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COMMENT

Ghosts in the Machine:

Comment on Sismondo

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Sociological interpretations of science, extending from Kuhn's (1962) *Structure of Scientific Revolutions* to the social constructivists of the 1980s, have enlivened the traditional debate about the foundations of science and the very idea of scientific progress. But there is perhaps no place to see the central flaw of such interpretations better than in academic medicine, for here the importance of reliable reporting of the data from empirical testing reveals clearly the distinction between genuine and sham science.

In his paper 'Ghosts in the Machine: Publication Planning in the Medical Sciences', Sergio Sismondo (2009) exposes the larger background of marketing and promotional activities in the vast network of pharmaceutical industry ghostwriting. By having infiltrated the ranks of marketers he brings a unique perspective to their activities, and his report on this experience is valuable. Outside of litigation one seldom sees the inner workings of this process. Sismondo, however, makes the serious mistake of claiming that pharmaceutical industry-sponsored research and ghostwriting produce genuine knowledge and science (albeit commercial science) not different from established medical science. He cites David Bloor, Karin Knorr Cetina, Andrew Pickering, and Harry Collins to support this claim and says that science is 'choice laden', implying in this case that it matters little whether it is produced by academic scientists or spun in marketing strategies of public relations firms.

It is widely acknowledged by the leading philosophers of science that science is 'choice laden' in the sense that as authors of scientific theories we create hypotheses by which experience is interpreted; but by subjecting these hypotheses to rigorous tests, we discover which ones are falsified and which ones will serve as our best, tentative solutions to problems (Popper, 1959). It is this crucial role of genuine and rigorous testing that demarcates real science from its impostors. Thus unlike Sismondo, I do not condone the activities of commercial science as merely part of a constructivist view of science, one that fails to distinguish between better and worse, genuine and sham.

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Sismondo says: 'Implicit in many of the exposés of ghostwriting in the medical science and popular literature is an assumption that ghostwritten science is formally inferior', and cites a high acceptance rate of ghost-managed papers as evidence against this alleged assumption (Sismondo, 2009: 193). Yet a high acceptance rate only demonstrates the failure of the journal editors to identify the suspect papers, not that genuine science is being produced. The most perfunctory examination of the literature on the subject reveals that the ghost-managed papers are inferior. In this regard, Sismondo has underestimated the known cases where ghostwriting has contributed to harming patients, including fatalities. Studies of many of these cases studies have documented scientific misconduct in manipulating the data by selective reporting or by faulty design to favor study medication. But there can be no such thing as scientific misconduct if the social constructivists are correct, and Sismondo has no complaint against ghostwriting.

If the results of industry-sponsored clinical trials were reported honestly, then aside from the question of deception and plagiarism, ghostwriting would not present a serious concern for advancing knowledge. However, medical communication companies and the pharmaceutical industry go to great lengths to conceal ghostwriting precisely because their efforts to promote the medications they study involve a corruption of clinical science. In the days before industry-sponsored trials largely conducted by contract research organizations and promoted through medical communication companies, the writing-up of trial results was merely a mundane task that a lead investigator could assign to a graduate assistant. Such reports were stolid but disinterested and honest (aside from outright fraud due to personal ambition). The aim was to provide a genuine test of a medication, not to engage in the marketing of a blockbuster.

The main problem with what Sismondo called ghost-managed papers is that the ghostwriter is only given a summary of the data, which the 'authors' typically accept as accurate. The carefully manipulated message of drug promotion is controlled by the sponsoring company. After all, they own the data and the manuscript. The manuscript only changes hands when the sponsoring company legally transfers ownership to the 'authors' in order to submit the paper for publication. The most serious cases of selective reporting leading to serious harm to patients have resulted from the failure of the lead investigators to demand the raw data from the industry sponsor of the study. Some of the most notable cases that have been investigated include:

Paroxetine (Paxil) – off-label prescribing for adolescent depression (Jureidini et al., 2008; McHenry & Jureidini, 2008);
Rofecoxib (Vioxx) – suppressed cardiovascular risks (Ross et al., 2008); and
Fenfluramine and Phentermine (Fen Phen) – diet drug promotion (Elliott, 2004).

