Behavior of influenza seasons in Mexico from 2010 to 2016: Analysis and prospective

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Abstract

The influenza virus spreads rapidly through recurring seasonal outbreaks during the fall and winter. Our country has the Epidemiological Surveillance System for Influenza (SISVEFLU), in operation since 2006, which has records of 558 health units of Influenza. According to the information recorded in it, we can see that the 2010-2016 influenza seasons have a biannual behavior, and that in the 2010-2011, 2012-2013, and 2014-2015 seasons, the predominant viral subtype was A (H3N2), while in the 2011-2012, 2013-2014, and 2015-2016 seasons, the predominant subtype was A (H1N1) pdm09, which was associated with an increased number of influenza cases and deaths. It is expected that the 2016-2017 season will have predominance of subtype A (H3N2) and in 2017-2018 the expected will be subtype A (H1N1) pmd09. During the 2010-2016 seasons, 53.5% of cases of influenza were women; 77% had no history of vaccination, and 36% had one or more comorbidities. As for deaths, 55% was observed in males, 85% had not been vaccinated, and 71.5% had one or more comorbidities.

KEY WORDS: *Flu. H1N1. SISVEFLU. Surveillance. Mortality. Seasons..*

Introduction

The influenza virus spreads rapidly in the entire world through seasonal outbreaks that are annually repeated during fall and winter in temperate regions. In the northern hemisphere, the influenza season start and duration can vary from one year to another, and although regularly it peaks in the months of January and February, it can start at late September or early October and last even up to May. In Mexico, it commonly occurs in the fall and winter months.

Our country has a special epidemiological surveillance procedure for influenza known as *Sistema de Vigilancia Epidemiológica de Influenza* (SISVEFLU), in operation since 2006. Nevertheless, it was only until October 2009 that an informatics platform became available, which would allow for information from the entire country to be concentrated in real time. Throughout their operation, both the platform and its procedures have improved and have been adapted to health services' needs. SISVEFLU is one of the most sensitive and robust systems coordinated by the Directorate General of Epidemiology in charge of the Sub-secretary of Prevention and Health Promotion of the Federal Ministry of Health. Currently, this surveillance system has a base of 558 Influenza-Monitoring Health Units, which by their Spanish acronym are known as USVIs.

According to information registered in SISVEFLU, we can identify that the influenza seasons recorded from 2010 to 2016 have a biannual behavior; i.e., in the 2010-2011, 2012-2013 and 2014-2015 seasons, the predominant viral subtype in the national territory was A (H3N2), whereas in the 2011-2012, 2013-2014 and 2015-2016 seasons, the predominant viral subtype was a (H1N1) pdm09. Similarly, influenza seasons with viral subtype

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A (H1N1) pdm09 predominance are observed to have higher records of influenza confirmed cases and increases in the number of deaths are observed with regard to seasons where there is predominance of the A (H3N2) viral subtype. Based on this behavior, the 2016-2017 season is expected to have influenza A (H3N2) predominance, and for the 2017-2018 season, predominance is expected to be of the A (H1N1) pmd09 viral subtype. If this is so, there would be an elevated number of deaths related to this disease in the second case.

During the 2010 to 2016 influenza seasons, out of all confirmed cases recorded by SISVEFLU, 53.5% corresponded to females, 77% of all cases had no history of influenza prevention vaccination and 36% had one or more comorbidities. With regard to deaths reported for this period, a predominance of the male gender was observed (55% out of them), 85% of total cases had not been vaccinated ore else didn't recall having been vaccinated in the last influenza season, and 71.5% had one or more comorbidities.

Influenza is a contagious respiratory disease caused by influenza viruses; it propagates easily and can spread rapidly in schools, community residences (old people's homes, boarding schools), workplaces and cities. This virus can cause mild or serious disease, and sometimes it can lead to death[1]. Influenza viruses circulate all over the world, can affect anybody at any age and cause outbreaks that in temperate regions peak at winter[2].

