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How ghost-writing threatens the credibility of medical knowledge and medical journals

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The past couple of years have seen some shocking exposés of violations of authorship in medical papers which suggest that one of the most important tenets in medical publishing – what it means to be named as an author on a paper – may not actually be as well accepted as previously believed.

In this article I shall briefly review some of the main cases that have led to these concerns, then I shall discuss the reasons why I think we have got to this point, why notions of authorship should concern us so much, and, finally, what I think is needed for integrity in authorship to become something that is again valued.

The evidence for ghost-writing

There has been much anecdotal evidence of the existence of ghost-writing – that is, someone who contributed substantially to a paper not being named as an author – (and its linked problem, guest authorship – that is, individuals not deserving of authorship being named as authors), in hematology journals[1] and in other journals.[2] However, until quite recently many involved in publishing felt that such authorship concerns were a marginal problem, and confined to a relatively small set of papers. But evidence is accumulating of a substantial, systematic problem in publishing. One of the first comprehensive surveys of the prevalence of ghost authors was published in 2007.[3] This survey, which took advantage of the availability of trial protocols from one source, and then compared the authorship of the protocols with that of the published papers, found evidence of ghost authorship for 75% of trials (33 of 44 trials). If the person qualifying for authorship was acknowledged rather than appearing as an author, then the prevalence of ghost authorship went up to 91% (40 of 44) articles.

An even more compelling indication that ghost-writing was a substantial, organized problem in medical literature came with the publication in 2008 of two related papers in *JAMA*.[4,5] One paper[4] laid out a campaign of what in the wider media world would be described as product placement – that is, papers reporting favorably on rofecoxib (Vioxx) being placed in a broad spectrum of medical journals and in a wide range of article types, from reviews to original articles. The case was especially shocking, to the general public as well as physicians, because of the furore that surrounded the safety of rofecoxib, and the ongoing court cases for damages. In fact it was these court cases that led to the documents which were described so compellingly in the *JAMA* papers being made publicly available at all. The message of the second paper,[5] which reported on mortality in trials of rofecoxib in patients with Alzheimer's disease or cognitive impairment, was more subtle, but equally important – i.e. what actually happens when papers are shaped for publication not by an impartial research agenda but by the need to sell a product. The conclusion of the paper, that substantial misinformation can be published relating to issues as important as mortality was, again, shocking to many people.

In 2009, *PLoS Medicine*, the journal where I work as Chief Editor, became involved in a further case in which evidence of a widespread campaign of ghost-writing was emerging.[6] *PLoS Medicine* and the *New York Times* acted as "intervenors" in litigation against menopausal hormone manufacturers by women who developed breast cancer while taking hormones. In July 2009, a US federal court decision resulted in the release of approximately 1500 documents which provided evidence of a substantial organized campaign by Wyeth of publication planning, including the use of ghost and guest authors.

If yet more evidence were needed of how ghost-writing has become integrated into the processes of pharmaceutical companies, a few weeks after the release of the documents from Wyeth, evidence came to light (again in court documents, this time concerning the drug paroxetine [Paxil]) of a program called CASPPER (named after the friendly ghost of US cartoons and standing for "Case Study Publications for Peer Review") which was used in the past by GlaxoSmithKline to involve clinical "authors" in promotional papers.[7] It is hard to avoid the conclusion that ghost authorship was something that was at some point so integrated into company practice that it was alright to make jokes about it.

Why does ghost-writing matter?

The International Committee of Medical Journal Editors says this about authorship:[8] "Authorship credit should be based on 1) substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; 2) drafting the article or revising it critically for important intellectual content; and 3) final approval of the version to be published. Authors should meet conditions 1, 2, and 3." Though a number of journals do not accept that all three criteria are needed, and instead use a contributorship system by which they allow authors to declare how they participated in the paper, the main reason for being proscriptive in the definition of an author is to remind authors about the responsibilities that go with authorship (as well, of course, as the privileges). To return to the title of this piece and address the question head on, ghost authorship matters because it threatens the fundamental understanding that exists between readers and authors: that whoever is named on the paper as an author deserves to be an author and that, in addition, the authors named on a paper indicate to the reader the actual provenance of the piece.

