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Seasonal influenza vaccine effectiveness against laboratory-confirmed influenza hospitalizations – Latin America, 2013 ☆

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ABSTRACT

Background: Despite widespread utilization of influenza vaccines, effectiveness (VE) has not been routinely measured in Latin America.
Methods: We used a case test-negative control design to estimate trivalent inactivated influenza VE against laboratory-confirmed influenza among hospitalized children aged 6 months-5 years and adults aged ≥60 years which are age-groups targeted for vaccination. We sought persons with severe acute respiratory infections (SARI), hospitalized at 71 sentinel hospitals in Argentina, Brazil, Chile, Colombia, Costa Rica, El Salvador, Honduras, Panama, and Paraguay during January–December 2013. Cases had an influenza virus infection confirmed by real-time reverse transcription PCR (rRT-PCR); controls had a negative rRT-PCR result for influenza viruses. We used a two-stage random effects model to estimate pooled VE per target age-group, adjusting for the month of illness onset, age and preexisting medical conditions.
Results: We identified 2620 SARI patients across sites: 246 influenza cases and 720 influenza-negative controls aged ≤5 years and 448 cases and 1206 controls aged ≥60 years. The most commonly identified subtype among participants (48%) was the influenza A(H1N1)pdm09 virus followed by influenza A (H3N2) (34%) and influenza B (18%) viruses. Among children, the adjusted VE of full vaccination (one dose for previously vaccinated or two if vaccine naïve) against any influenza virus SARI was 47% (95% confidence interval [CI]: 14–71%); VE was 58% (95% CI: 16–79%) against influenza A(H1N1)pdm09, and 65% (95% CI: −9; 89%) against influenza A(H3N2) viruses associated SARI. Crude VE of full vaccination against influenza B viruses associated SARI among children was 3% (95% CI: −150; 63). Among adults aged ≥60 years, adjusted VE against any influenza SARI was 48% (95% CI: 34–60%); VE was 54% (95% CI: 37–69%) against influenza A(H1N1)pdm09, 43% (95% CI: 18–61%) against influenza A(H3N2) and 34% (95% CI: −4; 58%) against B viruses associated SARI.
Conclusion: Influenza vaccine provided moderate protection against severe influenza illness among fully vaccinated young children and older adults, supporting current vaccination strategies.

☆ The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the US Centers for Disease Prevention and Control.

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1. Introduction

There is substantial use of influenza vaccines in the Latin American and the Caribbean (LAC) region as compared to other regions globally. As of 2014, 38 out of 43 LAC countries/territories offered influenza vaccines free of charge through their national expanded programs on immunization (EPI) [1]. The LAC EPIs target individuals at increased risk of exposure to influenza virus such as healthcare workers as well as those at heightened risk of developing secondary complications from influenza infections (e.g., pregnant women, children aged <5 years, older adults and individuals with underlying medical conditions (Table 1)) [1–5].

In South America, influenza virus activity typically peaks between April and September [6,7]. Thus, these countries administer the Southern Hemisphere influenza vaccine, which becomes available during March–April, the beginning of the austral winter. In Central America, situated in the American Tropics, influenza seasonality has been more difficult to define. However, recent epidemiological analyses suggest that epidemics start in May (±two months) when the Southern Hemisphere vaccine is also the most up-to-date formulation available [6,7].

High income countries that annually use influenza vaccines monitor their effectiveness in order to evaluate vaccination programs' investments and guide risk communication messages to the public and health professionals [8–14]. In these countries, the use of the test-negative design (TND) (which compares the odds of vaccination among influenza positive patients and influenza negative "controls") coupled with highly sensitive and specific molecular diagnostic has been established as an efficient evaluation method that minimizes bias due to health-seeking behavior while providing robust estimates [15–19].

Since 2013, the network for influenza VE in LAC denominated as REVELAC-i for its acronym in Spanish (*Red para la Evaluación de Vacunas En Latino América y el Caribe*–influenza) has been estimating influenza VE as an integral component of evaluating influenza prevention in the region [20,21]. We present the results of the REVELAC-i multicenter VE evaluation in nine Latin American countries during the 2013 influenza season.

