Paper to be presented at the DRUID Academy conference in Rebild, Aalborg, Denmark on January

21-23, 2015

Selective reporting in industrial research: the effect of innovation, uncertainty of science and competition on firm motivation

Rossella Salandra
Imperial College Business School
Innovation and Entrepreneurship Group
r.salandra12@imperial.ac.uk

Abstract

Although the existence of selective reporting in industrial research is well acknowledged, little is known about firms' incentives to selectively present or withhold research findings in scientific publications. Building on innovation theory's strategic use of science arguments, I suggest that the degree of innovation positively influence a firm?s likelihood to selectively publish research findings about its innovation, based on the ?direction? of the results. Moreover, acknowledging that firms may have multiple motivations to selective reporting, I argue that the uncertainty of the science underlying a firm?s innovation and the degree of competition are additional incentives to the strategic selection of research results for publication in academic journals. The analysis of 324 industry-funded scientific papers reporting clinical trial results partially supports my hypotheses.

Jelcodes:O32,O3

Selective reporting in industrial research: the effect of innovation, uncertainty of science and competition on firm motivation

Rossella Salandra

Imperial College Business School, London SW7 2AZ, United Kingdom, r.salandra12@imperial.ac.uk

Although the existence of selective reporting in industrial research is well acknowledged, little is known about firms' incentives to selectively present or withhold research findings in scientific publications. Building on innovation theory's strategic use of science arguments, I suggest that the degree of innovation positively influence a firm's likelihood to selectively publish research findings about its innovation, based on the "direction" of the results. Moreover, acknowledging that firms may have multiple motivations to selective reporting, I argue that the uncertainty of the science underlying a firm's innovation and the degree of competition are additional incentives to the strategic selection of research results for publication in academic journals. The analysis of 324 industry-funded scientific papers reporting clinical trial results partially supports my hypotheses.

1. Introduction

Firms can use scientific publications as a strategic weapon to compete in the marketplace and support the commercialization of their innovations (Azoulay 2002, Polidoro and Theeke 2012). As a result, innovating firms have strong incentives to approach what should or should not appear in scientific journals in a strategic way. Against this background, recent research has drawn attention to the practice of selective reporting i.e. the selection of a subset of research findings, on the basis of their "direction", for publication in scientific journals. Scholars have long documented the widespread diffusion of selective reporting, particularly in medical research, and discussed potential implications in the context of research misconduct (Chan, Hróbjartsson et al. 2004). However, little is known about specific factors that can tilt the balance of the firm away from the transparent publication of findings, further towards selective reporting. I thus set to investigate the following research question: "*What are the firms' incentives to selectively present or, in contrast, withhold research findings in scientific publications*"?

In addressing this question, I focus on the influences stemming from *degree of innovation*, *uncertainty of science* and *degree of competition*. I propose that on account of the promise of substantial rewards and of the resource commitment involved in pioneering research, the *degree of innovation* increases the firms' likelihood to resort to selective reporting, to mitigate the risk of seeing such promise unfulfilled or resource commitment not repaid. I additionally put forward that, by making it less likely to reach "positive" research findings and in turn by making it potentially easier to hide or twist "negative" results, the *uncertainty of science* underlying the firm innovation creates an inducement to select what findings should be included in scientific papers. I finally hypothesise that by increasing the firm's need to demonstrate its innovation's uniqueness, the *degree of competition* creates pressures to select results for publication on the basis of their significance.

To develop and test these hypotheses, I focus empirically on the context of pharmaceutical drugs development. Pharmaceutical companies are actively engaged in the production and publication of scientific research. The integrity of their research has come under intense scrutiny in recent time. The "Bad Pharma" debate, triggered by the publication of the homonymous book by Ben Goldacre, has drawn attention to the fact that drugs may be tested in poorly designed trials, and that companies are perfectly entitled to "hide" unflattering research results, resulting in distorted science Hence, this setting enables me to examine firms' deliberate strategies in the context of the creation and dissemination of research findings (Goldacre 2012).

With this study, I aim to make two primary contributions. First, in highlighting firms' incentives to selectively present or withhold information in scientific publications, I join recent research (e.g. Azoulay 2002) explaining how science supports firms' attempts to obtain competitive advantage from innovation and more specifically, how firms can use scientific publications strategically to compete in the market. In doing so, I respond to calls for research to examine the nature of pressures influencing the content of

firms' publications (Polidoro and Theeke 2012). In addition, in explaining firm-level motivations to selective reporting, I contribute to the growing literature on research misdemeanours, and specifically to studies exploring those forms of misconduct that lead to positive publication bias (Fanelli 2009)

2. Theory and hypotheses

Publication in peer-reviewed journals contributes to establishing the credibility of the firms' research (Latour 1987) and certifies that the evidence has been obtained by using scientific methods (Merton 1973). Scientific papers help evaluators develop collectively shared criteria that guide professional consensus (Nelson and Winter 1982) and shape the nature of further knowledge together with the scope for its future applications (Metcalfe, James et al. 2005). In the context of drug development, firms collect evidence around a drug's efficacy and potential side effects by running clinical trials. Evidence is submitted to the regulatory bodies, that review the efficacy and safety of new treatments before approving their market introduction, and is then made available to the medical community. Prior research has shown that scientific papers influence the extent to which of a certain drug achieve commercial success and can encourage its adoption facilitating consistent interpretation of the evidence and comparison of treatments (Azoulay 2002, Polidoro and Theeke 2012).

Taking into account the potential benefits of publication in academic journals described above, firms are likely to approach scientific publication strategically. Against this background, the excess of "positive" published research results has long been acknowledged in different fields, for example, biology (Csada, James et al. 1996), psychology (Sterling, Rosenbaum et al. 1995) and economics (Mookerjee 2006). First and foremost, researchers may decide against publication of a study, based on the whether or not the results are positive (Bekelman, Li et al. 2003, Lexchin, Bero et al. 2003, Dwan, Altman et al. 2008, Lee, Bacchetti et al. 2008, McGauran, Wieseler et al. 2010, Song, Parekh et al. 2010). What's more, for those studies that reach publication, researchers have shown to have substantial methodological flexibility to alter the study results. Specifically, recent literature provides empirical evidence for the existence of a distinct type of systematic behaviour, selective reporting, i.e. the selection of a subset of research findings, on the basis of their "direction", for publication in scientific journals. Selective reporting has been documented across a number of scientific areas (Bedeian, Taylor et al. 2010, Stroebe, Postmes et al. 2012)).

In term of selective reporting, clinical research has received a particular attention. The current debate around clinical trial transparency and quality (Goldacre 2012) and recent real cases including Merck's nonsteroidal anti-inflammatory drug Vioxx (Horton 2004), or Roche's influenza vaccine Tamiflu (Smith 2009) provide evidence that drug companies not only have the motivations but indeed also the means to adopt strategic behaviour in research publication. The skewed prevalence of positive results in medical research and the widespread diffusion of selective reporting has been extensively discussed (Chan, Hróbjartsson et al. 2004, Chan and Altman 2005, Dwan, Altman et al. 2008). In the context of medical research, selective reporting has been defined as the "selection of a subset of the original variables recorded, on the basis of the results, for inclusion in publication of trials" (Hutton and Williamson 2000). Outcome measures may be recorded but not reported (Tannock 1996), descriptions of outcomes as 'primary' or 'secondary' may be altered retrospectively in the light of the findings (Chan 2004a, Chan 2004b), reporting of adverse events and safety outcomes in clinical trials may be inadequate (Melander, Ahlqvist-Rastad et al. 2003). In this setting, selective reporting presents distinctive characteristics deriving from the unique nature of clinical research which I will discuss. First, selective reporting can be detected in ways that are specific to this field. Generally speaking, selective reporting can be assessed by consulting the methods and the results section within a specific publication. The published report can also be compared to abstracts of presentations relating to the same study. Since clinical investigations begin with the development of a clinical protocol i.e. a document describing how the trial will be conducted, selective reporting can also be detected by comparing the published report against the research protocol, if available. In addition, a detailed description of the study may be available in a trial registry. Selective reporting may also be detected from internal company documents following litigations.

