

Study: 2 Influenza Doses 85% Effective in Children

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WASHINGTON — Two doses of influenza vaccine were up to 55% effective against influenza-like illness and 85% effective against pneumonia or flu in children, Mandy Allison, M.D., said at the National Immunization Conference sponsored by the Centers for Disease Control and Prevention.

The aim of Dr. Allison and her colleagues at Children's Hospital, Denver, and the University of Colorado Health Sciences Center, was to gather more data on the flu vaccine's effectiveness in children, especially since the CDC's Advisory Committee on Immunization Practices advised in 2004 that the shot should be included as a routine immunization for children aged 6-23 months.

Dr. Allison said that one study in the *Journal of the American Medical Association* calculated the vaccine's effectiveness at 66% in any given year, but a recent systematic review published in the *Lancet* found very little data on vaccine efficacy in children under 2 years old (2005;365:773-80).

A study conducted by Kaiser and the CDC found that the flu vaccine was only 25% effective against influenza-like illness, and 49% effective against pneumonia and flu, which is defined as a subset of influenza-like illness (MMWR 2004;53:707-10), she said.

Her group analyzed billing and immunization registry data from 5,913 healthy 6- to 21-month-old children from five Denver area pediatric practices.

ICD-9 codes for office visits between Nov. 1 and Dec. 31 were reviewed to determine the first influenza-like illness; the same nine codes were used in the Denver study as in the Kaiser/CDC study, Dr. Allison said.

Children were dubbed either partially vaccinated—one shot during the current season and 14 days before the first influenza-like illness—or fully vaccinated, which was defined as two shots more than 14 days before the first influenza-like illness.

During Colorado's flu season, which peaked early, 36% of the children were unvaccinated, 24% were partially vaccinated, and 40% were fully vaccinated.

Only 6% were fully vaccinated by Nov. 1, and 36% by Jan. 1, Dr. Allison said.

Twenty-eight percent of children had an influenza-like illness, and 5% pneumonia or flu, during the season.

The researchers also calculated hazard ratios that accounted for age, gender, and immunization status.

They determined that fully vaccinated children were less likely to have influenza-like illness (a ratio of 0.45), when compared with unvaccinated children, which was not surprising.

But partially vaccinated children were more likely to have influenza-like illness, compared with unvaccinated children, Dr. Allison said. She said the researchers weren't sure why one dose seemed to increase the chance of illness, but said there might be something different about those children or families.

She also wasn't certain why the Denver study showed much higher efficacy than the Kaiser/CDC study but noted that it might be that there was a significantly higher vaccination rate in the Denver population.

All the children in the Denver practices came from more affluent socioeconomic groups, which may have made a difference. That also limited the study's conclusions, though, she added. ■

Most Flu-Related ED Visits Are By Patients Aged 5-49 Years

SAN DIEGO — Most emergency department visits for influenza in the United States are by patients aged 5-49 years who have no other diagnoses, results from a large analysis have shown.

The finding underscores the importance of vaccination in this segment of the population, Kimmie Kohlhase McLaurin reported in a poster session at the 100th International Conference of the American Thoracic Society.

"We don't know much about influenza in this age group," said Ms. McLaurin, a research analyst for MedImmune Inc., which manufactures FluMist, the intranasal vaccine that was approved in 2003 for healthy children and adults aged 5-49 years. "We know a lot more in the young and in the old. That's where our focus has been."

In a study funded by MedImmune, Ms. McLaurin and her associate, Shelah Leader, Ph.D., analyzed emergency department data from the 1997-2002 National Hospital Ambulatory Medical Care Surveys to identify visits with a primary diagnosis of influenza based on ICD-9 codes 487.0 (influenza with pneumonia), 487.1 (influenza with other respiratory manifestations), and 487.8 (influenza with other

manifestations). More than 1.1 million ED visits for influenza occurred during the 6-year study period. Of these, 69% were by patients aged 5-49 years.

Nearly three-quarters of ED visits by this age group (71%) had no secondary diagnoses, and visits were highest among 18-22-year-olds, non-whites, and females.

January was noted to be the peak month for visits, followed by February, December, and March.

