Word Count 3,326

Tables 3

AUTHORSHIPS & IMPACTS

Data on the Changing Face of Scientific Authorship

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Abstract

Context: A growing awareness of changes in the character of medical authorship.

Objective: To compare the impact of novel forms of authorship with those of traditional authorship.

Design: We have used Medline and Embase to catalogue articles dealing with the therapeutic effects of sertraline during 1998-2000. We have calculated and compared numbers of Medline listed articles per author and journal Impact Factors, as well as a literature profile for these articles constructed by multiplying Medline listings by impact factors, with a series of articles on sertraline prepared for Pfizer during this period.

Results: There were 39 articles on sertraline, which were probably authored in the traditional manner. These had a total of 107 authorships from 105 authors, an average of 2.7 authors per article, a mean length of 3.4 pages, a mean Medline listing rate of 36.7 per authorship (C.I. 26.6 – 46.8), and an overall literature profile of 252 per article (C.I. 115 – 388). There were 20 Pfizer sponsored articles on sertraline published in 1998 with a further 37 published in 1999/2000. These 57 articles had 123 authorships from 70 authors per year, an average length of 10.7 pages, an average of 6.5 authors per article, a mean Medline listing rate of 70.4 per academic authorship (C.I.

61.9 – 78.9), and a mean literature profile of 1824 per article (C.I 1084 - 2561). The literature profiles of the two series were significantly different.

Conclusions: An increasing proportion of the therapeutics literature is being written in a non-traditional manner. There is a significant difference between the likely impact of traditional and non-traditional authorships. The new style of authorship can deliver good quality articles, but it raises concerns for the scientific base of the therapeutics field and questions about the input to the new literature from academic “authors”.

INTRODUCTION

There has in recent years been increasing attention paid to authorship in the scientific literature (1). One concern has been the role of unacknowledged editorial or writing assistance to academic authors - so-called ghostwriters (2,3). Ghostwriters are often employed by medical communication agencies working to pharmaceutical companies. Efforts have been made to distinguish between ghostwriting and ghost authorship (4). Efforts have also been made to quantify the extent to which ghost writing is happening with Flanagin and colleagues (5) reporting that up to 11% of articles published in 6 peer reviewed journals in 1996 involved the use of ghostwriters.

Based on an unpublished Medline search for review articles on the treatment of depression against a background of other physical disorders, one of us (DH) found that as of 1997, 50% of the literature appeared in journal supplements or was authored by company personnel. This raises the possibility that up to 50% of the literature in pharmacotherapeutics, in certain domains such as psychiatry, might consist of articles that differ substantially in character from conventional notions of a scientific article (6). Traditionally the individuals whose names appear on the authorship line of a scientific article have authored all drafts of that article, and these individuals have worked with the raw data being reported on and can if required share this data with other investigators. By raw data here is meant data that has not been previously tabulated, which, we would argue, is a primary and key act of authorship.

There are a number of delicate issues that need to be teased out in this area ranging from the practicalities of regulating authorship to the more profound questions of whether ghostwriting is an unfortunate accidental development in the scientific enterprise or whether it reflects some fundamental aspect of the way modern science is conducted. There can be few if any of these issues or questions however that would not benefit from some quantification of what is happening. Against this background we have sought to quantify the literature profile of articles on one drug, sertraline, produced in 1998.

METHODS

We have used two data sources. First Medline and Embase literature retrieval services using the word sertraline, the year 1998, and searching under therapeutic uses. Second a document prepared for Pfizer Pharmaceuticals by Current Medical Directions Incorporated (CMED) on 1/29/1999, which gives a world-wide status update on articles on Pfizer's antidepressant sertraline, some of which had been published in 1998, while others were published in 1999, 2000 or early 2001. The CMED document was made available to us by Pfizer, in the course of legal proceedings on a non-confidential basis.

Rather than distinguishing between ghost authorship and ghostwriting, this article distinguishes between traditional and non-traditional authorships, with the primary criterion being whether the authors are likely to have seen the raw data they report on and whether they are free to share this data with others.