Importantly, the consequences of selective reporting could be particularly deleterious when the object of investigation and misreporting are the efficacy or adverse reporting of treatments. Particularly, if the results from clinical trials are published in a biased manner, informed medical decision-making and evidence-based medicine, the systematic review and appraisal of trials that investigate the benefits and harms of medical treatments, come under threat. Thus, in the context of life science, scholars have long described selective reporting as an issue with damaging consequences. Literature has discussed selective reporting in the broader context of research misconduct together with other forms such as data

fabrication, data falsification, plagiarism, multiple publications (i.e. publishing the same data in several publications) and highlighted that leading to false scientific knowledge being published, "cooking research data" could present greater threats to the scientific enterprise than those caused by high profile fraud cases (Martinson, Anderson et al. 2005).

Despite the increase in research on selective reporting, and its discussion in the context of research integrity, relatively few studies have addressed its causes and started to discuss general solutions. Scholars have highlighted the skewed prevalence of positive results, which may be indicative of the use of questionable practices (Fanelli 2009). Studies investigating motivations behind selective reporting tend to discuss it as a systemic characteristic of the scientific community. In the framework of research misconduct, the conflict of interest created by scientists' need to publish (Fanelli 2010) and the reward structure (Nosek, Spies et al. 2012) are frequently mentioned as key motivations. However, many analyses are based on prominent cases, which, while suggestive, are likely to capture only the tip of the icebergs. Other studies are based on reports about researchers who have been found committing frauds, or on surveys of researchers with the obvious limitations of self-reporting. Although quantitative studies have repeatedly shown that financial interests can influence the outcome of biomedical research (Melander, Ahlqvist-Rastad et al. 2003), the debate lacks a theoretical background that clarifies the underlying incentives of private institutions with regard to selective reporting strategies. Taken together, these gaps inform my approach in answering the following research question: "*What are the firms' incentives to selectively present or, in contrast, withhold research findings in scientific publications*"?

In the following sections, I examine how the *degree of innovation*, the *uncertainty of the science* underlying a firm innovation and the *degree of competition* can affect the decision of the firm to selectively report research results in scientific articles. Factors that reduce the benefits of selective reporting, increase its cost and intensify its detection should encourage a firm's transparent publication of findings about its innovation. Conversely, it is likely that in the absence of these conditions, the balance of the innovating firm's considerations should tilt further toward selective reporting. I develop predictions about the nature of these relationships in the context of the pharmaceutical industry.

2.1. Degree of innovation and selective reporting

Innovations are a central element of firm strategy (Barney 1991, Nelson 1991). Novel products embed a promise of substantial financial rewards for the innovating firm. In the context of pharmaceutical, innovative treatments, e.g. drugs that provide important therapeutic gain, are priced significantly higher than existing drugs used for the same purpose (e.g. (Lu and Comanor 1998), Ekelund and Persson (2003). Yet, the promise of high profits rooted in innovative projects is fulfilled only if such projects demonstrate success. To mitigate the risk of seeing substantial profits unfulfilled, firms are likely to choose to emphasise favourable project outcomes and, on the other hand, de-emphasise or remove from publications those results that do not put the project in a favourable light.

In the face of high expected profitability, the undertaking of projects which builds on novel scientific knowledge requires sizable resources. Because the technology necessary to generate radical innovations is increasingly complex, firms have to invest more time, financial resources and managerial attention to test compound building on new science. In pharmaceutical research (DiMasi, Hansen et al. 2003) found that more highly rated (i.e. innovative) drugs involve higher mean clinical phase costs, specifically US$ 207 million for priority drugs, compared to US$ 155 million for standard reviews. If radical innovations are more likely to arise from well-funded research projects, the firms' financial interest and desire to capitalise on such commitment are likely to create enticements to selectively withheld research outcome that are non-significant or negative.

In sum, when conducting scientifically unprecedented research, the promise of substantial rewards and the large commitment create incentives for the firm to resort in selective reporting. Thus, I hypothesize:

H1. The degree of innovation increases the likelihood of a firm's selective reporting of research findings about its product in scientific papers

2.2 Uncertainty of underlying science and selective reporting

I then turn my attention to the influences arising from the uncertainty of the science underlying the firm innovation. Such uncertainty is inherent in the differing scientific objectives and science knowledge base sustaining the firm's innovations. In the medical research setting, the knowledge base accumulated is varied across the different fields. For instance, in the case of oncology, more than 40% of the compounds in development for cancer are directed against 'unprecedented' mechanisms (Kola and Landis 2004). In highly uncertain fields, the number of scientific relationships that might be potentially postulated is very high. On the other hand, the number of relationships that have already been proved is very low. Because scientific knowledge builds upon previous science, the lesser the selection of tested relationships in a scientific field, the less likely the research findings are to be true. Essentially, true research findings are extremely unlikely to be true in uncertain, hypothesis-generating fields (Ioannidis 2005). In such circumstances, as negative or insignificant results are highly likely, firms are more likely to engage in selective reporting.

In uncertain fields, it is also true that theories are less clear and methods are less standardized. In the context of pharmaceutical research, for example, clinical endpoints (i.e. the target outcomes of a trial) can be clearly defined and assessed in certain diseases areas but are very unclear in others. For example, in a trial investigating the ability of an antibiotic medication, the clinical endpoint can generally be defined in a straightforward way as the point at which the infection is reduced or cured. In contrast, it can often be difficult to prove the efficacy of psychotropic compounds, since this would require a measurement of alteration of a mood or behaviour (DiMasi, Feldman et al. 2010). When analytical methods are still under experimentation and research outcomes are not unequivocally agreed, researchers have more "degrees of freedom" to produce the results they expect (Ioannidis 2008). The uncertainty of the basic science thus creates methodological flexibly which in turn making it easier for the researcher to produce the results they expect, with a potential for bias.

Overall, the decrease probability of reaching favourable results and the increased methodological flexibility to change those results that are not pointing to the "right" direction, make the firm's engagement in "poor science" more likely if the basic science underlying an innovation is highly uncertainty. Accordingly, I hypothesize:

H2. The uncertainty of the science underlying a firm product increases the likelihood of a firm's selective reporting of research findings about its product in scientific papers

2.3 Degree of competition and selective reporting

I finally shift my focus away from the influences arising from the level of innovativeness and the science underlying the firm's innovation, further towards the competitive environment surrounding the firm. Population density creates competitive pressures for a firm operating in a given technologic space (Hannan and Freeman 1977). Firms introducing innovations face technological competition from both similar innovations and from potential substitutes that deliver comparable functionality (Dosi 1982). The presence of competing technologies creates challenges for a firm in demonstrating the technical superiority and ultimately the uniqueness of its innovation, which is at the basis of sustained competitive advantage (Barney 1991).

