begin the process of inquiry into selective reporting. To frame my analysis, I consider my research question in the context of past literature and focus on two salient characteristics of research projects: (1) the source of *institutional support*; and, (2) the *type of innovation* evaluated.

3.1. Relationship between source of institutional support and selective reporting

A growing number of clinical trials are privately funded, possibly reflecting the fact that the pharmaceutical industry now spends more on research than government research centres e.g., the National Institute of Health (NIH) in the US (Moses et al., 2015). Pharmaceutical companies are more and more involved with academia, and a variety of financial interactions exist, ranging from academic institutions receiving industry funding, to personal financial ties with industry sponsors. Private institutions are also increasingly contributing to scientific discourse via publications in peer-reviewed journals and their outputs are often of a high standard and widely cited (Lim, 2004; Koenig, 1983; Hicks, 1995).

This well documented increase in industry-involvement is raising concerns related to its effect on the quality of published research (Bekelman et al., 2003), considering that firms have not only the motivation but also the means to stay in control of the outcomes of the publication process. In the pharmaceutical sector specifically, many studies have examined the motivations that lead firms to publish (Cockburn and Henderson, 1998; Zucker et al., 2002; Gittelman and Kogut, 2003). The publication of clinical trial results in academic papers is an important means for firms to communicate the benefits of approved compounds to prescribers and regulators (Polidoro and Theeke, 2012; Azoulay, 2002). Publishing positive results can help ensure that a treatment will be approved by the regulator and may translate in the wider use of a new product. On the other hand, negative results can put an end to the development of a new drug or reduce its market uptake.

Available evidence suggests that when firms make their research findings available in scientific journals, they indeed try to stay in control of the outcomes of the publication process (Sismondo, 2008; Gotzsche et al., 2007). Blumenthal et al. (1996) found evidence of both publication delay and nondisclosure restrictions, with reasons for not publishing including to postpone the dissemination of undesired results. Bekelman et al. (2003) found that industry funding is associated with limitations on data access or the publication of results. Czarnitzki et al. (2014) found a strong positive relationship between the degree of publication restrictions and the share of industry sponsorship.

The relationship between industry funding and publication bias specifically has been analysed extensively in recent years, particularly in medical research; results are mixed. Several studies have found that industry-sponsored studies are more likely to report favourable or

significant outcomes compared to privately-funded studies (Bekelman et al., 2003; Lexchin et al., 2003; Schott et al., 2010; Song et al., 2010; Lundh et al., 2012). However, another group of studies suggests that bias is not limited to industry-sponsored publications. A qualitative study of editors' and publishers' views on publication bias (Wager and Williams, 2013) found that there were disagreements among interviewees about the role of research funders in publication bias. Inconsistencies have also been recognized in the reporting of high-quality government-funded or academic trials (Ross et al., 2012; Linker et al., 2017; Chan et al., 2004; Berendt et al., 2016).

Taken together, the mechanisms underlying the prevalence of positive outcomes in industry trials remain to be fully understood: reporting bias is one of several possible explanations. It has been suggested that the lack of conclusive results regarding the relationship between bias in publication and source of funding is partly due to the complexities of industry involvement and the lack of a standardised methodology for its assessment (e.g., Van Lent et al., 2013). In particular, in determining the potential role of the funding source on non-publication, it is believed to be important to discriminate between different forms of support and disentangle the effect of funding from authorship (e.g., Ahn et al., 2017). Regarding selective reporting specifically, the most recent review of the available evidence (Dwan et al., 2013) concludes that although funding is an important factor to consider when investigating reporting bias, there are no definite results on the relationship between industry involvement and selective reporting.

This brief literature review indicates that findings are mixed with regard to the relationship between industry involvement and bias in scientific publication. While there is some evidence supporting an association between industry involvement and reported findings, the effect of the funding source on bias remains unclear, thus speculative.

3.2. Relationship between type of innovation and selective reporting

The association with private institutions is one among many features of clinical research projects and we can expect that industry involvement is not the only factor creating challenges for the complete reporting of research results. It seems reasonable to question whether different pressures or difficulties may arise for investigators based on whether the technologies evaluated are more or less novel.

Little is known about whether the type of innovation investigated in a research project may associate with bias in reporting. A better understanding of this issue is important for two reasons. Firstly, it would be interesting to know whether the pursuit of innovation comes at a price of increased bias in study conclusions. Secondly, if selective reporting is associated with specific types of research, then many policy initiatives that encourage research transparency might be re-aligned to consider the diverse nature of the research projects.

The review of past literature on publication bias and scientific misconduct indicates that the nature of research is likely to have an influence on the chances of selective reporting (Lacetera and Zirulia, 2011; Fanelli, 2011). The work of Lacetera and Zirulia (2011) suggests that there may be a mismatch between the type of research that is more likely to be fraudulently produced (incremental) and the type of research that is more likely to be uncovered if fraudulent (radical).

Considering pressures to publish, it is not clear whether these are more intense in radical as opposed to incremental research. On one hand, if the value of a published article (e.g., in terms of citations) is higher for ground-breaking research, incentives to highlight positive findings and alter or remove negative results may be stronger compared to incremental research. On the other hand, given that academic journals pursue the publication of new and original findings, novel research may have a higher chance of being published, making it more pressing for investigators involved in incremental research to engage in partial reporting to increase the chances of publication.

The likelihood of altering or removing study results may also depend on the probability that a research study reaches findings that are negative or insignificant (Ioannidis, 2005; Fanelli, 2010a). It is unclear how this probability may vary based on the type of innovation investigated. Incremental research relies on a great amount of prior information; thus, failure rates may be lower. In biomedical research, for example, development programmes are riskier for novel drugs compared to drugs that have therapeutic qualities similar to those of an already-marketed drug. However, prior knowledge in incremental research may also have the effect of increasing scientists' confirmation bias and theory tenacity, the persistent belief in a theory notwithstanding conflicting evidence (Loehle, 1987).

In addition, the chances of misreporting may depend on the rigour of research methodologies. In studies that address novel phenomena, the connection between theories and findings could be more open to interpretation. This would give scientists more freedom in deciding how to interpret data, which increases the chances that they will support the hypotheses they believe to be true (e.g., Ioannidis, 2005). However, flexible methodologies may also characterise incremental research. For example, in medical research, concerns have been raised about the quality of the evidence supporting incrementally new drugs (e.g., Hitchings et al., 2012).

The studies referred to above show that while the type of research undertaken may have an influence on what gets published, predictions on where poor reporting is more likely are often conflicting and have been empirically verified by very few studies.

4. Data source and measures

4.1. Data sources

The literature here reviewed indicates that prior work on scientific misconduct and publication bias is complicated by the limitation of data sources and the lack of a standardised methodology for the assessment of bias (e.g., Dechartres et al., 2011). To attempt to tackle these issues, this study relies on a hand-collected dataset that leverages expert-driven assessment of the risk of bias introduced by selective reporting.