The CMED paper suggests CMED were monitoring three kinds of articles on sertraline. First, there were a number of publications originating within communications agencies, with the authors' names listed as "to be determined". The published articles in this series have many prominent names attached to them, with the authorship line commonly including Pfizer personnel. Second was a series of articles with very similar academic and company authors, already published or being worked on without apparently originating in a communication agency. Third was a set of articles that do not appear to have been written within a communication agency, and do not have a Pfizer name on them. This latter group of articles acknowledge Pfizer funding; in some of these the authors appear likely to have had access to the raw data in that the studies have been run in either one or a small number of linked centers.

The Medline and Embase articles on sertraline include articles listed in the CMED series and some not listed in that series. Of those not listed by CMED, the majority are reports of studies not supported by Pfizer and involve authors who appear likely to have had access to the raw data.

We have attempted to estimate the impact of these different articles as follows. The impact factor for each journal was established using Journal Citation Reports for 1999 from the Institute for Scientific Information Inc. We have had to estimate impact factors for one journal in the CMED series and four in the non-CMED series. Using Medline, we systematically searched for the number of Medline citations in both the CMED and non-CMED author

series. This permits us to offer three estimates. First we have estimated the mean number of Medline listings associated with each authorship. Second, we have estimated the overall literature profile of each article by summing the Medline listings for each authorship line and multiplying by the journal impact factor. Third we have estimated an annual literature profile for each series of articles, by multiplying mean article profiles by the number of articles in the series.

RESULTS

It is probable that the literature search process and CMED document miss a number of articles, most likely to be found in company funded symposium supplements or in journals not then listed in literature databases. Using Medline with sertraline as a keyword threw up 58 articles in 1998. Embase threw up 56 articles for sertraline in 1998. The overlap between Embase and Medline was greatest for the CMED articles they had in common. Altogether for 1998, 1999 and 2000 Medline listed 81% of the CMED articles published in 1998, 1999 and 2000, if supplement articles and health economic articles are excluded. In 1998 only 9 of the 20 articles appearing in the CMED document as published in 1998 appeared in the Medline search with 11 of the 20 appearing in Embase. Of the 11 not appearing in Medline, 5 came from the only supplement in the CMED series and 3 from health economic journals.

Medline/Embase Articles

Excluding those articles listed by CMED, Medline listed 6 papers that offer results on therapeutic trials with sertraline, of which 5 reported positive results

for depression (3), for premature ejaculation (1), and for dialysis hypotension (1), while 1 offered a negative result for sertraline used in pelvic pain. Five of these were studies not supported by Pfizer.

There were 14 papers offering case studies of clinical effects of sertraline, of which 13 detail adverse effects, including serotonin syndrome, hypomania, suicide attempts, extrapyramidal problems, urinary retention and priapism. There was in addition one review paper on extrapyramidal problems associated with sertraline use.

We have excluded five groups of papers. First, two generic SSRI papers, one being a study reporting a positive result with SSRIs for post-stroke emotional incontinence and the other a review on antidepressants, including SSRIs, for the treatment of paraphilias. Second, two Pfizer funded large multicenter studies, which outlined therapeutic advantages for sertraline in depression. The nature of these papers and their funding argue suggest an overlap with the CMED series of articles laid out below. Third, 4 papers comprised of 3 studies and 1 review, funded by other companies, which listed disadvantages of sertraline. The problems surrounding authorship in the CMED series of articles are likely to affect these also. Fourth, a further 9 papers dealing with biochemical aspects of sertraline use or animal models in which it is used, which have little relevance to daily therapeutics. Fifth a series of 10 papers or letters or case conferences on issues to do with issues from the role of culture in psychiatric care and the force-feeding of patients with Alzheimer's dementia.

In addition to those articles retrieved by Medline, we have included a further 18 Embase listed papers not found in the CMED document. Of these 18, 8 listed negative results for sertraline, 1 gave an ambiguous result, while 9 gave positive results. Of these latter 9, 3 received support from Pfizer, but the authors appeared likely to be in possession of the raw data. Embase also retrieved a further 7 papers on toxicology, and 3 on biochemical studies, which are not considered further.