In the context of pharmaceutical drugs, the availability of alternative treatments makes it more difficult for a firm to assert the distinctiveness of its drug. Also, in the presence of fierce competition it is in the firms' interest to reach the market before any competitors to enjoy a greater time to respond to the introduction of competitive products. By increasing the firm's need to assert its drug's merits and by pressing a firm to be the first to reach the market, competitive pressures are likely to create firms inducement to take short cuts in the conduct and publications of their research outcomes.

All else being equal, by creating incentives for firms to present their innovation in a positive light and to reach conclusions before the others, pressures might arise in crowded competitive spaces for firms to select results for publication on the basis of their significance and "direction". Hence, I posit:

H3. The degree of competition increases the likelihood of a firm's selective reporting of its research findings

3. Methods

3.1. Sample

To test the hypothesized relationships, I examined the publication behaviour of firms in the pharmaceutical industry. The role of the firms in the production and publication of scientific research is particularly extensive in this industry. Pharmaceutical companies conduct clinical trials to add to the evidence related to the treatment of a certain disease and can decide upon making trial results available in scientific publications. Because of drug companies' engagement in publishing, a rich body of information is available.

In addition, partly as a result of the publication of Ben Goldacre's book Bad Pharma (Goldacre 2012), the public interest in the issues of clinical trial data quality and publication has increased significantly in the past few years. Goldacre's book suggests that drugs are tested in "poorly designed" trials, on "hopelessly small" numbers of patients, and analysed using techniques which exaggerate the benefits of the investigated treatment. In addition, Goldacre reviews evidence that when trials "throw up results that companies don't like", firms are perfectly entitled to hide them. Recent developments have provided substantial evidence supporting the "Bad Pharma" debate. Drug companies have been facing court action above manipulation of conduct and publication of clinical studies. Internal documents due to settlement agreements resulting from these litigations have been exposed to open scrutiny (Steinman, Bero et al. 2006, Ross, Hill et al. 2008). The media have brought to public attention several examples of company misconduct. For instance, the case of Merck's 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). Or Roche's influenza vaccine Tamiflu, stocked at great cost by the UK government notwithstanding concerns that the drug is no better than placebo (Smith 2009). The pharmaceutical setting thus provides and an interesting window into firms' strategies with regard to the creation and dissemination of research findings.

This study entailed an extensive data collection effort. I gathered data on clinical studies and underlying scientific publications from the Database of Systematic Reviews maintained by the Cochrane Collaboration.[1]. The Cochrane Collaboration is an international not-for-profit association founded in 1993. Cochrane's members prepare, maintain and promote systematic reviews to inform healthcare decisions. Their work has been fundamental with regard to the promotion of systematic reviews and the shift to evidence-based medicine (Guyatt, Cairns et al. 1992, Guyatt, Cook et al. 2004). Each Cochrane review addresses a specific question to establish whether or not there is convincing evidence about a certain intervention (e.g. Can antibiotics help in alleviating the symptoms of a sore throat?). Reviewers search for all available evidence on a certain topic, assess it using predefined guidelines, and present the results in a structured format described in the Cochrane Reviewers' Handbook (Higgins and Altman 2008). In particular, Cochrane reviews describe the methodological quality of trials focusing on five dimensions (Higgins, Green et al. 2008): Adequate sequence generation, Adequate measures to conceal allocation, Blinding, Completeness of outcome data and Free of selective reporting . For each appraised study, a "traffic-light" representation of bias is provided, where green indicates low risk of bias, amber an unknown bias risk and red a high risk.

In order to build a comprehensive dataset, I proceeded as follows. First, I investigated all the titles registered with the Cochrane Review Groups covering the 7 selected therapeutic areas that I will discuss later. I considered for inclusion only reviews that examined evidence around drug interventions, as opposed to other interventions such as medical devices. I then separately analysed each review and for all of the appraised studies I extracted a) the reference to the underlying publication[2], b) the risk for bias rating assigned by Cochrane and c) any additional study information. Duplicates and any study that was not matched to a published paper were then removed from the selection, with the aim of creating a dataset of clinical trials univocally paired to a scientific publication.

To fill any gaps at the level of the clinical study (such as sponsorship information), I additionally matched the sample against the records included in Clinicaltrials.gov, a US Web-based trial registry made available to the public. If necessary, individual trial publications were also accessed. For instance, when sponsorship information was not provided, I considered authors' contact information and affiliations, statements of sources of support, authors' affiliations and acknowledgments. I considered for inclusion only trials where industrial sponsorship was identified and where the trial intervention was a FDA-

[1] http://www.cochrane.org/

[2] A trial can have several publications. For each trial, I captured the first reference listed in the Cochrane review

approved drug.[3] For these trials, relevant information on the interventional drug, such as the classifications of chemical composition and therapeutic potential (used to test H1), were retrieved from the Drug@FDA database. [4] In addition, for each of the pharmaceutical firms included in the dataset[5], research pipeline data was extracted from IMS Lifecycle providing fine-grained data on R&D projects for a large number of pharmaceutical firms.

My final sample consists of 324 industry-sponsored clinical projects, matched to an equal number of scientific papers presenting their results. Altogether, these studies received financial support by 30 different pharmaceutical firms and investigated 59 distinct FDA-approved drugs in 7 separate therapeutic areas: Endocrinology, Respiratory, Infectious diseases/vaccines, Cardiology, Oncology, Mental disorder and Dermatology. The sample does not comprise all innovations of the firms in these therapeutic classes but rather those that the FDA eventually approved for market introduction and that were considered in a scientific publication subsequently assessed in one of considered Cochrane reviews. Also, while the trial to scientific publication matching is unique, it is possible that the same drug is investigated in many trials, by different firms and for several indications. For example Flovent Hfa (Fluticasone Propionate) appears in trials for chronic asthma but also in trial investigating Chronic Obstructive Pulmonary Disease (COPD).

3.2. Variables

3.2.1. Selective reporting

To operationalize selective reporting, I relied on data collected from the Cochrane Collaboration's systematic reviews. I created a binary variable (*selective_reporting*) indicating the presence of selective reporting in a publication, set to 1 when the Cochrane "free of selective reporting" risk of rating indicated high risk of bias and 0 otherwise (unknown or low risk of bias).

3.2.2 Degree of innovation (H1)

An attractive characteristic of the pharmaceutical industry is that an objective classification system for innovation is available. Based on the chemical composition of new applications, the FDA distinguishes between New Molecular Entities (NMEs) and incrementally modified drugs, which modify an existing drug to use it in improved formulations or other indications. The 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 (Kesselheim, Wang et al. 2013).

The FDA provides an additional classification on the basis of the drug therapeutic potential. Specifically, Priority review status is given to those drugs which appear to represent an advance over available therapies. Standard review drugs, on the other hand, have therapeutic qualities similar to those of an already marketed drug. [6]

I adopted the taxonomy proposed by (Sorescu, Chandy et al. 2003) and stratified the drugs in my sample based on chemical composition and therapeutic potential. Such categorisation was captured in the categorical variable *degree_of_innovation*, set to 0 for updates (Standard review and non-NMEs) [7], 1 for drugs that are New Molecular Entities (not not Priority) and 2 for radical innovations (Priority NMEs).

3.2.3. Uncertainty of underlying science (H2)

As uncertainty of basic science is a characteristic of the field rather than of a specific compound (Ioannidis 2005), I considered uncertainty at the level of the therapeutic area i.e. Endocrinology, Respiratory, Infectious diseases/vaccines, Cardiology, Oncology, Mental disorder and Dermatology.