Based on the virus types predominantly circulating in the previous season, those that will be included in next season's vaccine are selected. Furthermore, the sensitivity or resistance of circulating viruses to antiviral drugs is determined each year, in order to ensure the prescription of the adequate medication[3]. In the northern hemisphere, the start and duration of the influenza season can vary from one year to another, and although it regularly peaks in January and February, it can start since late September or early October and last even until May. In Mexico, it occurs commonly in fall and winter months[4].

The worldwide rate of influenza attack is 5% to 10% in adults and 20% to 30% in children. The disease is cause of hospitalization and death, especially in high-risk groups (very young children, old people and chronically ill individuals). These annual outbreaks cause about 3 to 5 million cases of serious disease and about 250,000 to 500,000 deaths[5].

In our country, children younger than 1 year, adults older than 60 years, pregnant women and young adults with comorbidities such as diabetes, obesity, heart disease, cancer, asthma or kidney failure have been identified as the population groups at higher risk to experience serious manifestations of this disease. Therefore, these groups, together with healthcare personnel, are the target group for annual vaccination[6].

Historical background

An influenza pandemic usually appears when a new influenza virus subtype or strain develops by antigenic change and spreads over the world. In the 20th century there were three pandemics, and all were caused by an antigenic change in influenza A virus[7].

Between 1918 and 1919, mankind suffered the most lethal pandemic in history: the so-called "Spanish flu", probably caused by a flu virus of animal origin, which evolved in most part of the world in three outbreaks, with the second of them, in 1918 fall, being the most severe[8]. According to most recent estimates, the number of fatal victims would range between 50 and 80 million people, which accounted for 2.5% to 5% of global population at that time. In Spain, 1.5% of the population died, and in the USA, nearly 675,000 people died[9].

Influenza maintained an annual frequency after the 1918 pandemic, but no new and virulent influenza type emerged until 1957. In February of that year, evidence began to be observed of a wave of severe flu making its way in China, which would be known as the 1957-1958 Asian influenza pandemic caused by the A (H2N2) viral subtype. Moreover, just as the pandemic that had emerged barely 10 years prior, the first signs of a new influenza A strain, the A (H3N2) viral subtype, appeared in Asia, which caused the Hong Kong influenza pandemic between 1968 and 1969.

The next significant threat emerging with influenza came again from Asia in 1997, when the A (H5N1) avian influenza virus infected birds and then was transmitted to humans. Several people got sick and died because of this lethal virus. According to the World Health Organization's (WHO) official records, from 2003 to February 2016, a total of 846 influenza A (H5N1) confirmed cases and 449 deaths for this cause are recorded, which renders this ailment reaching a lethality rate in humans of 53.1%[10]. It was until 2009 that a new influenza pandemic was activated by the A (H1N1) pdm09 viral subtype, with the first cases being identified in Mexico.

Basic concepts

There are three types of influenza virus, A, B and C, which belong to the *Orthomixoviridae* and have a RNA

genome. The different influenza virus subtypes have been generated by changes in protein surface antigens, the hemagglutinin (HA) and neuraminidase (NA) proteins[11]. Type A viruses are classified in subtypes according to HA and NA proteins different combinations. Among many subtype A flu viruses, viruses of the A (H1N1) and A (H3N2) subtypes are currently circulating in humans. Cases of C influenza are much less common than influenza A or B cases, and this is why only type A and B viruses are included in the vaccines against seasonal flu[12].

The virus can travel up to one meter distance through saliva droplets expelled when talking, coughing or sneezing, and, when inhaled, deposit an infectious inoculum on the respiratory tract epithelium, or else by contact with contaminated hands or surfaces. The virus survives between 48 and 72 hours on smooth surfaces such as hands, doorknobs and handrails, as well as in porous areas such as disposable tissues and fabrics; therefore, a person can be contaminated by fomites[13]. The influenza virus enters the body through the nose or throat, after which the person will develop symptoms 1 to 4 days later.

