Results of the First Mexican Consensus of Vaccination in the Adult

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Abstract

For years our efforts have been focused on vaccination during childhood. Today we know that this is not enough to ensure health in the rest of the life. Childhood is as important as any other stage and, therefore, vaccination must be permanent and differentiated, according to our age, throughout life. Introducing a life course perspective in vaccination programs, with emphasis on adult vaccination, particularly in older adults, offers us the opportunity to review the performance of health programs, actions, and services in the field of immunization, as well as strengthening health promotion actions. In this context, the first Mexican Consensus on Adult Vaccination was carried out in a joint effort of the National Institute of Geriatrics, bringing together a group of specialists who worked on three central objectives: establishing vaccination guidelines throughout the life course, with emphasis on new vaccines; defining priority groups according to their risk factors; and contributing to the effort to promote healthy aging.

KEY WORDS: *Adult. Consensus. Mexico. Vaccination. Vaccine.*

Basic concepts

We are facing a new challenge in public health: systematic use of all available vaccines given the chance. For years, we have been used to focus vaccination efforts on childhood, but now we know that this is not enough to ensure health for the rest of life. From the perspective of life course, childhood can be understood to be as important as any other stage, and vaccination should therefore be permanent and differentiated, according to our age, throughout life.

Vaccination and healthy aging

Evolution of the aging process depends on different factors, both personal (gender, ethnicity, genetic make-up, lifestyles, diseases and injuries) and environmental (health system characteristics, economic and social determinants, violence, etc.). Vaccination largely contributes to promote healthy aging, since it prevents transmittable diseases that continue to significantly contribute to morbidity and that frequently trigger events leading to catastrophic impairment[1]. For example, it is

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not the same dealing with heart failure with good general health than additionally doing it with a pneumonia that might have been well prevented. The World Report on Aging and Health, published by the World Health Organization (WHO) in October 2015, defines healthy aging as "the process of developing and maintaining the functional ability that enables wellbeing in old age"[1].

Vaccination as one of the elements articulating service exchange and promoter of national health system integration

Currently, any Mexican can access to vaccination at any health facility in the country. Owing to its high impact, vaccination is the core of prevention strategies, and is an invigorating agent of different involved stakeholders: health personnel, public, private and social institutions; investigator community and academic community, providers, society and users/beneficiaries[2,3].

Introducing a life-course perspective in vaccination programs, with an emphasis on adult vaccination, and particularly in the elderly, offers an opportunity to review the performance of the set of health programs, actions and services in the field of vaccination, as well as its monitoring and permanent assessment. It is also an opportunity to strengthen health promotion actions in concert with the social development sector, making use of social programs' joint responsibility actions, which represent a privileged opportunity to access to vaccination and other health services. In order to make the most of every vaccination opportunity, generating much clearer and simple information for the population is necessary, in order to allow for it to empower and undertake a more active commitment with both individual and collective health preservation. The social and health combined approach allows for vaccination programs' benefits to be maximized for the population[4,5].

It is in this context that the First Mexican Consensus on Adult Vaccination took place, which gathered a group of specialists who worked with three central objectives: to establish vaccination guidelines throughout the course of life with an emphasis on the new vaccines, to define priority groups for vaccination according to their risk factors, and to contribute to the effort for healthy aging promotion.

Here, the eight most important vaccines for adults and for the elderly, which were the subject of study of this First Mexican Consensus on Adult Vaccination, are described, with backgrounds of each pathology and type of vaccine being reviewed and schedules being proposed and consensus recommendations being established.

The vaccines recommended by this consensus were the diphtheria, pertussis and tetanus (DPT), hepatitis B, herpes zoster, influenza, meningococcal, pneumococcal, human papillomavirus and dengue vaccines.

Vaccine against diphtheria, pertussis and tetanus

In Mexico, no cases of diphtheria have occurred since 1991 (http://www.censia.salud.gob.mx/contenidos/vacunas/enfermedadesprev.html) and a decrease in non-neonatal tetanus cases has been observed since 1961, with an estimated incidence rate < 1/100,000 population. Although neonatal tetanus lethality rate is high (it exceeds 80%), it tends to decrease in Mexico[6]. However, in the case of pertussis, different reports indicate that it continues to be endemic worldwide, and that its incidence has been increasing over the last 30 years. The main causes that explain this increase are the progressive loss of vaccine-induced immunity, genetic changes in circulating strains, low exposure to naturally-circulating *Bordetella pertussis*[7,8], and better diagnostic and epidemiological surveillance methods[9]. The Ministry of Health (SSA – *Secretaría de Salud*) considers very important to prevent the reemergence of these diseases by means of children vaccination and adults and older adults' booster shots[6]. Vaccines against diphtheria, pertussis (whooping cough) and tetanus (e.g., Tdap [DPT, diphtheria, pertussis and tetanus] and Td [diphtheria and tetanus]) not only do protect the individual vaccinated for the disease, but also protect family members and people close to him/her. However, the type of recommended vaccine varies according to the consulted source (Centers for Disease Control and Prevention [www.cdc.gov/vaccines/hcp/acip-recs/index.html], Joint Commision[10], Advisory Committee on Immunization Practices [ACIP][11] and WHO [http://www.who.int/immunization/documents/positionpapers/]). Worldwide, the use of the Tdap/Td vaccine is recommended as booster in all 19-year-old or older people. In Mexico, the Td vaccine is included in the vaccination guidelines that the SSA has established for adults and older adults (http://www.promocion.salud.gob.mx/dgps/interior1/programas/cartillas.html) (Table 1).

The response of adolescent and adult antibodies to Tdap is not inferior than the antibody response of infants exposed to three DTaP doses[12,13]. In addition, maternal immunization with Tdap during the third trimester of pregnancy elicits an efficient placental transference of antibodies to the fetus[14].

Table 1. Vaccines against diphtheria, pertussis and tetanus available in Mexico for use in adults

Tetanol®	Novartis	40 UI tetanus toxoid
Tetadiph®	Novartis	20 IU tetanus toxoid and 2 IU diphtheria toxoid
Imovax DT® Adult	Sanofi	20 IU tetanus toxoid and 2 IU diphtheria toxoid
Adacelboost®	Sanofi	5 Lf tetanus toxoid and 2 Lf diphtheria toxoid and 2.5 µg pertussis toxoid
Boostrix®	GSK	20 IU tetanus toxoid and 2 IU diphtheria toxoid and 8 µg pertussis toxoid
Tetanus and diphtheria toxoids TD adult	Laboratorios de Biológicos y Reactivos de México	*Corynebacterium diphtheriae* Parker Williams 8 strain diphtheria toxoid 3-5 Lf, *Clostridium tetani* Massachusetts strain tetanus toxoid 10-20 Lf

Source: www.cofepris.gob.mx/AS/Documents/.../Vacunas/Vacunas.pdf

The safety of vaccines is well established, with local reactions being the most common side effect. There are only two medical conditions regarded as absolute contraindications: 1) history of anaphylactic reaction and 2) encephalopathy of unidentified cause within 7 days after the administration of a vaccine with a pertussis component[11]. Tdap can be administered regardless of the elapsed time interval since the last vaccination with diphtheria and tetanus toxoids.

