

HEAD TO HEAD

Should journals stop publishing research funded by the drug industry?

The *BMJ* no longer publishes research funded by tobacco companies. **Richard Smith** and **Peter Gøtzsche** say that research funded by drug companies is also flawed and published to encourage sales, but **Trish Groves** says that the industries are fundamentally different and that moves are afoot to increase integrity

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Yes— Richard Smith and Peter C Gøtzsche

The *BMJ* and its sibling journals have stopped publishing research funded by the tobacco industry for two main reasons: the research is corrupted and the companies publish their research to advance their commercial aims, oblivious of the harm they do.¹ But these arguments apply even more strongly to research funded by the drug industry, and we suggest there is a better way to communicate the results of trials that would be safer for patients.

Prescribed drugs are the third leading cause of death, partly because of flaws in the evidence published in journals. We have long known that clinical trials funded by the drug industry are much more likely than publicly funded trials to produce results favourable to the company.² The reason is obvious. The difference between an honest and a less than honest data analysis can be worth billions of euros, and the fraudulent trials of some cyclo-oxygenase-2 inhibitors for arthritis and selective serotonin reuptake inhibitors for depression are good examples.³⁻⁵

Industry cannot be trusted

There are many clever ways in which companies manipulate their research,⁶ and two recently published books give dozens of examples.^{3,7} Flaws in the coding of adverse events can distort results without leaving any trace of what has happened, as we cannot get access to the raw data the drug companies hold. Three large trials of prasugrel, rosiglitazone, and ticagrelor made by Daiichi Sankyo and Eli Lilly, GlaxoSmithKline, and AstraZeneca, respectively, published in the *New England Journal of Medicine* were shown to be seriously misleading.⁸ Such biased selection by the sponsor of “unclear cases” of serious adverse events for review by an independent adjudication committee also corrupts the evidence base.³ Less cleverly, the

companies publish favourable results in major journals and bury unfavourable ones. Half of trials are never published.⁹

In contrast to tobacco funded research, which is comparatively rare, two thirds of the clinical trials published in major journals such as the *Lancet* or *New England Journal of Medicine* are funded by the drug industry.¹⁰ In addition, companies use ghost writers to promote misleading trials in scores of secondary publications and reviews in major journals. These, just like the original research, often carry the names of opinion leaders, which seems to give the articles credibility.^{3,11} This common practice is scientific fraud.¹²

Readers of these journals are thus given a seriously corrupted view on the benefits and harms of drugs that they will be heavily persuaded to prescribe. The companies spend millions of dollars buying reprints of the studies they have sponsored, using the brand of the journal to promote their drugs.^{3,13} The journals make huge profits on these sales, a gigantic conflict of interest.^{3,10,14,15}

Sadly, there are many examples of drug companies advancing their business while causing harm to patients by promoting their drugs in journal articles. Pfizer was fined \$430m for fraudulent promotion of gabapentin (Neurontin) for unapproved uses.³ The drug was licensed for treatment resistant epilepsy but accumulated some 48 off-label uses. Kay Dickersin, director of the US Cochrane Center, analysed the studies used to promote gabapentin for migraine, bipolar disorder, and pain and found a “remarkable assemblage of evidence of reporting biases that amount to outright deception of the biomedical community, and suppression of scientific truth concerning the effectiveness of Neurontin.”¹⁶ Pfizer was convicted of organised crime and conspiracy.³

Merck scientists knew already in 1996 that rofecoxib (Vioxx) might cause thrombosis, but the company published numerous misleading studies in prominent journals to promote its licensed use and other uses, sometimes omitting cases of myocardial

infarction in patients taking the drug.^{3 4} More generally, the dishonesty in the research literature on non-steroidal anti-inflammatory drugs is legion and has resulted in the deaths of hundreds of thousands of patients, many of whom didn't even need the drug.³

Another dire example is antipsychotics. Many recent drug industry crimes are related to off-label promotion of antipsychotics, and in the United States they were the most sold drugs in 2009.³ However, they are so dangerous that just one of them, olanzapine (Zyprexa), has probably caused 200 000 deaths.³

New model

Fortunately, journals are no longer needed to communicate the results of trials to doctors; there are much better ways, without paywalls.¹⁷ Trial planning should begin with a systematic review of previous work, which would show whether a new trial was really needed—or whether it was simply promotion dressed up as science. The review would be posted on the web for anybody to comment, recognising that scrutiny by many eyes is better than scrutiny by a few. If a new trial was needed, the protocol would also be posted for anybody to comment. The statistical analysis plan would not be made up late in the trial, when the sponsor might already have evaluated some of the data behind closed doors,³ but would be posted with the protocol, and when the trial was done the entire anonymised dataset would be uploaded for everyone to analyse. It is a terrible misconception that drug companies can own trial data. According to the European ombudsman and other lawyers we have spoken to, the data belong to us all, not least the patients who have run an unknown risk by generating the data.

The role of journals would be to publish the results from the systematic reviews and contrasting analyses of the trial data by independent groups, and everybody would be able to see every part of the evidence. The journals, to be respected, would free themselves entirely from drug companies, as the French journal *Prescrire* has done.

