

Why the Intranasal Influenza Vaccine is not Recommended this Season

Each year, as autumn is well underway, seasonal influenza vaccinations become a topic of conversation for everyone in general and for those with children in particular. And with good reason. Depending on the circulating strains of influenza and the native immunity within any given community, the percentage of people in the United States who contract the flu annually can be between 5% and 20%, with an average of more than 200,000 patients hospitalised every year. The number of flu-related deaths can be even more staggering, ranging from as few as 3349 (1986-1987) to as many as 48,614 (2003-2004).

While these numbers vary year to year, and are subject to interpretation, there is little doubt that even at the lowest end of this range, the number is often surprisingly large. For this reason, the Centers for Disease Control and Prevention (CDC) has recommended a seasonal influenza vaccine prior to each season. Sometimes this vaccine matches the circulating strains, sometimes it does not (the

strains are chosen in February for a flu season that begins about 10 months later). The formulations, traditionally a three-virus strain “cocktail,” have recently added a fourth strain to increase the potential virus match of the annual vaccine.

Even when the vaccine content is a match for the circulating strains, the efficacy of the vaccine can fluctuate due to several factors, ranging from the recipient’s metabolism to which type of vaccine is used. Most vaccines are inactivated vaccines, that is, the virus within has been killed or taken apart so that only pieces remain. These pieces stimulate the immune system and potentially yield the desired immunity result.

A notable exception to the inactivated influenza vaccines is FluMist (in the US, Fluenz in Europe), which is different for not only containing live — though weakened — virus in the vaccine, but is also delivered intranasally.



This delivery method was popular with recipients who did not like needles (or pain) and was particularly favoured by paediatric patients.

The intranasal vaccine, a live attenuated *influenza vaccine* (LAIV), was determined to be as effective as injectable influenza vaccines and approved in 2003, but only in patients aged 5-49 years. It was approved later in the age group 2-5 years. The vaccine was popular with the paediatric population and data continued to appear to reflect comparable (or better) efficacy against the circulating strains of influenza as the injected inactivated vaccine.

However, starting three seasons ago, during the 2013-2014 season, there began a noticeable downward trend in vaccine effectiveness for the LAIV. That season's data showed no measurable efficacy against the H1N1 influenza A strain in the paediatric population, whereas the inactivated vaccine had a 60% effectiveness mid-point estimate. This difference was statistically significant against the predominant virus that season, which was the same strain that caused the 2009 pandemic.

These data were echoed the following year against the prevailing virus strain (H3N2), though it was acknowledged that neither the LAIV nor the inactivated vaccine worked particularly well against that virus. However, the inactivated vaccines showed a 15% mid-point vaccine effectiveness estimate while the same data point for the LAIV vaccine was -23%. Neither are great efficacy numbers, but one is markedly worse than the other.

Ultimately, at this year's meeting of the CDC's Advisory Committee on Immunization Practices (ACIP), citing preliminary data regarding the vaccine effectiveness of the vaccines in use during the 2015-2016 season, the committee noted that the downward efficacy trend had continued. The data appeared to show that the LAIV effectiveness in recipients aged 2-17 years was only 3%, while the injected inactivated vaccine had an effectiveness estimate of 63%.

The 3% estimate (with a confidence interval of -49% to 37%) for the LAIV meant that the vaccine imparted no measurable protective benefit. For this reason, the ACIP recommended that the intranasal LAIV not be used for the 2016-2017 influenza season. The committee still maintained its recommendation that everyone aged six months and older receive an inactivated or recombinant influenza injected vaccine.

Two months after the ACIP's recommendation, the CDC made the recommendation official CDC policy. The American Academy of Pediatrics followed suit soon thereafter, noting in its announcement that children who received the LAIV intranasal vaccine were 2.5 times more likely to contract the flu than those children who received an injected vaccine.

This loss of a popular formulation of the seasonal influenza vaccine had the potential to strain the supplies of other injectable vaccines. However, it is believed that the CDC acted soon enough to allow suppliers to increase production of recommended, still quite effective, vaccines. It was also hoped that this early action assisted doctors who had pre-ordered the intranasal vaccine in amending their supplies in order to be able to offer the injectable vaccine.

The CDC has noted that the reasons behind the reduction in efficacy of the LAIV vaccine in children are not understood and that the study data are being reviewed to aid in determining the cause. Current theories suggest that perhaps the virus strains in the vaccine are less effective in stimulating an immune response when administered nasally, or perhaps the target population has developed some resistance to the immunity reaction. Still, these theories are in the early stages of research and run counter to the previous data that had demonstrated improved effectiveness of the LAIV vaccine in children against the H1N1 pandemic strain in prior years relative to the inactivated injection.

As a result, the CDC is working not only with the manufacturer, but also with the US Food and Drug Administration, the US Department of Defense, and other public health organisations to determine the cause. In the meantime, the CDC has stressed that inactivated injectable vaccines have, for whatever reason, remained effective and recommends that everyone over six months of age, even those who dislike needles, get an influenza vaccination for the 2016-2017 season.



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