To explain differences in the uncertainty about the science underlying the different therapeutic area, I used the variability in attrition rate by therapeutic area. The nature of the basic science is adduced as a

3 I did not include biologic compounds as reporting requirements in the Drug@FDA are different

4 I considered only the drug assigned to intervention groups and not the drug assigned to the control group.

5 If a trial was sponsored by two or more firms in the same trial, the main sponsor mentioned in the article was selected for inclusion in this study.

6 For instance, a recombination (hence not-novel) drug that represents an advance over available therapies (e.g Malarone (Atovaquone-Proguanil) for malaria) is considered more innovative than a breakthrough treatment made available in a market where customer-needs have already been fulfilled.

7 Five trials in the sample related to priority review, non-NME drugs were included in the middle category

reason of high attrition rate in certain fields such as oncology (Booth, Glassman et al. 2003). As such, high attrition should be a good-enough proxy of a field's uncertainty.
I took into consideration two studies reporting clinical development success rates by speciality, Hay, Thomas et al. (2014) and DiMasi, Feldman et al. (2010) and classed as uncertain those therapeutic areas where the rate of success from Phase 3 to regulatory approval was below-average (or conversely, the rate of attrition was above-average). Since attrition for Dermatology was not specifically considered in this studies, I based my classification on attrition rates reported by (Pammolli, Magazzini et al. 2011). I then created a dummy variable *uncertainty_of_science* set to 1 for those therapeutic areas where the rate of success from Phase 3 to regulatory approval was below the average (Oncology, Cardiovascular and Mental Disorder) and 0 for the remaining (Endocrinology, Respiratory, Infectious diseases/vaccines, and Dermatology).

3.2.4. Degree of competition (H3)

Based on past research (Arora, Gambardella et al. 2009) I measured the degree of competition by the number of firms operating (in the USA) in the same therapeutic area as the interventional drug of the focal project. To capture this information, I relied on the IMS Lifecycle. [8]To qualify as a relevant project, the project had to satisfy two criteria. First, the project had to have been conducted in the US. Second, the project had to be in a clinical testing phase (PhaseI, PhaseII, PhaseIII) or marketed. [9] The degree of competition was assessed at the date of trial completion rather than the date of publication of an article.

3.2.5. Control variables

I controlled for a number of variables at the level of I) firm, II) indication, III) trial, IV) article and V) Cochrane review.

I. Firm-level control variables
I included fine-grained variables at the level of firm, to control for difference in the firm's propensity to selective reporting. First and foremost, I included firm size. As a measure of firm size I used the log transformation of the number of employees at the time of trial completion (*firm_size)*. To control for differences associated with geographic origin I defined a dummy variable (*is_usa*) that accounts for the national residence of firms in the USA (with firms from outside the USA representing the base category). Additionally, I considered whether or not firms trade on a stock exchange and are required to disclose their financial information (*is_public*, =0 for private companies and=1 for public companies). Moreover, to account for any variance due to the level of diversification of the firm, a dummy variable (*is_chemical*) was utilized to distinguish strictly pharmaceutical firms from those diversified in the chemical industry (e.g. Solvay, Bayer, 3M, BASF)

Finally, I introduced variables to account for the firm's level of specialisation in a certain therapeutic area and level of diversification into different fields. Using the IMS Lifecycle database I calculated the total number of ongoing clinical projects (Phase I-III plus marketed) in all therapeutic areas. Therapeutic specialisation (*therap_area_focus*) was calculated as the firm's percentage of projects in the therapeutic area (of the focal project considered). Scope was measured as the number of therapeutic areas in which the firm was active (*scope_of_research*). These measures are based on the literature (Danzon, Nicholson et al. 2005, Macher 2006). All time-variant characteristics were calculated at the time of trial completion.

II. Indication-level control variables
To control variations at the level of the indication, I developed a binary disease-level measure to show whether the disease was chronic or acute (is_*chronic*).

III. Trial-level control variables
To account for the possibility that if trial that is intrinsically better, the corresponding report is less likely to include selective reporting, I controlled for several dimensions of the trial's quality. First, I controlled for study size, using the log transformation of the number of enrolled participants (*trial_size).* I also

[8] A text analysis was performed on the project description to identify any firms that had subsequently merged (IMS retroactively updates the name of the firm to the parent group in case of acquisitions) and to validate project phase.
9 Some project did not report duration. In this instances, the average trial duration by phase and by therapeutic area as measured in the remaining sample projects was considered

examined the control group used in the trial. Specifically, I considered whether the control group used a placebo (*trial_control*=1), whether it investigated a drug in the same class as the interventional drug (*trial_control*=2*)*, or none of the previous (baseline category). Duration of the trial was also taken into account (*trial_duration*). The trial length was operationalised as a categorical variable (0=11 weeks or less, 1=12 to 51 weeks, 2=52 weeks and more).
I additional included a study-level dummy measure to capture whether the trial was open (i.e. involved parties know which patients are allocated the interventional drug as opposed to, say, the placebo) or blinded (is_*blinded* =1). Due to the concealment of the intervention allocation, blinded trials are generally considered of better methodological quality.

IV. Article-level control variables

The quality of a study, hence the likelihood of misreporting, may be associated with the probability of publication in a high impact journal (Lee Kp 2002). Hence, I controlled for journal quality using impact factors (*journal_jcr*). These were extracted from Journal Citation Reports of the Institute for Scientific Information (JCR-ICI). [10]

The sample firms had published an article at various times from 1990 to 2009. Over this time period, two major events attempting to increase transparency of research enterprise occurred. First, the International Committee of Medical Journal Editors (ICMJE) announced that journals would only consider a trial for publication only if it has been registered before the enrolment of the first patient. Second, in 2007, the FDA established the creation of ClinicalTrials.gov and required the registration of all trials. Although academic studies (Zarin, Tse et al. 2005, Mathieu, Boutron et al. 2009, Zarin, Tse et al. 2011, Prayle, Hurley et al. 2012) indicate that the JCMJE's and FDA's initiatives may have failed in some respect, I expect selective reporting to be less frequent in recent trials because, if a detailed description of the study is available in a trial registry, the detection of selective reporting may become easier. I therefore added a dummy variable *published_after_2007* to show whether the trial was published after 2007.

Pharmaceutical companies have been accused of using post-approval trials for marketing purpose with the primary objective of skewing the evidence available around a certain treatment (Sismondo 2008). Hence, I include a dummy variable (*pub_post_approval)* to indicate whether or not the trial was published after the marketing approval of the intervention been investigated.

Lastly, I included the count of the authors of the article (*authors_count).*[11]

V. Review-level control variables

The Cochrane reviews included in the sample were published from 2008 through 2012. To capture for methodological differences in Cochrane appraisal system, I distinguish the most recent reviews (*reviewed_after_2012=1)* from the ones published in the preceding years. To take into account possible influences deriving from differential attention to details which might reduce the likelihood of bias detection, I added to the model the number of trials included in a review (*trials_count*) and the number of reviewers (*reviews_count).*

3.3. Analytical methods

In order to test my hypotheses, I needed to select a model that appropriately takes into account the nature of my sample and the dependent variable. As my dependent variable is binary, I applied a logistic regression model estimating. Since the observations where derived by different reviews, to control for within-review error correlation, which could lead to very small standard errors, and consequent misleadingly low p-values, standard errors were clustered by review_id.

[10] Impact factors were extracted for each study year and average values were used in the analyses. For 29 observations, the impact factor was not available and therefore it was set to 0.
[11] The author count was truncated at 10 authors

3.4. Results

Descriptive statistics of my main and control variables are given in Table 1. From the table it can be seen that selective reporting was identified in 25.9% of the trials in the sample. Simple correlations between my explanatory variables can be found in Table 2. In Table 3 I present the results from my analysis.