My main source of information on clinical papers, including their risk of bias ratings, was the Database of Systematic Reviews maintained by the Cochrane Collaboration. This organisation is an international not-for-profit association delivering reliable summaries of health information that are used to inform policies (Bunn et al., 2015). The work of the Cochrane Collaboration has been fundamental with regard to the promotion of systematic reviews and the shift to evidence-based medicine (Guyatt et al., 1992; Guyatt et al., 2004). Among others, they provide input on the way research evidence is identified and assessed by the Word Health Organization (WHO). Cochrane reviews are compiled following a thorough appraisal of published and unpublished evidence by review authors who are experts in the subject area.

Each Cochrane review addresses a specific question to establish whether or not there is convincing evidence about certain interventions, for instance, *Can antibiotics help in alleviating the symptoms of a sore throat?* After searching for all available evidence on a certain topic, reviewers assess findings using predefined guidelines, and present the results in a structured format as described in the Cochrane Handbook (Higgins and Green, 2011). Cochrane reviews describe the methodological quality of all appraised trials focusing on five characteristics that may introduce a risk of bias in the study results: (1) adequate sequence generation; (2) adequate measures to conceal allocation; (3) blinding; (4) completeness of outcome data; and, (5) selective reporting − the key dimension considered in my analysis. Each risk of bias dimension is assessed systematically and in duplicate by expert reviewers who reach consensus. A 'traffic–light' representation is then provided for each study, where green indicates a low-risk of bias, amber an unknown bias risk and red a high-risk of bias.

To build a comprehensive dataset, I started by investigating all the titles registered with the Cochrane Review Groups covering seven

therapeutic areas: Endocrinology, Respiratory, Infectious Diseases, Cardiology, Oncology, Mental Health and Dermatology. My search strategy generated 764 reviews, of which I identified 75 for inclusion. The included reviews appraised 1839 clinical trials. For each trial, Cochrane reviews listed one or more publications reporting the trial results. To build a dataset of projects univocally paired to scientific papers, in case of multiple publications I linked each trial to the reference that most closely resembled the trial code name used in the Cochrane review (e.g., for a trial coded as 'Meltzer 2003′ I would link the reference authored by Meltzer in 2003). Duplicates, trials that were not matched to a published paper (e.g., conference abstracts and posters) and studies with no selective reporting rating were then removed from the selection, leaving 1068 clinical trial/publication pairs. For these studies, I extracted the risk of bias rating assigned by Cochrane and any additional study information. Due to the lack of a standardised reporting format across reviews, cleaning the data and matching the relevant trial information to build a structured dataset entailed considerable effort.

I extended the data in three directions. First, I used SCOPUS to collect bibliometric data for the full set of trial publications. I was specifically interested in extracting information about authors' affiliations, which I used to explore the relationship between institutional support and selective reporting (see Section 5.2). A total of 39 (4%) publications were not retrieved in SCOPUS or Web of Science, resulting in a total of 1029 articles for the final sample. Second, I manually searched all publications and accessed the full-text versions to collect any information on funding and conflicts of interest (e.g., from acknowledgements and footnotes). Finally, I analysed the titles of all the papers to extract the name of the focal drug investigated in each trial and I attempted to match these drugs with the list of all the New Drug Applications (NDAs) approved in the U.S. by the Food and Drug Administration (FDA).[5] The matching was conducted based on brand and generic drug names. Because drugs can be approved in several dosages and they can have different formulations, I also tried to match the FDA's approval record corresponding to the precise dosage/formulation investigated in each trial. Studies concerning (1) biologics; (2) vaccines; (3) non-drug interventions; and, (4) long established drugs (approved before 1982) were excluded because reporting requirements in the FDA databases are different. For the drugs that were retrieved in the FDA's database, I collected the assigned chemical type (e.g., whether the approved NDA was for a New Molecular Entity) and therapeutic significance rating (e.g., P for priority reviews drugs). These categorisations are used in my analysis on the relationship between type of innovation and selective reporting (see Section 5.3). I was also interested in checking whether each drug was specifically approved for the indication(s) investigated in the included studies and whether these were the first or subsequent indications approved. To collect this information, I read approval letters (for never-before-approved drugs) as well as any efficacy supplements (for drugs approved for new uses).[6]

From the initial list of 1029 publications included in the dataset, the matching process identified 471 papers examining 78 FDA approved drugs. These treatments were specifically approved in the formulations and indications investigated in the included trials. The remaining trials included: 226 studies that were excluded because reporting requirements in the FDA databases were different (e.g., biologics); 195 studies concerning drugs that could not be retrieved in the FDA approval dataset (e.g., drugs that were not approved by the FDA); and, 137 studies where I was unable to identify the focal drug or resolve ambiguities regarding the specific indication/patient population under study.

4.2. Measures

To operationalise selective reporting in my analysis, I relied on the risk of bias from selective reporting ratings indicated in the Cochrane reviews. These ratings are based on expert judgment made applying specific and unambiguous criteria listed in the Cochrane Handbook (see Section 4.3). Specifically, the Handbook indicates as criteria for a judgement of a 'high risk' of bias due to selective reporting any one of the following: (1) "not all of the study's pre-specified primary outcomes have been reported"; (2) "one or more primary outcome is reported using measurements, analysis methods or subsets of the data (e.g., subscales) that were not pre–specified"; (3) "one or more reported primary outcomes were not pre–specified (unless clear justification for their reporting is provided, such as an unexpected adverse effect)"; (4) "one or more outcomes of interest in the review are reported incompletely so that they cannot be entered in a meta–analysis"; and, (5) "the study report fails to include results for a key outcome that would be expected to have been reported for such a study". I created a binary variable ('Selective Reporting') set to 1 when the Cochrane reporting rating indicated high-risk of bias from selective reporting and 0 otherwise (unknown or low-risk of bias from selective reporting).[7]

To examine the correlates of selective reporting, I identified and developed the following independent variables.

4.2.1. Source of institutional support

The role of the source of support in drug trials involves a variety of levels ranging from financial support and donation of study medication by a drug company, to input from the manufacturer in the trial design, conduct, data analysis and publication of results. Focusing on direct founding alone may neglect other important types of personal financial interests and associations such as employment, consultancy, stock ownership and honoraria (Van Lent et al., 2013). Accordingly, in this study I have explored both (1) direct *funding*; and, (2) personal *financial interests*.

