Vaccination against Influenza

IMPACT AND PREVENTIÓN

Asociación Colombiana de Gerontología y Geriatría

Which vaccines are recommended in the elderly?

Within the recommendations issued by the CDC- ACIP, the vaccines that an adult over the age of 65 must receive this year are as follows: the vaccine against influenza, pneumococcus, Zoster and Tdap, while vaccination against Hepatitis A/B, meningococcus and H.influenzae are recommended in those over the age of 65 with additional risk factors and other indications[1].

Table 1 Recommended Adult Immunization Schedule by Age Group, United States, 2020

Vaccine	19–26 years	27–49 years	50–64 years	≥65 years
Influenza inactivated (IIV) or **Influenza recombinant** (RIV)	1 dose annually or			
Influenza live, attenuated (LAIV)	1 dose annually			
Tetanus, diphtheria, pertussis (Tdap or Td)	1 dose Tdap, then Td or Tdap booster every 10 years			
Measles, mumps, rubella (MMR)	1 or 2 doses depending on indication (if born in 1957 or later)			
Varicella (VAR)	2 doses (if born in 1980 or later)		2 doses	
Zoster recombinant (RZV) *(preferred)*			2 doses or	
Zoster live (ZVL)			1 dose	
Human papillomavirus (HPV)	2 or 3 doses depending on age at initial vaccination or condition	27 through 45 years		
Pneumococcal conjugate (PCV13)	1 dose			65 years and older
Pneumococcal polysaccharide (PPSV23)	1 or 2 doses depending on indication			1 dose
Hepatitis A (HepA)	2 or 3 doses depending on vaccine			
Hepatitis B (HepB)	2 or 3 doses depending on vaccine			
Meningococcal A, C, W, Y (MenACWY)	1 or 2 doses depending on indication, see notes for booster recommendations			
Meningococcal B (MenB)	2 or 3 doses depending on vaccine and indication, see notes for booster recommendations; 19 through 23 years			
***Haemophilus influenzae* type b** (Hib)	1 or 3 doses depending on indication			

Recommended vaccination for adults who meet age requirement, lack documentation of vaccination, or lack evidence of past infection

Recommended vaccination for adults with an additional risk factor or another indication

Recommended vaccination based on shared

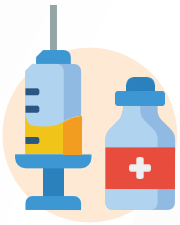
No recommendation/ Not applicable

Influenza – Risk Groups

Regarding influenza, the WHO and the CDC have established that certain groups are more at risk because they are more susceptible to hospitalizations, complications, and death due to the disease. This group includes children under the age of 5 years old, pregnant woman, adults over the age of 60 years of age and patients with chronic diseases.

It is in these groups in which the prevention campaigns of the disease are focused, and in whom vaccination is prioritized. Additionally, the WHO and the have established other groups in which the annual vaccination against influenza must be received, not only because they may be part of the risk groups due to the increase in exposure and infection of the virus, such as healthcare professionals. Furthermore, the following groups need to prevent the disease and avoid infections due to the environment in which they live, such as: People that are residents of old age homes and persons receiving long-term attention; Contacts at home and caregivers to children under the age of 5 years old and adults over the age of 50 years old; as well as contacts at home and caregivers of people with medical conditions that place them at higher risk of severe diseases and complications due to influenza[2].

Effectiveness of the Influenza Vaccines



It has been demonstrated that the influenza vaccine reduces the risk of morbidity and mortality in the elderly. Nevertheless, the effectiveness of the influenza vaccines depends on various factors, such as age and the state of health of the recipient, the types and subtypes of the circulating influenza virus and the degree of similarity between the circulating virus and those included in the vaccine[3]. Despite the estimations of vaccine efficacy (VE) varying between 20-80% depending on the study, vaccination against influenza provides a high level of protection against the disease and its complications[4].