Model 1 reports the baseline model including only the control variables. Some of the results for the control variables are interesting to note.

At a firm level, the model shows that firms from the USA (is_usa=1) are more likely to engage in selective reporting. This finding is in line with previous literature suggesting that, due to stronger publication pressures, research misconduct may be more likely in the U.S. (Fanelli 2010). The results also show that firms in the sample trading on the stock exchange (is_public=1) are more likely to engage in selective reporting. One possible explanation is that institutional pressures from the investors' community might increase firm's pressures to deliver positive results, in turn generating incentives to selective reporting. The count of the number of a firm's therapeutic areas (scope_of_research) has a negative significant coefficient, suggesting that, for the firms included in the sample, the broader the scope of the firm's research, the less likely the firm engagement in selective reporting. It may be the case that if a firm is active in several research fields, the need to adjust or withdraw negative results attained in specific area is less pressing.

At indication level, trials investigating treatments for chronic diseases were more likely to be biased. With pharmaceuticals, repeat purchases are more likely for drugs designed for acute than for chronic diseases. Given the prospects of high profit generated by repeat purchases, the benefit of selective reporting may be higher in chronic circumstances, making selective reporting more likely.

At trial level, as expected, common measures of trial quality appear with a 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. The linear coefficients of blinding and duration are also negative, however they are not significant. The results also show that head-to-head trials (*trial_control=2*) are at higher risk of selective reporting. These findings support the hypothesis frequently suggested in the literature that comparative trials might originate from the firm marketing department and may be used as a sophisticated form of advertising.

Interestingly, at the level of the paper, the number of authors of a trial is a significant predictor of selective reporting. These results should be investigated further: according to some research, the size of a research team is a proxy for the hardness of a field , alternative arguments however suggest that team size is the result of funding availability (Fanelli and Glänzel 2013). It is possible that, if many have access to the data and are involved in the collection and analysis, the "diffusion of responsibility" may compensate for the increased risk of detection of malfeasances.

Models 2–4 add the independent variables sequentially. I discuss results based on the full model (Model 4). Hypothesis 1 predicts that the degree of innovation has a positive impact on selective reporting. Consistent with the prediction, the coefficient on degree of innovation is positive and statistically significant for NMEs ($\beta = 1.091$ $p<0.1$) and radical innovations ($\beta = 2.960$, $p<0.01$). In other terms, investigating radical innovation increases the log odds of selective reporting by 2.7. Talking in odds ratio term, if a pharmaceutical company investigates a drug that is very innovative (i.e. a new molecule that provides high therapeutic potential) as opposed to an update (e.g. a drug that is just a recombination and does not provide substantial therapeutic improvement) the firm's odds of selective reporting increase by a factor of 19.2 The findings also support Hypothesis 2, that uncertainty of science increase the likelihood of selective reporting. Consistent with the expectation, the coefficient of uncertainty of science is significantly positive ($\beta = 1.343$, $p<0.1$). In other words, conducting research in fields characterised by uncertain science (as oppose to running investigations in established fields) increases the firm's odds of selective reporting by a factor of 3.8. Considering as an example the "average sized" trial, run by a "mediums sized" public USA firm and reviewed before 2012 (i.e. setting firm_size=0.497, is_usa=1, is_public=1, is_chronic=1, trial_size=2.5, reviewed_after_2012=0) the probability of selective reporting increases by 0.3376 if the compound investigated is a radical innovation. For the same trial, the probability of selective reporting increases by 0.2660 if the underlying science is uncertain.

Hypothesis 3 predicts that the degree of competition contribute to increasing a firm's rate of scientific publication about its drug. The linear coefficient of competition is positive as expected however it is not significant therefore Hypothesis 3 is not supported.

When using a logit model, none of the pseudo R2 measures are equivalent to the R2 in OLS however the McKelvey and Zavoina's R2 is mentioned as the measure that most closely approximates the R2 obtained from regressions (Hoetker 2007). The explained variance increases from model to model, and the McKelvey and Zavoina's R2 for Model 4 is 70%. Adj Count R2, another measure mentioned as a measure of corrected prediction of the model (Hoetker 2007), was 46% in Model 4.

3.5. Robustness analysis

As evident from the correlation table (Table2), correlations between variables are not distinctly high. However, to guard against multicollinearity, I calculated the variance inflation factor (VIF) for all variables. The mean VIF was 1.76, and all obtained VIFs were well below the concerning value of 10 (Neter, Kutner et al. 1996) .

As previously discussed, my sample was chosen opportunistically. To validate the representativeness of the analysed trials in 3 clinical specialities (oncology, cardiovascular and mental health) I compared key trial features such as size and duration to the characteristics of the trial registered in clinicaltrials.gov (Califf, Zarin et al. 2012). The test showed no major discrepancies in terms of trial features.

In order to test the representativeness of the sample in term of bias, I considered the incidence of selective reporting in a broader sample of trials (including trials that were eventually excluded because they were not industry sponsored or where industry sponsorship was not identified). I found that my subsample had a slightly higher percentage of biased trials. I thus tested the data for the dependent variable on the broad sample. Although a full model specification for this bigger dataset was not feasible, I found that the presence of sponsorship was a significant predictor of selective reporting. These findings provides support to the premise that financial conflict plays a role in research misconduct and validate my focus on financial roots for selective reporting. In addition, the results for the relationship between degree of innovation and selective reporting (albeit in a simplified model) remained largely consistent in direction and significance, increasing confidence in the results.

An alternative interpretation of my findings is that some unobserved sources of variation at the level of the review might drive the assessment of the risk of bias. As discussed earlier, the analysis controlled for potential sources of heterogeneity across reviews, which minimizes this potential concern. Given that statistical methods to detect within-study selective reporting are, as yet, not well developed (Higgins, Green et al. 2008), the possibility remains, however, that my specification may still leave out some heterogeneity across review author e.g. that a reviewer may systematically apply more stringent assessment criteria. To further probe this possibility, I considered a subset of publications in my sample that were rated in more than one review (such duplicates were subsequently excluded in the analysis). No major discrepancies were detected in the assessment of bias, increasing confidence that my findings were not simply driven by such unobserved processes affecting scientific appraisal.

4. Discussion

In this study, I sought to further our understanding firm's incentives to selectively report research results in scientific journals. I argued that in studying firm motivations behind selective reporting, the *degree of innovation* should be taken into account. Moreover, I reasoned that selective reporting is likely to be impacted by the *uncertainty of the underlying science* and the *degree of competition*. My results confirm the positive and significant effects of degree of innovation and uncertainty of science. The positive direct effect of competition was not significant.

Generalizability of findings

A potential concern is that the firm's strategic selection of results to be included in publication is a phenomenon specific to the empirical setting that I examine, which may limit the generalizability of my results. However, selective reporting is not an exclusive feature of this industry. Existing literature has extensively documented an excess of positive results in different fields, for example, biological research (Csada, James et al. 1996), psychology (Sterling, Rosenbaum et al. 1995) and economics (Mookerjee 2006). Thus, the opportunity exists to extend this research beyond the context of pharmaceutical drugs.

Implications for practice

My findings about how degree of innovation and uncertainty of underlying science create firm's inducements to selectively withhold results about their innovations in scientific articles have significant implications for practice. In particular, this paper draws managers' attention to how the innovative nature of a project might tilt the balance of firms' considerations closer to poor reporting, or more generally, to poor science. This is also relevant to those firms exploring projects in fields characterised by high uncertainty.