Consensus Recommendations

The recommendations for the use of the Tdap and Td vaccines are the following:

- Universal vaccination of 19 to 64-year-old adults, starting with a Tdap dose and applying Td boosters every 10 years; 65-year-old and older population shall receive an additional Tdap dose followed by a Td booster every 10 years.
- Adults who are or expect to be in contact with children younger than 12 months.
- Tdap to healthcare personnel.
- Tdap to pregnant women, ideally between week 27 and 36, and it should be applied at each pregnancy.
- Patients with contaminated wounds should receive a tetanus toxoid-containing vaccine[10,15,16].

According to recently-generated scientific evidence from all over the world, it will be important to consider Td substitution with Tdap every 10 years, with the purpose not to leave the population unprotected against *B. pertussis*[17]. Another point to consider will be the shortening of intervals between boosters, since evidence indicates that vaccine-conferred immunity lasts approximately 7 years and, therefore, there would be a considerable period during which the patient would be unprotected. Individuals who have acquired the natural infection should be immunized as well, since having the disease does confer permanent immunity.

Hepatitis B vaccine

Hepatitis B (HB) is a viral disease caused by a hepatotropic virus. The initially acute condition can progress to chronic, which is associated with serious complications on the long-term, such as liver cirrhosis or hepatocarcinoma[18-20]. HB is a disease that is preventable by means of a specific vaccine.

The HB vaccine is produced by recombinant engineering. It contains subunits of HB s antigen (HBsAG), it doesn't contain infecting elements and is highly immunogenic.

Since 1998, all newborns in Mexico must be vaccinated according to the WHO universal vaccination program. For this reason, the vast majority of adults and older adults are not vaccinated or ignore their immunoserologic status with regard to HB. Older adults should be assessed according to their risk factors for contracting this disease, such as an active sex life, promiscuity, treatments affecting immunity or being carriers of chronic-degenerative conditions (subjects with kidney disease under dialysis procedures, diabetics, etc.), without forgetting that immunosenescence becomes patent since 60 years of age in most cases[21].

The recommended administration schedule is three doses by the intramuscular route (at 0, 2 and 6 months). Vaccinated patients preserve immunity for a long time and booster is usually not required if the above-mentioned schedule was completed. Vaccinated subjects show anti-HBsAg antibodies in serologic determinations. No boosters are required, since vaccine-conferred immunity persists until 24 years of age[22] in those vaccinated during childhood; for those vaccinated after 20 years of age, booster might be required[23].

It is important to improve health personnel knowledge on HB prevention in older adults. This knowledge should include vaccination, with special emphasis on those who work in, live in or attend healthcare or

rresidential institutions or prisons, and in establishments that due to their nature imply an increased risk for contracting this disease.

The individualized HB vaccination schedule for adults and older adults implies the necessity to know their immunization history and immunoserologic status, which in turn implies an additional cost. Therefore, complete vaccination should be promoted at least in adults older than 60 years with diabetes[24]. Not only chronic hepatitis and associated cirrhosis would be prevented, but also hepatocarcinoma associated with this infection would.

Consensus Recommendations

Liver diseases are the sixth cause of mortality (influenza and pneumonia are the seventh) in older adults in Mexico[25], and HB vaccination is therefore suggested to be included in the NOM-036-SSA2-2012 standard[26], in addition to including it in the 2014 SS older adult National Health Record Chart. This measure is also suggested by Michel[27] for subjects older than 60 years.

Herpes zoster vaccine

Herpes zoster (HZ) is characterized by painful unilateral vesicular exanthema distributed in dermatomas[28], the evolution of which is self-limited in approximately 4 weeks[29]. It is a manifestation of latent varicella-zoster virus (VZV) reactivation, resulting from previous varicella[28]. After varicella recovery, the virus remains lifelong latent in dorsal root ganglia[29,30], and as age advances, VZV can be reactivated and manifest itself as a result of a decrease in VZV-specific T cell immunity[29]. Life-long risk for the development of HZ is reported to be approximately 25%-35%, but it disproportionally affects older adults and immunocompromised people[30]. Aging is associated with immunosenescence, which is the innate and adaptive immune system natural decline to produce an efficacious immune response[31]. HZ main complication is postherpetic neuralgia (PHN), a painful chronic syndrome that can develop after a HZ episode. It is a neuropathic pain that persists beyond exanthema disappearance and it is defined as at least 90 days of documented pain[32]. HZ overall incidence in immunocompetent subjects ranges from 1.2 to 4.8 per 1000 years-person, and it markedly increases with age, with an estimated of up to 14.2 per 1000 years-person after 50 years of age[33]. In immunosuppressed patients, incidence rates range from 14.5 to 53.6 per 1000 years-person[33]. Although HZ is less contagious than varicella, taking preventive measures is indispensable, since VZV can be transmitted to susceptible people[32]. The reduction of disease burden, HZ incidence and PHN incidence in subjects vaccinated against VZV is 61%, 51% and 67%, respectively[30,34].

The purpose of the vaccine is to elicit sufficient immunity against inactive VZV in such a way that, when reactivated, the disease is attenuated[35], in addition to reduce medical and psychosocial elevated costs of HZ and its complications[28]. The Oka/Merck vaccine contains live-attenuated viruses[34]. It markedly reduces HZ and PHN morbidity in older adults[36]. The effectiveness of the vaccine against HZ was demonstrated in a large, randomized, double-blind study that included 38,546 adults aged ≥ 60 years, with a 3-year follow-up and demonstrated that the vaccine reduced HZ incidence by 51%. Secondary benefits included a decrease in PHN incidence in 67% of vaccinated subjects who had developed HZ[34]. Although vaccine efficacy decreases with age, the efficacy to prevent PHN was maintained at all studied ages[37]. Schmader et al.[36] found that the efficacy to prevent HZ was 69.8% in 11,211 individuals (50 and 59 years of age). Mean severity by pain duration was lower (0.13) in the group with the VZV vaccine than in the group that received placebo (0.49), with an estimated relative reduction of pain between both groups of 73%. The most common adverse event that has been found in clinical trials is reaction in the site of injection, which is generally mild[38,39].