A systematic review by Cochrane estimated that the combined effectiveness against a disease similar to that of influenza was of 41% and a laboratory confirmed efficacy against influenza was of 58%[5]. Another meta-analysis regarding influenza vaccination in adults over 65 years of age found an effectiveness of 35% against the disease similar to influenza, 33% against hospitalizations due to pneumonia and influenza, 47% against pneumonia and mortality due to influenza, and 50% against mortality due to all causes[6]. Other studies have reported that vaccination may be up to 80% effective in the reduction of mortality associated to influenza[7,8]. It must be considered that the effectiveness of the vaccination could vary among the elderly residents of the community compared with those that are institutionalized. A Cochrane review published in 2006 evidenced a difference in the prevention of hospitalizations among the elderly of the community by around 25% versus 45% in the elderly, long-term residents of care centers[9].

A multicenter study that included over 4000 elderly patients found a 60% efficacy in the prevention of disease[10]. An observational study evidenced that during influenza outbreaks in geriatric homes, the elderly residents that were not vaccinated against influenza, not only had higher probabilities of disease than those who were vaccinated (RR 2,6 CI95% 1,8-3.6), but also of being hospitalized (RR: 2.4 CI95% 1.2 -4.8), developing pneumonia (RR: 2.9; CI95% 1.6-5.3), or dying (RR:5.6; CI95% 1.2-9.1). These findings suggest that vaccination against influenza may reduce the incidence and severity of the infections due to the influenza virus among the elderly and those with chronic diseases[11]. Another study performed in geriatric homes in 2003-2004 evidenced how the influenza attack rates in the vaccine group (6.4, 4.6 and 2.4%) were significantly less than when compared with that of the unvaccinated group (V17.7, 13.8 and 10.1%.) over 3 periods of 2 months. It was discovered that the vaccine efficacy to reduce the appearance of influenza varied between 55 and 76% during the six-month follow-up of the study. The elderly adults that received the vaccine had less episodes of fever, cough, muscle pain, nasal secretion ($p < 0.001$) and experienced less disease days due to respiratory diseases[12].

Estimations regarding the seasonal incidence of influenza, the burden associated with severe disease and the effectiveness of the influenza vaccine over six influenza seasons (2010-2011 to 2015-2016) in the United States allowed the estimation that vaccination against influenza has prevented between 1.6 million and 6.7 million cases of the disease, 790,000 - 3.1 million outpatient medical visits, 39,000 - 87,000 hospitalizations and 3,000 - 10,000 deaths due to respiratory and cardiovascular disease related with influenza in each season[13].

The estimations of the vaccination effect against influenza during the 2017-2018 season in the United States found that Vaccine Efficacy (VE) to avoid laboratory confirmed influenza cases that required medical attention was 38% in general (CI 95%, 31% - 43%). Despite this VE, the influenza vaccine substantially reduced the burden of the disease associated with influenza, around 7.1 million diseases (95% Credibility Interval [Crl], 5.4 million - 9.3 million), 3.7 million (95% Crl, 2.8 million - 4.9 million) medical visits, 109,000 (95% Crl, 39,000 - 231, 000) hospitalizations and 8,000 (95% Crl, 1,100 - 21,000) deaths. Vaccination prevented 10% of the generally expected hospitalizations and 41% of the hospitalizations among young children aged 6 months to 4 years of age[14].

All of this data demonstrates the importance of performing vaccination programs focused on people above 65 years of age that also present with associated chronic pathologies, in both those residents of the community and long-term residents in geriatric homes or centers.

Safety of the Influenza Vaccines

The influenza vaccines available in the country are inactivated fractionated vaccines so they do not have the risk of causing influenza disease after vaccination. Their use is thus safe in patients with chronic disease, even in those with respiratory diseases where it has been observed that there is no causing of exacerbation and complications in COPD, and neither do they cause disease such as post-vaccination pneumonia[15].

Regarding the reactions expected after the application of the vaccine, different control studies in the elderly have demonstrated that the most common reaction is a local reaction which corresponds to pain at the injection site, which is mild and short in duration, and does not interfere with the ability to perform daily activities. These studies also demonstrated that the administration of the vaccine is not associated to higher incidences of systemic symptoms (fever, myalgia, headache, and general malaise). During the influenza seasons 2013-14 and 2014-2015, the Vaccine Safety Datalink discovered that there were no higher risks presented in the health of the adults and the elderly after the application of the inactivated influenza vaccine for acute disseminated encephalomyelitis, anaphylaxis, Bell's palsy, SGB, encephalitis and transverse myelitis[16]. There was also no greater risk of venous thromboembolism in adults ≥ 50 years of age[17].