Most people recover in 1 or 2 weeks without requiring any treatment. In life extremes (infancy and old age), as well as in people with preexisting conditions (chronic respiratory diseases, diabetes mellitus, kidney or heart conditions), influenza can become a serious threat to life. In these people, the infection can develop serious complications, worsen underlying conditions and even result in pneumonia and death.

Influenza epidemiological surveillance functioning in Mexico

In 1947, the WHO World Flu Surveillance Network (FluNet) was established, and it is currently comprised by 116 national centers against influenza with laboratories in 87 countries and 4 WHO collaborative influenza reference and research centers. FluNet is an international influenza epidemiological tool that detects and publishes serotypes found, which constitutes essential information for this viral disease's follow-up[14].

In Mexico, influenza virus isolates are carried out since 1955 by the Institute of Epidemiological Diagnosis and Reference (inDRE – *Instituto de Diagnóstico y Referencia Epidemiológicos*) and, since 1941, influenza is an ailment subjected to epidemiological surveillance and mandatory and immediate report according to Mexican Official Standard NOM-017-SSA2.2012 for epidemiological surveillance, and is part of the National Epidemiological Surveillance System (SINAVE – *Sistema Nacional de Vigilancia Epidemiológica*)[15]. Since 2000, our country belongs to the FluNet international network, and by 2006, the SISVEFLU had already been generated. However, its operative activation with an informatics platform that would enable real-time concentration of information from the entire country took place in 2009. Throughout its operation, both the platform and this system's processes have been improved and adapted to our country's public health needs.

Since the beginning, influenza surveillance was intended to follow the sentinel surveillance model, where information is not collected in all health units, but in a small set of selected health centers and hospitals, known as USMI. The sentinel surveillance strategy is based on the WHO-recommended model and is similar to the one used by the US Centers for Disease Control and Prevention and by the Public Health Agency of Canada. In Mexico, this system is comprised by primary, secondary and tertiary care USMIs distributed across the 32 states of the country[13].

SISVEFLU's main objective is to opportunely detect influenza suspected or confirmed cases and deaths in order to generalize epidemiological information for the making of decisions that guide control actions and mitigate the damage to the population's health. SISVEFLU actions include all the sector's institutions, with the purpose to have permanent surveillance covering a sample of the Mexican population[16].

For SISVEFLU operative purposes, the operational definitions proposed by the WHO are used and, therefore, screening for suspected cases is carried out by identifying patients meeting the influenza-type disease or serious acute respiratory infection criteria[17]. Currently, the Public Health Laboratories National Network, coordinated by InDRE's Dr. Manuel Martínez Báez, in charge of the Directorate General of Epidemiology, has a network of 37 validated reference laboratories for the processing of samples of influenza suspected cases. Of note, the test conducted to confirm or rule out influenza cases is real-time polymerase chain reaction and, in turn, negative samples are processed again with the purpose to identify other possibilities of etiologic viruses, such as the respiratory syncytial virus, among others.

The purpose of SISVEFLU is to guide prevention and control measures, to opportunely identify circulating influenza virus types and subtypes, to describe risk groups and areas, to carry out an epidemiological data analysis that allows for risk identification and for the corresponding recommendations to be issued in order