Consensus Recommendations

The VZV vaccine currently available in Mexico(Oka/Merck) is indicated to prevent HZ and PHN, and to decrease HZ-associated acute or chronic pain[40]. A single dose is systematically recommended in 60-year-old or older adults, regardless of having experienced a previous HZ episode, and it can be administered to 50 to 59-year-old adults. Subjects aged 60 years or older with any chronic medical condition can be vaccinated, unless their condition constitutes a contraindication, such as severe immunodeficiency[41]. It can be administered to people with a history of HZ, although the optimal timing to apply the vaccine after an acute episode is not known. Delaying vaccination for 3 years is feasible in immunocompromised individuals with recent history of HZ, as long as the HZ diagnosis is well documented by the health professional[32]. The vaccine is contraindicated in people with hematological malignancies whose disease is not on remission and in those who received cytotoxic chemotherapy within the last

3 months, in individuals with T cell immunodeficiency (e.g., human immunodeficiency virus [HIV] infection with a CD4 cell count ≤ 200 per cubic millimeter or < 15% of total lymphocyte count) and in those receiving high-dose immunosuppressant therapy (e.g., > 20 mg of prednisone per day for ≥ 2 weeks or therapy with tumor necrosis factor inhibitors)[32]. Patients with solid organ transplant who receive immunosuppressants should not receive the vaccine[42].

It can be co-administered with other vaccines (e.g., influenza vaccines), at separate injection sites and with different syringes. However, pneumococcal vaccine should not be simultaneously administered with the HZ vaccine because a reduced antibody response to the HZ vaccine occurs[43].

A recombinant vaccine that contains VZV E glycoprotein and the AS01B adjuvant system (known as HZ/su) for the prevention of HZ in older adults is currently under evaluation. Previous phase I-II clinical trials that were carried out in older adults and immunosuppressed subjects showed that HZ/su had an acceptable clinical safety profile and that it produced a robust immune response that persisted for at least 3 years in older adults. The vaccine showed an efficacy ranging from 96.6% to 97.9% for all age groups[43].

Influenza vaccine

Seasonal influenza is a disease caused by three types on viruses that belong to the *Orthomyxoviridae* family: the influenza A, B and C viruses[44]. The influenza A virus is designated according to the hemagglutinin (H) and neuraminidase (N) subtypes it possesses[45]. The viruses accumulate genetic point mutations during replication that lead to the appearance of viral variants, which produces the so-called seasonal influenza caused by viruses A and B every year[46,47]. This antigenic variation is due to genetic mutations and rearrangements that originate minor annual changes, known as genetic drifts, and major changes or shifts, generally every 40 years. With these mechanisms, the virus eludes the host's adaptive immune system[44]. Most times, the infection affects the upper airway, but in severe cases, there can be pulmonary involvement[48]. Disease severity depends on people's age and comorbidity, and clinical manifestations vary from one person to another[49].

In Mexico, the National Committee fir Epidemiological Surveillance reported, until February 2016 (2015-2016 season), 870 influenza cases and 34 deaths; 88% of people who died were not vaccinated against influenza. The main consequences of influenza are influenza-related primary pneumonia and secondary bacterial pneumonia[47,50].

Annual vaccination is the main influenza prevention and control measure, although the protection conferred by available vaccines is not homogeneous owing to the antigenic difference that usually exists between environmental viruses and those contained by vaccines[51].

In a retrospective, case-series, ecological study, Kuri-Morales et al.[52] found that, in January, there are more influenza-associated deaths in people older than 65 years (mean: 1,154), and that the lowest mortality is in June (mean: 445). During the assessed period (1990-2005) a descending trend was observed in the number of deaths (29 less per year) in this age group, and it was concluded that vaccination has a positive effect on death and hospitalization decrease, as well as on quality of life[52].

In a retrospective study of 18 cohorts of elderly residents in community-based old-people's homes during 10 influenza seasons, a significant decrease in the risk for hospitalization (27%) and death (48%) was observed. The vaccine effectiveness was 37% when the included strains barely matched the environmental strains and 52% when there was higher matching[53]. Other cohort and case-control studies have reported 60% efficacy in disease decrease, lower risk for death during winter in vaccinated elderly individuals in comparison with non-vaccinated elderly subjects, and an up to 50% decrease in the rate of winter deaths[52], as well as 51% efficacy in people aged from 9 to 49 years[54].

The influenza vaccine rarely causes serious allergic or anaphylactic reactions. In general, adverse reactions are common to those of any parenteral vaccine: reactions at the site of injection, headache, fatigue, muscle pain, general malaise and fever[49].

In Mexico, there are 14 influenza vaccines available (three for pandemic influenza and 11 A and B-type trivalent vaccines) authorized by the Federal Commission for the Protection against Sanitary Risk (COFEPRIS – *Comisión Federal para la Protección Contra Riesgos Sanitarios*)[55].

According to the National System of Health Record Charts, vaccination against influenza should be applied in pregnant women at any trimester of pregnancy, in adult non-pregnant women (20 to 59 years of age), in adult men (20 to 59 years' old) and in older adults (60-year-old and older)[56].

Meningococcal vaccine

Meningococcal disease has different forms of presentation: meningitis (leptomeningitis), sepsis, pneumonia and arthritis, among others. However, meningitis

Table 2. Meningococcal conjugate vaccines available in Mexico. Adult schedules

Vaccine	Brand (manufacturer)	Dose	Route	Schedule
Meningococcal polysaccharide and diphtheria toxoid conjugate vaccine (MenACWY-D)	Menactra® (Sanofi Pasteur)	0.5 ml	IM	1 dose*
Meningococcal oligosaccharide CRM 197 and diphtheria toxoid conjugate vaccine (MenACWY-CRM)	Menveo® (Novartis)	0.5 ml	IM	1 dose*
Meningococcal conjugate vaccine for serogroup C	Menjugate® (Novartis)	0.5 ml	IM	1 dose*
Meningococcal conjugate vaccine for serogroup C	Neissvac® (Baxter)	0.5 ml	IM	1 dose

IM: intramuscular.
*Booster dose is recommended every 5 years in case of asplenia or immunodeficiency of any other type.

and sepsis are predominant and represent a public health problem in some regions, owing to their elevated mortality rate (around 50%), even in spite of treatment, and impairment they generate in at least 30% of those affected[57].

Neisseria meningitidis transmission occurs by person-to-person contact through inhalation of respiratory secretions droplets. Disease propagation is facilitated by close and prolonged contact with an infected person. Mean incubation period is 4 days, but it can range from 2 to 10 days[57]. Based on capsular polysaccharides immune reaction, it is classified in 12 serogroups, and according to the external membrane protein composition, they are classified in subtypes. By means of molecular analysis, different genetic types or clonal complexes are identified; this is related to strain virulence. Between 10 and 20% of the population is thought to be *N. meningitidis* carrier, although the carrier rate can be higher in epidemic situations[58-60].

