Effectiveness of Trivalent Flu Vaccine in Healthy Young Children

**WHAT’S KNOWN ON THIS SUBJECT:** In the United States, given the high burden of disease, influenza vaccine is recommended for all children from age 6 months. The paucity of vaccine effectiveness data in children <2 years has led some to argue against routine vaccination in this age group.

**WHAT THIS STUDY ADDS:** This study reveals the effectiveness of trivalent influenza vaccine in young children and supports the current Advisory Committee on Immunization Practices recommendation. This study provides the strongest evidence to date confirming the effectiveness of trivalent influenza vaccine in children <2 years of age.

**BACKGROUND:** There are few studies evaluating the effectiveness of trivalent influenza vaccination (TIV) in young children, particularly in children <2 years. The Western Australian Influenza Vaccine Effectiveness Study commenced in 2008 to evaluate a program providing TIV to children aged 6 to 59 months.

**METHODS:** An observational study enrolling children with influenza-like illness presenting to a tertiary pediatric hospital was conducted (2008–2012). Vaccination status was determined by parental questionnaire and confirmed via the national immunization register and/or vaccine providers. Respiratory virus polymerase chain reaction and culture were performed on nasopharyngeal samples. The test-negative design was used to estimate vaccine effectiveness (VE) by using 2 control groups: all influenza test-negative subjects and other-virus-detected (OVD) subjects. Adjusted odds ratios were estimated from models (VE) by using 2 control groups: all influenza test-negative subjects and other-virus-detected (OVD) subjects. Adjusted odds ratios were estimated from models (VE) by using 2 control groups: all influenza test-negative subjects and other-virus-detected (OVD) subjects. Adjusted odds ratios were estimated from models (VE) by using 2 control groups: all influenza test-negative subjects and other-virus-detected (OVD) subjects.

**RESULTS:** Of 2001 children enrolled, influenza was identified in 389 (20.4%) children. Another respiratory virus was identified in 1134 (59.6%) children. Overall, 295 of 1903 (15.5%) children were fully vaccinated and 161 of 1903 (8.4%) children were partially vaccinated. Vaccine uptake was significantly lower in 2010–2012 after increased febrile adverse events observed in 2010. Using test-negative controls, VE was 84.7% (95% confidence interval [CI]: 33.7%–81.2%). No difference in VE was observed with OVD controls (85.8%; 95% CI: 32.1%–82.8%). The VE for children <2 years was 85.8% (95% CI: 37.9%–96.7%).

**CONCLUSIONS:** This study reveals the effectiveness of TIV in young children over 4 seasons by using test-negative and OVD controls. TIV was effective in children aged <2 years. Despite demonstrated vaccine effectiveness, uptake of TIV remains suboptimal. *Pediatrics* 2014;133:e1218–e1225

**AUTHORS:** Christopher C. Blyth, MBBS,a,b,c,d Peter Jacoby, MSc,e Paul V. Effer, MD, MPH,f Heath Kelly, MPH,f,g David W. Smith, MBBS,ah Christine Robins,c Gabriela A. Willis, MBBS,c Avram Levy, PhD,i Anthony D. Keil, MBBS,i and Peter C. Richmond, MBBS,a,b,c on behalf of the WAIVE Study Team

aSchool of Paediatrics and Child Health and bSchool of Pathology and Laboratory Medicine, University of Western Australia, Perth, Australia; cPrincess Margaret Hospital for Children, Perth, Australia; dTelethon Institute of Child Health Research, West Perth, Australia; ePathWest Laboratory Medicine, Nedlands, Australia; fCommunicable Disease Control Directorate, Department of Health, Perth, Australia; gVictorian Infectious Diseases Reference Laboratory, Melbourne, Australia; and hAustralian National University, Australian Capital Territory, Australia