To identify the source of funding (industry as opposed to non-industry) I considered statements of sources of support and acknowledgments declared in the individual publications (e.g., "trial funded by industry", "trial sponsored by industry" "financial support received from a pharmaceutical company", "unrestricted educational grants"). I then distinguished between studies wholly or partially funded by industry ('Industry') and studies funded independently of industry ('Non-Industry'). The remaining studies that lacked sufficient information on funding to be categorised as funded by industry or other sources, fell into two groups: studies explicitly reporting no funding ('None Declared') and studies with no funding information reported ('Not Reported').[8]

No consensus exists on how financial interests are best conceptualised and measured. A common approach in biomedical research is to rely on published information such as disclosures or the authors' affiliations to infer the existence of conflicts of interest (e.g., Perlis et al., 2005). In line with these studies, I defined financial interests as any report of consulting or speaking fees, stock ownership or employment by a firm. However, I also inferred financial interests where no disclosure was made, but the study authors were affiliated to a pharmaceutical company. Specifically, I considered whether: (1) at least one author had a professional affiliation to a pharmaceutical company ('Employment'); (2) at least one author had declared a personal financial interest including: consulting or speaking fees, stock ownership

[5] FDA's Drug Approvals Databases is available at: http://www.fda.gov/Drugs/InformationOnDrugs/default.htm.

[6] A relatively small number of efficacy supplements for new indications are submitted via a full original new drug application (type 6 NDA). All others efficacy supplements are submitted as supplements to original NDAs (supplemental NDAs). Approval letters are publicly available at: http://www.accessdata.fda.gov/.

[7] To test for the thoroughness of the ratings, I took into consideration any comments that reviewers might have provided alongside the rating (this sense-check was suggested by one of the editors of the Cochrane Collaboration). Reassuringly, the vast majority of the trials with a high-risk of bias from selective reporting had a comment, indicating meticulousness.

[8] For 59 publications, I could not access the full text online. These were flagged in the dataset as records with funding 'Not Investigated'.

('Other Financial Associations'); and, (3) the study included provision of study medication ('Donation of Medication').[9]

4.2.2. Type of innovation

On the basis of the *drug composition* of new applications, the FDA distinguishes between (1) New Molecular Entities (NMEs) and (2) incrementally modified drugs, which modify an existing drug to use it in improved formulations or other indications. Being based on active ingredients that have never been marketed before, NMEs are considered the most technologically advanced drugs. Given that NME status is the most commonly adopted measure of innovation e.g., the more NMEs approved by the FDA in a given year, the more innovation in the industry (e.g., Kesselheim et al., 2013), I started by investigating whether a trial was evaluating an NME ('NME' = 1 if the drug is New Molecular Entity).

Depending on the *therapeutic potential* of new drug applications, the FDA also separates Priority and Standard review applications. Priority review status is given to those drugs which appear to represent an advance over available therapies and can fill important unmet medical unmet needs. Standard review drugs, on the other hand, have therapeutic qualities like those of an already marketed drug. Accordingly, I distinguished between (1) NME that also received Priority status ('Priority NME') and (2) NME that only received Standard review designation ('Standard NME').

Several control variables were added to the model at the level of: the trial; the article; the Cochrane review; and, the research area. First, I collected data on characteristics of trials that could influence bias. These include study size ('Participants', the natural log transformation of the number of enrolled participants), duration ('Weeks', the log transformation of the number of weeks), choice of comparator ('Placebo', 1 = trial was placebo-controlled) and blinding ('Blinding Bias', 1 = trial was rated as at high risk of bias due to blinding in the Cochrane reviews).[10] I also considered the risk of bias ratings along the remaining three dimensions assessed by Cochrane ('Any Other Bias', 1 = trial was rated as at high risk of bias in at least one of the reported dimensions e.g., adequate sequence generation, adequate measures to conceal allocation and completeness of outcome data).

Given that the quality of a study may be associated with publication in a high impact journal (Lee et al., 2002), I controlled for journal quality ('JCR', the log transformation of impact factors from Journal Citation Reports of the Institute for Scientific Information). The sample includes articles published at various times from 1983 to 2012. Over this period, two major events attempting to increase the transparency of research occurred: (1) in 2005, the International Committee of Medical Journal Editors (ICMJE) announced that journals would consider a trial for publication only if it had been previously registered; and, (2) in 2007, the FDA required the registration of all trials in ClinicalTrials.gov. Although academic studies indicate that the ICMJE's and FDA's initiatives may have failed in some respect (Zarin et al., 2005; Zarin et al., 2011; Prayle et al., 2012; Hooft et al., 2014), I anticipate selective reporting to be less frequent in more recent trials. To capture the influences of both initiatives (considering a lag of 2 years for the ICMJE initiative), I added a variable 'Published After 2007′ (1 = year of article publication > = 2007).

Past studies have indicated that the production of multiple publications from single studies can lead to bias in a number of ways (e.g., Huston and Moher, 1996). Thus, I added the natural log transformation of the number of references that are associated to the trial, as reported in the Cochrane reviews ('Papers'). Given that the geographical origin of the research may be a potential source of bias, in line with previous evidence on national origin and corrupt behaviour (Fisman and Miguel, 2007) I also included a dummy ('First Affiliation USA',1 = if the corresponding author affiliation was from the United States). Finally, I included the log transformation of the count of the affiliations of the article ('Affiliations'). To capture methodological differences in the Cochrane appraisal system over time, I distinguished the most recent reviews ('Reviewed After 2012′ = 1) from those published before 2012. Finally, to account for differences across scientific fields, I included dummies at the level of the seven therapeutic areas ('Oncology', 'Mental Health', 'Infectious Diseases', 'Cardiology', 'Endocrinology', 'Respiratory' and 'Dermatology').

4.3. Validity and reliability of the selective reporting measure

To address potential concerns regarding the validity of the measure of selective reporting used in this study, I gathered detailed information about the process of preparing Cochrane reviews, specifically focussing on how review authors arrive at rating risk of bias from selective reporting. First, I examined the Cochrane reviewers' official guide, the Handbook (Higgins and Green, 2011). Second, I interviewed four Cochrane review authors from three different fields.

The interviews and the inspection of the Handbook indicate that writing a Cochrane review requires considerable time, coordination, and expertise. All reviews are undertaken by a team of authors, which must include expertise in the topic area and in systematic review methodology. The editorial team of each Cochrane Review Group is ultimately responsible for the decision to publish a review following peer evaluation. 'Risk of bias' ratings are based on expert judgment, grounded upon a set of clear-cut criteria listed in the Handbook. To allow for validation and replication of the ratings, any risk of bias judgement includes a comment that can be verified. Furthermore, to overcome the dangers of individual bias, all ratings are assessed separately by at least two authors; divergences are resolved by consensus discussion or with the intervention of a third expert.

A specific worry may be that review authors adopt more (or less) stringent criteria to appraise industry-funded studies. All interviewees reported that articles are assessed merely on their scientific merit, using the same criteria, regardless of the funding source. In addition, the Collaboration has a code of conduct for avoiding potential conflicts of interest e.g., reviews cannot be funded through commercial sources.

