Meta-analysis of the Efficacy of Live Attenuated Influenza Vaccine in Children 2 Through 17 Years of Age

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Background

- Children are among the most susceptible to influenza infection and are primarily responsible for transmitting the illness to others.[1-6]
- In several countries, live attenuated influenza vaccine (LAIV) is approved for use in eligible children and adolescents 2 years of age and older.
- Multiple randomized controlled clinical trials have evaluated the efficacy of LAIV against culture-confirmed influenza illness compared with placebo or trivalent inactivated influenza vaccine (TIV).[7-16]
- These data have not been collectively analyzed for children 2–17 years of age,[17] the age group for whom LAIV is approved for use.

Objective

- To evaluate the efficacy of LAIV in children 2–17 years of age, using data from all available randomized, controlled clinical trials

Methods

- 8 randomized, controlled trials enrolled children 2–17 years of age **(Table 1)**.[7,9-16]
  - 5 compared LAIV with placebo; 3 compared LAIV with TIV.
- Illnesses caused by drifted influenza B viruses were analyzed as originally classified by the trials and secondarily by classifying all antigenic B variants as dissimilar.
- The meta-analysis was conducted using a fixed-effects model. A log-binomial model was used to calculate LAIV relative risk adjusting for study variation.

Table 1. Trials Comparing LAIV With Placebo or TIV in Children 2–17 Years of Age

Study Location	Time Period	Population	Age Range	Treatment Group (Doses)	Subjects, n
Placebo studies					
AV006[7,9] United States	Year 1: Aug 1996–Apr 1997	Previously unvaccinated children	24–71 mo	LAIV (2) Placebo (2)	717 342
	Year 2: Sep 1997–May 1998		24–83 mo	LAIV (1) Placebo (1)	748 362
D153-P501[12] China, Hong Kong, India, Malaysia, Philippines, Singapore, Taiwan, Thailand	Year 1: Sep 2000–Oct 2001	Previously unvaccinated children	24–35 mo	LAIV (2) Placebo (2)	782 534
	Year 2: Nov 2001–Oct 2002		24–47 mo	LAIV (1) Placebo (1)	771 494
D153-P502[13] Belgium, Finland, Israel, Spain, United Kingdom	Year 1: Oct 2000–May 2001	Previously unvaccinated children attending day care	24–35 mo	LAIV (2) Placebo (2)	490 356
	Year 2: Dec 2001–May 2002		24–47 mo	LAIV (1) Placebo (1)	570 403
D153-P504[10] South Africa, Brazil, Argentina	Year 1: Apr 2001–Nov 2001	Previously unvaccinated children	24–35 mo	LAIV (2) Placebo (2)	344 332
	Year 2: Mar 2002–Nov 2002		24–47 mo	LAIV (1) Placebo (1)	265 276
D153-P513[11] Philippines, Thailand	Feb 2002–Nov 2002	Previously unvaccinated children	24–35 mo	LAIV (2) Placebo (2)	209 182
TIV studies					
D153-P514[14] Belgium, Czech Republic, Finland, Germany, Israel, Italy, Poland, Spain, Switzerland, United Kingdom	Oct 2002–June 2003	Children who had experienced 2 or more practitioner-attended RTIs in the past 12 mo, regardless of previous influenza vaccination	24–71 mo	LAIV (2) TIV (2)	790 819
D153-P515[16] Belgium, Finland, Germany, Greece, Israel, Italy, Netherlands, Norway, Poland, Portugal, Spain, Switzerland, United Kingdom	Oct 2002–May 2003	Children with a diagnosis of asthma, regardless of previous influenza vaccination	6–17 y	LAIV (1) TIV (1)	1109 1102
MI-CP111[15] Belgium, Czech Republic, Finland, Germany, Greece, Hong Kong, Iceland, Israel, Italy, Korea, Lebanon, Spain, Sweden, Taiwan, United Kingdom, United States	Oct 2004–Aug 2005	Children, regardless of previous influenza vaccination	24–59 mo	LAIV (1/2)* TIV (1/2)*	2083 2083

LAIV=live attenuated influenza vaccine; RTI=respiratory tract infection; TIV=trivalent inactivated influenza vaccine.
*2 doses were administered to those previously unvaccinated; 1 dose was administered to those previously vaccinated.

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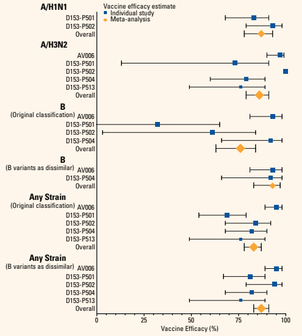
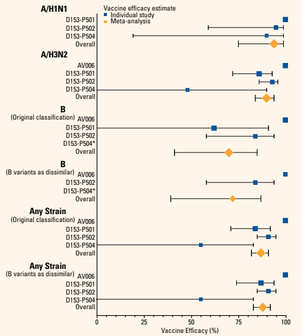
Results

Figure 1. Meta-analyses of vaccine efficacy for LAIV vs placebo (year 1, 2 doses) for antigenically similar subtypes.



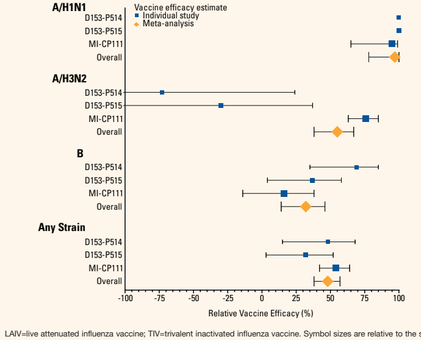
LAIV=live attenuated influenza vaccine. Symbol sizes are relative to the study population sizes.

Figure 2. Meta-analyses of vaccine efficacy for LAIV vs placebo (year 1, 2 doses; year 2, 1 dose) for antigenically similar subtypes.



LAIV=live attenuated influenza vaccine. Symbol sizes are relative to the study population sizes.
*Efficacy could not be estimated because there were no cases among placebo recipients.

Figure 3. Meta-analyses of vaccine relative efficacy for LAIV vs TIV (year 1, 1 and 2 doses) for subtypes regardless of antigenic similarity.



LAIV=live attenuated influenza vaccine; TIV=trivalent inactivated influenza vaccine. Symbol sizes are relative to the study population sizes.

Conclusions

- **This meta-analysis provides precise estimates of LAIV efficacy among children 2–17 years of age, the age group for whom the vaccine is approved for use.**
- **In children 2–17 years of age, LAIV has demonstrated**
  - **High efficacy after 2 doses in year 1**
  - **High efficacy after revaccination in year 2**
  - **Greater efficacy compared with TIV**
- **LAIV efficacy estimates relative to placebo and TIV for only those subjects from the United States were robust and were similar to or higher than those observed overall.**
- **The most common adverse reactions with LAIV in children are runny nose/nasal congestion and fever >100°F.**

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