**KEY WORDS**

influenza, trivalent influenza vaccine, vaccine effectiveness, children

**ABBREVIATIONS**

ACIP—Advisory Committee on Immunization Practices

CI—confidence interval

ILI—influenza-like illness

LAIV—live-attenuated influenza vaccine

OVD—other virus detected

PCR—polymerase chain reaction

TIV—trivalent influenza vaccine

VE—vaccine effectiveness

Dr Blyth supervised the project, analyzed the data, and wrote the first draft of the manuscript; Mr Jacoby assisted in designing the study, analyzed the data, and assisted with writing the manuscript; Professors Effer, Kelly, Smith, and Richmond designed the study, supervised analysis, and assisted in writing the manuscript; Ms Robins enrolled patients, supervised research assistants, collated and cleaned the data, and assisted with writing the manuscript; Dr Willis assisted in designing the study, collated and cleaned the data, and assisted with writing the manuscript; Dr Levy performed virologic studies, collated and cleaned the data, and assisted with writing the manuscript; and all authors reviewed and approved the final manuscript as submitted.

The data in this article were presented at the Infectious Diseases Society of America Annual Scientific Meeting (IDWeek); October 2013, San Francisco, CA; Abstract 342.

www.pediatrics.org/cgi/doi/10.1542/peds.2013-3707
doi:10.1542/peds.2013-3707

Accepted for publication Feb 4, 2014

(Continued on last page)
Influenza viral infections remain a major contributor to the global burden of acute respiratory infection.1 Young children, the elderly, and others with underlying medical conditions are at greatest risk of hospitalization, morbidity, and death.2–4 Annual influenza vaccination is the most effective method for preventing influenza virus infection and its complications.5

National recommendations for influenza vaccination vary significantly between countries, particularly for young children. Since 2003, the Advisory Committee on Immunization Practices (ACIP) in the United States has recommended influenza vaccination for all children from 6 to 23 months of age.2 From 2008, the ACIP extended its recommendation to include vaccination of all children with either trivalent influenza vaccine (TIV) from 6 months of age or with live-attenuated influenza vaccine (LAIV) from age 2 years.2 Since 2007, Finland has recommended annual TIV in children aged 6 months to 3 years.5 Before 2013, the UK Joint Committee on Vaccination and Immunization recommended influenza vaccination in children aged ≥6 months with underlying medical conditions associated with severe influenza.6 From September 2013, influenza vaccination has been recommended for all children aged 2 to 17 years in the United Kingdom, with LAIV being preferred over TIV; children aged 6 to 23 months with underlying medical conditions are recommended to receive TIV. In Australia, TIV is licensed for all children aged ≥6 months. The Australian Technical Advisory Group on Immunization recommends influenza vaccination for children aged ≥6 months with underlying medical conditions associated with severe influenza.8 LAIV is unavailable in Australia.

There remains ongoing controversy about the role of influenza vaccination in the very young, particularly children <2 years. Because LAIV is licensed for children ≥2 years, TIV remains the only licensed option in this age group. There is a paucity of published data demonstrating effectiveness of TIV in children younger than 2 years, leading some authors to argue against the recommendation for routine TIV in this age group.9–11

After several influenza-related deaths in previously healthy preschool children in 2007,12 the state of Western Australia implemented its own pediatric influenza vaccination program. TIV was recommended and provided free for all children aged 6 months to 5 years. This program was in addition to the national program, which recommended vaccination in children ≥6 months with underlying medical conditions associated with severe influenza. The Western Australian Influenza Vaccine Effectiveness (WAIVE) Study commenced in 2008 to assess influenza vaccine effectiveness (VE) with the use of the test-negative design, with the outcome being medically attended, laboratory-confirmed influenza. VE estimates from the year 2008 have been presented previously.13,14 Influenza-positive cases were compared against 2 different control groups: test-negative and other-virus-detected (OVD) controls. The second analysis was undertaken on the assumption that if any respiratory virus was detected, influenza virus would also have been identified if present (ie, excluding false-negative controls).