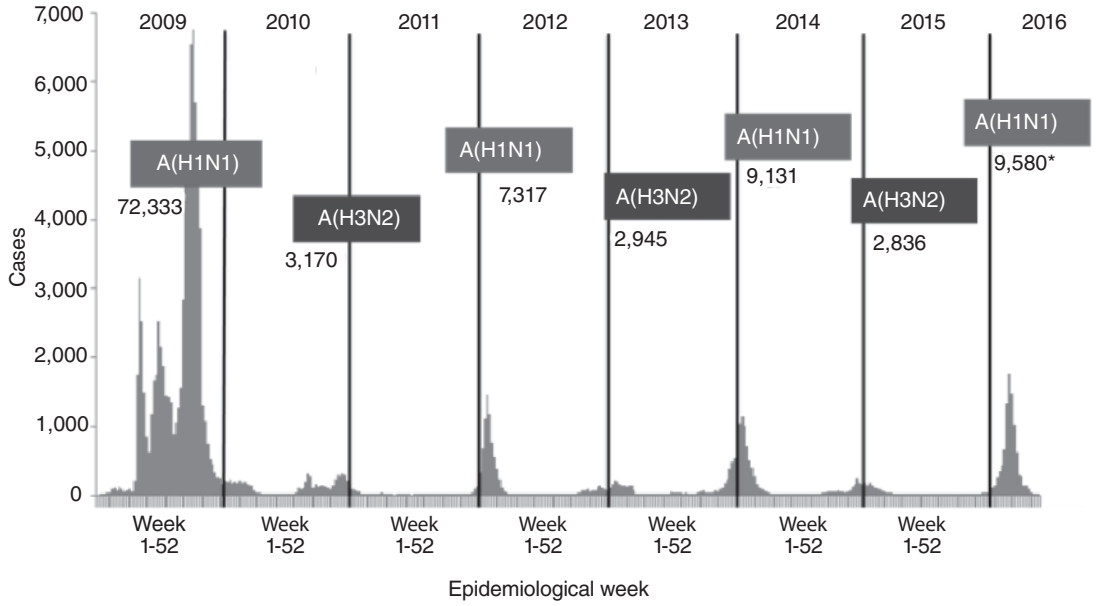

Figure 1. *Confirmed influenza cases, per occurrence week, Mexico, 2009-2016. Note: The number of confirmed cases is indicated for each season. *Preliminary cutoff by May 19, 2016.* (source: SINAVE/DGE/SOSVEFLU/January 2009-May 19, 2016).

for prevention and control measures to be established, to promote the diffusion and use of epidemiological information for decision making, and to put together multidisciplinary and multi-sector groups that enable to permanently assess influenza control measures[18]. The USMIs generate the report of all suspected and confirmed cases detected in their facilities. In addition, SISVEFLU captures all influenza-related deaths recorded in the country, whether occurred in a USMI or not, or through the Mortality Epidemiological Statistical System.

Influenza seasons behavior

According to data concentrated in the SISVEFLU on the 2009 through 2016 influenza seasons, in the 2009 pandemic, the observed behavior was atypical with regard to temporality and affected population groups. However, after the pandemic, a biannual pattern has been identified in the occurrence of predominance of two circulating viral subtypes in the Mexican population and, hence, in the number of cases occurrence and detected lethality. In the 2010-2011, 2012-2013 and 2014-2015 seasons, it has been evident that the predominant viral subtype in the national territory was A (H3N2), whereas in the 2011-2012, 2013-2014 and 2015-2016 seasons, the predominant viral subtype was A (H1N1) pdm09 (Fig. 1).

The number of deaths recorded at different influenza seasons in our country shows a similar behavior pattern than that of the number of cases. It should be noted that, after the pandemic, opportune report and confirmation procedures both of cases and influenza-suspected deaths were improved. Similarly, it should be pointed out that, according to the aforementioned biannual pattern, in the 2011-2012, 2013-2014 and 2015-2016 seasons, since there was predominance of the A (H1N1) pdm09 viral subtype, there was also an increase in the number of deaths (Fig. 2).

The lethality rate observed over the past 6 years shows a biannually-fluctuating behavior, with the lowest point being observed in 2010-201, with a rate of 1.36%, and the highest peak in the 2013-2014 season, with a rate of 12.27% (Table 1 and Fig. 3).

Description of epidemiological surveillance obtained results with regard to cases and deaths occurred in Mexico in the 2010 to 2016 influenza seasons

With regard to confirmed cases between 2010 and 2016, we can appreciate that during the 2011-2012, 2013-2014 and 2015-2016 seasons there was predominance of the A (H1N1) viral subtype, which ranged from 45% to 87% in comparison with other circulating viral subtypes. This is why it is readily identified that the number of cases surpasses those occurred in the 2010-2011, 2012-2013 and 2014-2015 seasons, thus confirming the biannual behavior of this ailment. The main affected group in winter seasons, when there is circulation

