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Influenza seasonality goes south in the Yucatan Peninsula: The case for a different influenza vaccine calendar in this Mexican region

Guadalupe Ayora-Talavera [a], Gerardo Montalvo-Zurbia Flores [a], Jesus Gómez-Carballo [a], Refugio González-Losa [a], Laura Conde-Ferraez [a], Marylin Puerto-Solís [a], Irma López-Martínez [b], Alberto Díaz-Quiñonez [b], Gisela Barrera-Badillo [b], Rodolfo Acuna-Soto [c], Alicia A. Livinski [d], Wladimir J. Alonso [e,*]

[a] *Centro de Investigaciones Regionales Dr. Hideyo Noguchi, Universidad Autónoma de Yucatán, Av. Itzaes #490x59, Centro, C. P. 97000 Merida, Yucatan, Mexico*
[b] *Instituto de Diagnóstico y Referencia Epidemiológicos "Dr. Manuel Martínez Báez" (InDRE), Secretaría de Salud, Francisco de P. Miranda 177, Lomas de Plateros, 01480 Álvaro Obregón, Mexico City, Mexico*
[c] *Departamento de Microbiologia y Parasitologia, Facultad de Medicina, Universidad Nacional Autonoma de Mexico, Ciudad Universitaria, Avenida Insurgentes Sur 3000, Del. Coyoacán, C.P. 04510 Ciudad de México, Mexico*
[d] *National Institute of Health Library, Division of Library Services, Office of Research Services, 10 Center Drive, Bethesda, MD 20892, USA*
[e] *Fogarty International Center, National Institutes of Health, 16 Center Drive, Bethesda, MD 20892, USA*

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ABSTRACT

Introduction: While vaccination may be relatively straightforward for regions with a well-defined winter season, the situation is quite different for tropical regions. Influenza activity in tropical regions might be out of phase with the dynamics predicted for their hemispheric group thereby impacting the effectiveness of the immunization campaign.

Objective: To investigate how the climatic diversity of Mexico hinders its existing influenza immunization strategy and to suggest that the hemispheric vaccine recommendations be tailored to the regional level in order to optimize vaccine effectiveness.

Methods: We studied the seasonality of influenza throughout Mexico by modeling virological and mortality data. De-trended time series of each Mexican state were analyzed by Fourier decomposition to describe the amplitude and timing of annual influenza epidemic cycles and to compare with each the timing of the WHO's Northern and Southern Hemispheric vaccination schedule.

Findings: The timings of the primary (major) peaks of both virological and mortality data for most Mexican states are well aligned with the Northern Hemisphere winter (December–February) and vaccine schedule. However, influenza peaks in September in the three states of the Yucatan Peninsula. Influenza-related mortality also peaks in September in Quintana Roo and Yucatan whereas it peaks in May in Campeche. As the current timing of vaccination in Mexico is between October and November, more than half of the annual influenza cases have already occurred in the Yucatan Peninsula states by the time the Northern Hemispheric vaccine is delivered and administered.

Conclusion: The current Northern Hemispheric influenza calendar adopted for Mexico is not optimal for the Yucatan Peninsula states thereby likely reducing the effectiveness of the immunization of the population. We recommend that Mexico tailor its immunization strategy to better reflect its climatologic and epidemiological diversity and adopt the WHO Southern Hemisphere influenza vaccine and schedule for the Yucatan Peninsula.

* Corresponding author.
E-mail addresses: talavera@correo.uady.mx (G. Ayora-Talavera), gerardomontalvozf@gmail.com (G.M.-Z. Flores), jesus.gomez@correo.uady.mx (J. Gómez-Carballo), glosa@correo.uady.mx (R. González-Losa), laura.conde@correo.uady.mx (L. Conde-Ferraez), psolis@correo.uady.mx (M. Puerto-Solís), irma.lopez@salud.gob.mx (I. López-Martínez), alberto.diaz@salud.gob.mx (A. Díaz-Quiñonez), gisela.barrera20@yahoo.com.mx (G. Barrera-Badillo), acunasoto.rodolfo@gmail.com (R. Acuna-Soto), alicia.livinski@nih.gov (A.A. Livinski), wladimir.j.alonso@gmail.com (W.J. Alonso).

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1. Introduction

In order to produce influenza vaccines with the composition that best reflects the most up-to-date circulating strains, the WHO established the Global Influenza Surveillance and Response System (GISRS) to provide data to experts of the WHO Global Influenza Program (GIP) who meet twice a year to generate the composition for the next influenza season for each hemisphere. Virus strains circulating in the Northern Hemisphere are reviewed in February and the vaccine is distributed between September and October. Likewise, the viruses circulating in the Southern Hemisphere are reviewed in September and vaccination usually takes place between April and May [1]. The current six-month delay between the WHO decision on composition and the actual availability of the vaccine is mostly due to limitations of the current technology used for the vaccine manufacturing process. These limitations represent a severe challenge to vaccine efficacy, given the frequent obsoleteness of the strains present in the composition by the time the population is vaccinated [2,3,4].