In summary, in addition to studies and papers sponsored by pharmaceutical companies, literature retrieval processes pulled up 39 probably independent papers on aspects of sertraline's use in therapeutics, with 15 offering positive results and 24 detailing adverse effects.

Of these 39 papers, 4 appeared in the Journal of Clinical Psychiatry, 3 in the Journal of Clinical Psychopharmacology, 2 in Psychosomatics, 1 in the American Journal of Psychiatry with the rest in a number of minor journals, including some foreign language journals. There were 107 authorships from 105 individuals, an average of 2.7 authors per article. These articles were 3.4 pages in length on average; seven were in fact letters rather than articles.

CMED Articles

CMED's document outlined 85 papers in the production process during 1998. Of these 57 had been published by mid 2001, with 20 appearing in 1998, 19 in 1999 and 18 in 2000 or early 2001. We have not considered the results for

1998 in isolation in that a large number of further articles not listed in CMED come on stream in 1999 and 2000 in addition to those that were being worked on or had already been submitted for publication in 1998. Some of the 1998 listed articles remained in the publication process for 3 or more years suggesting that communication agency involvement means that articles handled in this way do not retire to the filing cabinet after serial rejection.

The 85 articles cover depression (14), seasonal affective disorders (1), dysthymia (7), panic disorder (8), post-traumatic stress disorder (2), general anxiety (2), obsessive-compulsive disorder (1), differentiation between SSRIs (17), what is termed “outcomes research” (largely pharmacoeconomic articles) (10), the use of sertraline in the elderly (10), the use of sertraline in children (6), the use of sertraline in women (4), sertraline pharmacokinetics (2) and sertraline in pedophilia (1).

The 57 published articles have a mean length of 10.7 pages, with 370 authorships listed, drawn from a total of 210 individual authors, giving a mean of 6.5 authorships per article. Of these, there are 185 academic and 25 company authors. Two of these articles acknowledge writing support from non-authors. These 57 articles offer the results of 25 clinical trials from a number of different therapeutic areas, including areas in which Pfizer were seeking licenses at that time for sertraline, in addition to 9 review articles and 6 articles offering economic models based on Pfizer trial data. All of the clinical trial results were favorable to Pfizer as were the economic analyses. Two of the review articles however listed adverse events in some detail. One

of these, from a Pfizer author, offered a frank acknowledgment of the capacity of sertraline to induce agitation/akathisia and the links between this and treatment-induced suicidality (7). The 57 papers appeared in the journals listed in Table 1.

TABLE 1: JOURNALS TAKING PFIZER SUPPORTED ARTICLES ON SERTRALINE

NAME of JOURNAL	No of Articles	Journal Impact Factor
Journal of Clinical Psychiatry	7	4.2
Journal of Psychopharmacology	7	2.8
American Journal of Psychiatry	6	6.3
Journal of the American Medical Association.	3	11.4
Archives of General Psychiatry	3	11.0
Journal of Affective Disorders	3	2.1
J American Acad Child & Adolescent Psychiatry	3	3.6
Journal of Clinical Psychopharmacology	3	5.7
International Clinical Psychopharmacology	2	1.1
Archives of Family Medicine	2	1.4

Impact factors for journals -1999 ISI data

Other journals in which one article was published included the British Medical Journal, European Psychiatry, the British Journal of Psychiatry, the American Heart Journal, Pharmacoeconomics and 13 other journals.

Of the 85 articles, 23 are listed as originating within communications agencies (see Table 2). Of the 57 published articles, the names of several senior academics appear on between 5 and 10 articles. In the CMED document, 13 articles do not appear to have a company author or to have been through an agency. Four of these articles involve economic models based on data provided by Pfizer, and it is assumed these authors do not have access to the raw data. Four appear in a company sponsored symposium supplement. The remaining five articles acknowledge support funding. Of these five articles, two at least have been reviewed by Pfizer personnel. Although more likely to have been authored in a traditional manner, these articles are included in the CMED series; their impact factor is well below the mean for the other articles in the series.