We present the estimated VE of TIV in children aged 6 months to 5 years (2008–2012, excluding 2009) calculated from children presenting with an influenza-like illness (ILI) to the major pediatric teaching hospital emergency department in Perth, Western Australia.

METHODS

From 2008 onward, all children in Western Australia aged 6 to 59 months were eligible for free TIV. Children receiving vaccine for the first time were recommended to receive 2 doses at least 1 month apart.8 Princess Margaret Hospital is the sole tertiary pediatric hospital for the state of Western Australia (population 2.4 million people). The hospital manages >70,000 emergency visits per year (~25% of pediatric emergency visits in the state), 15% to 20% of which require hospital admission (M. Borland, MBBS and L. Brennan, BSc, MBA, personal communication). The commencement and cessation of the influenza season in Western Australia were determined by using data on influenza virus detection from community influenza surveillance and routine diagnostic samples; these data were analyzed weekly.15 All children presenting to the Princess Margaret Hospital emergency department during the influenza season (2008–2012) were eligible for enrollment.

All children with an ILI were eligible for enrollment, except for those with a known immunodeficiency disorder, receiving current or who received recent immunosuppressive treatment, or who received immunoglobulin in the previous 3 months.8 ILI was defined by at least 1 acute respiratory symptom or sign plus either a documented fever ≥37.5°C or history of fever in the past 96 hours. After written consent from parents or guardians, clinical data and nasopharyngeal samples were collected by nurses or medical students who had been instructed on correct sampling techniques. Vaccination status was assessed during the parental interview and then confirmed by either the Australian Childhood Immunization Register or by contacting immunization providers. “Fully vaccinated” was defined as (1) 2 doses of TIV at least 21 days apart and at least 14 days before presentation or (2) 1 dose of TIV at least 14 days before presentation and ≥2 doses in a previous year.8

Bilateral midturbinate nasal swabs (Copan Diagnostics, Murrieta, CA) placed into viral transport medium or

PEDIATRICS Volume 133, Number 5, May 2014
nasopharyngeal aspirates were collected for all enrolled children. With the use of previously published methods, nasopharyngeal samples were tested by polymerase chain reaction (PCR) assay for respiratory viruses including influenza A/B/C, respiratory syncytial virus A/B, human metapneumoviruses, human parainfluenza virus types 1 to 4, picornaviruses (including human rhinoviruses and enteroviruses), human adenoviruses B through D, human coronaviruses OC43/229E, and human bocaviruses. Viral culture was performed by using centrifuge-enhanced inoculation onto Madin-Darby canine kidney cells and diploid human lung fibroblasts and confirmed by using immunofluorescent antibody detection with monoclonal antibodies directed at influenza A or B (Oxoid Microbiology; ThermoFisher; Waltham, MA). In addition, hospital inpatients underwent antigen detection by using a standard direct immunofluorescence method (Chemicon; Millipore Corporation, Billerica, MA).

With the use of the test-negative design, children testing positive for influenza viruses (PCR and/or viral culture) were identified as cases. These were compared with 2 different control groups. The first control group included all enrolled children testing negative for influenza viruses (test-negative controls). The second control group comprised enrolled children who tested positive for respiratory viruses other than influenza (OVD controls).

Statistical analysis was performed by using SPSS 20.0.0 (IBM SPSS Statistics, IBM Corporation, Armonk, NY). Differences in categorical variables were tested by χ² test or Fisher’s exact test. With laboratory-confirmed influenza as the primary outcome and vaccine status as the primary exposure, odds ratios and 95% confidence intervals (CIs) were calculated by using logistic regression models. Season, month of disease onset, age, gender, indigenous status, prematurity, and the presence of comorbidities (yes/no) were included as covariates on the basis of their theoretical potential as confounders and/or effect modifiers. VE was calculated as 1-OR. In addition, VE was assessed by year, in specific age groups, and for individual influenza types/subtypes.