To test for the reliability of the measure (e.g., if the risk of bias ratings were to be done a second time, would they yield the same outcomes?) I considered a subset of publications in my sample that were rated in more than one review. The risk of bias ratings for trials assessed more than once were largely consistent.[11]

5. Modelling strategy and results

5.1. Descriptive statistics

Descriptive statistics of the variables for the full dataset (1029 papers used for the first analysis on the relationship between institutional support and selective reporting) are given in Table 1.

Selective reporting was identified in 21.7% of the trials in the sample. Most of the studies (59.4%) received industry funding and just over half of all papers (51.4%) have at least one author with some personal financial interest. T-tests show that, in the sample considered,

[9] These were built as mutually exclusive variables e.g. 'Other personal associations' identifies records with personal associations other than employment (captured in 'Employment').

[10] In over one third of cases the trial duration was either missing from the characteristics reported in the Cochrane review or it was just provided as a range e.g. 8–26 weeks. In these cases, duration was estimated using the mean duration for the trials in my dataset investigating the same condition (where duration was missing) or the median point of the given range (e.g. 16 weeks for the '8 to 26 weeks' range). I created an indicator variable ('Duration Estimate') to flag these instances.

[11] 105 publications were assessed in more than one review. Out of these, 10 had different selective reporting ratings, changing over time from low to high (n = 5) or from high to low (n = 5). In my final sample, I included the most recent rating for these studies.

Table 1
Descriptive statistics (Full sample used for the first analysis, N = 1029).

VARIABLES	N	Mean	sd	min	max
Selective Reporting	1029	0.217	0.412	0	1
Funding					
Industry	1029	0.594	0.491	0	1
Industry Sole	1029	0.53	0.499	0	1
Industry Partial	1029	0.0641	0.245	0	1
Non-Industry (ref. category, removed)	1029	0.19	0.393	0	1
None Declared	1029	0.0233	0.151	0	1
Not Reported	1029	0.135	0.342	0	1
Not Investigated	1029	0.0573	0.233	0	1
Personal Financial Interests					
Any	1029	0.514	0.5	0	1
Employment	1029	0.379	0.485	0	1
Other Financial Associations	1029	0.0632	0.243	0	1
Donation Of Medication	1029	0.0719	0.258	0	1
Interaction (Industry Funding And Employment)					
None (ref. category, removed)	1029	0.18	0.384	0	1
Employment Only	1029	0.0107	0.103	0	1
Industry Funding Only	1029	0.261	0.44	0	1
Industry Funding And Employment	1029	0.332	0.471	0	1
Controls					
Participants (log)	1029	5.282	1.475	1.386	11.15
Weeks (log)	1029	2.722	1.136	0	6.254
Duration Estimate	1029	0.342	0.475	0	1
Placebo	1029	0.246	0.431	0	1
Blinding Bias	1029	0.206	0.405	0	1
Any Other Bias	1029	0.257	0.437	0	1
JCR (log)	1029	1.018	0.552	0	2.353
Published After 2007	1029	0.292	0.455	0	1
Papers (log)	1029	0.356	0.629	0	2.773
First Affiliation USA	1029	0.348	0.477	0	1
Affiliations (log)	1029	1.114	0.841	0	3.045
Reviewed After 2012	1029	0.478	0.5	0	1
Area Dummies					
Oncology (ref. category, removed)	1029	0.0632	0.243	0	1
Endocrinology	1029	0.0496	0.217	0	1
Cardiology	1029	0.119	0.323	0	1
Mental Health	1029	0.253	0.435	0	1
Respiratory	1029	0.137	0.344	0	1
Infectious Diseases	1029	0.225	0.418	0	1
Dermatology	1029	0.154	0.361	0	1
Year Paper	1029	2002	6.299	1983	2012
Journal JCR	1029	2.261	2.094	0	9.514
Participants (count)	1029	1046	5010	4	69,274
Weeks (count)	1029	31.17	54.06	1	520
Papers (count)	1029	1.911	2.296	1	16
Affiliations (count)	1029	4.266	3.601	1	21
Selective Reporting Unknown	1029	0.149	0.356	0	1
FDA Approved (included in Part II)	1029	0.457	0.498	0	1

Table 2
Descriptive statistics (Sub-sample used for the second analysis, N = 471).

VARIABLES	N	mean	sd	min	Max
Selective Reporting	471	0.231	0.422	0	1
Funding					
Industry	471	0.701	0.458	0	1
Industry Sole	471	0.650	0.478	0	1
Industry Partial	471	0.051	0.220	0	1
Non-Industry (ref. category, removed)	471	0.110	0.314	0	1
None Declared	471	0.011	0.103	0	1
Not Reported	471	0.136	0.343	0	1
Not Investigated	471	0.042	0.202	0	1
Personal Financial Interests					
Any	471	0.580	0.494	0	1
Employment	471	0.476	0.500	0	1
Other Financial Associations	471	0.049	0.216	0	1
Donation Of Medication	471	0.055	0.229	0	1
Interaction (Industry Funding And Employment)					
None (ref. category, removed)	471	0.106	0.308	0	1
Employment Only	471	0.004	0.065	0	1
Industry Funding Only	471	0.265	0.442	0	1
Industry Funding And Employment	471	0.435	0.496	0	1
Type of Innovation					
NME	471	0.645	0.479	0	1
Priority NME	471	0.157	0.364	0	1
Standard NME	471	0.488	0.500	0	1
Others (ref. category, removed)	471	0.355	0.479	0	1
Controls					
Participants (log)	471	5.221	1.327	2.079	10.42
Weeks (log)	471	2.626	0.941	0.693	5.624
Duration Estimate	471	0.231	0.422	0	1
Placebo	471	0.261	0.439	0	1
Blinding Bias	471	0.119	0.324	0	1
Any Other Bias	471	0.280	0.449	0	1
JCR (log)	471	1.009	0.518	0	2.353
Published After 2007	471	0.288	0.453	0	1
Papers (log)	471	0.379	0.650	0	2.773
First Affiliation USA	471	0.426	0.495	0	1
Affiliations (log)	471	1.119	0.807	0	3.045
Reviewed After 2012	471	0.494	0.500	0	1
Area Dummies					
Oncology (ref. category, removed)	471	0.019	0.137	0	1
Endocrinology	471	0.070	0.256	0	1
Cardiology	471	0.066	0.248	0	1
Mental Health	471	0.386	0.487	0	1
Respiratory	471	0.263	0.441	0	1
Infectious Diseases	471	0.083	0.276	0	1
Dermatology	471	0.113	0.316	0	1

industry-funded projects are broadly of better methodological quality (e.g., they are more likely to be of a greater size and to have a longer duration), compared to trials receiving funding from other sources. These results are consistent with past research indicating that privately-funded studies may have different characteristics compared to publicly-funded trials (Procyshyn et al., 2004; Djulbegovic et al., 2000). T-tests also show that there are no substantial differences between industry and non-industry funded trials in the sample regarding year of publication and journal quality. Reflecting a general evolution over time towards better reporting of funding information, trials with no reported funding tend to be older and to be published in lower quality journals compared to the studies that include funding information.