Meningococcal meningitis cases occur basically in children younger than 15 years, with them being more prevalent in children younger than 2 years. In adults older than 55 years, meningococcal infection occurs more commonly as pneumonia that is clinically indistinguishable from that produced by other bacterial agents. However, the following patients are recognized as being at high risk for contracting the disease: hyperendemic zones inhabitants, tourists travelling to a hyperendemic or epidemic zone, recent exposure to a meningococcal meningitis outbreak, microbiologists, patients with anatomic or functional asplenia, terminal complement system deficiency or other state of immunodeficiency[58-61].

Consensus Recommendations

Prevention is carried out by means of meningococcal vaccine application. Capsular polysaccharide available vaccines have only demonstrated usefulness in outbreaks, since they do not modify the carrier status or provide herd immunity. Conjugate vaccines with an antigen are the only ones that are internationally recommended. In Mexico, adult universal vaccination is not required, but risk-focused vaccination[61] (Table 2).

Pneumococcal vaccine

Diseases caused by *Streptococcus pneumonia* (pneumococcus), on its invasive and non invasive form, are the cause of great morbidity and mortality, with higher risk in adults older than 60 years, who are particularly susceptible to infection owing to comorbidity and immunosenescence[62,63]. This bacterium is the most common cause of community-acquired pneumonia (CAP) in the world, and it is estimated to cause between 30% and 50% of CAP cases requiring hospitalization in adults[64]. Currently, there are two types of vaccines for the prevention of diseases caused pneumococcus in adults: the 23-valent purified polysaccharide polyvalent vaccine (PPSV23)[65] and the 13-valent conjugate vaccine (PCV13)[66]. Purified pneumococcal polysaccharide-derived vaccines behave as thymus-independent antigens, with primary response antigens of the IgM and IgG1 class being produced, but since these are not memory antigens, conjugating the polysaccharides to carrying proteins was necessary, since this way they behave as thymus-dependent antigens, able to induce primary and memory immune responses, and thus were the pneumococcal serotype conjugate vaccines born, such as PCV13[66]. PCV13 is more immunogenic for serotypes contained by PPSV23[65], with both being safe and well tolerated[67]. Immunization with both vaccines has managed to decrease specific or complication-attributable morbidity, need for hospitalization and associated mortality.

Immunization strategies against pneumococcus vary with regard to age groups, risk groups to be immunized and type of vaccine used (PPSV23, PCV13 or both). According to available epidemiological evidence, the best anti-pneumococcal immunization strategy should be based on age and risk factors. Actually, although the risk-based strategy has many disadvantages, such as difficult access to health services, required participation of different health professionals and difficulty to achieve elevated coverage, it must be implemented at large scale and be associated with the age strategy[66]. This is why, in August 2014, the USA ACIP recommended systematic use of a PCV13 dose followed by a PPSV23 dose. The application interval between both vaccines, according to the last ACIP recommendations published in February 2016[68,69], is one year or more, and it consists in the following: for 65-year-old and older immunocompetent adults without any previous immunization, a PCV13 dose should be applied, followed by a PPSV23 dose after 1 year. The same schedule is recommended for this age and for those younger than 65 years in case of chronic conditions or any type of immunosuppression. If prior to 65 years of age, an immunocompetent patient received a PPSV23 dose sometime in life, from 65 years of age on he/she can be administered one PCV13 and another PPSV23 dose after 1 year, provided at least 5 years have elapsed since the first PPSV23 administration.

Consensus Recommendations

According to current scientific evidence, and considering our population's epidemiology, the present consensus recommends adult pneumococcal vaccination with PPSV23, at a universal vaccination age from 60 years on, and taking into account risk factors and revaccination indications pointed out by the National Vaccination Council as follows[70]:

- Universal vaccination age: from 60 years on.
- People of 2 to 60 years of age with chronic conditions of the cardiovascular or pulmonary type, diabetes, alcoholism or cirrhosis, or cerebrospinal fluid fistulas: one dose without revaccination.
- People aged 2 to 60 years with functional or anatomical asplenia: one dose with a single revaccination 5 years later in those older than 10 years, and 3 years after the first one in those younger than 10 years.
- People older than 2 years with immunosuppression (including asymptomatic or symptomatic HIV infection, leukemia, lymphoma, Hodgkin's disease, myeloma multiple, disseminated neoplasms, chronic kidney failure and nephrotic syndrome): one dose with a single revaccination 5 years after the first dose in those older than 10 years, and 3 years after the first one in those younger than 10 years. In case the patient receives some type of immunosuppressant therapy, vaccine administration will be until 2 weeks after having received said therapy.
- People aged 2 to 60 years residing in foundling or old people's homes: no revaccination is required.
- Apply the vaccine at discharge of every adult patient hospitalized for pneumonia who hasn't received it previously.
- In can be simultaneously applied with the influenza vaccine.
- Whenever possible, according to PCV13 availability, the vaccination algorithm suggested by the ACIP can be followed, with one PCV13 dose followed by a PPSV23 dose with ACIP-indicated time-intervals.

Human papillomavirus vaccine

Cervical cancer is the second malignant disease most common in women worldwide[71]. Approximately 530,000 cases are estimated to occur per year, with a mortality of 274,000 women annually[71-78]. Persistent infection with oncogenic human papillomaviruses (HPV) is a necessary cause for the development of cervical cancer[72,73]. HPV's constitute a group of DNA viruses associated with the appearance of benign and malignant lesions of the genital tract, the respiratory tract and the skin. Most common high-risk viruses are HPV 16 and 18, which are related to more than 70% of cervical cancer and 90% of cervical adenocarcinoma cases, as well as with an increased incidence of vulva, vagina, penis, anus, oral cavity, pharynx and larynx cancer. Low-risk viruses are HPV 6 and 11, which are associated with more than 90% of genital warts[74-81]. HPV infection is transmitted by sexual contact. HPV 16 and 18 tend to persist for long time and progress more frequently to high-grade lesions. One hundred percent of cervical cancers are attributed to HPV[75], and approximately 80% of women will present HPV infection in their lifetime[75,76]. Most common oncogenic types are HPV 16 and 18, followed by HPV 45, 31 and 33 in terms of frequency; all these are associated with cervical cancer and cervical adenocarcinoma[77,79,81,82].

HPV infection is generally asymptomatic. The main risk factors for acquiring the infection are sexual

intercourse initiation at early age, having multiple sexual partners, prolonged use of oral contraceptives, smoking and alcoholism[78,79,82]. The diagnosis of HPV infection and low and high-grade cervical lesions is carried out by exfoliative cytology, colposcopy and histopathological and molecular studies. Treatments include from low-grade lesions surveillance to methods that destroy the lesion (5-fluorouracyl, immunoregulators) or ablative procedures (electrocauterization, laser, cryotherapy and cervical conization)[75,79,81,82].