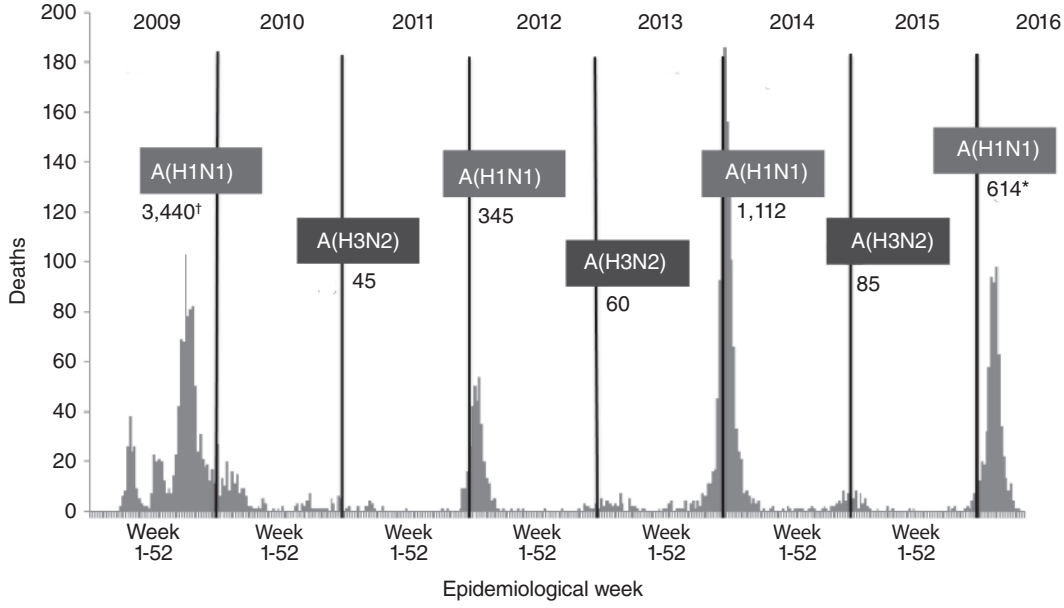

Figure 2. *Influenza-related confirmed deaths, per occurrence week. Mexico, 2009-2016. Note: The number of influenza-related confirmed deaths is indicated for each season. In addition, it should be noted that, as of the 2013-2014 season, all deaths occurring in the country began to be notified to SISVEFLU. Previously, the system only recorded deaths occurring at sentinel units that were part of the SISVEFLU. *Preliminary cutoff by May 19, 2016. †Total number of deaths is comprised by 2,196 that were clinically diagnosed and 1,244 laboratory-confirmed* (source: SINAVE/DGE/SOSVEFLU/January 2009-May 19, 2016).

Table 1. Influenza lethality rate per season, Mexico 2010-2015

Influenza season	Cases	Deaths	Lethality rate
2010-2011	3,160	43	1.36
2011-2012	7,281	344	4.72
2012-2013	2,891	56	1.94
2013-2014	9,051	1,111	12.27
2014-2015	2,785	84	3.02
2015-2016	9,721	537	5.52

Source: SINAVE/SISVEFLU/2010 to 2015 period.

