Did Tamiflu work? How can we know if we can't find out?

Medical science frequently favours commercial interests over free speech, writes Deborah Cohen of the BMJ.

If one of the principles of free speech is the ability to make “well informed decisions” then medical science may find itself wanting. Pharmaceutical companies and device manufacturers have come in for stinging criticism over the past few years for preventing fair and objective assessments over the benefits and harms of their products.

Take Tamiflu (Oseltamivir) - a multibillion dollar drug stockpiled globally to fight pandemic influenza - as a case in point.

The UK spent around £1.2bn on the pandemic with just under half of that on global healthcare company Roche’s pills. The premise was that wide availability of the drug would ease pressure on over-stretched health services by preventing otherwise healthy people infected with influenza from developing more serious illness. Health authorities also trumpeted the ability of Tamiflu to stop the virus spreading to other people - hardly surprising that it quickly became a prized asset in the fight against pandemic flu.

Replication and repetition is the essence of science - it helps to show that a previous finding wasn't fraudulent or simply due to chance. But when the Cochrane Collaboration, a group of respected international independent academics, tried to assess if the claims about preventing serious complications stacked up in 2009 they found a few barriers in their way.

Even though they had been funded to do this with public money, a straightforward exercise to confirm the evidence base for current policy and practice became instead a complex investigation involving the Cochrane Collaboration, the BMJ and Channel 4 News.

When the group went about surveying the medical literature, not all of the trials they knew existed about the effects of the drug in healthy people appeared in the medical press. To fairly reflect the evidence, they needed to know exactly what all trials said. But they couldn't access all the data they needed - the majority of trials were unpublished. This included the biggest, and therefore arguably the most important, trial conducted.

The bold claims about cutting down serious illness and reducing the burden on hospitals hinged on a single research paper published in 2003 that was supported by Roche. It used company statisticians and one of the two "independent" academics included as authors on the study had financial ties to the company too. This study amalgamated the results of ten Roche-funded trials to see what they said overall. This is often done in medicine to get a better picture the benefits and harms of a drug or device.

They asked the authors of the study - supposedly the guardians of views expressed in the 2003 research paper - for the unpublished trials, but they were unable to produce them. So they then turned to Roche. And whilst the company produced some data, it was not enough to satisfy the Cochrane Collaboration and answer their question: did Tamiflu really help to reduce the number of people going to hospital from serious complications of influenza? This what international health authorities had said.

(Further investigations also found that Roche funded some of the experts who advised the likes of the WHO and the European Medicines Agency on the benefits of Tamiflu in pandemic planning.)

Clearly, neither the company nor the 2003 study authors were in a position or wanted to help the Cochrane group make a well-informed decision based on the trial data. And Roche were well within their legal rights. Nevertheless, they have provided a litany of reasons for not complying with the Cochrane Collaboration's requests. Reasons, perhaps, that might undermine the fundamental principles of freedom of expression as described on this very site.

These include the fact that the Cochrane group refused to sign a confidentiality agreement with the company; a similar study to that proposed by the Cochrane Collaboration is commencing and there are concerns that the request may conflict with this; and also, the initial request for data came from the media.

Even the key health organisations responsible for devising public policy - and determining how valuable resources are allocated - were seemingly unwilling to help figure out what the data really said and enter into discussions with the Cochrane group.

But commercial sensitivity - in theory - should not carry any truck with the European and US drug authorities. Legislation dictates that companies have to provide regulators with a thorough scientific dossier on all trials conducted on a drug so the data can be scrutinised before it can be sold. Clinical data is available in both jurisdictions under the Freedom of Information Act.

So the drug regulators were the next port of call. In early 2010, the researchers asked both the European Medicines Agency and the US Food and Drug Administration for all the clinical data they had on file - this could potentially amount to tens of thousands of documents.

After just over four months, the European Medicines Agency turned over what they had. (The US Food and Drugs Administration are yet to comply with the request.) But far from having a complete dataset themselves, the European drug authorities did not have everything the Cochrane group wanted. The agency later confirmed that it had not exercised their rights to ask Roche for all data relating to the trial - something the new EMA head, Guido Rasi, has pledged to do in future.

After nearly three years of mounting a simple but crucial task, the Cochrane Collaboration has been left with more questions than answers. But one conclusion they have been able to draw is that medicine does not always adhere to the principles of freedom of speech - the ability to make “well informed decisions” for the public good may be trumped by commercial interests.

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