Others in which promotional claims in ghostwriting overstated efficacy or involved the use of key opinion leaders to manipulate evidence in competitive issues include:

> Vagus nerve stimulator – undisclosed background promotion (Holden, 2006);
> Paroxetine (Paxil) – battle between Eli Lilly and SmithKline Beecham over selective seratonin reuptake inhibitors (SSRIs) withdrawal/discontinuation (McHenry, 2005),
> Gabapentin (Neurontin) – sponsorship of scientific papers (Steinman et al., 2006).

Sismondo briefly mentions the cases of refecoxib, dexfenfluramine (an anti-obesity drug related to fenfluramine and phentermine), and gabapentin, but only to make the point about how these industry-sponsored ghost-written publications were also ghost-managed projects and not to expose the scientific misconduct or the harm to patients (Sismondo, 2009: 172–73). In the rofecoxib case alone, Graham et al. (2005: 480) estimate that the drug may have caused up to 120,000 cardiovascular events in the US, including 40,000–60,000 that were fatal.

In other cases where investigators have refused to read the data in the way prescribed by the industry, there have been serious consequences for careers. Witness for example the cases of academic researchers David Healy, Nancy Olivieri, Aubrey Blumsohm, and Betty Dong. This has demonstrated a serious problem for the academic–industry partnerships that largely formed in the wake of the Bayh-Dole Act of 1980 (Krimsky, 2003).

Where there is a profit motive involved in the testing of a medication, there can be no science if indeed the test does not involve a real risk of failure. Consider the gold standard of clinical research, the double-blind, randomized, placebo-controlled trial. The test of a study medication is reaching statistical significance in the primary measures against placebo or a comparator drug. Yet, if the sponsor company's investment in a new molecular entity is challenged by either of the other two arms of the study, the design of the trial can be rigged by manipulating the dosage or by choosing a weak comparator. If this isn't sufficient, when writing up the results, the primary and secondary measures can be conflated or adverse events that affect the risk ratio can be miscoded so that the study medication is declared the winner by the ghostwriter (Jureidini et al., 2008).

It is notoriously difficult to get any reliable numbers about ghost-managed papers, since this process is meant to conceal conflicts of interest and manipulation of results. The only way we know of these, as Sismondo well knows, is from litigation and whistleblowers, of which there are few cases. While the known cases are merely the proverbial tip of the iceberg, they are sufficient to demonstrate my point against Sismondo. But let us consider another fact of the invisibility of the process. The crucial data needed to settle the matter of whether commercial science is producing real science are carefully guarded by industry. This puts Sismondo and me at

equal disadvantage, but the fact that industry must invoke the Trade Secrets Act in the US to ensure that crucial documents remain confidential demonstrates that they have much to hide. Furthermore, if any of this comes close to full exposure, industry will then threaten libel actions or withdraw journal sponsorship (Healy, 2008).

Elsewhere, Sismondo and Doucet propose what I consider to be the most radical but sensible recommendation for restoring the integrity of the medical literature. They write: 'if the medical journals want to ensure that the research they publish is ethically sound, they should not publish articles that are commercially sponsored' (Sismondo & Doucet, 2009). But if as Sismondo has maintained, commercial science is not inferior science and the ghost-managed publications have passed the tests of peer review with flying colors, then upon what grounds can he now condemn the current editorial practices? I suggest that the problem with professional ethics overlaps with the problem of scientific misconduct and this is precisely why this recommendation is so sensible, but in the end shows an inconsistency in Sismondo's argument. He cannot maintain without contradiction that industry-sponsored clinical trial reports should be banned from the medical journals and that the science behind these reports is not inferior.

The commercial medical science that has created the ghostwriting industry is a corruption of science, and not merely as Sismondo puts it 'science done in a new, corporate mode' (Sismondo, 2009: 193).

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