Theoretical contributions and potential for future research

This paper highlights degree of innovation, uncertainty of underlying science and degree of competition (albeit not significantly) as important reasons for firms to conduct and publish less-than-rigorous research. Motivations other than these are unaccounted for in this study. Future studies could explore the possibility that selective reporting is shaped by the collaboration formed by the firms. For example, it might be the case that, as a result of diffusion of responsibility, incentives to selective publication differ if more than one firm is involved in a research project. Also, the patterns of collaboration ties that firms form with prestigious universities could be investigated. Gaining institutional support for specific innovations may alleviate the firm's propensity to engage in poor reporting.

Another avenue for extensions may concern the analysis of the relationship between a firm performance and propensity to selective reporting. Research has long suggested that performance influences the need and the costs to consider engaging in unethical activities (Mishina, Dykes et al. 2010). A history of poor performance might provide a variety of benefits and opportunities for organizations to engage in selective reporting.

One of the propositions in this study relates to the degree of competition that a firm faces from firms competing in the same therapeutic area. Prospective studies could refine this analysis by taking into account the specific nature of the competitive threat faced by the firms. Specifically, technological competition at the level of the mechanisms of action underlying drugs in a therapeutic class should be taken into account. In line with Polidoro and Theeke (2012)'s findings, it is possible that the presence of similar or substitute drugs alters a firm incentives to selective publication. Because competition permeates into the scholarly domain of scientific publications (Polidoro and Theeke 2012), future research could also investigate whether the competition for publication in top journal create unique incentives for selective reporting.

Because of my focus on firms' scientific publication behaviour, this study is silent about non-financial roots and individual-researches motivations for selective reporting. Adding to the growing body of empirical evidence on research behaviour (Fanelli 2009), future research could further investigate how pressures at an individual level (e.g. number of papers published on a certain class of drugs, number of retractions, pressure for promotion or tenure) impact the selective reporting of information in clinical research.

In conclusion, this research expands our understanding about the relationship between science and private firms by delineating the conditions under which firms are more likely to selectively report, or in contrast withhold, their research findings. To my knowledge, this is the first study examining the relationship between innovation, uncertainty of science, competitive pressures and selective reporting. The strength of this study also rests in its use of Cochrane risk of bias rating to provide valuable insight into the decision making process from the planning to the publication stage of clinical trials.

Acknowledgements

I gratefully acknowledge the insightful comments and suggestions provided by Paola Criscuolo and Ammon Salter and the financial support received by the UK Engineering and Physical Sciences Research Council (EPSRC).

Tables

Table1 – Descriptive statistics

VARIABLES	(1) N	(2) mean	(3) sd	(4) min	(5) max
select_reporting	324	0.259	0.439	0	1
degree_of_innovation (H1)	324	0.960	0.590	0	2
uncertainty_of_science (H2)	324	0.540	0.499	0	1
degree_of_competition (H3)	324	3.566	0.527	1.609	5.468
Firm-level					
firm_size	324	4.540	0.756	2	5
is_usa	324	0.497	0.501	0	1
is_public	324	0.920	0.272	0	1
is_chemical	324	0.0988	0.299	0	1
therap_area_focus	324	0.153	0.212	0	1
scope_of_research	324	5.806	3.683	0	13
Indication-level					
is_chronic	324	0.778	0.416	0	1
Trial-level					
trial_size	324	2.525	0.627	1	4
trial_control	324	0.864	0.779	0	2
trial_duration	324	0.849	0.629	0	2
is_blinded	324	0.901	0.299	0	1
Publication-level					
journal_jcr	324	2.273	2.046	0	9.510
published_after_2007	324	0.333	0.472	0	1
published_post_approval	324	0.747	0.435	0	1
authors_count	324	5.929	1.877	1	10
Review-level					
reviewed_after_2012	324	0.429	0.496	0	1
trials_count	324	34.10	21.96	4	83
reviewers_count	324	4.951	2.242	1	9
firms_in_TA	324	41.47	30.30	5	237
employees	324	44,100	30,224	90	122,000
participants	324	834.5	2,286	17	20,078

Table2 – Correlations among the independent variables (N=324)

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
1	-																			
2	0.24	-																		
3	0.19	0.00	-																	
4	0.06	0.25	0.14	-																
5	0.18	-0.13	0.29	0.07	-															
6	-0.06	0.12	0.23	-0.06	0.25	-														
7	-0.01	-0.16	0.12	-0.28	-0.14	0.10	-													
8	0.20	0.42	-0.06	-0.17	-0.12	-0.01	-0.02	-												
9	0.15	0.22	0.11	0.43	0.29	0.19	-0.20	-0.09	-											
10	-0.46	-0.17	-0.02	0.11	-0.02	-0.10	0.05	-0.16	-0.12	-										
11	0.15	0.20	0.04	0.11	-0.02	-0.10	-0.15	0.07	0.02	-0.09	-									
12	-0.05	0.00	0.24	0.17	0.14	0.04	-0.21	-0.15	-0.05	0.14	0.04	-								
13	0.24	0.38	-0.15	0.04	-0.07	-0.05	-0.15	0.27	0.11	-0.32	0.28	0.11	-							
14	-0.20	-0.26	0.19	-0.01	0.04	-0.06	0.01	-0.24	-0.05	0.12	0.13	0.16	-0.03	-						
15	0.25	0.21	0.16	0.01	-0.01	0.19	-0.02	0.11	0.10	-0.32	0.25	0.05	0.23	0.05	-					
16	-0.09	0.41	-0.23	0.02	-0.07	-0.08	-0.15	0.23	-0.10	0.17	0.06	-0.04	0.05	-0.12	-0.12	-				
17	0.18	0.04	0.13	0.02	0.34	-0.02	0.05	0.02	0.12	0.00	-0.08	0.20	0.11	0.02	-0.04	0.13	-			
18	0.08	0.16	0.02	0.23	0.04	-0.03	-0.10	-0.02	-0.01	0.08	-0.02	0.10	0.04	-0.07	0.18	0.11	0.02	-		
19	-0.18	-0.14	-0.36	-0.03	-0.11	-0.25	-0.10	-0.15	-0.09	0.13	0.10	-0.31	0.06	0.18	-0.09	0.15	-0.16	-0.05	-	
20	-0.11	-0.39	-0.22	-0.11	0.08	0.16	0.20	-0.15	0.02	0.14	-0.29	-0.21	-0.12	0.08	-0.13	-0.21	-0.12	-0.07	0.33	-
21	0.03	-0.20	0.58	-0.12	0.23	0.16	0.12	0.13	0.12	0.06	-0.19	0.20	-0.11	0.03	-0.06	-0.26	0.13	-0.07	-0.50	0.00

1	degree_of_innovation
2	degree_of_competition
3	uncertainty_of_science
4	firm_size
5	is_usa
6	is_public
7	is_chemical
8	therap_area_focus
9	scope_of_research
10	is_chronic
11	trial_size
12	trial_control
13	trial_duration
14	is_blinded
15	journal_jcr
16	published_after_2007
17	published_post_approval
18	authors_count
19	reviewed_after_2012
20	trials_count
21	reviewers_count

Table 3 – Logistic regression results, dependent variable: Selective reporting.