The basic descriptive statistics for the sub-sample of 471 studies used for the second analysis on the relationship between type of innovation and selective reporting are presented in Table 2.

The vast majority of the trials included in this sample evaluated NMEs (64.5%). About one in four of these trials investigated drugs that also received a priority rating ('Priority NMEs' = 1 for 15.7% of the sample). Due to the exclusion criteria discussed earlier, this sample is highly selected. Nevertheless, the comparison of the 471 included papers against the 558 papers that I removed shows that the trials included in the sub-set are broadly of similar methodological quality to the others (t-tests show no significant difference in the journal JCR score or in the choice of comparator). In addition, selective reporting is more frequent in this sample (23.1% of trials in the sub-sample compared to 20.4% of the remaining trials); however, a test of proportions shows that this difference is not significant.

Simple correlations between my explanatory variables in both the full and sub-sample are not distinctly high. However, to guard against multicollinearity, I calculated the variance inflation factor (VIF) for all variables in both samples. None of the obtained VIFs were above the concerning value of 10 (Neter et al., 1996).[12]

[12] For brevity, the correlation table and additional tests are not reported here. However, these are available upon request.

Table 3
Logistic regression results, dependent variable: selective reporting. (first analysis, N = 1029).

VARIABLES	(1)	(2)	(3)	(4)	(5)	(6)	(7)
	Baseline	Funding	Funding - Strat.	Fin. Int. - Any	Fin. Int. - Strat.	Funding & Fin. Int	FDA Approved
Funding							
Industry		0.474**					
		(0.241)					
Industry Sole			0.497**				
			(0.248)				
Industry Partial			0.311				
			(0.507)				
None Declared		1.008*	1.011*			0.982	0.933
		(0.596)	(0.595)			(0.607)	(0.612)
Not Reported		0.137	0.146			0.123	0.119
		(0.408)	(0.413)			(0.426)	(0.436)
Not Investigated		0.922**	0.937**			0.886*	0.977**
		(0.459)	(0.473)			(0.454)	(0.465)
Personal Financial Interests							
Any				0.19			
				(0.177)			
Employment					0.336*		
					(0.176)		
Other Financial Associations					−0.431		
					(0.445)		
Donation Of Medication					−0.00227		
					(0.309)		
Interaction (Funding And Empl.)							
Employment Only						0.126	0.124
						(0.811)	(0.788)
Industry Funding Only						0.289	0.314
						(0.296)	(0.296)
Industry Funding And Employment						0.728***	0.803***
						(0.237)	(0.225)
FDA Approved (included in Part II)							−0.580*
							(0.352)
Controls							
Participants (log)	−0.194**	−0.187**	−0.194**	−0.205**	−0.232***	−0.216**	−0.214**
	(0.0811)	(0.0858)	(0.0796)	(0.0864)	(0.088)	(0.0938)	(0.0954)
Weeks (log)	−0.205	−0.188	−0.183	−0.207	−0.2	−0.191	−0.157
	(0.178)	(0.194)	(0.196)	(0.177)	(0.175)	(0.195)	(0.192)
Duration Estimate	0.559	0.515	0.511	0.567	0.549	0.516	0.532
	(0.393)	(0.395)	(0.397)	(0.391)	(0.395)	(0.393)	(0.383)
Placebo	−0.652	−0.676*	−0.673*	−0.668	−0.746*	−0.747*	−0.707*
	(0.412)	(0.403)	(0.399)	(0.409)	(0.412)	(0.393)	(0.415)
Blinding Bias	0.0551	0.104	0.112	0.0618	0.0879	0.109	0.12
	(0.337)	(0.349)	(0.338)	(0.336)	(0.341)	(0.343)	(0.342)
Any Other Bias	0.656***	0.648**	0.647**	0.657***	0.656***	0.664**	0.688***
	(0.245)	(0.253)	(0.253)	(0.246)	(0.251)	(0.26)	(0.249)
JCR (log)	0.239	0.315	0.329	0.233	0.309	0.357	0.401*
	(0.228)	(0.236)	(0.24)	(0.229)	(0.226)	(0.244)	(0.235)
Published After 2007	0.00201	0.0222	0.0301	−0.024	0.0515	0.00151	0.017
	(0.214)	(0.211)	(0.215)	(0.223)	(0.236)	(0.205)	(0.208)
Papers (log)	0.540***	0.473***	0.474***	0.532***	0.524***	0.468***	0.439**
	(0.169)	(0.173)	(0.173)	(0.168)	(0.168)	(0.173)	(0.173)
First Affiliation USA	0.358	0.35	0.354	0.337	0.334	0.334	0.401
	(0.277)	(0.3)	(0.303)	(0.282)	(0.281)	(0.294)	(0.314)
Affiliations (log)	0.0323	0.0438	0.0479	−0.00324	−0.0297	−0.0283	−0.0372
	(0.12)	(0.125)	(0.125)	(0.122)	(0.119)	(0.115)	(0.115)
Reviewed After 2012	−0.099	−0.113	−0.12	−0.0994	−0.125	−0.143	−0.0877
	(0.391)	(0.39)	(0.388)	(0.39)	(0.396)	(0.393)	(0.392)
Area Dummies							
Endocrinology	0.159	0.14	0.132	0.0929	−0.0652	−0.0285	0.302
	(1.35)	(1.342)	(1.339)	(1.34)	(1.336)	(1.335)	(1.361)
Cardiology	−1.006	−0.975	−0.951	−0.991	−0.904	−0.879	−0.793
	(0.98)	(0.978)	(1.004)	(0.978)	(0.992)	(0.989)	(0.986)
Mental Health	2.739***	2.847***	2.857***	2.708***	2.678***	2.800***	3.277***
	(0.936)	(0.922)	(0.936)	(0.928)	(0.928)	(0.927)	(0.977)
Respiratory	−0.995	−0.797	−0.782	−1.034	−0.986	−0.809	−0.326
	(1.024)	(1.009)	(1.023)	(1.019)	(1.038)	(1.015)	(1.029)
Infectious Diseases	0.671	0.904	0.926	0.661	0.675	0.875	1.006
	(0.823)	(0.775)	(0.796)	(0.812)	(0.821)	(0.774)	(0.743)
Dermatology	2.138***	2.191***	2.195***	2.097***	2.143***	2.197***	2.405***
	(0.794)	(0.802)	(0.812)	(0.784)	(0.803)	(0.824)	(0.802)
Constant	−2.084**	−2.724***	−2.740***		−1.965**	−2.511***	−2.783***