HPV prevention at early ages (from 9 years of age onwards) has a notorious impact on cost-benefit, since in addition to decreasing the mortality index, it reduces the number of abnormal cytologies by up to 20%, colposcopy by up to 26% and excisional therapies by up to 40-60%, with evident economic impact and decrease in the demand of medical services for HPV-associated diseases[78,81,82].

In Mexico, there are two vaccines for HPV prevention: the quadrivalent vaccine Gardasil® (Silgard, Merck & Co. Inc, NJ, USA) and the bivalent vaccine Cervarix® (Glaxo Smith Kline, Middleses, UK)[83]; both are approved by the US Food and Drug Administration the Mexican Ministry of Health. These vaccines are synthesized by recombinant use of capsid L1 proteins, which are arranged in a similar form to the viral structure (virus-like particles, VLP), the purpose o which is to produce high serum titers of neutralizing antibodies in order to prevent host cells infection. Vaccination highest efficacy and greatest benefits are reported in women younger than 25 years[78,79,81], given that HPV infection and low grade dysplasias (75.9%) are more common in this age group, and high grade lesions (65.3%) occur mainly after 38 years of age. Several studies show that older women would benefit from vaccination, since an efficacy higher than 48% has been demonstrated in the prevention of new cervical lesions by any HPV type in women who were previously carriers of low-grade lesions and grade II cervical intraepithelial neoplasias[80-82,84,85].

The vaccines are administered in a three-dose schedule by intramuscular injection, preferably on the deltoid area[79,81,86]. The two-dose schedule (0 and 6 months) is used in Mexico, Canada, Chile, Colombia, Switzerland and India with satisfactory results based on immunogenicity and protection against HPV that are similar to those obtained with the three-dose schedule in females younger than 15 years[86-88]. Most common side effects are pain at the injection site (70%-97%), sweating (24.2%), erythema (23.6%), headache (26%), nausea (6%) and gastrointestinal disorders (6%); anaphylaxis has been observed in 2.6 per 100,000 doses. Serious adverse reactions are reported in 0.3% of cases and have not been associated with the vaccine application, but with preexisting conditions[78,79,81,83,89]. Adverse reactions are self-limited and are resolved spontaneously[79,81,83,86,90,91].

More than 175 million doses have been applied in the entire world. Vaccination al early ages and prior to active sex life initiation (from 9 years of age onwards) confers nearly 100% protection against HPV 6, 11, 16 and 18. The Universal Vaccination Program general guidelines in Mexico mention that current schedule is to apply the first dose of the vaccine in primary school 5th grade girls, or at 11 years of age if they are not in school[79,81-83,87]. In Mexico, applying the vaccine in males has not shown, epidemiologically, a good cost-benefit contribution for cervical cancer, but studies are underway for its validation. In men who have sex with men, its cost-benefit has been shown for HPV-associated diseases[92,93].

Consensus Recommendations

- Applying the HPV vaccines is not recommended during pregnancy, although there is no evidence that there is an increase in congenital anomalies or obstetric complications in vaccinated women.
- Both available HPV vaccines are indicated in females from 9 to 26 years of age.
- In both genders, the quadrivalent vaccine is indicated between 9 and 26 years of age.
- Administer the first dose of the vaccine in primary school 5th-grade girls or at 11 years if not in school.
- The vaccination schedule consists of two doses (0 and 6 months).

Administer the vaccine by intramuscular route, in the deltoid area of the right upper arm.

- The vaccine should be stored in refrigeration at 2-8 °C, and be administered as soon as possible after being removed from the refrigerator.
- Vaccinees should be observed for approximately 15 minutes after vaccine administration.
- The vaccine is contraindicated in case of hypersensitivity to the active substances or any of the excipients, acute disease or fever, and in patients on anticoagulation or suffering from blood dyscrasias.
- Avoid subsequent administration if anaphylaxis occurred with the previous dose.
- Vaccination is preventive, not therapeutic.

Dengue vaccine

Dengue is produced by any of Dengue flavivirus (DENV) serotypes (1, 2, 3 or 4)[94,95]. The infection produces immunity throughout life, but the most serious forms of dengue infection frequently occur in individuals with a second infection with a different serotype[96].

Mexico is an endemic zone for dengue[97], and the serotypes most commonly identified in the country are, in decreasing order, 1, 2, 4 and 3. In 2015, the highest incidence of dengue fever and dengue hemorrhagic fever cases was observed in the population aged from 15 to 19 years, with an incidence gradual decrease until 60 to 64 years of age and an upturn from 65 years of age on[98].

Primary prevention strategies against dengue include epidemiological and entomological surveillance; control of the vector, the *Aedes* mosquito, by means of breeding grounds' control and by protecting water storages by means of potable water supply and good drainage systems; use of larvicides, use of net canopies and intra-domiciliary insecticides, use of insect repellent and installation of screen doors and windows[95,97,99,100]. Other primary prevention strategies include the development of vaccines against the virus, among which live attenuated virus (LAV), purified inactivated virus (PIV) viroid particle recombinant subunits and virus-like particles (VLP)-derived vaccines are under investigation. One of the recombinant chimeric yellow fever attenuated virus-derived LAV vaccines[96,101,102], CYD-TDV, is the only one that has completed phase III trials and has been authorized for commercialization by national regulatory authorities from different Asian and Latin American countries.

The results of different studies on CYD-TDV point out the efficacy of the vaccine in the prevention of severe dengue and hospitalizations, although with great variability with regard to circulating serotypes; in efficacy decreasing order: DENV 3 and 4 > DENV 1 > DENV 2. Efficacy was higher in those who had preexisting neutralizing antibodies and older age cohorts than in seronegative individuals and younger age cohorts[103,104].

According to COFEPRIS, the CYD-TDV vaccine is indicated for individuals aged between 9 and 45 years previously exposed to the virus in populations where dengue is endemic and seroprevalence is ≥ 60%[105]. On the other hand, the WHO Strategic Advisory Group of Experts (SAGE) on Immunization recommends administration of this vaccine in three 0.5-ml reconstituted doses by subcutaneous injection in the deltoid area, separated by 6 months ± 20 days intervals (0, 6 and 12 months), both in children and adults[101,105], in those endemic regions where seroprevalence is ≥ 70%, to be applied in individuals 9 to 45-60 years of age who live in said areas, whereas in places where seroprevalence at 9 years of age is > 50% and < 90%, the recommended age is from 11-14 years on, since there is the possibility that immunization may be inefficacious or even increase the risk for dengue-related hospitalization in seronegative subjects at first dose, as it occurred in the 2 to 5-year-old studied group[106].