2. Methods

The populations targeted for government-sponsored influenza vaccination varied among REVELAC-i countries (Table 1). All countries targeted young children but differed in age cut-offs and their focus on preexisting conditions, including the following groups: all children aged 6–59 months (El Salvador and Panama), all aged 6–23 months (Argentina, Brazil, Chile, and Colombia), all aged 6–35 months (Paraguay), children aged 6–35 months with preexisting conditions (Honduras), and those aged 6 months–11 years with preexisting conditions (Costa-Rica). All countries also targeted older adults aged ≥60 years (Brazil, Colombia, El Salvador, Honduras, Panama, and Paraguay) or ≥65 years (Argentina, Chile, and Costa-Rica), regardless of preexisting conditions. For this study, each country contributed children and older adults within their local targeted age ranges which resulted in a combined sample that included children aged 6 months–5 years and older adults aged ≥60 years.

We used a common protocol, as previously described [20–22], to conduct the study at 71 severe acute respiratory infections (SARI) sentinel surveillance hospitals (4 in Argentina, 29 in Brazil, 6 in Chile, 7 in Colombia, 6 in Costa-Rica, 4 in El Salvador, 3 in Honduras, 10 in Panama and 2 in Paraguay) during 2013 (Fig. 1.) Surveillance staff identified SARI patients as persons presenting with fever (i.e., measured temperature ≥38 °C or parental- or self-reported history of fever), cough, and difficulty breathing who were hospitalized [22] and collected a respiratory specimen, using one or more standard collection methods (i.e., combined mid-turbinate nasal and oropharyngeal swabs, nasopharyngeal aspirates, nasopharyngeal swabs, or pharyngeal washes). Hospitals aimed to collect specimens from all SARI patients in Argentina, Brazil, Chile, Costa-Rica, Honduras and Paraguay and from a convenience sample of five weekly SARI patients in Colombia, El Salvador and Panama. Specimens were tested for influenza through real-time reverse transcription polymerase chain reaction (rRT-PCR) at national reference laboratories, using US-CDC protocols, primers, and probes [23,24].

The study start date for each country was (1) after the start of the country's 2013 national influenza vaccination campaign, (2) after confirmation of the start of local influenza circulation by study leads, and (3) after the identification of the first SARI patient with rRT-PCR confirmed influenza. The study period ended on the last day of local influenza circulation in 2013 as determined by study leads. A case was defined as a SARI patient with rRT-PCR confirmed infection with influenza A or B viruses. A "control" was a SARI patient who tested negative for influenza by rRT-PCR. Argentina, Chile, Honduras, and Panama contributed all their available influenza-negative controls. Due to limitations in resources to review vaccination cards records, Brazil, Colombia, Costa-Rica, El Salvador, and Paraguay randomly selected three influenza-negative controls per case (frequency-matched by children versus adults and by month of illness onset).

We extracted information from the SARI case report forms, including age, sex, date of illness onset, date of respiratory specimen collection, diagnosed preexisting medical conditions, dates of admission and discharge, receipt of antiviral treatment, intensive care unit admission, death, influenza vaccination status and dates in the current and prior seasons, number of doses of influenza vaccine among children. Preexisting conditions common to all SARI case-report forms included diabetes, cardiovascular disease, chronic respiratory diseases (including chronic pulmonary disease), renal diseases, obesity, hepatic diseases, immunosuppression, and immunodeficiency. Reference laboratories for influenza provided information on influenza rRT-PCR results, influenza type/subtype, and positivity for other respiratory viruses (using indirect immunofluorescence assay).

Influenza vaccination status was documented in three ways. The SARI case report form at all study hospitals required staff to document influenza vaccination status (including the number and dates of vaccine doses) by reviewing vaccination cards brought in by patients or family members during hospitalization. For SARI patients without vaccination cards, surveillance staff liaised with EPI local/regional teams to obtain information from local sources of vaccination records, including EPI records. In Chile, Colombia (Bogota), Costa-Rica and Panama where a national electronic immunization registry was available, the national surveillance team retrieved the vaccination status by linking the SARI surveillance database and the vaccination registry through a unique citizen or national identifiers. Patients without documentation through any of these methods were considered unvaccinated. Investigations to document status took place for all patients regardless of self-reported vaccination status.

We calculated the minimum sample size needed to estimate regional, age-group specific VEs. To detect a hypothetical VE of 50% with 80% power, an alpha-type error of 5%, and an estimated vaccine coverage of 30% among the controls, we anticipated needing at least 138 influenza cases and 414 controls per age-group from the region [20]. Assuming that approximately 13% of SARI patients would test positive for influenza in the participating countries [CDC's World Health Organization (WHO) Collaborating Center for Surveillance, Epidemiology and Control of Influenza and National Influenza Centers in participating countries, unpublished

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