TABLE 2: BREAKDOWN OF ORIGIN & PLACEMENT of CMED ARTICLES

CMED Articles	85
Communication Agency Articles	23
Published Articles with Company Name	44
Published Articles without Company Name	13
Articles in Pfizer Sponsored Supplements	5
Articles involving Economic Models	6
Articles without Company Names or Communication Agency Input	5

CMED and Traditional Articles Compared

In Table 3, we list the mean number of authors per article, the mean number of pages per article, and the mean number of Medline listings per authorship

for each series. There are significant differences between the two series of articles on each of these features. In addition, we have estimated the literature profile of each article by summing the Medline listing rates for all authorships for each article and multiplying by the journal impact factor in which the article appeared. Finally, we have estimated an annual literature profile for each series by multiplying the mean literature profile of articles in each series by the number of articles that year. Using a Wilcoxon's Signed Ranks test, the two series of articles differed significantly in terms of Medline listing per authorship [$z = -3.74$; $p \leq 0.01$), and literature profile per article ($z = -4.32$; $p \leq 0.01$).

In addition, there was a mean journal impact factor of 3.0 (C.I 1.9 – 4.1) for articles reporting beneficial effects of sertraline versus 1.78 (C.I. 1.1 – 2.5) for those reporting negative effects. The mean literature profile for favorable articles was 351 (C.I. 59 – 643) versus 172 (C.I 7 – 337) for negative articles.

TABLE 3: THE LITERATURE PROFILE OF CMED & NON-CMED ARTICLES

MEDLINE/EMBASE	39 Articles
No Authorships/No Authors	107/105
Mean No. Authors/ Article	2.7
Mean No. Pages/ Article	3.4
Mean Medline Listing /Authorship	36.7 (C.I. 26.6 - 46.8)
Mean Literature Profile / Article	252 (C.I. 115 – 388)
Overall Literature Profile for 1998	9,828.
CMED	57 (19 p.a.)
No Authorships/No of Authors	370/210 (123/70 p.a.)
Mean No Authors/ Article	6.5
Mean No Pages/ Article	10.7
Mean Medline Listing /Academic Authorship	70.4 (C.I.61.9 - 78.9)
Mean Medline Listing /Company Authorship	17 (C.I. 14 – 20)
Mean Literature Profile / Article	1823 (C.I 1084 – 2561)
Overall Literature Impact Per Annum	34, 637 (19 x 1823)

DISCUSSION

Traditionally authors generate and have access to raw data and prepare an article that disinterested observers would accept reflects the most appropriate interpretation of that data. Authorship has been changing, however, and journals now accept that articles may be authored by individuals who have

made a substantial contribution to the conception and design, or acquisition of data or analysis and interpretation of data in a study or who have drafted or critically revised the intellectual content of an article and who have approved the final version of the published article (8, 9). This new authorship matrix is consistent with many articles being ghostwritten.

There are a number of good aspects to the ghostwriting process. First authorship by a communications agency or within a company makes it more likely that the results of research will enter the public domain than if the production of articles were left to the senior clinicians involved in clinical trials. Second, the quality of the writing is probably consistently superior as a consequence. Third, there is every reason to believe that at least some communications agencies and companies will take the efforts by journal editors to encourage the disclosure of interests and inputs more seriously than many academic investigators will. Fourth, there is data to indicate that the reporting of adverse events in company sponsored and monitored clinical trials is more comprehensive than the reporting of adverse events in government sponsored or other independent studies (10). While the analysis of published results on antidepressant studies in recent years, many of which have been written in the manner outlined here, have made it clear that a significant proportion of negative results are not published, to the extent that the sponsorship of a published study is now a demonstrable predictor of the findings of that study (11,12), this bias almost certainly affects the entire domain of therapeutics, including psychotherapy, and alternative therapies.

