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# Increasing uptake of live attenuated influenza vaccine among children in the United States, 2008–2014

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## Abstract

The Advisory Committee on Immunization Practices (ACIP) recommends annual influenza vaccination for all persons in the United States aged 6 months. On June 25, 2014, ACIP preferentially recommended live attenuated influenza vaccine (LAIV) for healthy children aged 2–8 years [1]. Little is known about national LAIV uptake. To determine uptake of LAIV relative to inactivated influenza vaccine, we analyzed vaccination records from six immunization information system sentinel sites (approximately 10% of U.S. population). LAIV usage increased over time in all sites. Among children 2–8 years of age vaccinated for influenza, exclusive LAIV usage in the collective sentinel site area increased from 20.1% (2008–09 season) to 38.0% (2013–14). During 2013–14, at least half of vaccinated children received LAIV in Minnesota (50.0%) and North Dakota (55.5%). Increasing LAIV usage suggests formulation acceptability, and this preexisting trend offers a favorable context for implementation of ACIP's preferential recommendation.

## Keywords

Immunization Information Systems; Registries; Vaccine Coverage; Vaccination; Influenza Vaccines; Influenza, Human; Child, preschool

**Conflicts of Interest** 

#### Disclosure

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## Introduction

The Advisory Committee on Immunization Practices (ACIP) recommends annual influenza vaccination for all persons in the United States aged 6 months. Two comparative studies have reported that the nasal spray formulation (live attenuated influenza virus vaccine, or LAIV) confers more protection among children 6 to 71 months of age, compared with the injectable formulation (inactivated influenza vaccine, or IIV) [2, 3]. On June 25, 2014, ACIP recommended that LAIV be used, when immediately available, for healthy children aged 2-8 years (e.g., those without chronic medical conditions conferring higher risk for severe illness and complications due to influenza). Previously, ACIP stated no preference between LAIV and IIV for healthy children aged 2 years. This recommendation is expected to result in increased uptake of LAIV compared with IIV in otherwise healthy children 2-8 year of age, and monitoring the recommendation's impact will require an understanding of prior trends in LAIV usage. LAIV is currently thought to be administered less frequently than IIV, although few studies have quantified uptake of the alternate influenza vaccine formulations. One pediatric practice-based survey indicated that LAIV composed 30% of influenza vaccinations among 2–18 year olds during the 2008–09 influenza season [4]. In order to understand pre-recommendation characteristics of LAIV usage, we used population-based vaccination surveillance data to assess the relative uptake of LAIV among vaccinated children aged 2-8 years in the United States. We additionally assessed LAIV usage among children 9–12 years of age; although the ACIP recommendation did not include this age group, the impact of the recommendation beyond the targeted ages should be monitored. Therefore, we sought to assess preexisting trends in LAIV usage.

## **Methods**

Immunization information systems (IIS) are confidential, population-based systems that consolidate data from vaccine providers [5, 6]. IIS sentinel sites, which meet high data quality standards and are funded by the Centers for Disease Control and Prevention to evaluate vaccine coverage in their populations, are located in Michigan, Minnesota, North Dakota, New York City, Oregon (six contiguous counties containing 56% of the Oregon population), and Wisconsin [7]. This collective area contains approximately 10% of the United States population aged 2–12 years.

IIS sentinel sites queried their respective IIS during April, 2014 to obtain de-identified vaccination records for seasonal influenza vaccine doses given during July 1, 2008 to March 31, 2014 to children born during April 1, 1996 through July 1, 2011. Pandemic influenza vaccines were excluded. IIS sentinel sites transmitted record-level data to CDC for analysis. We defined influenza vaccination periods as July 1 through March 31 of the following year. For each influenza vaccination period, children vaccinated with seasonal influenza vaccine were classified as having received LAIV only, IIV only, or any of the following: at least one dose of recombinant influenza vaccine, at least one dose of an unknown formulation, or at least one dose of more than one formulation. We used SAS<sup>®</sup>, version 9.3 (SAS Institute, Inc.) and Microsoft<sup>®</sup> Excel<sup>®</sup> 2010 (Microsoft Corp.) to calculate vaccination coverage using 2013 Census denominators and percentages of vaccinated children who received LAIV, IIV, or both (the latter includes children who received unknown formulations) during each

influenza vaccination period. Aggregate measures describe pooled sentinel site vaccination records.

## Results

Seasonal influenza vaccinations were reported for each influenza vaccination periodduring 2008–09 through 2013–14 for a mean of 1,179,788 children aged 2–12 years (range: 885,485–1,347,162) per vaccination period. During this period, overall coverage of 1 dose of influenza vaccine increased from 29.2% to 39.9% among children 2–8 years of age (Figure 1A). During the same period, coverage among children 9–12 years of age was lower, and increased from 18.2% to 33.3%.