Consensus Recommendations

Dengue is a health problem in the Mexican adult population, which requires additional prevention and control measures to those already existing, with administration of a vaccine and vector control methods standing out, particularly within the context of the presence and propagation of two emerging viruses in the country: chikungunya and zika. It is highly important to continue and intensify individual and community-based protection measures against the vector (see section on Primary prevention), and not promoting the idea that dengue vaccine administration eliminates the need for preventive actions. It would be convenient to have national and individual studies on seroprevalence prior to the vaccine administration (reduced efficacy in seronegative patients), as well as to carry out studies on efficacy and safety specifically in the adult population. In addition, it is necessary for the effect of the vaccine added to age-related comorbidity to be investigated.

Since the CYD-TDV vaccine is already approved to be used in Mexico, it is indispensable for health professionals to participate in the report of events supposedly attributable to vaccination or immunization (ESAVI), given the increased risk for hospitalization in 2 to 5-year-old children[107], while waiting to obtain further data on safety in populations older than 16 years, since whether this is related to patient age or serologic status is not known.

Considering current evidence, strict adherence to COFEPRIS and SAGE administration indications for CYD-TDV vaccine administration is necessary, according to each patient's age and serologic status with regard to dengue and to the demographic region he/she inhabits.

Vaccination has a positive impact on the population's health and aging. Its application should not be an issue limited by age, but a permanent and continuous action, conceived as part of a model of disease prevention and healthy aging promotion with a life-course perspective. From the presented information, it is clear that there

are many stakeholders involved in a national vaccination program that comprises the national health system as a whole, with its institutions, specific action programs, budget and personnel. But that is not sufficient; being successful requires active, responsible and informed participation of people, communities and the media.

Conclusions

A vaccination program with a life-course perspective implies not only the need to improve vaccination programs performance and coverage, but it offers us an opportunity to review actions and infrastructures as a whole, as well as for their monitoring and permanent evaluation. It is also an opportunity to strengthen social development actions and to reduce health disadvantage gap, while improving health education, which represents an opportunity or not to access to information and, therefore, to services. To progress, we will have to generate much clearer and simpler information for the population, which allows for it to empower and to undertake a more active commitment with the responsibility for individual and collective health.

Vaccines can significantly alleviate the burden of the diseases exposed throughout this text, but a significant reduction of these diseases requires a comprehensive approach that includes disease prevention and control by combining the use of vaccines with basic actions as personal as hand washing or adequate nutrition, and with collective actions such as pollution reduction.

Once again, social and health synchronic approach is proposed not as “a” strategy, but as “the” strategy that allows for the benefits of vaccination programs to be maximized in the population (Table 3).

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Table 3. Summary of recommendations

Tdap and Td	HB	HZ	Influenza	Meningococcal	Pneumococcal	HPV	Dengue
– 19 to 64-year-old adults, start with one Tdap dose and apply Td boosters every 10 years – Adults older than 65 years should receive an additional Tdap dose followed by a Td booster every 10 years – Adults who are or expect being in contact with children younger than 12 months – Tdap to healthcare personnel – Tdap to pregnant women (between weeks 27 and 36) and at each pregnancy. – Patients with contaminated wounds should receive a vaccine containing tetanus toxoid	– Inclusion of older adult HB vaccine in NOM-036-SSA2-2012 – Inclusion in 2014 SS National Health Record Chart.	– One dose in older than 60 years without previous HZ episode – 50 to 59-year-old adults – In those older than 60 years with chronic conditions without severe immunodeficiency – People with a history of HZ – Delay vaccination 3 years in immunocompromised subjects with recent history of HZ with well documented diagnosis – Contraindicated in: • Active hematologic cancer • Patients on cytotoxic chemotherapy within last 3 months • T cell immunodeficiency (e.g., HIV infection with CD4 ≤ 200/mm^3 or < 15% of total lymphocyte count) • Patients on high-dose immunosuppressant therapy (e.g., > 20 mg/day of prednisone for ≥ 2 weeks or therapy with tumor necrosis factor inhibitors • Patients with solid organ transplant receiving immunosuppressants	– In pregnant women at any trimester of pregnancy – Non-pregnant adult women (20 to 59 years) – Adult men (20 to 59 years) – Older adults (60 years and older)	Prevention by means of meningococcal vaccine administration Available capsular polysaccharide vaccines have demonstrated usefulness only in outbreaks, since they don't modify the carrier status or provide herd immunity Antigen conjugate vaccines are the only ones internationally recommended In Mexico, adult universal vaccination is not required, but risk-focused vaccination	– Universal vaccination from 60 years of age on – One dose without revaccination in 2 to 60-year-old patients with chronic conditions (cardiovascular, pulmonary, diabetes, alcoholism, cirrhosis, cerebrospinal fluid fistula) – 2 to 60-year-old subjects with functional or anatomical asplenia, one dose with one single revaccination 5 years later in those older than 10 years, or 3 years after the first one in children younger than 10 years – Subjects older than 2 years with immunosuppression (asymptomatic or symptomatic HIV infection, leukemia, lymphoma, Hodgkin's disease, myeloma multiple disseminated neoplasims, chronic kidney failure, nephrotic syndrome), one dose with a single revaccination 5 years after the first dose in those older than 10 years, or 3 years after the first one in children younger than 10 years – In patients receiving immunosuppressant therapy, administration will be until 2 weeks after having received said therapy – 2 to 60-year-old subjects residing in foundling or old people's homes do not require revaccination – At discharge of every patient hospitalized for pneumonia who has not received it previously – It can be simultaneously applied with the influenza vaccine	– Administration during pregnancy is not recommended – Both available HPV vaccines are indicated in 9 to 26-year-old females – Apply the first dose in primary school-5th grade girls or at 11 years of age if not in school – The vaccination schedule consists of two doses (the second 6 months after the first) – In Mexico, administration of the vaccine in males has not shown a cost-benefit contribution for cervical cancer – In men who have sex with men, cost-benefit has been shown for HPV-associated diseases – Contraindicated in case of hypersensitivity to the active substances or any of the excipients, acute diseases or fever, patients on anticoagulation or suffering from blood dyscrasias	– Continue and intensify individual and community protection measures against the vector – Do not promote the idea that dengue vaccine administration eliminates the need for preventive actions – Indispensable for health professionals to participate in ESAVI reporting – Adherence to COFEPRIS and SAGE recommendations for CYD-TDV vaccine administration according to age, serologic status and demographic region