Regarding the inactivated tetravalent influenza vaccines, it was discovered that the most common consults in terms of safety were for pain in the site where the injection was applied and systemic reactions such as myalgia, headache, and fatigue. There was a similar safety profile to that of the inactivated trivalent influenza vaccine. No specific safety concerns were identified[18-21].

Vaccination against Influenza in Times of the COVID-19 Pandemic

We are currently starting the influenza season in the southern hemisphere, which for Colombia means there will be an increase in the circulation of the influenza virus and due to the current pandemic situation that has resulted in quarantine and social distancing, increases the risk of a disruption in routine immunization, as well as a decrease in the demand for immunization, causing an increase in the risk of re-emergence and outbreaks of immuno preventable diseases among the susceptible populations. Therefore, it is essential to decrease the number of cases due to respiratory infections mainly resulting from influenza and pneumococcus via vaccination, in the context of the situation we currently find ourselves in with COVID-19. Clinic and hospital consults which could increase the risk of infection must be avoided, and the collapse of the healthcare system must be prevented by reducing the burden of morbidity[22].

The World Health Organization, the Pan-American Health Organization and the Ministry of Health have established that immunization is a critical health service that must be continued with at all costs during the time of the pandemic. The essential healthcare services such as the fixed immunization services and the surveillance of vaccine preventable diseases must be executed where the capacity of the healthcare system is intact, maintaining the protection measures and social distancing, prioritizing vaccination against influenza, pneumococcus and vaccine series in the at risk population, healthcare workers, the elderly, and pregnant women[23,24].

Can Vaccination against Influenza in the Elderly Increase the Risk of COVID-19 or Infection by SARS-CoV2?

There is no evidence that relates vaccination against influenza as a risk condition to suffering from COVID-19 or being infected by SARS CoV-2. Some authors have studied the viral interference phenomenon associated with the vaccine. The purpose of these studies was to evaluate the possible bias in the effectiveness estimates of the influenza vaccine from the observational studies that use test-negatives. There is today limited evidence that the influenza vaccine in reality could be associated with the interference process of the virus[25,26].

The result of these studies is limited due to the small sample size, as well as due to the reduced number of outcomes that did not allow the construction of solid inferences of the results, in accordance with that indicated by the authors. Further to evaluating only upper respiratory tract infections that in a significant number did not require medical attention compared with influenza and its complications, which could minimize the burden of disease and the secondary impact of the influenza diseases. Other studies have not found any association between vaccination against influenza and the increase in the risk of respiratory virus[25,27]. Even in the studies that found significant differences between the non-influenza virus infections in vaccinated children, the investigators have considered that blaming only

vaccination as a cause would be a biologically implausible explanation and conclude that the control of diseases similar to influenza are appropriate to compare both groups and determine the efficacy of the vaccine[28].

Wolff y cols., in a study performed to evaluate the negative test methodology to evaluate the VE of the influenza vaccine also studied the viral interference in the receptor of the influenza vaccine. No association was discovered between the influenza vaccine and viral interference. Upon studying the viral interference due to specific respiratory viruses, it was observed that there is a significant association with the coronavirus OR 1.36 (CI 95% 1.14 - 1.63) and the human metapneumovirus OR 1.36 (CI 95% 1.14 - 1.63). The authors compared their results with other similar studies and found statistical inconsistencies that included significance and opposite direction associations when comparing children and adults, so they concluded that the results of this study did not support a possible bias in the study of effectiveness of the vaccine based on test-negatives. They highlighted that, in a study design with a test-negative, the selection criteria of the patients must be that they are ill with a disease similar to influenza. Given that the population must be ill, the vaccinated population in fact has more probabilities of having other respiratory viruses in comparison with the unvaccinated population; in turn, it is less likely that they have influenza[29].

Rikin y cols., evaluated acute respiratory disease related with time after vaccination against influenza. The studies demonstrate that the risk of respiratory pathogen agents that are not influenza was higher during the same period (HR 1.65, CI 95% 1.14 - 2.38); when stratified by age, the risk continued being higher in children (HR 1.71, CI 95% 1.16 - 2.53) but not in adults (HR 0.88, CI 95% 0.21 - 3.69) (26). This is a cohort that followed up the cases of respiratory diseases that compared subjects vaccinated against influenza with unvaccinated subjects. As in other studies, the monitoring was only performed in sick patients; as the patients are sick and vaccinated against influenza, the possibility that other respiratory viruses are present could be higher. To the contrary of that which could be concluded, the purpose of this study was to demonstrate that respiratory infections after vaccination is due to other viruses that are not influenza and increase confidence in vaccination.