Among children 2–8 years of age vaccinated for influenza, exclusive use of LAIV increased from 20.1% in the 2008–09 vaccination period to 38.0% during the 2013–14 vaccination period (Figure 1B). During the latter vaccination period, exclusive LAIV use was highest among 5–8 year olds (42.1% of vaccinated children), and lowest among children 2–4 years (32.8%) (data not shown). Upward trends in use of LAIV were observed in all six sentinel sites, although there was substantial variability between sites. North Dakota, Minnesota, Oregon, and Wisconsin had higher LAIV relative uptake (55.5%, 50.0%, 46.1%, and 44.6% of children vaccinated for influenza, respectively) than Michigan and New York City (32.8% and 26.9% of vaccinated children, respectively) during the 2013–14 vaccination period (Figure 2).

## Discussion

This is the first report of population-based, provider-verified data describing the use of LAIV among children in the United States. From 2008 to 2014, the percentage of children 2-8 years of age vaccinated for influenza who received LAIV has nearly doubled (from 20.1% to 38.0%). The increase in proportional use of LAIV was similar among children age 9-12 years, although the percentage of children receiving any influenza vaccine was lower in this older age group. In North Dakota and Minnesota, at least 50% of children 2-8 years of age who received an influenza vaccination during the 2013-14 influenza vaccination period exclusively received LAIV, indicating that for some states, LAIV is no longer the less frequently administered formulation. Documenting uptake of LAIV in the United States is important since this formulation is more effective than IIV among young healthy children [2, 3], and LAIV usage will likely increase as a result of an ACIP preferential recommendation [1]. This report describes increasing use of LAIV prior to the June 25, 2014 recommendation, and thus future studies seeking to measure the impact of the recommendation should consider this preexisting trend. The ACIP position could influence patient or parent preferences for age groups beyond those specified in the recommendation, and thus monitoring use of LAIV in additional age groups is warranted to monitor potential impacts.

IIV remains recommended for healthy children aged 6 months to less than two years, and for certain persons ineligible for LAIV; contraindications and precautions for LAIV include immunosuppression, egg allergy, asthma, pregnancy, and receipt of certain drugs including

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aspirin antiviral medications [1]. IIV should be administered to eligible children who present for care during encounters in which LAIV is unavailable, which could occur for providers that placed IIV orders for the 2014–15 influenza season prior to ACIP's preferential recommendation; ACIP notes that vaccination should not be delayed in such instances. Uptake is thus influenced by programmatic factors, and the American Academy of Pediatrics has described a need for research on the health services components that influence influenza vaccine usage [8]. Purchasing decisions might be affected by price, which is higher for LAIV compared with IIV, although one study found LAIV to be more cost effective when administered to healthy children 24–59 months of age due to greater reduction of illness and associated healthcare costs [9]. Additionally, shelf life, storage requirements, and availability from manufacturers, might influence programmatic choices between formulations, and differences between public influenza vaccination programs could potentially contribute to geographic variability in LAIV uptake. These factors should be investigated in order to optimize coverage and inform policy makers considering preferentially recommending LAIV to young children.

This report demonstrates that overall coverage with 1 dose of influenza vaccine is generally increasing among children 2-12 years of age. For some children, ACIP recommends two doses of influenza vaccine, depending on age, vaccination history, and influenza season, and the proportion of the population that is fully vaccinated for influenza is likely lower than the coverage described in this report. IIS sentinel site data are not necessarily nationally representative, although increasing use of LAIV among all sites suggests a generalized trend. Moreover, a previous analysis examined influenza vaccination records in an area that largely overlapped with the jurisdiction of our analysis, and found that trends in influenza vaccine coverage in the examined area were comparable to national survey data [10]. These provider-verified IIS data allow for timely assessments in selected populations and can identify coverage issues warranting further study or intervention. IIS do not universally collect in-depth demographic data on vaccinated children, and this limitation prevented analysis of predictors of LAIV usage. Exploration of factors that influence relative and absolute uptake of LAIV could be useful to inform influenza vaccination programs and future policy regarding preferential use of vaccine formulations. Our results indicate increasing use of LAIV among younger children in the United States, demonstrating broad acceptability of the formulation. Implementation of ACIP's recommendation is thus supported by a preexisting trend of increasing use of LAIV, and this underlying factor should be considered when evaluating the impact of the ACIP's preferential recommendation for use of LAIV.

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А.



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B.



### Vacinee age, by influenza vaccination period

**Figure 1. Uptake of Influenza Vaccine among children 2–12 years of age (A) and Use of LAIV Compared with IIV among Children Receiving Influenza Vaccine (B)** — **2008–2014** Data obtained from Immunization Information System sentinel sites located in Michigan, Minnesota, North Dakota, New York City, Oregon, and Wisconsin. Collectively, a mean of 1,179,788 children aged 2–12 years were reported as annually vaccinated for influenza. Children who received 1 dose of any influenza vaccine are reported among Census populations for each influenza vaccination period during 2008–14 (A) and the relative use of each formulation among vaccinated children is reported (B).

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Figure 2. Relative Uptake of LAIV among Children Aged 2–8 Years Receiving Influenza Vaccine by Immunization Information System Sentinel Sites — 2008–2014 The percentage of pediatric LAIV recipients was defined as the number of 2–8 year olds who received one or more doses of LAIV without IIV or unknown formulations, among

children who received any influenza vaccine of any formulation.