Though many types of authors can be either ghosts or guests and none is acceptable there are some that should concern us very much. In the paper by Gøtzsche and colleagues[3] the high prevalence of ghost statisticians was particularly troubling. If no one named on a paper was actually responsible for the analysis, which was instead done by a shadowy group of unnamed individuals, then it is hard to have any confidence in the findings overall. Conversely, it is also troubling that authors agree to be guest authors, particularly in a senior position on the paper. In return for a publication (which they often may not need given their senior position) they allow

their name to legitimize something they cannot really vouch for. Though, more often than not, authors get away with it, authors should be very wary of being guests. In a number of recent high profile cases of fraud some senior authors have protested that they knew nothing about the alleged misconduct, only to have their protestations met with incredulity.[9] It is a forceful reminder that authorship is a responsibility not just a privilege and should be offered or accepted with appropriate consideration.

What can be done?

If there is one lesson to be learned from all these cases of ghost, guests and other illegitimate authors it is that authorship has somehow slipped recently from something to be earned through a specific, meaningful contribution to a superficial designation that can be traded. These slippery notions of authorship have not come out of a vacuum, and were certainly not invented by pharmaceutical companies. The issue of guest authorship – of including the head of department among the list of authors of a paper for no other reason than esteemed status – has been widespread in academia for many years. I would argue that it is this culture that pharmaceutical companies have tapped into, rather than inventing a new type of author. But by flattering academics into being guest authors, they have created, and then filled, a need for ghost authors to actually write the papers. The academics accepting the apparent honor of authorship thus provide cover – as accomplices or as dupes – for manipulative marketing practices.

Some have interpreted the anxiety over ghost authors as a call to remove all medical writers from papers but that is not the case. Medical writers do have a role to play in writing papers, but somehow, as we have argued before,[10] without appropriate standards this legitimate role can be turned into something that subverts and threatens medical publishing more widely.

It is clear then that the responsibility for addressing the mismatch between what an author should be and what authorship has come to mean lies with many groups. Journals clearly have a role to play in identifying and correcting the most egregious examples. And pharmaceutical companies must accept that trying to hide ghost, or entice guest authors is not acceptable. But the primary responsibility for prevention lies much further back, within the institutions where authors work, and where medical academics are trained. Authorship of a scientific or medical paper must be returned to something that can be a source of pride, and which is deserved and earned – and declared.

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Rac GTPases play multiple roles in erythropoiesis

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The four members of the Rac family of GTPases – Rac1, Rac2, Rac3 and RhoG – are members of the Rho superfamily that regulates the organization, dynamics, and function of the actin cytoskeleton. Rac GTPases play significant roles in many cellular processes including migration, cytokinesis, lamellipodia formation, and cell polarity.[1] Genetically modified mice deficient in each of the Racs are available;[2-6] deficiency of Rac1 causes intrauterine death, whereas mice defective in Rac2, Rac3 or RhoG develop fairly normally. Rac proteins may have redundant functions in certain types of cells and unique functions in others.

As shown by single- and double knock-outs of Rac genes, the Rac GTPases play important roles in many hematopoietic cells.[7] Rac2 is specifically expressed in hematopoietic cells, and is directly involved in chemotaxis and superoxide production in neutrophils and macrophages.[3,8-11] In addition, Rac2, together with Rac1, mediates B-cell receptor signaling pathways.[12] T-cell activation is also affected in Rac2-deficient mice[13] and hematopoietic stem cells from Rac2$^{-/-}$ mice show defective long-term engraftment.[14]

In contrast, Rac1 is ubiquitously expressed and plays essential roles in several organ systems, including