Influenza Epidemiological Situation United States – Colombia

Acute respiratory influenza infection, which affects to a large extent the elderly, makes up part of one of the reportable epidemiological events. The elderly have a high risk of developing severe influenza complications in comparison with young adults. This is due, in part, to the aging of the immune system and to the high morbidity resulting from pluripathologies that increase the risk of disease, complications and death in this population. Even though the influenza seasons may vary in severity, people aged 65 years of age or older present a major burden of disease due to influenza during a majority of the seasons.

In the United States from 1976 to 2007, the elderly older than 65 years of age represented approximately 90% of all the deaths related with influenza during this period; estimations that were similar to those obtained in Hong Kong. In Singapore, influenza deaths are reported as 11.3 times more likely among individuals older than 65 years of age versus the general population.

In the United Kingdom between 1999 and 2010, it was estimated that 2.5-8.1% of the deaths among individuals ≥75 years of age was due to influenza. It was even established that the risk of death associated with influenza is higher among the elderly older than 85 years of age because they are 16 times more prone to die from diseases associated with influenza than those aged between 65 and 69 years of age[30].

Excess mortality models due to all of the causes used in Portugal and Australia evidenced a considerable increase in mortality in this age group, above that which was estimated via direct laboratory confirmation of the influenza virus (31,32). Nevertheless, the burden of disease is not given only as a result of mortality in this population, but due to the increase in the number of hospitalizations. It is estimated that the hospitalization rates of this population in the United States is between 125-228 hospitalizations/100,000 people without high-risk conditions and around 399-528 hospitalizations/ 100,000 high risk people ≥65 years of age. This reflects an increase of 4-10 times more than the hospitalizations due to influenza among the young adults with or without risk[33,34].

Furthermore, it must be taken into account that the institutionalized elderly run a higher risk of influenza infection due to the occurrence of documented regular outbreaks in the different institutions and long-term care centers throughout the year. The risk of transmission during the year in institutionalized environments must be taken into account in order to guarantee the management and protection of this population [35-37].

Over the past years, it has been estimated that between 70% - 85% of the deaths, and between 50%-70% of the hospitalizations related with seasonal influenza occur among people belonging to this age group in the United States[38]. Over the past two influenza seasons (2018-2019 and 2019-2020) in the United States, the CDC for 2018-2019 reported a general hospitalization rate during this season of 63.6 per 100,000 inhabitants. However, the highest hospitalization rate was presented in the population >65 years of age (212/100,000 inhabitants), followed by the adults aged 50-64 years of age (79.2/100,000 inhabitants), and in third place by children 0-4 years of age (70.9/ 100,000 inhabitants). For the 2019-2020 season, the general hospitalization rate was 68.2 per 100,000 inhabitants, being the highest reported in comparison with all of the recent seasons for this time of the year. Nevertheless, upon consideration thereof according to age group, the highest hospitalization rates were presented in first place by those older than 65 years of age (179.7/100.000 inhabitants), followed by children aged 0-4 years of age (94.1/100.000 inhabitants) and the age group 50-64 years of age (90.2/100.000 inhabitants). Of the adults hospitalized with information regarding their pathologies, 92.3% had at least one associated comorbidity, the most frequently reported were cardiovascular disease, metabolic disorder, obesity and chronic pulmonary disease[39].

In Colombia for 2018, 7,026,693 outpatient and emergency consults due to acute respiratory infection, 247.368 hospitalizations due to severe acute respiratory infection, and 22,748 hospitalizations due to severe acute respiratory infection hospitalizaciones in intensive care units of 262,028 were notified accross the country. According to the NHI, the age groups that were most affected were people between 40 and 59 years of age, and those older than 60 years of age. The intensive care unit hospitalizations due to SARI surpassed the upper historical limit established for the greater part of the year[40]. Of the laboratory identified viruses, 1425 were positive for Influenza, with a predominance mainly of subtype A(H1N1)pdm09 with 1.177 positive cases, followed by subtype A(H3N2) with 120 positive cases and in a lesser proportion by influenza B. Even though we do not have clarity regarding the number of cases by B/Yamagata or B/victoria, it was once again observed in 2018 that that just like in previous years, there was the presence of co-circulation of the two influenza B lines throughout the year in the country[41].

