

New research assesses use of Tamiflu, Relenza to prevent flu

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Two common anti-influenza drugs — Relenza and Tamiflu — appear equally effective at preventing common flu symptoms when given before infection, say researchers from the Stanford University School of Medicine. However, data is lacking on the effectiveness and safety of the two drugs in vulnerable groups such as the very young and people with compromised immune systems.

The researchers pooled and analyzed the data from seven previously published studies because countries around the world are stockpiling these and other drugs for possible use in the current H1N1 pandemic, as well as for future influenza pandemics. Their results will be published in the *Annals of Internal Medicine* on Aug. 4.

Together, the studies, published between 1999 and 2007, indicated that individuals treated with either of the drugs were less likely to develop symptomatic influenza (that is, to both test positive for influenza infection in laboratory tests and to experience [flu symptoms](#) like fever, headache, muscle aches and coughing) than did those who had received the placebo. Those who received the drugs were, however, no less likely to become infected. The two drugs are best known for their ability to reduce or shorten flu symptoms in already-infected individuals.

Three of the studies investigated the effectiveness or safety of zanamivir, marketed by [GlaxoSmithKline](#) as [Relenza](#). The four others explored the effectiveness and safety of oseltamivir, marketed by Roche Pharmaceuticals as [Tamiflu](#). None of the studies compared the two drugs

with each other, and all of the studies were funded by pharmaceutical manufacturers. Six of the seven studies included authors that had served as paid consultants of the sponsoring pharmaceutical company.

"These are still high-quality studies," said Stanford pulmonologist and critical care specialist Nayer Khazeni, MD, the lead author of the study, "but we always like to see research that is independently funded, and we don't have that in this case."

Khazeni also added: "There's a paucity of data for children and people with weakened immune systems even though they've been identified by the Department of Health and Human Services and other public health agencies as priority groups in an influenza pandemic. We were hoping to find a much broader distribution of participants in the studies."

Khazeni and her collaborators selected from nearly 1,900 studies to perform a meta-analysis, a rigorous statistical methodology that can detect statistically or clinically significant results not apparent in smaller, individual studies. They analyzed the results of seven studies comprising more than 7,000 uninfected people who received either of the two drugs for four or more weeks, looking at not just the studies' results but also at their participants and sponsors. They included only those that were randomized, placebo-controlled and double-blinded.

The researchers estimated that about one case of symptomatic influenza would be prevented for every 25 people who received zanamivir or oseltamivir. Of course, not all of these 25 people would become infected during a normal flu season; the baseline risk for seasonal symptomatic influenza in the seven studies varied between about 6 and 14 percent.

In general, the two drugs appeared to be relatively well-tolerated, although there was an increase in the risk of nausea and vomiting in individuals receiving oseltamivir, which was further increased for those

receiving higher-than-recommended preventive doses of oseltamivir. None of the studies enrolled enough people to detect the extremely rare events, including neurological and psychological disorders, which have been associated with these antiviral drugs in certain ethnic and age groups.

Khazeni outlined some of the limitations of the studies: "Nearly all the participants were Caucasian, with the exception of one study of Japanese adults. Children under 12 years of age were not studied, nor were immune-compromised adults or people who had received the live-attenuated influenza virus vaccine." Live-attenuated vaccine is delivered in the form of an inhaled nasal spray and is increasingly used as an alternative to the more-familiar injected vaccine, especially in children.

Khazeni also noted that although the authors performed a thorough search of studies published in all languages, it is possible that there were studies that did not replicate these findings, but were not published.

Because zanamivir appears to be as effective as oseltamivir in preventing symptoms, it may be useful in combating the increasing number of cases of oseltamivir-resistant influenza observed worldwide. Still, zanamivir is not recommended for people with preexisting lung conditions, as it is inhaled as a powder rather than taken orally.

Although the results suggest that administering the drugs to uninfected people may lessen the chance of symptoms after infection, it is not yet known whether asymptotically infected people are still infectious. Khazeni, together with another group of colleagues, is currently mathematically modeling a hypothetical [influenza pandemic](#) in New York City in which extended-administration of this class of anti-influenza medications, known as neuraminidase inhibitors, is one strategy used to prevent infection.

Source: Stanford University Medical Center ([news](#) : [web](#))

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