Ethical approval for the study was obtained from the ethics committees of Princess Margaret Hospital for Children (1673/EP), the South Metropolitan Area Health Service, and the Western Australian Aboriginal Health Information and Ethics Committee.

RESULTS

A total of 2001 children were recruited for the study between 2008 and 2012, of whom 98 (4.9%) were excluded from the analysis (consent was withdrawn in 38, 50 were older than 59 months, 4 had no respiratory sample obtained, 6 had unknown vaccination status). The numbers of children enrolled each year varied from 169 in 2010 to 643 in 2012 (Table 1). The median age of children enrolled was 1.9 years. The majority of children had no preexisting conditions associated with severe influenza: comorbidities were present in 219 of 1306 (17.5%), with chronic asthma (n = 156), other chronic respiratory disease (n = 22), chronic neurologic disease (n = 20), and heart disease (n = 17) being most common.

Influenza was identified in 389 children (20.4%; influenza A: 14.1%; influenza B: 6.3%; Table 1). Another respiratory virus was identified in 1134 children (59.6%; Fig 1). The most frequently detected noninfluenza viruses were human picornaviruses (n = 673), respiratory syncytial virus A/B (n = 312), human parainfluenza virus types 1 to 4 (n = 193), adenoviruses B through D (n = 157), bocaviruses (n = 126), and coronaviruses OC43/229E (n = 61). Two or more respiratory viruses were detected in 467 children, including 115 children with influenza, and another respiratory virus detected in the same sample.

Vaccine uptake was 24.0% overall (fully vaccinated: 295 of 1903, 15.5%; partially vaccinated: 161 of 1903, 8.5%) and decreased significantly from 2008–2009 to 2010–2012 (127 of 1306, 9.7%; P < .001). Vaccine uptake in children with comorbidities was higher than in children without comorbidities (66 of 219 [30.1%] vs 389 of 1635 [23.8%]; P = .045), yet remained low.

Seventy-five children were identified as having influenza in 2009, of whom 72 were infected with the 2009 pandemic influenza A/H1N1 (2009), 2 with A/H3N2, and 1 with both A/H1N109 and A/H3N2 viruses. Given the significant mismatch between the seasonal influenza vaccine and the 2009 pandemic influenza A/H1N1 strain, all 2009 cases and controls were excluded from VE calculations.

Vaccine Effectiveness

Summary VE was calculated from the remaining 1514 children (Table 2). Unadjusted VE was calculated by season by using both test-negative and OVD controls (Table 3). After adjustment for season, month of disease onset, age, gender, indigenousity, prematurity, and comorbidities, fully vaccinated and unvaccinated children were compared (Table 4).

The overall adjusted VE using test-negative controls was 64.7% (95% CI: 33.7% to 81.2%). No difference in VE was observed when OVD controls were used: VE = 65.8% (95% CI: 32.1% to 82.8%). In children aged <2 years, VE was calculated to be 85.8% (95% CI: 37.9% to 96.7%) for test-negative controls and as 85.5% (95% CI: 34.7% to 96.8%) for OVD controls.

VE was calculated by influenza type/subtype. With the use of test-negative controls, a trend toward greater VE was observed for influenza A compared with
influenza B (overall influenza A: VE = 79.6%; 95% CI: 41.6% to 92.9%; influenza B: VE = 47.8%; 95% CI: −12.4% to 75.8%). When influenza A/H1N1 and influenza A/H3N2 were compared using test-negative controls, VE was 86.5% (95% CI: 4.2% to 98.2%) for A/H1N1 and 74.8% (95% CI: 13.5% to 92.7%) for A/H3N2. Insufficient cases were available to calculate VE against separate influenza B lineages.