The work by Flanagin et al (15) gives some indication of the extent of the ghostwriting phenomenon. Our work gives a further quantification based on a single drug. It suggests that the proportion of the therapeutics literature for a high profile therapeutic agent in any one-year being authored in a non-traditional manner is at least 50%. Furthermore, the impact of this non-traditional authorship greatly outweighs the impact of articles written in the traditional way.

These data suggest CMED and Pfizer recruited authors, whose background increased the possibility of the company's publications appearing in the most prestigious journals, and specific journals seem to have been targeted. The combination of distinguished journal, distinguished author, an efficient distribution system and sponsored platforms makes it highly likely that the impact on the therapeutics domain from non-traditionally produced articles will be greatly in excess of 50% of the impact of the literature linked to any particular pharmacotherapeutic agent.

The question of literature impact is tied closely to the nature of ghostwriting. Authorship lines from perceived opinion-leaders with minimal company representation and non-declaration of other authorship inputs increase the likelihood that these articles will be influential with prescribers and purchasers. One of the expressed concerns about ghostwriting, hitherto, has been the way this process leads to a lack of recognition for the people who actually do the writing of the articles. The converse of this point is that academics become opinion leaders in a therapeutics field because they appear to have their

names on a larger proportion of the literature appearing in the most prestigious journals than do others and because they get asked to national and international meetings to present this data, with which they may not have first hand acquaintance. Whether or not these academic authors authored any of the CMED articles in a traditional sense, there must be a non-traditional authoring involved in most cases in the sense that these authors cannot share proprietary raw data with colleagues in the way that has been traditional in the scientific domain. This allied to the volume of non-traditional authorship indicates a process of changing scientific authorship that could conceivably culminate in a situation in which the dominant figures in therapeutics actually have comparatively little first hand research experience and little raw data that they can share with others.

The data in this study suggest that the non-traditional method of authorship makes the publication process both more efficient and more effective. It does not seem right to say that an efficient and effective publication process is problematic per se. Arguably concerns about an efficient publication process are a substitute for recognizing that an additional bias in the field of therapeutics must stem from the fact that most studies are now sponsored, designed, and analyzed, as well as efficiently written by pharmaceutical companies. This is a process that in psychopharmacology picked up pace from 1980 (14). While the greatest proportion of studies are sponsored, designed and analyzed by companies, the primary questions being asked in the therapeutics domain will relate to the marketing interests of pharmaceutical companies rather than to unanswered scientific questions.

Recent efforts to encourage pharmaceutical companies to publish the results of all of their studies imply that therapeutics will become scientific if all studies are published. Complete publication of studies would in fact only bring the field of therapeutics up to an acceptable business ethics standard.

A field is only scientific if scientific questions are addressed. But in addition, authors must be able to share their data with others. Company assertions of proprietary rights over raw data are in fact incompatible with the canons of scientific methodology. To appreciate the significance of the proprietary control of raw data, consider the following. In a meta-analysis of trials on recent antidepressants submitted to the FDA, Khan et al (15) found no difference between rates of suicidal acts between placebo and investigational agents including sertraline. However, a substantial proportion of the suicidal acts categorized as occurring on placebo in sertraline and paroxetine trials actually occurred during the washout phase of trials rather than on placebo. The same categorization is shared by a number of other articles, suggesting these authors are all using data previously tabulated by the respective companies. When suicidal acts on investigational drugs are compared to suicidal acts on placebo omitting washout, there is a statistically significant difference favoring placebo.

Making raw data from therapeutic trials available may be seen as a counsel of perfection, but if pharmacotherapy is to be a scientific business rather than just a business adopting the appearances of science, no less than this is needed. It should be remembered that the capitalization of the industry

depends entirely on the voluntary participation of healthcare consumers in studies of the kind reviewed here. This study suggests that there is a greater discrepancy between appearance and reality in the behavior of academic contributors to articles in the therapeutic domain than has hitherto been appreciated. These same authors are better placed than most parties to scientific authorship to help move the field forward.

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