While vaccination may be relatively straightforward for regions with a well-defined winter season, the situation is quite different for tropical regions. Influenza activity in tropical regions is frequently out of phase with the dynamics predicted for their hemispheric group [2,3,5,6,7,8,9] and the optimal timing for routine influenza vaccination does not correspond to the one expected for their hemisphere. A number of studies have illustrated this issue, including in South and Central America [2,5,9,10], Southern and South-Eastern Asia [7], China [8], and Africa [11,12,13]. In these tropical regions, multiple peaks and year-round influenza activity make deciding on the optimal timing of vaccination particularly difficult [3].

Mexico is a very diverse country, located above the Equator between 32°43′N and 14°32′S to 118°27W and 86°42E. This vast geographic expanse includes a variety of climate conditions from temperate (central Mexico) to arid (northern Mexico) to tropical (Gulf coast, Pacific coast, and Yucatan Peninsula). In particular, the Yucatan Peninsula which is situated in southeastern Mexico is characterized by a tropical climate with summer rains.

The influenza vaccination program in Mexico is based on the WHO's Northern Hemispheric recommendation and covers a variety of risk groups (e.g., pregnant women, individuals with obesity [Body Mass Index, BMI > 30 kg/m^2], asthma or pulmonary chronic diseases, diabetes mellitus, and HIV positive), children (from 5 months to 6 years old), and those aged 60 years and older [14]. Results from cross-sectional analysis of the National Health and Nutrition Survey, ESANUT 2012, estimated among adults 20–59 years old a 56% coverage with influenza vaccine, whereas in children aged <1 year to 6 years, a coverage of 50% for a six vaccine scheme which includes influenza [15,16,17]. Since 2004, the Mexican Ministry of Health (MMH) has included influenza vaccination as a priority, and has used the WHO's Northern Hemisphere influenza vaccine recommendations [18]. The selection of the Northern Hemisphere vaccine with data aggregated at the national level was supported by a global mapping of influenza circulation timing informed by the WHO FluNet dataset [3] and an American tropics-specific study using WHO FluNet and Pan American Health Organization (PAHO) viral datasets [10]. However, like other large countries with heterogeneous geographies which include temperate and tropical regions, vaccination recommendations chosen on the basis of national data may not fully or accurately account for the diversity of influenza patterns [2,5,8,9].

Here we investigate how climatic diversity in Mexico may hinder the current influenza immunization strategy and to provide a recommendation for the Yucatan Peninsula that is regionally tailored in order to optimize vaccine effectiveness.

2. Methods

2.1. Virological data

Virological data from each of the 31 Mexican states and Mexico City were obtained from PAHO and WHO covering 2010–2014. These data are collected from countries throughout the Americas, including from Mexico's National Influenza Centre (InDRE, Mexico City, Mexico). The system compiles influenza laboratory results from respiratory specimens tested through routine clinical practice, outbreak investigations, program evaluations, and surveillance for influenza-like illness and severe acute respiratory infections [19,20].

Influenza diagnosis was performed by real time RT-PCR [21] through the National Influenza Network (SINAVE) by each of the 30 Regional Laboratories. All laboratory results were loaded into the SINAVE platform, and classified as positive to: influenza A, A (H1), A(H1N1pdm09), A(H3), and B based on a real time RT-PCR protocol [22]. The dates used in our analyses were obtained from the data field "date of onset of symptoms".

2.2. Mortality data

Mortality data for 1998–2014 was obtained from the Sistema Nacional de Informacion en Salud (SINAIS) of the Mexican Ministry of Health (MMH) [23]; 1998 was the first year that International Statistical Classification of Diseases and Related Health Problems 10th revision 2015 (ICD-10) was used. This database represents mortality from all death certificates (compulsory in Mexico) issued by judicial authorities or in cases of non-violent deaths, by public and private health services. The data are collected by the Civil Registry and shared with the National Institute of Geography and Statistics (INEGI) for analysis, which then provide a copy to the MMH for epidemiological and policy studies; the data are publicly available [23]. All mortality records coded as Influenza and Pneumonia (i.e., from J09 to J18, except J17: "Pneumonia in diseases classified elsewhere") were extracted for our analyses (see http://apps.who.int/classifications/icd10/browse/2015/en#/J09-J18 for list of codes used). Several studies have demonstrated Pneumonia and Influenza (P&I) deaths to be the most specific endpoint for studying the timing and amplitude of influenza-related mortality, both at the local and national scales [24,25,26].

2.3. Data analyses

Seasonal parameters were extracted from time series analyses in different areas of the country, as published previously [5,27]. The same spatio-temporal analyses were performed independently for both virological and mortality data. Counts of virus positive specimens and deaths were aggregated and organized into a 3-D matrix, containing the following units in each one of the "dimensions" of the matrix:

- Time: monthly aggregated data
- Space: 32 geographic units (the 31 states plus Mexico City)
- Variables: Influenza types for the virological data and ICD-10 codes (J09, J10, J11, J12, J13, J14, J15, J16, J18) for the mortality data.

The 3-D matrices, organized in Excel spreadsheets, were loaded to the free analytical software Epipoi (version 2016) [27] for descriptive statistics and spatio-temporal analyses. The spatio-temporal analyses consisted of comparing the parameters describing influenza seasonality in each state as a function of longitude and latitude. Therefore, each time series was first de-trended with

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