

Did seasonal flu vaccination increase the risk of infection with pandemic H1N1 flu?

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In September 2009, news stories reported that researchers in Canada had found an increased risk of pandemic H1N1 (pH1N1) influenza in people who had previously been vaccinated against seasonal influenza. Their research, consisting of four different studies, has now undergone further scientific peer review and is published in the open access journal *PLoS Medicine*.

Did previous vaccination against [seasonal flu](#) increase the risk of getting pH1N1 flu? Based on these studies - conducted by a large network of investigators across Canada led by Principal Investigator Danuta Skowronski of the British Columbia Centre for Disease Control in Vancouver, in collaboration with provincial leads Gaston De Serres in Quebec, Natasha Crowcroft in Ontario and Jim Dickinson in Alberta - the answer remains: "possibly."

In a school outbreak of pH1N1 in spring 2009, people with cough and fever were found to have received prior seasonal [flu vaccination](#) more often than those without. Several public health agencies in Canada therefore undertook four additional studies during the summer of 2009 to investigate further. Taken together, the four studies included approximately 2,700 people with and without pH1N1.

The first of the studies used an ongoing sentinel monitoring system to assess the frequency of prior vaccination with the 2008-09 seasonal vaccine in people with pH1N1 [influenza](#) (cases) compared to people without evidence of infection with an influenza virus (controls). This

study confirmed that the seasonal vaccine provided protection against seasonal influenza, but found it to be associated with an increased risk of approximately 68% for pH1N1 disease.

The further 3 studies (which included additional case-control investigations in Ontario and Quebec, as well as a transmission study in 47 Quebec households where pH1N1 influenza had occurred) similarly found between 1.4-1.5 times increased likelihood of pH1N1 illness in people who had received the seasonal vaccine compared to those who had not. Prior seasonal vaccination was not associated with an increase in hospitalization among those who developed pH1N1 illness.

These studies do not show whether there was a true cause-and-effect relationship between seasonal [flu](#) vaccination and subsequent pH1N1 illness (as might occur if, for example, the seasonal vaccine modified the immune response to pH1N1), or whether the observed association was not a result of vaccination, but was instead due to differences in some unidentified factor(s) among the groups being studied.

If the findings from these studies are real they raise important questions about the biological interactions between pre-existing and novel [pandemic](#) influenza strains. The researchers note, however, that the World Health Organization has recommended that pH1N1 be included in subsequent seasonal vaccine formulations. This will provide direct protection against pH1N1 and thereby obviate any risk that might have been due to the seasonal vaccine in 2009, which did not include pH1N1.

In an accompanying commentary in [PLoS Medicine](#), Lone Simonsen and Cécile Viboud, who were not involved in the studies, write: "Given the uncertainty associated with observational studies, we believe it would be premature to conclude that increased the risk of 2009 pandemic illness, especially in light of six other contemporaneous observational studies in civilian populations that have produced highly conflicting results." They

conclude that "this perplexing experience should teach us how to best react to disparate and conflicting studies and prepare us for the next public health crisis, so that we can better manage future alerts for unexpected risk factors."

More information: * Skowronski DM, De Serres G, Crowcroft NS, Janjua NZ, Boulianne N, et al. (2010) Association between the 2008 Seasonal Influenza Vaccine and Pandemic H1N1 Illness during Spring-Summer 2009: Four Observational Studies from Canada. PLoS Med 7(4): e1000258. [doi:10.1371/journal.pmed.1000258](https://doi.org/10.1371/journal.pmed.1000258)

* Viboud C, Simonsen L (2010) Does Seasonal Influenza Vaccination Increase the Risk of Illness with the 2009 A/H1N1 Pandemic Virus? PLoS Med 7(4): e1000259. [doi:10.1371/journal.pmed.1000259](https://doi.org/10.1371/journal.pmed.1000259)

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