(*continued on next page*)

Table 3 (*continued*)

VARIABLES	(1)	(2)	(3)	(4)	(5)	(6)	(7)
	Baseline	Funding	Funding - Strat.	Fin. Int. - Any	Fin. Int. - Strat.	Funding & Fin. Int	FDA Approved
	(1.014)	(0.963)	(0.993)		(0.991)	(0.951)	(0.913)
Adj Count R2	0.211	0.22	0.22	0.22	0.224	0.202	0.242
McKelvey & Zavoina's R2	0.47	0.476	0.477	0.471	0.475	0.481	0.49
Log-Likelihood Full Model	−390.263	−386.396	−386.31	−389.839	−388.291	−385.025	−381.528
Observations	1029	1029	1029	1029	1029	1029	1029

Positive coefficient = predicting selective reporting.
Robust standard errors clustered by reviewer *** p < 0.01, ** p < 0.05, * p < 0.1.

5.2. Source of institutional support and selective reporting

To explore the relationship between source of institutional support and selective reporting, I used the whole sample of trials (n = 1029). As my dependent variable ('Selective Reporting') is binary, I applied a logistic regression model. Since the observations where derived from different Cochrane reviews, compiled by different authors, standard errors were clustered by reviewer. For each review, I considered the first author listed, which left me with 48 clusters.

In Table 3 I present the results of my analysis.

The model predicts selective reporting, thus positive coefficients indicate an increased likelihood of selective reporting. Column (1) reports the baseline model including only the control variables. At trial level, as expected, common measures of trial quality appear with negative coefficients i.e. predict a low chance of selective reporting. The larger the study size, the lower the probability that selective reporting occurs in the published paper reporting the study results. On the other hand, as expected, the coefficient of 'Any Other Bias' is positive and significant, indicating that selective reporting is more likely if a trial is at high-risk of bias due to any of the other risk dimensions assessed by Cochrane. Interestingly, the number of papers associated to a trial is also strongly and positively correlated with the chances of selective reporting. A possible explanation for this result is that bias is generally more likely when multiple publications are produced from a single study. For example, prior work shows that studies with significant results are more likely to appear in multiple publications (Easterbrook et al., 1991).

The coefficients of field-level dummies indicate that selective reporting is more likely in Mental Health and Dermatology trials, compared to Oncology (reference category, removed). Past literature has provided evidence that 'softer' fields report more positive outcomes (Fanelli, 2010b). Following this line of argument, we would expect selective reporting to be more likely in the 'softer' scientific fields. The model results, and the high incidence of selective reporting in Mental Health, a field that is generally considered 'soft', are intuitively consistent with the hypothesis that bias is more common in 'softer' sciences. Although no direct measure of hardness is available, certain parameters may reflect theoretical and methodological consensus in a field (Fanelli, 2010b). Exploratory analyses involving testing for some of these parameters indicatively confirmed that both Mental Health and Dermatology have certain characteristics of 'soft' fields. For example, trials in these areas tend to be published in journals specialising in applied research (as opposed to basic research) and are unlikely to include 'hard' measures, such as mortality.

Columns (2)–(7) report the results for five different specifications of the model. Column (2) explores the role of the source of funding. The results indicate that selective reporting is more likely in industry-funded projects, compared to projects funded by other institutions (reference category, removed).[13] In the stratified analysis reported in Column (3), I refined the 'Industry' variable separating studies funded solely by industry ('Industry Sole') from those only partially funded by industry ('Industry Partial'). While the coefficient of 'Industry Sole' is significantly positive, the coefficient of 'Industry Partial' is positive and not significant. Although these results should be interpreted with caution given that partial funding was identified only in a small number of trials, they provide some support to the direction of the main findings on funding source.

Columns (4)–(5) explore the role of personal financial interest. I tried two different specifications that consider any financial interest (Column 4) or specific types of financial interest (employment as opposed to other personal associations as opposed to the donation of study medications). The results show that employment alone (i.e. the presence of one or more company employees among the study authors) is significantly associated with selective reporting. In Column (6) I interact 'Industry Funding' and 'Employment'. The results indicate that the significance of industry funding for selective reporting is restricted to those projects that receive direct funding *and* have at least one author that is an employee. Industry affiliation alone ('Employment Only') is not significantly correlated to selective reporting. However, only a very limited number of trials in the sample have an industry affiliation and public funding, therefore we cannot draw any solid conclusions about the effect of authorship alone. Finally, in Column (7) I include the variable 'FDA Approved (included in Part II)' to broadly test for differences between trials included in Part II and those that have been excluded regarding the likelihood of selective reporting. The variable has a negative and weakly significant coefficient (i.e., controlling for all the other variables, the trials included in Part II have lower chances of selective reporting). Reassuringly, the inclusion of the variable does not affect the main results of the model.

5.3. Type of innovation and selective reporting

To assess the impact of the type of innovation, I used the smaller sample including only those trials where I could identify the focal drug that was FDA-approved for use in the indication(s) investigated in the trial dataset (n = 471). Table 4 summarises the results for five different model specifications.

Column (1) reports the baseline model; Column (2) includes the variable 'NME', capturing whether a trial is evaluating a New Molecular Entity. The results show no significant difference in the incidence of selective reporting in projects investigating NMEs compared to those investigating incrementally modified drugs. In Column (3) I stratify the trials exploring NMEs based on the FDA therapeutic rating (Priority or Standard review). The coefficient of 'Priority NME' is positive and significant, indicating that selective reporting is more likely when research projects investigate Priority NME drugs compared to incrementally modified drugs (reference category, removed). Column (4) includes the interaction between source of funding and personal interests (tested in the first part of the analysis). The coefficient of 'Industry Funding and Employment' is still positive and significant, confirming that my results for the full model are robust to restricting to

[13] The chances of selective reporting are also high in those papers where funding could not be investigated. Although I control for year and journal quality, it is possible that these trials (where full text version was not available online) have other specific characteristics linked to quality of publication and bias.

Table 4
Logistic regression results, dependent variable: selective reporting. (second analysis, N = 471).