When partially vaccinated and unvaccinated children were compared (ie, excluding fully vaccinated children), VE was 81.5% (95% CI: 54.7% to 92.4%) for test-negative controls and 83.8% (95% CI: 58.8% to 93.2%) for OVD controls). Receipt of ≥1 doses of seasonal influenza vaccine was shown in both the younger and older age groups (VE = 78.4% [95% CI: 43.2% to 94.8%] and 78.4% [95% CI: 41.6% to 92.0%] for age <2 years and VE = 69.3% [95% CI: 41.1% to 84.0%] and 73.3% [95% CI:...
VE against non–influenza virus infection was calculated by comparing other virus-positive cases with all virus-negative controls; VE was calculated to be 20.5% (95% CI: 25.6% to 34.3%).

**DISCUSSION**

Studies assessing TIV VE against laboratory-confirmed influenza in older children and adults have frequently revealed a protective effect.9–11 In children <2 years of age, there are fewer studies to guide immunization practice. Only 1 randomized controlled trial has been performed: Hoberman et al estimated TIV VE against laboratory-confirmed influenza in children aged 6 to 23 months with acute otitis media during 2 North American influenza seasons to be 27% (95% CI: 2247% to 67%) and 66% (95% CI: 34% to 84%). A number of prospective observational studies of TIV VE against laboratory-confirmed influenza have been performed: Heinonen et al estimated VE in fully vaccinated Finnish children aged 9 to 23 months enrolled in a single influenza season to be 67% (95% CI: 0 to 89). Of note, the dose of TIV administered in this study was double the dose recommended in other settings.2,8 Eisenberg et al estimated VE in children aged 6 to 23 months presenting to 3 US centers in 2 seasons to vary from 28% (95% CI: –130% to 77%) to 55% (95% CI: 13% to 77%). Shuler et al estimated VE in children aged 6 to 23 months enrolled in a single influenza season to be 52% (95% CI: 20% to 70%). Maeda et al failed to show protection against laboratory-proven influenza in children aged 6 to 24 months over 3 influenza seasons in Japan.

The paucity of published data in this age group has led to suggestions that there are insufficient data to support the routine use of TIV in children aged 2 years.9,10 Despite the paucity of data, given the high burden of influenza infection in this population, many international immunization advisory bodies

---


<table>
<thead>
<tr>
<th>Demographic characteristics and risk factors, n/n (%)</th>
<th>Influenza-Positive Cases (n = 314)</th>
<th>Test-Negative Controls (n = 1200)</th>
<th>OVD Controls (n = 794)</th>
<th>Total (N = 1514)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &lt;2 years</td>
<td>105/314 (33.4)</td>
<td>701/1200 (58.5)</td>
<td>481/794 (60.7)</td>
<td>886/1514 (55.3)</td>
</tr>
<tr>
<td>Male gender</td>
<td>156/311 (50.2)</td>
<td>650/1187 (54.8)</td>
<td>435/785 (55.4)</td>
<td>861/1498 (55.8)</td>
</tr>
<tr>
<td>Indigenous</td>
<td>22/305 (7.2)</td>
<td>51/1185 (4.4)</td>
<td>38/773 (4.9)</td>
<td>71/1470 (5.0)</td>
</tr>
<tr>
<td>Preterm birth</td>
<td>23/305 (7.9)</td>
<td>39/1185 (3.3)</td>
<td>16/769 (2.1)</td>
<td>39/1370 (2.9)</td>
</tr>
<tr>
<td>Any comorbidities</td>
<td>27/303 (8.9)</td>
<td>137/1182 (11.8)</td>
<td>85/769 (11.1)</td>
<td>115/1485 (7.9)</td>
</tr>
<tr>
<td>Asthma</td>
<td>21/303 (6.9)</td>
<td>102/1182 (8.8)</td>
<td>61/769 (7.9)</td>
<td>123/1470 (8.1)</td>
</tr>
<tr>
<td>Other chronic respiratory disease</td>
<td>3/303 (1.0)</td>
<td>15/1182 (1.3)</td>
<td>11/769 (1.4)</td>
<td>19/1370 (1.4)</td>
</tr>
<tr>
<td>Chronic cardiac disease</td>
<td>1/303 (0.3)</td>
<td>12/1182 (1.0)</td>
<td>9/769 (1.2)</td>
<td>13/1370 (1.2)</td>
</tr>
<tr>
<td>Chronic neurologic disease</td>
<td>3/303 (1.0)</td>
<td>11/1182 (0.9)</td>
<td>7/769 (0.9)</td>
<td>14/1370 (0.9)</td>
</tr>
<tr>
<td>Vaccination status, n (%)</td>
<td>Fully vaccinated</td>
<td>14 (4.5)</td>
<td>128 (10.7)</td>
<td>85 (10.7)</td>
</tr>
<tr>
<td>Partially vaccinated</td>
<td>8 (1.9)</td>
<td>84 (7.0)</td>
<td>57 (7.2)</td>
<td>90 (5.9)</td>
</tr>
<tr>
<td>Unvaccinated</td>
<td>294 (93.6)</td>
<td>988 (82.3)</td>
<td>652 (82.1)</td>
<td>1282 (84.7)</td>
</tr>
</tbody>
</table>