219 deaths related with influenza A(H1N1)pdm09 were confirmed; surpassing the deaths in comparison with the previous years 2014-2019. The age groups in which the greatest number of deaths were reported were, in first place, the group of 40 to 59 years of age with 40,6 % followed by the people of 60 years of age and up, with 23,3%. Of the people who died, 65.8% had at least one risk factor; these characteristics pertaining to the population 40-59 and 60 years of age and older. The risk factor with the highest proportion was Age Group (under 2 years of age and older than 60 years of age) with 34,7 %, followed by Diabetes with 18,8 % and Obesity with 15,3 %, Cardiovascular Antecedents, and Immunosuppression among others were also reported. By taking into account all of the respiratory viruses identified in the population, it was observed how RSV predominates in those under the age of one year old, while in those older than 5 years of age, the influenza A(H1N1)pdm09 virus represents the highest proportion in the patient deaths and those hospitalized in the ICU[40].

During 2019, 6.706.324 emergency and outpatient consults due to acute respiratory infection occurred in Colombia, 223.424 hospitalizations in the general ward and 21.444 hospitalizations in the ICU. These last two events registered mainly in those under 1 year of age and those older than 60 years of age. Regarding the uncommon severe acute respiratory infection, the cases in those under one year of age were predominantly due to RSV, while as of one year and on, the compromise was mainly due to the influenza virus AH1N1 in first place, followed by AH3N2 and influenza B, mainly in the age groups of 40-59 years of age and those older than 60 years of age[42]. In accordance with the last event reports corresponding to the epidemiological period IV, 1.729.342 emergency room and outpatient consults due to acute respiratory infection, 54.859 general ward hospitalizations and 6.250 ICU hospitalizations, have been reported. These two events registered mainly in those under 1 year of age and those older than 60 years of age. An increase has been reported of uncommon severe acute respiratory infection associated with the current context of the COVID-19 pandemic[43].

Conclusions:

- According to the WHO and the CDC, the elderly aged 60 years old have a greater risk of hospitalizations, complications and death due to influenza; therefore this group must be vaccinated every year as a priority.
- The influenza vaccine is indicated annually by different international organizations for all healthy people or people with associated chronic diseases, older than 60 years of age.
- The influenza vaccine does not cause influenza disease nor secondary respiratory cases such as as pneumonia.
- The influenza vaccine is effective, safe and it is highly indicated in the captive population such as geriatric, long-term attention centers, clubs for the elderly, among others.
- It has been demonstrated that the influenza vaccines reduce the risk of morbidity and mortality in the elderly.