VARIABLES	(1)	(2)	(3)	(4)	(5)
	Baseline	NME	NME - Strat.	Funding & Fin. Int	Full Model
Type of Innovation					
NME		0.74			
		(0.714)			
Priority NME			1.858**		2.019**
			(0.818)		(0.885)
Standard NME			0.692		0.749
			(0.717)		(0.727)
Interaction (Industry Funding And Employment)					
Employment Only				0.0632	0.616
				(0.879)	(1.199)
Industry Funding Only				0.0582	0.222
				(0.211)	(0.254)
Industry Funding And Employment				0.549**	0.806**
				(0.276)	(0.352)
None Declared				0.543	0.88
				(1.699)	(1.751)
Not Reported				0.382	0.486
				(0.84)	(0.958)
Not Investigated				1.642	1.838
				(0.998)	(1.161)
Controls					
Participants (log)	−0.233*	−0.211	−0.155	−0.289*	−0.22
	(0.134)	(0.13)	(0.124)	(0.148)	(0.141)
Weeks (log)	−0.214	−0.222	−0.271	−0.115	−0.166
	(0.331)	(0.322)	(0.341)	(0.321)	(0.334)
Duration Estimate	0.544	0.509	0.415	0.52	0.34
	(0.612)	(0.618)	(0.659)	(0.674)	(0.717)
Placebo	−0.65	−0.577	−0.522	−0.783	−0.682*
	(0.516)	(0.475)	(0.443)	(0.491)	(0.412)
Blinding Bias	0.583*	0.554	0.581*	0.496	0.52
	(0.34)	(0.346)	(0.328)	(0.432)	(0.414)
Any Other Bias	0.751***	0.675***	0.731***	0.734***	0.719***
	(0.189)	(0.178)	(0.205)	(0.176)	(0.185)
JCR (log)	0.415*	0.362*	0.275	0.625***	0.457*
	(0.217)	(0.203)	(0.235)	(0.241)	(0.266)
Published After 2007	0.439	0.489	0.543*	0.529*	0.659*
	(0.292)	(0.31)	(0.32)	(0.31)	(0.339)
Papers (log)	0.456*	0.379	0.267	0.317	0.108
	(0.249)	(0.234)	(0.217)	(0.292)	(0.268)
First Affiliation USA	0.368	0.428	0.382	0.359	0.382
	(0.433)	(0.466)	(0.481)	(0.456)	(0.508)
Affiliations (log)	−0.0313	−0.0056	0.0145	−0.0759	−0.0596
	(0.141)	(0.14)	(0.131)	(0.209)	(0.212)
Reviewed After 2012	−0.245	−0.158	−0.0613	−0.155	0.0391
	(0.504)	(0.508)	(0.498)	(0.521)	(0.522)
Constant	−16.68***	−14.85***	−16.59***	−17.12***	−17.21***
	(1.689)	(1.542)	(1.702)	(1.3)	(2.071)
Adj Count R2	0.156	0.211	0.174	0.257	0.275
McKelvey & Zavoina's R2	0.7	0.658	0.676	0.706	0.685
Log-Likelihood Full Model	−180.159	−178.572	−176.334	−176.715	−172.421
Observations	471	471	471	471	471

Positive coefficient = predicting selective reporting.
Robust standard errors clustered by reviewer *** p < 0.01, ** p < 0.05, * p < 0.1.
Area dummies included and not reported.

the sub-sample. Column (5) reports all the variables. The sign and significance of the coefficient of Priority NME is unchanged after the introduction of the industry support variables.

In robustness checks, I re-estimated my core model, excluding those records where the risk of bias from selective reporting rating was 'unknown'.[14] In other checks, as a proxy to identify trials conducted post-regulatory approval, I created a variable 'Published post approval' (1 = the year of publication of the paper was 2 or more years after the year the drug was approved). 'Published post approval' was not significantly associated to selective reporting and the introduction of this variable did not significantly change the results for my key variables. In additional checks, I removed the variable 'Published after 2007′ and added year dummies. In such models, not reported in the paper, my main results are largely unchanged.

6. Discussion and conclusion

Although several studies have tried to assess the prevalence of selective reporting in clinical trials, few studies to date have explored the

[14] The Cochrane Handbook indicates that risk of bias should be considered unclear when there is insufficient information to permit judgment of low or high-risk.

factors associated with selective reporting. This paper takes a first step to filling this gap by examining a sample of clinical trials and leveraging the information contained in the Cochrane reviews.

6.1. Discussion of source of institutional support and selective reporting

The first aim of this study was to test the relationship between the source of institutional support and selective reporting. Within my sample, the odds of selective reporting are 1.6 higher for industry-funded compared to studies funded by other institutions. In the stratified analysis, industry funding was significantly associated with selective reporting only for studies where one or more authors had an employee relationship with a pharmaceutical company (odds ratio = 2.07, baseline category: non-industry funded trials). These findings are consistent with recent research on the role of financial ties in the reporting of positive trial outcomes (Ahn et al., 2017). There are many possible explanations for these results.

In line with past research on misconduct, and specifically on scientific fraud and organisational misconduct (Greve et al., 2010; Lacetera and Zirulia, 2011), in for-profit companies, where performance pressure and conflict of interests are assumed to be high, practices that may limit full disclosure of research findings may be more likely to occur. While accepting funding from a pharmaceutical company may create unconscious obligations to repay the 'gift' in some manner (Sismondo, 2008), financial ties and specifically employment, may give researchers additional personal interests in the direction of results. Although we cannot measure the magnitude of the inducements (e.g., stock ownership, honoraria), these results are consistent with prior work on misrepresentation of firm performance outcomes, indicating that the likelihood of impropriety may rise with the strength of inducements (e.g., Harris and Bromiley, 2007).

Another possibility is that the presence of company-employed authors indicates a high level of involvement of the firm and increased ability for the firm to influence the conduct and reporting of the trial. For example, it has been suggested that trials that are funded by industry can be formally classified as industry-sponsored (thus, the firm will likely participate in the conduct and reporting of the trial) only if there are company-employed co-authors (Van Lent et al., 2013). In line with the body of research viewing industrial and academic science as characterised by conflicting logics (Aghion et al., 2008; Gittelman and Kogut, 2003; Murray, 2010), we can also speculate that the results reflect differences in the scientists' preferences, norms and values. Industrial scientists may have reduced personal constraints to engaging in imperfect publication practices, compared to researchers in academia.

Finally, conflicts of interest disclosures may influence authors' conclusions. For example, disclosures may compromise transparency further through moral licensing, "the often unconscious feeling that biased advice is justifiable because the advisee has been warned" (Loewenstein et al., 2012, p. 669).

