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Vaccine Effectiveness of the Southern Hemisphere Trivalent Inactivated Vaccine in Healthy Young Children using Test Negative and Other Virus Detected Controls

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Background:

National recommendations for influenza vaccination vary significantly between countries. There remains ongoing controversy about the role of influenza vaccination in the very young, particularly children <2 years. There is a paucity of published data demonstrating effectiveness of Trivalent Influenza Vaccine (TIV) in children <2 years leading some authors to argue against routine use for healthy children in this age group. The Western Australian Influenza Vaccine Effectiveness study commenced in 2008 to evaluate a program providing TIV to children aged 6-59 months.

Methods:

From 2008 onwards, all children in Western Australia aged six to 59 months were eligible for free TIV. Children presenting to Princess Margaret Hospital with an influenza-like illness (ILI) during the influenza season (2008-2012) were eligible. ILI was defined by acute respiratory symptoms or signs plus either a documented fever ≥37.5°C or history of fever in the past 96 hours. Following parental consent, clinical data and nasopharyngeal samples were collected.

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Bilateral nasal swabs (Copan Diagnostics Inc, Murrieta, CA) placed into viral transport medium or nasopharyngeal aspirates were collected on all enrolled children. Nasopharyngeal samples were tested by polymerase chain reaction (PCR) for influenza A/B/C and other pathogenic respiratory viruses. Vaccination status was assessed during the parental interview and confirmed by either the Australia Childhood Immunisation Register (ACIR) or by contacting immunisation providers. Fully vaccinated was defined as i) two doses of TIV at least 21 days apart and at least 14 days prior to presentation or ii) one dose of TIV at least 14 days prior to presentation and two or more doses in a previous year.

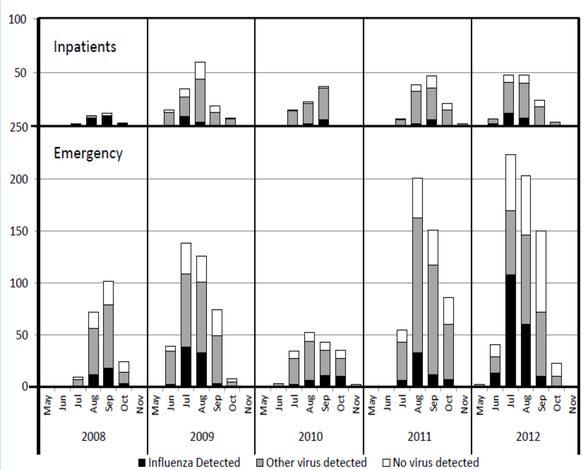
Using the test-negative design, children testing positive for influenza viruses were identified as cases. These were compared with two different control groups. The first control group were all enrolled children testing negative for influenza viruses: test-negative controls. The second control group were enrolled children who tested positive for respiratory viruses other than influenza: other virus detected (OVD) controls. Subjects enrolled in 2009 were excluded from VE calculations. With laboratory-confirmed influenza as the primary outcome and vaccine status as the primary exposure, odds ratios (OR) and 95% confidence intervals (CIs) were calculated using logistic regression models. Season, month of disease onset, age, sex, Indigeneity, prematurity and the presence of comorbidities (yes/no) were included as covariates. Vaccine effectiveness was calculated as 1-OR.

Results:

Of 2408 children enrolled (median: 1.9y), 21.0% required hospital admission. Only 15.3% of children had any comorbidities. Overall, 16.6% children were fully vaccinated and 8.4% partially vaccinated. Influenza was identified in 469 children (influenza A, 13.7%; influenza B: 5.8%). Another respiratory virus was identified in 1493 children (62.0%; Figure 1).

Unadjusted VE were calculated for children recruited through the emergency department (table 1). Following adjustment for covariates, fully vaccinated and unvaccinated children were compared. Using test negative controls, VE for children recruited through the emergency department was 64.7% (95%CI: 33.7, 81.2; table 2). No significant difference in VE was observed with OVD controls (65.8%; 95%CI: 32.1, 82.8). The VE for children < 2 years was 85.8% (95%CI: 37.9-96.7). A trend towards greater VE was observed for influenza A compared with influenza B.

Figure 1



*children with both influenza and other respiratory virus are included in influenza detected only

Table 1	Fully vaccinated		Unvaccinated		Unadjusted VE (95% CI)*
	Cases	Controls	Cases	Controls	
Test –ve controls	14	128	294	988	63.2% (35.2, 79.1)
OVD controls	14	85	294	652	63.5% (34.6, 79.6

Table 2	Vaccine Effectiveness (95% confidence interval)*	
	Test negative controls	Other virus detected controls
All children	64.7% (33.7, 81.2)	65.8% (32.1, 82.8)
Children < 2 years	85.8% (37.9, 96.7)	85.5% (34.7, 96.8)
Children ≥ 2 Years	52.1% (-0.1, 77.1)	55.0% (-3.6, 80.5)
Influenza A	79.6% (41.6, 92.9)	78.3% (34.8, 92.8)
Influenza B	47.8% (-12.4, 75.8)	53.2% (9.4, 79.6)

* VE calculations are for years 2008, 2010-2012

Conclusions:

This study demonstrates the effectiveness of TIV in young children over multiple seasons using both test negative controls and other virus detected controls. TIV was effective in children aged <2 years. Despite demonstrated vaccine effectiveness, uptake of TIV remains suboptimal.

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