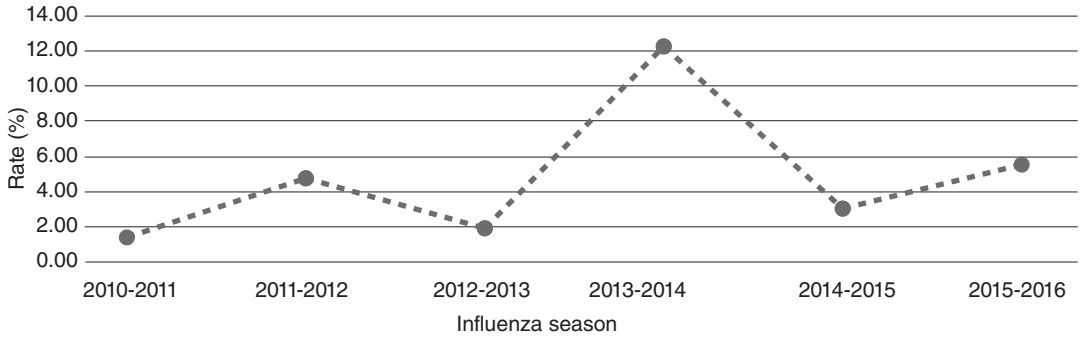

Figure 3. *Lethality rate per season. Mexico, 2010-2015.*

Table 2. Characterization of confirmed influenza cases in Mexico during the 2010-2011 to 2015-2016 seasons

	(Influenza season)*					
Characteristics	**2010-2011**	**2011-2012**	**2012-2013**	**2013-2014**	**2014-2015**	**2015-2016†**
Cases per season	3,170	7,317	2,945	9,131	2,836	9,580
Predominant subtype in deaths						
Cases	AH3N2 (39%)	AH1N1 (87%)	AH3N2 (51%)	AH1N1 (76%)	AH3N2 (39%)	AH1N1 (45%)
Gender	Females (56%)	Females (54%)	Females (53%)	Females (50%)	Females (55%)	Females (53%)
Median age	27	28	28	37	33	35
Age groups (years)	1 to 9 (22%), 30 to 39 (18%) and 20 to 29 (15%)	20 to 29 (22%), 1 to 9 (17%) and 30 to 39 (17%)	1 to 9 (23%), 30 to 39 (16%) and 10 to 14 (14%)	40 to 49 (19%), 30 to 39 (17%) and 50 to 59 (14%)	Older than 60 (20%), 1 to 9 (18%) and 30 to 39 (15%)	1 to 9 (18%), 30 to 39 (16%) and 40 to 49 (16%)
Without vaccine	72%	81%	75%	81%	74%	80%
One or more comorbidities in cases	29%	33%	31%	42%	41%	42%

*Complete seasons from 2010-2011 season to 2014-2015 season.
†2015-2016 data with cutoff at epidemiological week 20_2016.
Source: SINAVE/DGE/Sistema de Vigilancia Epidemiológica de Influenza, downloaded on 5/19/2016.

predominance of the A (H1N1) influenza virus, is the 30 to 39-year old group. On average, 36.3% of this condition confirmed cases had one or more comorbidities, and between 72% and 81% of the population who fell sick had not been vaccinated that year to prevent influenza (Table 2).

With regard to deaths recorded during the influenza seasons from the year 2010 through year 2016, the number of deaths can be observed to be low when there is A (H3N2) viral subtype circulation predominance; however, when in the season there is higher circulation of A (H1N1) influenza virus, a larger number of deaths is observed in the population with one or more comorbidities or that didn't receive the preventive vaccine on that season. It should be noted that during the 2013-2014 season there was higher number of deaths in comparison with other seasons, a phenomenon that was due to A(H1N1) influenza virus predominance, but also due to the fact that, as of that year, influenza-related deaths recorded in the entire country were included in the SISVEFLU operation (previously, only deaths occurring at the USMIs were recorded) (Table 3).

If in this last season, the most affected age groups are arranged by decades, mortality predominance is observed from 40 years of age on (Fig. 4).

Conclusions

Influenza seasons' biannual behavior is clearly observed, and the virologic mosaic of the influenza subtypes present in the Mexican Republic is readily identifiable. Generated evidence enables to predict that in the 2016-2017 season there will be predominance of the A (H3N2) viral subtype and that in the 2017-2018 season, the A (H1N1) pdm09 viral subtype will predominate, which will entail larger numbers of cases and deaths.

The influenza epidemiological surveillance system of Mexico is regarded by the WHO as one of the best systems, since it has real-time reliable data available and two supporting networks: the Epidemiologists National Network and operative team in the public health branch, which belong to the entire Health Sector, and the National Network of Public Health Laboratories, which has the highest quality standards in the country. The information generated day to day in this system supports public health decision-making in our country. However, it is necessary for Health Sector private part to join forces and become part of this national reporting sentinel network, and thereby having a broader perspective on what is going on in private institutions that provide health services.