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References

1. Informe Mundial sobre el Envejecimiento y la Salud. Ginebra: Organización Mundial de la Salud. Ginebra;2015. http://apps.who.int/iris/bitstream/10665/186471/1/WHO_FWC_ALC_15.01_spa.pdf?ua=1
2. Cortez-Alcalá R, Luna-Guzmán P, Grajales-Muñiz C, Ortiz-García F, et al. Grupo Técnico Interinstitucional del Comité Nacional para la Vigilancia Epidemiológica (CONAVE). Manual de procedimientos estandarizados para la vigilancia epidemiológica de las enfermedades prevenibles por vacunación. Dirección General de Epidemiología. Secretaría de Salud. Septiembre de 2012.
3. Gutiérrez Robledo LM, Garcia Garcia ML. Editores. Vacunación en el adulto mayor: perspectiva de curso de vida. Academia Nacional de Medicina de México. ISBN 978-607-443-565-8 Editorial Intersistemas CDMX, México 2015
4 WHO. Increasing RI Coverage by Reducing Missed Opportunities for Vaccination http://www.who.int/immunization/global_vaccine_action_plan/SAGE_GVAP_Assessment_Report_2016_ES.pdf?ua=1
5. O.M.S. Grupo de expertos de la OMS en asesoramiento estratégico sobre inmunización 2016. Examen a mitad de ejecución del plan de acción mundial sobre vacunas. http://www.who.int/immunization/global_vaccine_action_plan/SAGE_GVAP_Assessment_Report_2016_ES.pdf?ua=1
6. Hara M, Okada K, Yamaguchi Y, et al. Immunogenicity and safety after booster vaccination of diphtheria, tetanus, and acellular pertussis in young adults: an open randomized controlled trial in Japan. Clin Vacc Immunol. 2013;20:1799-804.
7. Águas R, Goncalves G, Gomes MGM. Pertussis: increasing disease as a consequence of reducing transmission. Lancet Infect Dis. 2006;6:112-7.
8. Quishui H, Mersola J. Factors contributing to pertussis resurgence. Future Microbiol. 2008;3:329-39.
9. The Joint Commission. Tdap vaccination strategies for adolescents and adults, including health care personnel. Strategies from research and practice. Disponible en: https://www.jointcommission.org/assets/1/6/Tdap_Monograpgh.pdf
10. Kim D, Bridges CB, Harriman K. Advisory Committee on Immunization Practices recommended immunization schedule for adults aged 19 years or older: United States, 2015. Ann Inter Med. 2015;162:214-24.
11. Ward JI, Cherry JD, Chang SJ, et al. Efficacy of an acellular pertussis vaccine among adolescents and adults. N Engl J Med. 2005;353:1555-63.
12. Wei SC, Tatti K, Cushing K, et al. Effectiveness of adolescent and adult tetanus, reduced-dose diphtheria, and acellular pertussis vaccine against pertussis. Clin Infect Dis. 2010;51:315-21.