References

1. Esquema de inmunización recomendado para adultos. CDC. https://www.cdc.gov/vaccines/schedules/downloads/adult/adult-combined-schedule.pdf [Consultado 24 mayo 2020]
2. Who Should and Who Should NOT get a Flu Vaccine. Influenza (Flu). Centers for disease control and prevention CDC. https://www.cdc.gov/flu/prevent/whoshouldvax.htm [consultado 7 mayo 2020]
3. Datos clave de la vacuna contra la influenza estacional. Influenza (gripe) CDC. https://espanol.cdc.gov/flu/prevent/keyfacts.htm [Consultado 6 mayo 2020]
4. Groskopf L. , Influenza Update. CDC. Current Issues in Immunization Webinar. 10-2-19)
5. Jefferson, T., et al., Vaccines for preventing influenza in the elderly. Cochrane Database of Systematic Reviews, 2010:CD004876
6. Vu, T., et al., A meta-analysis of effectiveness of influenza vaccine in persons aged 65 years and over living in the community. Vaccine, 2002. 20:1831-6
7. Govaert, T.M., et al., The efficacy of influenza vaccination in elderly individuals. A randomized double-blind placebo-controlled trial. The Journal of the American Medical Association, 1994. 272:1661-5
8. Kelly, H. and A.T. Newall, Mortality benefits of influenza vaccination in elderly people. The Lancet Infectious Diseases, 2008. 8:462-3; author reply 463-5.
9. Rivetti, D., et al., Vaccines for preventing influenza in the elderly. Cochrane Database of Systematic Reviews, 2006. 3:CD004876
10. Kissling, E., et al., I-MOVE Multi-Centre Case Control Study 2010-11: Overall and Stratified Estimates of Influenza Vaccine Effectiveness in Europe. PloS One, 2011. 6:e27622
11. Patriarca, P.A., et al., Efficacy of influenza vaccine in nursing homes. Reduction in illness and complications during an influenza A (H3N2) epidemic. The Journal of the American Medical Association, 1985. 253:1136-9
12. Isahak, I., A.A. Mahayiddin, and R. Ismail, Effectiveness of influenza vaccination in prevention of influenza-like illness among inhabitants of old folk homes. The Southeast Asian Journal of Tropical Medicine and Public Health, 2007. 38:841-8.
13. Rolfes MA et al. Annual estimates of the burden of seasonal influenza in the United States: A tool for strengthening influenza surveillance and preparedness. Influenza Other Respir Viruses. 2018 Jan;12(1):132-137. doi: 10.1111/irv.12486. Epub 2018 Feb 14.
14. Rolfes M Et al. Effects of Influenza Vaccination in the United States During the 2017-2018 Influenza Season. Clin Infect Dis. 2019 Nov 13;69(11):1845-1853. doi: 10.1093/cid/ciz075
15. Montserrat- Capdevilla J et al. Efectividad de la vacunación antigripal para evitar el ingreso hospitalario por agudización de la enfermedad pulmonar obstructiva crónica. Enferm Infecc Microbiol Clin. 2014;32(2):70–75. http://dx.doi.org/10.1016/j.eimc.2013.02.009.
16. Li R, Stewart B, McNeil MM, Duffy J, Nelson J, Kawai AT, et al. Post licensure surveillance of influenza vaccines in the Vaccine Safety Datalink in the 2013-2014 and 2014-2015 seasons. Pharmacoepidemiol Drug Saf. 2016 Aug;25(8):928-34.
17. Vickers ER, McClure DL, Naleway AL, Jacobsen SJ, Klein NP, Glanz JM, et al. Risk of venous thromboembolism following influenza vaccination in adults aged 50years and older in the Vaccine Safety Datalink. Vaccine. 2017 Oct 13;35(43):5872-7.
18. Beran J, Peeters M, Dewe W, Raupachova J, Hobzova L, Devaster JM. Immunogenicity and safety of quadrivalent versus trivalent inactivated influenza vaccine: a randomized, controlled trial in adults. BMC Infect Dis. 2013 May 20;13:224.
19. Kieninger D, Sheldon E, Lin WY, Yu CJ, Bayas JM, Gabor JJ, et al. Immunogenicity, reactogenicity and safety of an inactivated quadrivalent influenza vaccine candidate versus inactivated trivalent influenza vaccine: a phase III, randomized trial in adults aged >/=18 years. BMC Infect Dis. 2013 Jul 24;13:343
20. Greenberg D et al. Safety and immunogenicity of a quadrivalent influenza vaccine in adults 65 y of age and older. HUMAN VACCINES & IMMUNOTHERAPEUTICS. 2017, VOL. 13, NO. 9, 2058–2064. https://doi.org/10.1080/21645515.2017.1344375
21. Pepin S, Donazzolo Y, Jambrecina A, Salamand C, Saville M. Safety and immunogenicity of a quadrivalent inactivated influenza vaccine in adults. Vaccine. 2013 Nov 12;31(47):5572-8.
22. Rodríguez C y Cols. Rev Panam Salud Publica 29(3), 2011)
23. World Health Organization. 2020. 26 de March. Último acceso: 08 mayo 2020. https://apps.who.int/iris/bitstream/handle/10665/331590/WHO-2019-nCoV-immunization_services-2020.1-eng.pdf?sequence=1&isAllowed=y
24. LINEAMIENTOS GENERALES PARA EL PROGRAMA AMPLIADO DE INMUNIZACIONES (PAI) EN EL CONTEXTO DE LA PANDEMIA DE COVID-19. COLOMBIA 2020.