6.2. Discussion of type of innovation and selective reporting

The second objective of this study was to examine the relationship between type of innovation and selective reporting. The findings suggest that the likelihood of selective reporting is higher for trials exploring Priority NME drugs compared to trials investigating an incrementally modified drug. There could be many explanations for these results. In line with Sorescu et al. (2003) and Sternitzke (2010), Priority NME drugs can be considered *radical innovations* i.e. they represent both a technological and market improvement over existing treatments. It might be that only ground-breaking projects bring adequately high benefits (or high enough risks of failure) to justify resorting to selective reporting. This interpretation contrasts with some existing literature on misconduct e.g., with Lacetera and Zirulia (2011)'s prediction that fraud is more likely in incremental research, although it should be noted that their model anticipates that misconduct is more likely to be detected in radical research. Considering that priority-rated drugs have the potential to treat diseases where current treatment is limited, it may also be the case that the potential high social repercussions of such drugs offers some latitude for rationalisation of substandard reporting practices. In other words, scientists may implicitly justify poor research decisions, considering the overarching benefit of bringing a breakthrough treatment to market. Also, Priority review designation means that the FDA aims to take action on a drug application within 6 months, compared to 10 months under a Standard review. Past research has shown that deadlines shape the quality of decisions around FDA drug approvals, e.g., 'just-before-deadline' approvals are linked with higher rates of postmarked safety problems (Carpenter et al., 2012). Thus, it is possible that scientists may feel that the standard of the quality of the evidence necessary are lowered for Priority-rated drugs.

Finally, we cannot exclude a reviewer effect. For example, in line with the results on retractions of Furman et al. (2012), pressure to detect false science in high-profile papers may be greater, so that the 'bar' for selective reporting bias may be lower for such papers. Likewise, if scientific knowledge underlying radical innovations evolves very rapidly, the standards of trial conduct, reporting and assessment in place at the time of the trial and at the time of the review, may be different, thus ex-post evaluations may penalise radical treatments.[15]

I also find evidence of a scientific field effect: within my sample, Mental Health and Dermatology trials are more likely to be at high-risk of bias due to selective reporting, compared to Oncology trials (reference category). Conditional on the limitation that this study cannot measure the absolute prevalence of selective reporting, these results provide some empirical support to the hypothesis that bias is more common in 'softer' sciences.

6.3. Implications for policy

Overall, the results confirm that contextual factors play a role in selective reporting, with implications for research policy and practice. Professional communities (e.g., prescribers) as well as regulatory bodies (e.g., the FDA) should be mindful that certain project features, such as the conduct of cutting-edge research, may create additional enticements to mispresent or withhold selected findings. This paper also draws the attention of individual scientists and scientific teams to how a project's characteristics might tilt the balance of their considerations closer to poor reporting. The finding that industry affiliation is associated to biased reporting is particularly interesting, given that high research investment should be protected from the unnecessary waste of inadequately reporting research findings irrespective of sponsors.

Besides a broad recommendation to interpret with caution results of studies where industry involvement is high and where radical innovation is being studied, the findings confirm that there may not be a general solution to detect and deter poor reporting practices. Specifically, the results of this study provide evidence of differences across projects and across scientific disciplines, e.g., medical fields. This confirms that a one-size-fits-all approach to preventing bias in reporting may not be ideal and that specific measures for specific topics should be sought (Fanelli et al., 2017). As far as quality control measures and monitoring are concerned, it has been noted that although cross-checking of all trials submitted for publication should be the final aim for all parties involved (e.g., investigators, editors, journals), considering the large number of trials submitted for publication, priority could be given to the studies that are most likely to have substantial clinical impact (Ioannidis et al., 2017). The results of this study support this recommendation, since studies investigating radical treatments appear more likely to suffer from bias.

[15] I am grateful to a referee for suggesting this explanation.

6.4. Limitations

This analysis has many limitations. The dataset includes only certain trials in selected therapeutic areas (and an especially small number in Oncology). It is possible that the associations I observed may not generalise to different disease areas. Yet, past studies have indicated that reporting bias is spread across several indications and drug classes (Downing et al., 2014; Mcgauran et al., 2010). Also, the opportunity exists to extend this research beyond the context of clinical investigations given that literature has documented an excess of positive results in many other fields e.g., biological research (Csada et al., 1996), psychology (Sterling et al., 1995) and economics (Mookerjee, 2006).

Regarding the first analysis (*institutional support and selective reporting*), it is important to note that data on funding and financial ties were extracted from the information contained in the published articles. Thus, we cannot exclude the possibility of inaccurate reporting of funding or authorship contributions. In addition, notwithstanding the quality procedures of Cochrane reviews (e.g., bias is separately assessed by at least two authors), we cannot exclude that conflicts of interest disclosures may influence reviewers' perceptions of the validity of published studies.

The second part of the analysis (*type of innovation and selective reporting*) uses a sample that is smaller and biased in favour of those trials that evaluate FDA approved drugs. Larger samples are needed to validate presented results and further work is needed to test the robustness of the results with regard to the heterogeneity of trial characteristics and changes over time.[16] For example, as time passes, trials reporting 'contradicting' results (e.g., favouring the control group) may become attractive for publication, as they are 'different' (Dwan et al., 2013). All these shortcomings call for some caution in the interpretation of the results.

This study aims to analyse the relationship between certain salient project-level factors and selective reporting. Future studies could explore the possibility that selective reporting is shaped by individual-level characteristics. For example, in alignment with theoretical predictions (Lacetera and Zirulia, 2011) and past research investigating the incidence of retractions and corrections amongst early-career scientists (Fanelli et al., 2015), different career stages might bring a range of benefits and opportunities to engage in misreporting. Taking into account past work on the role of publishing in firms' battles for market dominance (Polidoro and Theeke, 2012), future studies could also examine how competitive conditions shape a firm's propensity to engage in strategic publishing behaviours. In line with prior work on retractions (Furman et al., 2012; Azoulay et al., 2017), prospect studies could also scrutinise the implications of selective reporting for knowledge dissemination, e.g., whether or not, and to what degree, the scientific community reacts to the publication of partial or invalid scientific information.

To conclude, I hope that this exploratory analysis can offer new insight into the links between the characteristics of a research project and the chances that its results are selectively reported, bringing attention to the contextual factors that shape scientific reporting and, more generally, bias in published research.

Acknowledgements

This work would not have been possible without the outstanding advice provided by Ammon Salter and Paola Criscuolo. Helpful suggestions were provided by Keld Laursen and two anonymous referees. Early versions of this paper were presented during internal workshops at Imperial College Business School, at the DRUID Academy Conference in 2015, at DRUID17 and at the Strategy Entrepreneurship and Innovation (SEI) Doctoral Consortium 2017. I am grateful for comments received at these events. I am also indebted to Corrado Barbui, Teresa Anna Cantisani, Maria Grazia Celani, Andrea Cipriani, Daniele Fanelli, Hans Frankort, Jarno Hoekman, Robert Mathie and Joel West. I gratefully acknowledge the financial support received by the UK Engineering and Physical Sciences Research Council (EPSRC) [Grant No. EP/K502856/1].

[16] Unfortunately, I do not have enough degrees of freedom to explore whether the results hold for each of the scientific fields because some fields have very few observations (see Table 1).

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