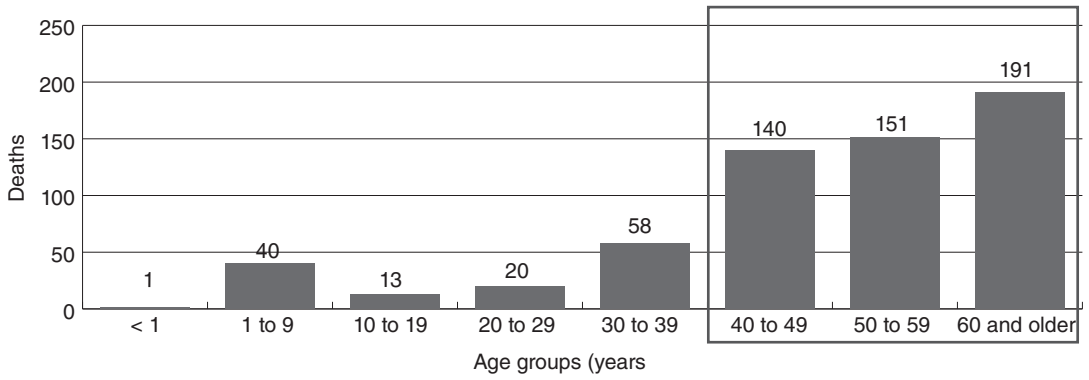

Figure 4. *Deaths by 10-year age groups, Mexico 2015-2016 (source: Dirección General de Epidemiología/SINAVE/SISVEFLU/Temporada Influenza 2015-2016, hasta semana epidemiológica 20_2016).*

Table 2. Characterization of influenza-related deaths in Mexico confirmed to SISVEFLU from the 2010-2011 season to the 2015-2016 season

Influenza season*						
Characteristics	**2010-2011**	**2011-2012**	**2012-2013**	**2013-2014**	**2014-2015**	**2015-2016†**
Season predominant subtype	AH3N2	A(H1N1) pdm09	A(H3N2)	A(H1N1) pdm09	A(H3N2)	A(H1N1)
Deaths per season	45	345	60	1112	85	614
Predominant subtype in deaths	AH1N1 (33%)	AH1N1 (86%)	AH3N2 (45%)	AH1N1 (90%)	AH3N2 (59%)	AH1N1 (77%)
Gender	Males (53%)	Males (63%)	Males (62%)	Males (62%)	Males (58%)	Males (61%)
Median age	54	51	53	49	71	53
Age groups (years)	Older than 60 (42%), 40 to 49 (22%) and 50 to 59 (11%)	Older than 60 (31%), 50 to 59 (21%) and 40 to 49 (17%)	Older than 60 (37%), 50 to 59 (15%) and 1 to 9 (15%)	50 to 59 (25%), 40 to 49 (25%) and older than 60 (24%)	Older than 60 (65%), 50 to 59 (8%) and 30 to 39 (7%)	Older than 60 (31%), 50 to 59 (25%) and 40 to 49 (23%)
Without vaccine	67%	63%	70%	85%	89%	85%
One or more comorbidities in cases	84%	63%	70%	69%	74%	66%

*Influenza season, from week 40 to week 20 next year.
†Data up to week 20.
Source: SINAVE/DGE/Sistema de Vigilancia Epidemiológica de Influenza, downloaded on 5/19/2016.

The biannual behavior of influenza detected with information generated by the SISVEFLU allows for the risks posed by this disease to be identified, as well as for anticipated decisions to be taken for the generation of preventive and promotion actions that enable the mitigation of harm to the Mexican population.

Available information enables to uphold that the Mexican working-age population without vaccination history and with one or more chronic comorbidities is at higher risk to die from influenza. This is why the need to strengthen prevention and health promotion actions has to be highlighted, focusing on vulnerable population, and lay the foundations for people empowerment, with the purpose for citizen participation to join these actions.

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