*NATURE* | NEWS: EXPLAINER

# Analysis of trial data revives flu-drug row

**What are the benefits of Tamiflu, and why is it so controversial?**

**Daniel Cressey**

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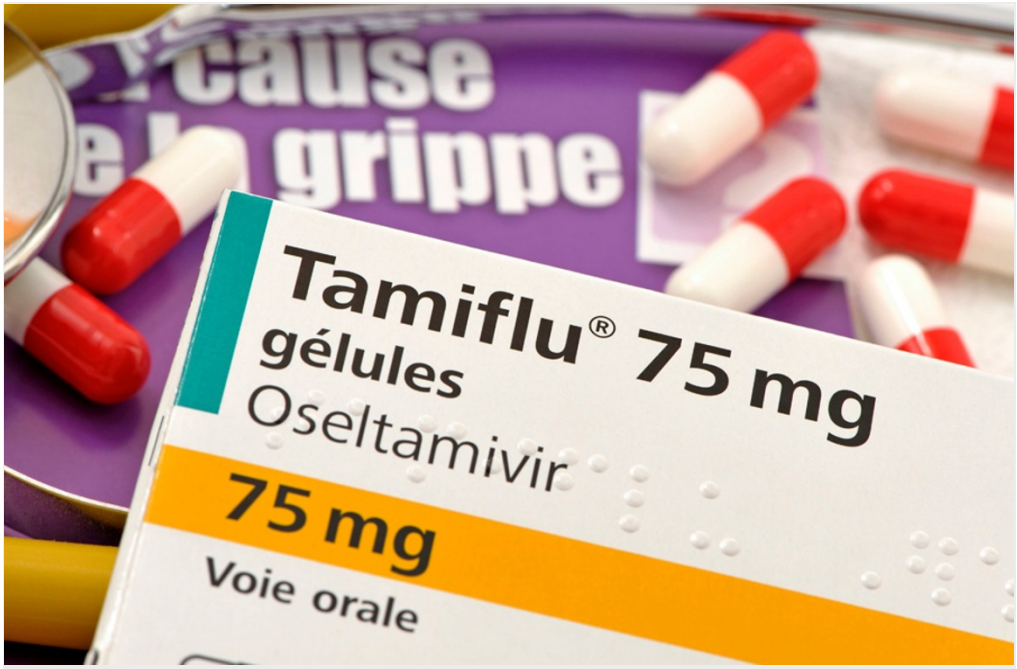


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Tamiflu has been approved as an influenza drug, but some doubt its effectiveness.

Governments around the world have between them spent billions of dollars stockpiling the drug oseltamivir, marketed as Tamiflu, in preparation for unusually severe influenza outbreaks. But scientists have debated — frequently acrimoniously — whether the drug is actually of much use in treating flu. Now, a team of researchers supported by the company that makes Tamiflu has reviewed existing clinical trials of the drug and concluded that it does reduce the duration of the illness and the need for hospitalization[1]. So the row is starting again.

**So why is this such a contentious subject?**

Whether Tamiflu is useful has become an issue that is about much more than just the drug's ability to fight flu.

At first, manufacturer Roche, which is headquartered in Basel, Switzerland, refused to allow independent researchers access to all its data on clinical trials of Tamiflu. This made the drug a rallying point for those campaigning for more openness in clinical trials. Some scientists, notably the Cochrane group of medical reviewers and the journal *BMJ*, feel that the pharmaceutical industry has distorted medical research to portray its drugs as more beneficial than they actually are, and that this case is an example of this. Others say that the work from the *BMJ* and the Cochrane group unfairly downplays the drug's real benefits.

**What does the latest study add?**

The research, published in *The Lancet*[1], is based on individual patient data provided by Roche — which provided some funding for the work but was not otherwise involved, according to the authors. It combines data from different trials in a process called meta-analysis, and is, according to a press release from *The Lancet*, the “most thorough analysis” of Tamiflu so far.

Led by epidemiologist Arnold Monto of the University of Michigan in Ann Arbor, the team looked at data from 9 clinical trials, which included 4,328 participants. People given a placebo saw their influenza symptoms pass in a little more than five days on average, whereas those given Tamiflu felt better after four days. The team also found that among those infected with influenza, Tamiflu reduced the risk of ending up in hospital by 63%.

**This result sounds familiar, somehow…**

An analysis from the Cochrane group, published in the *BMJ* last year[2], also aggregated data from multiple trials. That study found that compared with a placebo, Tamiflu reduced the duration of symptoms from 7 days to 6.3 days — or by about 17 hours — on average. But it found no difference in admissions to hospital.

**So Tamiflu is useful?**

Neither published paper makes an explicit recommendation for or against using Tamiflu to treat influenza. Both teams found significant side effects, including nausea and vomiting. The *Lancet* paper concludes that the drug does offer benefits, but it adds that whether these outweigh the side effects is something to be "carefully considered".

Media reports have sometimes characterized the *BMJ* study as showing the drug to be useless, and study co-author Carl Heneghan, director of the Centre for Evidence-Based Medicine at the University of Oxford, UK, said last year that money spent on stockpiles had been "thrown down the drain". The study itself said only that the results "provide reason to question the stockpiling of oseltamivir … and its use in clinical practice as an anti-influenza drug".

**Is the latest study really independent?**

That depends on whom you believe. Tom Jefferson, a reviewer with the Cochrane group and a co-author of the *BMJ* meta-analysis, says that the *Lancet* study should be viewed in the light of the fact that it was funded by Roche and that some of the authors have links to the pharmaceutical industry. Two of the four authors have accepted money from Roche separately from the study, and one of these also serves on the board of pharma company Gilead Sciences, based in Foster City, California, which invented Tamiflu and licensed it to Roche.

"These authors are not neutral," says Jefferson.

Stuart Pocock, a medical statistician at the London School of Hygiene and Tropical Medicine and one of the authors of the *Lancet* paper, disagrees. He stresses that Roche had no involvement in the study design, and that although his co-authors may have links to the company, their experience is crucial for good science. "One needs co-authors who really know about influenza," he says. "There's a great danger independence becomes ignorance if you push it too far."

**Where do we go from here?**

Jefferson says that the *Lancet* paper adds nothing new to the science on Tamiflu. "What they say there has been said before," he says. Pocock counters that the study is the first to use the "totality of data" from trials, so it should "greatly defuse any uncertainty" about the risks and benefits of the drug. Now it is up to policy-makers and health economists to decide how this evidence should be turned into policy, he says.

Pocock adds, "There tends to be an antagonistic arrangement that can occur between, on the one hand, defensive companies wanting to promote their drugs and, on the other, extreme activists who wish to claim that anything a company finds is nonsense. In reality, objective evidence lies between those two extremes."

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## References

1. Dobson, J., Whitley, R. J., Pocock, S. & Monto, A. S. *Lancet* http://dx.doi.org/10.1016/S0140-6736(14)62449-1 (2015).
2. Jefferson, T. *et al*. *Br. Med. J.* **348**, g2545 (2014).