NS, not significant.

---

**TABLE 3** VE by Year Against Laboratory-Confirmed Influenza Using Test-Negative and OVD Controls (unadjusted)

<table>
<thead>
<tr>
<th>Season</th>
<th>Number of Cases and Controls</th>
<th>Unadjusted VE, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Fully Vaccinated Cases</td>
<td>Unvaccinated Cases</td>
</tr>
<tr>
<td>Test-negative controls</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2008</td>
<td>9</td>
<td>21</td>
</tr>
<tr>
<td>2010</td>
<td>0</td>
<td>29</td>
</tr>
<tr>
<td>2011</td>
<td>2</td>
<td>57</td>
</tr>
<tr>
<td>2012</td>
<td>3</td>
<td>187</td>
</tr>
<tr>
<td>Total</td>
<td>14</td>
<td>294</td>
</tr>
</tbody>
</table>

---

OVD controls |

<table>
<thead>
<tr>
<th></th>
<th>Fully Vaccinated Cases</th>
<th>Unvaccinated Cases</th>
<th>Fully Vaccinated Controls</th>
<th>Unvaccinated Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>2008</td>
<td>9</td>
<td>21</td>
<td>53</td>
<td>54</td>
</tr>
<tr>
<td>2010</td>
<td>0</td>
<td>29</td>
<td>6</td>
<td>92</td>
</tr>
<tr>
<td>2011</td>
<td>2</td>
<td>57</td>
<td>13</td>
<td>300</td>
</tr>
<tr>
<td>2012</td>
<td>3</td>
<td>187</td>
<td>13</td>
<td>206</td>
</tr>
<tr>
<td>Total</td>
<td>14</td>
<td>294</td>
<td>85</td>
<td>652</td>
</tr>
</tbody>
</table>
recommend influenza vaccine for young children. In the absence of a randomized controlled trial (which may be considered unethical in populations for whom vaccination is already recommended), we are reliant on observational studies that assess outcomes associated with laboratory-confirmed influenza infection. This study reveals the effectiveness of TIV against medically attended, laboratory-proven influenza in Australian children aged 6 months to 5 years over 4 seasons. Of particular importance, this study provides the strongest evidence to date supporting the effectiveness of TIV in children younger than 2 years of age.

The Australian National Immunization Program strongly recommends and provides free influenza vaccine in all children and adults with risk factors for severe disease. In Australia, uptake of influenza vaccination in the elderly (≥65 years) is ~75%. Current uptake of TIV in Australian children with risk factors for severe disease is uncertain: in this cohort, only 30% of those with preexisting risk factors for severe influenza infection had previously received TIV in the year of enrolment. Because Western Australia is the only Australian state with a publicly funded preschool influenza vaccination program, uptake in other states is expected to be even lower. The optimal methods to improve vaccine uptake in children have not been defined and are likely to vary in different jurisdictions. As has been observed in other countries, a recommendation for annual influenza vaccination is likely to improve coverage.