VARIABLES	(1)	(2)	(3)	(4)
1.degree_of_innov NMEs (H1>0)		0.906*	0.911*	1.091*
		(0.549)	(0.524)	(0.610)
2.degree_of_innov Radical (H1>0)		3.953***	3.355***	2.960***
		(1.210)	(1.241)	(1.104)
uncertainty_of_science (H2>0)			1.306*	1.343*
			(0.783)	(0.730)
degree_of_competition (H3>0				1.213
				(1.226)
firm_size	0.115	0.0272	-0.169	-0.241
	(0.295)	(0.298)	(0.317)	(0.293)
is_usa	1.128*	1.295**	1.187**	1.449**
	(0.597)	(0.560)	(0.573)	(0.610)
is_public	0.975	1.791*	1.786*	1.890*
	(0.969)	(0.924)	(0.929)	(1.090)
is_chemical	0.441	0.178	0.0863	0.176
	(0.862)	(0.829)	(0.824)	(0.751)
therap_area_focus	-2.092	-2.507	-2.243	-3.686
	(1.843)	(1.810)	(1.724)	(3.089)
scope_of_research	-0.149	-0.233**	-0.200**	-0.248**
	(0.0918)	(0.0979)	(0.0989)	(0.121)
is_chronic	0.926	2.564***	2.313***	2.116***
	(1.001)	(0.803)	(0.710)	(0.743)
trial_size	-0.457	-0.597**	-0.612*	-0.621**
	(0.291)	(0.294)	(0.320)	(0.304)
1.trial_controlPlacebo	0.558	1.089	1.033	0.862
	(0.970)	(0.828)	(0.829)	(0.960)
2.trial_control Head-to-Head	1.593*	1.526*	1.493*	1.493*
	(0.890)	(0.863)	(0.869)	(0.878)
1.trial_duration 12-51 wks	-0.380	-0.429	-0.0582	-0.146
	(0.443)	(0.431)	(0.372)	(0.368)
2.trial_duration 52+wks	-0.290	-0.736	-0.422	-0.720
	(0.710)	(0.689)	(0.648)	(0.666)
is_blinded	-0.491	-0.356	-0.746	-0.758
	(0.583)	(0.581)	(0.547)	(0.555)
journal_jcr	-0.0912	-0.131	-0.147	-0.134
	(0.0990)	(0.115)	(0.122)	(0.124)
published_after_2007	-0.438	-0.532	-0.471	-0.767
	(0.495)	(0.490)	(0.522)	(0.680)
published_post_approval	0.0354	-0.0702	-0.243	-0.333
	(0.530)	(0.562)	(0.570)	(0.544)
authors_count	0.286***	0.290*	0.286*	0.280*
	(0.109)	(0.149)	(0.155)	(0.160)
reviewed_after_2012	-1.570**	-1.697**	-1.804**	-1.736**
	(0.793)	(0.716)	(0.701)	(0.696)
trials_count	0.0148	0.00984	0.0174	0.0221
	(0.0161)	(0.0153)	(0.0181)	(0.0175)
reviewers_count	0.191	0.327*	0.140	0.209
	(0.194)	(0.185)	(0.194)	(0.211)
Constant	-4.196	-6.793***	-5.514**	-9.456**
	(2.704)	(2.442)	(2.471)	(4.558)
Observations	324	324	324	324

Positive coefficient = predicting selective reporting
Robust standard errors in parentheses *** p<0.01, ** p<0.05, * p<0.1

References

Arora, A., A. Gambardella, L. Magazzini and F. Pammolli (2009). "A Breath of Fresh Air? Firm Type, Scale, Scope, and Selection Effects in Drug Development." Manage. Sci. **55**(10): 1638-1653.

Azoulay, P. (2002). "Do pharmaceutical sales respond to scientific evidence?" Journal of Economics & Management Strategy **11**(4): 551-594.

Barney, J. (1991). "FIRM RESOURCES AND SUSTAINED COMPETITIVE ADVANTAGE." J. Manage. **17**(1): 99-120.

Bedeian, A. G., S. G. Taylor and A. N. Miller (2010). "Management science on the credibility bubble: Cardinal sins and various misdemeanors." Academy of Management Learning & Education **9**(4): 715-725.

Bekelman, J. E., Y. Li and C. P. Gross (2003). "Scope and impact of financial conflicts of interest in biomedical research." JAMA: the journal of the American Medical Association **289**(4): 454-465.

Booth, B., R. Glassman and P. Ma (2003). "Oncology's trials." Nature Reviews Drug Discovery **2**(8): 609-610.

Califf, R. M., D. A. Zarin, J. M. Kramer, R. E. Sherman, L. H. Aberle and A. Tasneem (2012). "Characteristics of clinical trials registered in ClinicalTrials. gov, 2007-2010." JAMA: The Journal of the American Medical Association **307**(17): 1838-1847.

Chan, A.-W. and D. G. Altman (2005). "Identifying outcome reporting bias in randomised trials on PubMed: review of publications and survey of authors." bmj **330**(7494): 753.

Chan, A.-W., A. Hróbjartsson, M. T. Haahr, P. C. Gøtzsche and D. G. Altman (2004). "Empirical evidence for selective reporting of outcomes in randomized trials: comparison of protocols to published articles." Jama **291**(20): 2457-2465.

Csada, R. D., P. C. James and R. H. Espie (1996). "The" file drawer problem" of non-significant results: does it apply to biological research?" Oikos: 591-593.

Danzon, P. M., S. Nicholson and N. S. Pereira (2005). "Productivity in pharmaceutical–biotechnology R&D: the role of experience and alliances." Journal of health economics **24**(2): 317-339.

DiMasi, J. A., L. Feldman, A. Seckler and A. Wilson (2010). "Trends in risks associated with new drug development: success rates for investigational drugs." Clinical Pharmacology & Therapeutics **87**(3): 272-277.

DiMasi, J. A., R. W. Hansen and H. G. Grabowski (2003). "The price of innovation: new estimates of drug development costs." Journal of health economics **22**(2): 151-186.

Dosi, G. (1982). "Technological paradigms and technological trajectories: a suggested interpretation of the determinants and directions of technical change." Research policy **11**(3): 147-162.

Dwan, K., D. G. Altman, J. A. Arnaiz, J. Bloom, A.-W. Chan, E. Cronin, E. Decullier, P. J. Easterbrook, E. Von Elm and C. Gamble (2008). "Systematic review of the empirical evidence of study publication bias and outcome reporting bias." PLoS One **3**(8): e3081.

Ekelund, M. and B. Persson (2003). "Pharmaceutical pricing in a regulated market." Review of Economics and Statistics **85**(2): 298-306.

Fanelli, D. (2009). "How many scientists fabricate and falsify research? A systematic review and meta-analysis of survey data." PLOS one **4**(5): e5738.

Fanelli, D. (2010). "Do pressures to publish increase scientists' bias? An empirical support from US States Data." PloS one **5**(4): e10271.

Fanelli, D. and W. Glänzel (2013). "Bibliometric evidence for a hierarchy of the sciences." PloS one **8**(6): e66938.

Goldacre, B. (2012). "Bad Pharma." Fourth Estate.

Guyatt, G., J. Cairns, D. Churchill, D. Cook, B. Haynes, J. Hirsh, J. Irvine, M. Levine, M. Levine and J. Nishikawa (1992). "Evidence-based medicine." JAMA: the journal of the American Medical Association **268**(17): 2420-2425.

Guyatt, G., D. Cook and B. Haynes (2004). "Evidence based medicine has come a long way: The second decade will be as exciting as the first." BMJ: British Medical Journal **329**(7473): 990.

Hannan, M. T. and J. Freeman (1977). "The population ecology of organizations." American journal of sociology: 929-964.