24. LINEAMIENTOS GENERALES PARA EL PROGRAMA AMPLIADO DE INMUNIZACIONES (PAI) EN EL CONTEXTO DE LA PANDEMIA DE COVID-19. COLOMBIA 2020.
25. Cowling et al Increased Risk of Noninfluenza Respiratory Virus Infections Associated with Receipt of Inactivated Influenza Vaccine. Clinical Infectious Diseases 2012;54(12):1778-83
26. Rikin S et al Assessment of temporally-related acute respiratory illness following influenza vaccination Vaccine (36) 2018; 1958-1964.
27. Sundaram ME, McClure DL, Belomgia EA, et al. 2013. «Influenza vaccination is not associated with detection of noninfluenza respiratory viruses in seasonal studies of influenza vaccine effectiveness.» Clin Infect Dis 57:789-93
28. Kelly H, Jacoby P, Dixon G et al. 2011. «Vaccine effectiveness against Laboratory-confirmed influenza in Healthy Young Children: A cases-Control Study.» Pediatric Infectious Disease Journal 107-111
29. Wolff, Greg. 2020. «Influenza vaccination and respiratory virus intererence among Department of Defense during the 2017-2018 influenza season.» Vaccine (38)350-354)
30. Background Paper on Influenza Vaccines and Immunization SAGE Working Group 2012. World Health Organization WHO.
https://www.who.int/immunization/sage/meetings/2012/april/1_Background_Paper_Mar26_v13_cleaned.pdf [consultado 5 mayo 2020]
31. Thompson, W.W., et al., Mortality associated with influenza and respiratory syncytial virus in the United States. The Journal of the American Medical Association, 2003. 289:179-86. 193.
32. Nunes, B., et al., Excess mortality associated with influenza epidemics in Portugal, 1980 to 2004. PloS One, 2011. 6:e20661.
33. Simonsen, L., et al., The impact of influenza epidemics on hospitalizations. The Journal of Infectious Diseases, 2000. 181:831-7
34. Barker, W.H. and J.P. Mullooly, Impact of epidemic type A influenza in a defined adult population. American Journal of Epidemiology, 1980. 112:798-811
35. Burette, P., et al., Influenza outbreak in a well-vaccinated nursing home population in Belgium. Acta Clinica Belgica, 2009. 64:324-8
36. Ferson, M.J., et al., Concurrent summer influenza and pertussis outbreaks in a nursing home in Sydney, Australia. Infection Control and Hospital Epidemiology, 2004. 25:962-6
37. Gaillat, J., et al., Summer influenza outbreak in a home for the elderly: application of preventive measures. Journal of Hospital Infection, 2008. 70:272-7.
38. People 65 Years and Older & Influenza. Influenza (Flu). Centers for disease control and preventions CDC. https://www.cdc.gov/flu/highrisk/65over.htm [Consultado 4 mayo 2020].
39. Key updates for week 14, ending Abril 4, 2020. Weekly U.S. Influenza Surveillance Report. Fluview CDC https://www.cdc.gov/flu/weekly/weeklyarchives2019-2020/Week14.htm [consultado 4 mayo 2020]
40. Informe de evento infección respiratoria aguda 2018
https://www.ins.gov.co/buscador-eventos/Informesdeevento/INFECCI%C3%93N%20RESPIRATORIA%20AGUDA_2018.pdf [consultado 4 mayo 2020]
41. Colombia 2018 influenza laboratory surveillance information. GISRS. OMS
https://apps.who.int/flumart/Default?ReportNo=7 [consultado 4 mayo 2020]
42. Informe de evento IRAG Periodo epidemiológico XIII. Colombia, 2019
https://www.ins.gov.co/buscador-eventos/Informesdeevento/INFECCI%C3%93N%20RESPITATORIA%20AGUDA%20PE%20XIII%202019.pdf [consultado 5 mayo 2020]
43. Informe de evento IRAG Periodo epidemiológico IV. Colombia 2020
https://www.ins.gov.co/buscador-eventos/Informesdeevento/INFECCI%C3%93N%20RESPIRATORIA%20AGUDA%20PE%20IV%202020.pdf [Consultado 6 mayo 2020]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