Public and provider confidence in the safety of influenza vaccination is also paramount to the success of any vaccination program. Immunogenicity studies with both pandemic and seasonal vaccines reveal that young children frequently require a second dose of vaccine to achieve protective anti-influenza antibody levels. It is therefore recommended that children <9 years (ACIP, United States; Joint Committee on Vaccination and Immunization, United Kingdom) or ≤9 years (Australian Technical Advisory Group on Immunization, Australia) receive 2 doses of vaccine in the first year they are immunized. In our setting, partial immunization had demonstrable vaccine effectiveness (VE: 81.5%–83.8%). This result needs to be interpreted with caution and requires confirmation in other populations and over multiple influenza seasons.

Our intent in including both the test-negative and OVD control groups was to reduce the number of children having false-negative influenza results due to inadequate specimen collection, storage, and/or transport and to reduce the number whose symptoms were due to noninfectious causes. All viruses were detected by using the same laboratory diagnoses; and inclusion of both test-negative and OVD control groups may reduce the number of control children presenting with an ILI reveals difficulty in interpreting studies calculating VE against ILI. The limitations of the clinical definition of influenza and further highlights the difficulty in interpreting studies calculating VE against ILI.

This study was limited by the significant decrease in vaccine uptake during and after 2010. In 2010, the Western Australian preschool influenza vaccination program was temporarily suspended after a significant increase in the rate of febrile adverse events after immunization.
These adverse events were attributed to 1 manufacturer’s brands of influenza vaccine (Fluax and Fluax Junior; CSL Biotherapies Australia, now bioCSL). In 2010, the administration of Fluax and Fluax Junior was associated with a 44-fold increase in febrile convulsion compared with previous seasons. Despite this dramatic decrease in vaccination, we were able to show significant VE in preschool children by increased recruiting in the latter years of the study.

CONCLUSIONS
Influenza vaccination in children aged <2 years has been a contentious issue due to the paucity of data showing VE. Our findings reveal the effectiveness of TIV in healthy young children, including those younger than 2 years of age and support the current ACIP recommendations for young children. Consistent results were shown by using 2 different control groups. The inclusion of influenza vaccine in routine childhood immunization schedules will result in increased vaccine uptake. Ensuring access to a safe TIV is paramount to the successful implementation of a pediatric influenza vaccination program.

ACKNOWLEDGMENTS
The Western Australian Influenza Vaccine Effectiveness (WAIVE) study team includes Dr Christopher Blyth, A/Prof Meredith Borland, Dr Dale Carcione, Prof Paul Effler, Prof Gary Geelhoed, Mr Peter Jacoby, Dr Anthony Keil, Prof Heath Kelly, Dr Alan Leeb, Dr Avram Levy, Dr Katie Lindsay, Dr Hannah Moore, Ms Christine Robins, Prof Peter Richmond, Prof David Smith, Ms Simone Tempone, Simon Williams, and Dr Gabriela Willis.

The authors thank all of the nurses and research assistants of the Vaccine Trials Group who recruited children for this study as well as all of the study participants and their parents. The authors also thank the staff of the Emergency, General Paediatrics, and Microbiology Departments of Princess Margaret Hospital for Children, Perth, Western Australia. The authors thank all of the staff from PathWest Laboratory Medicine, Western Australia, involved in processing and reporting study samples.

REFERENCES

(Continued from first page)
Effectiveness of Trivalent Flu Vaccine in Healthy Young Children

Christopher C. Blyth, Peter Jacoby, Paul V. Effler, Heath Kelly, David W. Smith, Christine Robins, Gabriela A. Willis, Avram Levy, Anthony D. Keil and Peter C. Richmond

*Pediatrics* 2014;133:e1218; originally published online April 21, 2014;
DOI: 10.1542/peds.2013-3707

The online version of this article, along with updated information and services, is located on the World Wide Web at:
/content/133/5/e1218.full.html