Hay, M., D. W. Thomas, J. L. Craighead, C. Economides and J. Rosenthal (2014). "Clinical development success rates for investigational drugs." Nature biotechnology **32**(1): 40-51.

Higgins, J. and D. G. Altman (2008). "Assessing risk of bias in included studies." Cochrane Handbook for Systematic Reviews of Interventions: Cochrane Book Series: 187-241.

Higgins, J. P., S. Green and C. Collaboration (2008). Cochrane handbook for systematic reviews of interventions, Wiley Online Library.

Hoetker, G. (2007). "The use of logit and probit models in strategic management research: Critical issues." Strategic Management Journal **28**(4): 331-343.

Horton, R. (2004). "Vioxx, the implosion of Merck, and aftershocks at the FDA." Lancet **364**(9450): 1995.

Hutton, J. and P. R. Williamson (2000). "Bias in meta-analysis due to outcome variable selection within studies." Journal of the Royal Statistical Society: Series C (Applied Statistics) **49**(3): 359-370.
Ioannidis, J. P. (2005). "Why most published research findings are false." PLoS medicine **2**(8): e124.
Ioannidis, J. P. (2008). "Why most discovered true associations are inflated." Epidemiology **19**(5): 640-648.
Kesselheim, A. S., B. Wang and J. Avorn (2013). "Defining "innovativeness" in drug development: a systematic review." Clinical Pharmacology & Therapeutics **94**(3): 336-348.
Kola, I. and J. Landis (2004). "Can the pharmaceutical industry reduce attrition rates?" Nature reviews Drug discovery **3**(8): 711-716.
Latour, B. (1987). Science in action: How to follow scientists and engineers through society, Harvard university press.
Lee, K., P. Bacchetti and I. Sim (2008). "Publication of clinical trials supporting successful new drug applications: a literature analysis." PLoS medicine **5**(9): e191.
Lee Kp, S. M. B. P. B. L. A. (2002). "ASsociation of journal quality indicators with methodological quality of clinical research articles." JAMA **287**(21): 2805-2808.
Lexchin, J., L. A. Bero, B. Djulbegovic and O. Clark (2003). "Pharmaceutical industry sponsorship and research outcome and quality: systematic review." Bmj **326**(7400): 1167-1170.
Lu, Z. J. and W. S. Comanor (1998). "Strategic pricing of new pharmaceuticals." Review of Economics and Statistics **80**(1): 108-118.
Macher, J. T. (2006). "Technological development and the boundaries of the firm: A knowledge-based examination in semiconductor manufacturing." Management Science **52**(6): 826-843.
Martinson, B. C., M. S. Anderson and R. De Vries (2005). "Scientists behaving badly." Nature **435**(7043): 737-738.
Mathieu, S., I. Boutron, D. Moher, D. G. Altman and P. Ravaud (2009). "Comparison of registered and published primary outcomes in randomized controlled trials." JAMA: the journal of the American Medical Association **302**(9): 977-984.
McGauran, N., B. Wieseler, J. Kreis, Y. B. Schüler, H. Kölsch and T. Kaiser (2010). "Review Reporting bias in medical research-a narrative."
Melander, H., J. Ahlqvist-Rastad, G. Meijer and B. Beermann (2003). "Evidence b (i) ased medicine—selective reporting from studies sponsored by pharmaceutical industry: review of studies in new drug applications." Bmj **326**(7400): 1171-1173.
Merton, R. K. (1973). The sociology of science: Theoretical and empirical investigations, University of Chicago press.
Metcalfe, J. S., A. James and A. Mina (2005). "Emergent innovation systems and the delivery of clinical services: The case of intra-ocular lenses." Research Policy **34**(9): 1283-1304.
Mishina, Y., B. J. Dykes, E. S. Block and T. G. Pollock (2010). "WHY "GOOD" FIRMS DO BAD THINGS: THE EFFECTS OF HIGH ASPIRATIONS, HIGH EXPECTATIONS, AND PROMINENCE ON THE INCIDENCE OF CORPORATE ILLEGALITY." Academy of Management Journal **53**(4): 701-722.
Mookerjee, R. (2006). "A meta-analysis of the export growth hypothesis." Economics Letters **91**(3): 395-401.
Nelson, R. R. (1991). "Why do firms differ, and how does it matter?" Strategic management journal **12**(S2): 61-74.
Nelson, R. R. and G. Sidney (1982). "Winter. 1982." An evolutionary theory of economic change: 929-964.
Neter, J., M. H. Kutner, C. J. Nachtsheim and W. Wasserman (1996). "Applied linear statistical methods." Irwin, Chicago.
Nosek, B. A., J. R. Spies and M. Motyl (2012). "Scientific utopia II. Restructuring incentives and practices to promote truth over publishability." Perspectives on Psychological Science **7**(6): 615-631.
Pammolli, F., L. Magazzini and M. Riccaboni (2011). "The productivity crisis in pharmaceutical R&D." Nature reviews Drug discovery **10**(6): 428-438.
Polidoro, F. and M. Theeke (2012). "Getting competition down to a science: The effects of technological competition on firms' scientific publications." Organization Science **23**(4): 1135-1153.
Prayle, A. P., M. N. Hurley and A. R. Smyth (2012). "Compliance with mandatory reporting of clinical trial results on ClinicalTrials. gov: cross sectional study." BMJ **344**.
Ross, J. S., K. P. Hill, D. S. Egilman and H. M. Krumholz (2008). "Guest authorship and ghostwriting in publications related to rofecoxib." JAMA: the journal of the American Medical Association **299**(15): 1800-1812.
Sismondo, S. (2008). "How pharmaceutical industry funding affects trial outcomes: causal structures and responses." Social science & medicine **66**(9): 1909-1914.
Smith, J. (2009). "Point-by-point response from Roche to BMJ questions." BMJ **339**.
Song, F., S. Parekh, L. Hooper, Y. Loke, J. Ryder, A. Sutton, C. Hing, C. Kwok, C. Pang and I. Harvey (2010). Dissemination and publication of research findings: an updated review of related biases, Prepress Projects Limited.

Sorescu, A. B., R. K. Chandy and J. C. Prabhu (2003). "Sources and financial consequences of radical innovation: Insights from pharmaceuticals." J. Mark. **67**(4): 82-102.
Steinman, M. A., L. A. Bero, M.-M. Chren and C. S. Landefeld (2006). "Narrative review: the promotion of gabapentin: an analysis of internal industry documents." Annals of Internal Medicine **145**(4): 284-293.
Sterling, T. D., W. Rosenbaum and J. Weinkam (1995). "Publication decisions revisited: The effect of the outcome of statistical tests on the decision to publish and vice versa." The American Statistician **49**(1): 108-112.
Stroebe, W., T. Postmes and R. Spears (2012). "Scientific misconduct and the myth of self-correction in science." Perspectives on Psychological Science **7**(6): 670-688.
Tannock, I. F. (1996). "False-positive results in clinical trials: multiple significance tests and the problem of unreported comparisons." Journal of the National Cancer Institute **88**(3-4): 206-207.
Zarin, D. A., T. Tse and N. C. Ide (2005). "Trial registration at ClinicalTrials. gov between May and October 2005." New England Journal of Medicine **353**(26): 2779-2787.
Zarin, D. A., T. Tse, R. J. Williams, R. M. Califf and N. C. Ide (2011). "The ClinicalTrials. gov results database—update and key issues." New England Journal of Medicine **364**(9): 852-860.