The most common procedures ordered by clinicians were CBC (35%), chest x-ray (26%), pulse oximetry (19%), and administration of IV fluids (14%).

Most visits (84%) resulted in prescriptions for analgesics (43%), cold/flu remedies (30%), and antibiotics (21%).

Reasons for the visit as reported by the patient were fever/chills (47%), cough (33%), myalgia (20%), throat symptoms (17%), flu (14%), vomiting (14%), and headache (12%).

Ms. McLaurin noted that the estimated direct medical costs of the ED visits during this time period were \$576 million. The estimate was based on 1999 data published by the Medical Expenditure Panel Survey Household Component.

—Doug Brunk

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FDA Approves Another Flu Shot

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► Caregivers and household contacts of children younger than 6 months, or someone who is severely immunocompromised.

This year's supply of influenza vaccine was boosted by the expedited Food and Drug Administration approval last month of Fluarix, a TIV marketed by Glaxo-SmithKline. Fluarix is approved for healthy adults aged 18 years and older.

Approximately 8 million doses of Fluarix will be available for this flu season, Amanda Foley, GlaxoSmithKline spokesperson said in an interview. Shipments to wholesalers began in August, which means that physicians should be able to acquire the vaccine in time for injections at the start of October.

At press time, the CDC anticipated that Sanofi Pasteur Inc. would deliver approximately 60 million doses of its TIV, called Fluzone, and that MedImmune Vaccines Inc. would deliver approximately 3 million doses of FluMist, the live attenuated influenza vaccine (MMWR 2005; 54:850). Another 18-26 million doses of TIV are expected from British-based Chiron Corp.

Chiron's license to produce its Fluvirin TIV was suspended in last year due to contamination problems at the manufacturing plant. Chiron has made progress toward solving their manufacturing problems, but the amount of vaccine the company will provide for the upcoming flu season remains uncertain, and the FDA will continue to evaluate Chiron's activities, according to an FDA statement.

"We are pleased that the Chiron Corporation has taken steps to address issues at their facility in Liverpool as they prepare for the upcoming flu season," Jesse Goodman, M.D., director of FDA's Center for Biologics Evaluation and Research, said in a statement. "FDA will evaluate the implementation and effectiveness of their corrective actions going forward. In addition, any vaccine produced must pass all tests for safety and potency before it can be marketed in the U.S."

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The bulk of the Sanofi Pasteur vaccine will be available for the start of flu season, Raymond A. Strikas, M.D., of the Centers for Disease Control and Prevention, said in an interview.

"We realize that there are challenges every year for companies in terms of vaccine production and distribution," he said, adding that the addition of Fluarix to the vaccine arsenal is "good news."

The FDA's approval of Fluarix was based largely on a phase III clinical trial of approximately 1,000 adults aged 18-64 years. Fluarix was determined to be safe and immunogenic, compared with a placebo in this randomized, double-blind study. The most common adverse event associated with the vaccine was pain at the injection site. Other complications included headaches, muscle aches, and fatigue.

Adverse events were typical of those seen with flu vaccines, John Treanor, M.D., one of the investigators in the study, said in an interview. "Systemic symptoms were no different from a placebo group."

The trial did not evaluate children under age 18 years or adults aged 65 years and older. There was a sense of urgency to collect data that could be used to obtain U.S. licensure in time for this year's flu season, said Dr. Treanor of the infectious diseases unit at the University of Rochester, New York.

"There's a lot of information on the use of the vaccine in the elderly and other populations, it's just not from the United States," he said. The vaccine has been used in Europe since 1992, and studies that meet the European Union vaccine registration requirements have shown safety and efficacy in children, the elderly, and high-risk populations.

The FDA took the strong European data into consideration when it extended the approval to all healthy adults aged 18 years and older, even though the phase III trial in the United States only included adults aged 18-64 years, FDA spokesperson Lenore Gelb said in an interview. ■

For more information about influenza, visit www.cdc.gov/flu. For more information about individual influenza vaccines, visit www.fluarix.com, www.flumist.com, www.chiron.com, www.vaccineshoppe.com (for Fluzone).