The result? Drugs would no longer be the third leading cause of death, after heart disease and cancer.³

No—Trish Groves

Several BMJ journals, including the *BMJ*, recently banned submissions of research partly or wholly funded by the tobacco industry.¹⁸ This prompted Christopher Proctor, chief scientific officer at British American Tobacco, to accuse us of being antiscience and of lacking confidence in our own peer review processes.¹⁹ Richard Smith, who was editor of the *BMJ* when we previously decided against such a ban, added, “So will the editors [also] stop publishing research funded by the pharmaceutical industry, and if not why not?”²⁰ Here's why not.

The drug and tobacco industries, notwithstanding the inescapable fact that both are out to make money, have very different aims. The drug industry makes and sells products aimed at improving health. Medical journals aim to publish research that will improve health. It's a good fit. The tobacco industry, meanwhile, makes and sells products that harm health. As Gro Harlem Brundtland put it in 1999, when she was director general of the World Health Organization, “It is rare—if not impossible—to find examples in history that match tobacco's programmed trail of death and destruction. I use the word programmed carefully. A cigarette is the only consumer product which when used as directed kills its consumer.”²¹ Whatever your concerns about

the drug industry and the safety of drugs, you'd be hard pushed to make the same allegation.

Available evidence can be improved

There are, of course, many concerns about drug industry funded research. Only about one in 10 newly approved drugs substantially benefits patients,²² not least because patients are too often excluded from identifying gaps in treatment and in setting research questions.²³ Garattini and Chalmers argue that governments should work to improve the relevance and yield of drug research and to get better value for the substantial amounts of public money that already support industry led drug development.²³ They propose four strategies: involving patients in shaping the research agenda, making transparency in drug evaluation a legal requirement, requiring and resourcing independent evaluation of drugs (by national institutes of health research and national drugs agencies), and requiring proof of added value for all new drugs. More openness could help to transform the drug industry's image and performance, they say, and perhaps in return governments could extend patent time.

How much can we trust the evidence base for drugs in current use? It's hard to tell, given the woeful legacy of widespread non-registration, non-publication, and selective reporting of clinical trials.²⁴ Much of this reporting bias also applies to investigator led trials,²⁵ and the many steps now being taken to mandate prospective trial registration, ensure reporting of all results, and access patient level data on interventions' benefits and harms, as called for by the AllTrials campaign,²⁶ must apply to them as much as to industry led trials. Moreover, new rules on transparency need to be applied retrospectively: laudable plans to provide access to data on new drugs aren't enough.

That's why the *BMJ* is keen to publish papers from the RIAT (Restoring Invisible and Abandoned Trials) initiative, through which academics who find previously unreported trials can write them up and publish them if the original investigators decline to do so.²⁷ We also welcome “negative” trials that find no evidence of benefit, as long as their research questions are important and their methods robust, and we're particularly interested in publishing trials of comparative effectiveness. Both these types of study can be much more useful to clinical practice than the placebo controlled trials that regulators demand. We have many policies aimed at maximising the scientific and ethical transparency of papers about drug trials (www.bmj.com/about-bmj/resources-authors/article-types/research), but a journal article can convey only so much detail. Hence the *BMJ* considers drug and devices trials only if the authors also commit to making the relevant anonymised patient level data available on reasonable request.²⁸ This policy applies to any research article that reports the main end points of a randomised controlled trial of one or more drugs or medical devices in current use, whether or not the trial was funded by industry.

Taking a stand

Couldn't we have come up with some similarly tough policies for tobacco funded research, rather than banning it from our journals? Yes, we could. But we have decided that the likely harms of publishing tobacco funded studies we can't trust¹⁸ greatly outweigh any possible benefits of publishing such research. And, until we can rely fully on academia or governments to conduct all the important drug trials that the pharmaceutical industry won't do (and perhaps shouldn't do),²³ we will be happy to publish high quality, relevant studies from the industry while continuing to campaign for even greater relevance and more transparency.

So is this the whole story? Or are we just taking the moral high ground in banning tobacco research from our journals? To some extent we are; but it's ground we're happy to occupy, given our ultimate mission to improve outcomes for patients. More worryingly, are we editors afraid or unable to extend the ban to pharmaceutical research because our journals receive advertising, reprint, and some sponsorship income from the drug industry (www.bmj.com/about-bmj)? No; that's not the reason. As Fiona Godlee, the *BMJ*'s editor in chief, said in her response to Richard Smith's challenge, "If these efforts do not soon bring about a necessary sea change in the way industry funded trials are performed, the *BMJ* may well decide to stop publishing them. Whether an editor would survive such a decision is a question I may have to test."²⁹

Competing interests: The authors have read and understood the *BMJ* policy on declaration of interests and declare the following interests: TG is editor in chief of *BMJ Open* and head of research at the *BMJ*, which is a wholly owned subsidiary of the BMA. *BMJ* (the company) receives revenues from drug and device manufacturers in the form of advertising, reprint sales, and sponsorship. She receives a bonus based in part on the financial performance of the *BMJ*. The *BMJ* is an open access journal that charges author fees for publication of research articles, as does *BMJ Open*. She is responsible for encouraging authors to submit research to the *BMJ*. She chairs the *BMJ*'s weekly manuscript committee meeting where we decide which research to publish. She helped to develop and, in some instances, coauthored some of the published guidance that she has cited in this article. RS was editor of the *BMJ* and receives a pension from the BMA, the owners of the *BMJ*. The pension fund is underfunded for its commitments, and the profits from *BMJ* are important for the finances of the BMA. Some of those profits depend on revenue made from pharmaceutical companies. Join the authors live on Twitter to debate the issue on 21 January, 1200-1230 GMT at #pharmaban.

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