13. Muñoz FM, Bond NH, Maccato M, et al. Safety and immunogenicity of tetanus, diphtheria and acellular pertussis (Tdap) immunization during pregnancy in mothers and infants: a randomized clinical trial. JAMA. 2014;311:1760-9.
14. Koepke R, Kahn D, Petit A, et al. Centers for Disease Control and Prevention (CDC). Pertussis and influenza vaccination among insured pregnant women – Wisconsin, 2013-2014. MMWR Morb Mortal Wkly Rep. 2015;64:746-50.
15. Farhat F, Wortmann G. Vaccinating adults who are pregnant, older, or immunocompromised, or have chronic kidney disease. Clev Clin J Med. 2015;82:341-7.
16. Trucchi C, Zoppi G. Decennial diphtheria-tetanus adult boosters: are they really necessary? J Prev Med Hyg. 2015;56:E44-8.
17. Hepatitis B. Centro de prensa de la OMS. Nota descriptiva No. 204, 2015.
18. Hou J, Liu Z, Gu F. Epidemiology and prevention of hepatitis B virus infection. Int J Med Sci. 2005;(1):50-7.
19. Kao JH. Hepatitis B vaccination and prevention of hepatocellular carcinoma. Best Pract Res Clin Gastroenterol. 2015;29:907-17.
20. Gruver AL, Hudson LL, Sempowski GD. Immunosenescence of ageing. J Pathol. 2007;211:144-56.
21. Mendy M. Observational study of vaccine efficacy 24 years after the start of hepatitis B vaccination in two Gambian villages: no need for a booster dose. PLOS One. 2013;8:1-9.
22. Dehesa M. Hepatitis B. Rev Gastroenterol Mex. 2013;78(Supl 1):90-2.
23. CDC. Use of hepatitis B vaccination for adults with diabetes mellitus: recommendations of the Advisory Committee on immunization practices (ACIP). MMWR Morb Mortal Wkly Rep. 2011;60:1709-11.
24. INEGI. Los adultos mayores en México. Perfil Sociodemográfico; 2005. p. 107.
25. SS. NOM-036-SSA 2-2012. Prevención y control de enfermedades. Aplicación de vacunas, toxoides, faboterápicos (sueros) en SS, inmunoglobulinas en el humano.
26. SS. Cartilla Nacional de Salud del Adulto Mayor, 2014.
27. Michel JP. Coalition of advocates to vaccinate of Western European citizens aged 60 years and older. Aging Clin Exp Res. 2009:21:1-4.
28. Cunningham AL, Breuer J, Dwyer DE, et al. The prevention and management of herpes zoster. MJA. 2008;188:171-6.
29. Ultsch B, Weidermann F, Reinhold T, Siedler A, Krause G, Wichmann O. Health economic evaluation of vaccination strategies for the prevention of herpes zoster and postherpetic neuralgia in Germany. BMC Health Serv Res. 2013;13:359.
30. Sanford M, Keating GM. Zoster vaccine (Zostavax®). A review of its use in preventing herpes zoster and postherpetic neuralgia in older adults. Drugs Aging. 2010;27:159-76.
31. Arnou R, Fiquet A, Thomas S, Sadorge C. Immunogenicity and safety of ZOSTAVAX® approaching expiry potency in individuals aged ≥ 50 years. Human Vaccines. 2011;7:1060-5.
32. Cohen JI. Herpes zoster. N Engl J Med. 2013;369:255-63.
33. Forbes H, Thomas SL, Langan SM. The epidemiology and prevention of herpes zoster. Curr Derm Rep. 2012;1:39-47.
34. Oxman MN, Levin MJ, Johnson GR, et al. A vaccine to prevent herpes zoster and posherpetic neuralgia in older adults. N Engl J Med. 2005;352:2271-84.
35. Aspinall R, Lang PO. Vaccine responsiveness in the elderly: best practice for the clinic. Expert Rev Vaccines 2014;13:885-94.
36. Schmader K, Levin MJ, Gnann JW, et al. Efficacy, safety and tolerability of herpes zoster vaccine in persons aged 50-59 years. Clin Infect Dis. 2012;54:922-8.
37. Pilkinton MA, Talbot HK. Update on vaccination guidelines for older adults. J Am Geriatr Soc. 2015;63:584-8.
38. Baxter R, Nam TT, Hansen J, et al. Safety of ZostavaxTM - A cohort study in a managed care organization. Vaccine. 2012;30:6636-41.
39. Información para prescribir amplia de Zostavax® (Oka/Merck), 30-04-2009.
40. Advisory Committee Statement (ACS) – National Advisory Committee on Immunization (NACI). Update on the use of herpes zoster vaccine. January 2014. Disponible en: http://www.phac-aspc.gc.ca/naci-ccni/hzv-vcz-eng.php
41. Advisory Committee Statement. Statement on the recommended use of herpes zoster vaccine. CCDR RMTC 2010;36:ACS-1. Disponible en: http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/10vol36/acs-1/index-eng.php
42. Komara FA. Herpes zoster vaccination: benefits and barriers. JAOA. 2009;109(Suppl 2):522-4.
43. Lal H, Cunningham AL, Godeauz O, et al. Efficacy of an adjuvanted herpes zoster subunit vaccine in older adults. N Engl J Med. 2015; 372:2087-96.
44. Geier D, King PG, Geier MR. Influenza vaccine: review of effectiveness of the U.S. Immunization Program, and policy considerations. J Am Phys Surg. 2006;11:69-74.
45. OPS-CDC. Protocolo genérico para la vigilancia de la influenza. Washington D.C.; 2009. Disponible en: http://new.paho.org/hq/dmdocuments/2009/Protocolo_Gen_ESP.pdf
46. Influenza. Documento técnico. Secretaría de Salud, México 2014. Disponible en: http://www.epidemiologia.salud.gob.mx/doctos/lineamientos/influenza/documento_tecnico_influenza.pdf
47. Solórzano-Santos F, Miranda-Novales MG. Influenza. Bol Med Hosp Infant Mex. 2009;66:461-73.
48. Lade KS, Sawant SD, Singh MC. Review on influenza with special emphasis on swine flu. Int J Curr Pharm Res. 2011;3:97-107.
49. Prevención, diagnóstico y tratamiento de la influenza estacional. Guía de evidencias y recomendaciones. México: Secretaría de Salud, CENETEC-Salud; 2015. Fecha de publicación 2 de julio de 2015. Disponible en: www.cenetec.salud.gob.mx/contenidos/gpc/catalogoMaestro
50. Aviso Epidemiológico de Influenza. CONAVE/01/2016/Influenza. Actualización de la situación de influenza durante la temporada 2015-2016. Comité Nacional para la Vigilancia Epidemiológica, 10 de febrero de 2016. Disponible en: https://www.gob.mx/cms/uploads/attachment/file/56389/Aviso_Epi_influenza_130216.pdf
51. Lambert LC, Fauci AS. Influenza vaccines for the future. N Engl J Med. 2010;363:2036-44.
52. Kuri-Morales P, Galván F, Cravioto P, et al. Mortalidad en México por influenza y neumonía (1990-2005). Salud Publica Mex. 2006;48:379-84.
53. Nichol KL, Nordin JD, Nelson DB, et al. Effectiveness of influenza vaccine in the community-dwelling elderly. N Engl J Med. 2007;357:1373-81.
54. Treanor JJ, Talbot HK, Ohmit SE, et al. Effectiveness of seasonal influenza vaccines in the United States during a season with circulation of all three vaccine strains. Clin Infect Dis. 2012;55:951-9.
55. Vacunas autorizadas en México incluyendo fichas técnicas. Comisión Federal para la Protección contra Riesgos Sanitarios. Actualización del 27 de julio de 2015. Secretaría de Salud, 2015.
56. Cartillas Nacionales de Salud. Secretaría de Salud, México 2015. (Consultado el 15 de enero de 2016.) Consultado el 1 de abril de 2017. Disponible en: http://www.gob.mx/salud/articulos/cartillas-nacionales-de-salud-12270
57. Atkinson W, Hamborsky J, McIntyre L, Wolfe S, editores. Centers for Disease Control and Prevention. Epidemiology and prevention of vaccine-preventable diseases. 10th ed. Washington DC: Public Health Foundation; 2007. p. 271-82.
58. OMS. Meningococcal vaccines: position paper, November 2011. Wkly Epidemiol Rec. 2011;47:521-39.
59. CDC. Prevention and control of meningococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Morb Mortal Wkly Rep. 2013;62:1-28.
60. Kim DK, Bridges CB, Harriman KH. Advisory Committee on Immunization Practices recommended immunization schedule for adults aged 19 years or older: United States, 2015. Ann Intern Med. 2015;162:214-25.
61. Consejo Nacional de Vacunación. Vacuna antimeningocócica. En: Manual de Vacunación 2008-2009. México: Secretaría de Salud; 2008. p. 158-63.
62. Almirall J, Bolíbar I, Vidal J, et al. Epidemiology of community-acquired pneumonia in adults: a population-based study. Eur Respir J. 2000;15:757-63vv
63. Millett ER, Quint JK, Smeeth L, et al. Incidence of community-acquired lower respiratory tract infections and pneumonia among older adults in the United Kingdom: a population-based study. PLoS One. 2013;8:e75131.
64. Báez-Saldaña R, Gómez-Zamora C, López-Elizondo C, et al. Neumonía adquirida en la comunidad. Revisión y actualización con una perspectiva orientada a la calidad de la atención médica. Neumol Cir Torax. 2013;72(Supl 1):6-43.
65. Shapiro ED, Berg AT, Austrian R, et.al. The protective efficacy of polyvalent pneumococcal polysaccharide vaccine. N Engl J Med. 1991; 325:1453-60.
66. Ansaldi F, Orsi A, Trucchi C, et al. Potential effect of PCV13 introduction on emergency department accesses for lower respiratory tract infections in elderly and at risk adults. Hum Vaccin Immunother. 2015;11:166-71.
67. Jackson LA, Gurtman A, van Cleeff M, et al. Immunogenicity and safety of a 13-valent pneumococcal conjugate vaccine compared to a 23-valent pneumococcal polysaccharide vaccine in pneumococcal vaccine-naïve adults. Vaccine. 2013;31:3577-84.
68. Kim DD, Bridges CB, Harriman K. Advisory Committee on Immunization Practices recommended immunization schedule for adults aged 19 years or older: United States, 2016. Ann Intern Med. 2016;164:184-94.
69. Lindsey NP, Lehman JA, Staples JE, Fischer M. West Nile virus and other nationally notifiable arboviral diseases – United States, 2014. MMWR Morb Mortal Wkly Rep. 2015;64:929-34.
70. Consejo Nacional de Vacunación. Vacuna polisacárida contra neumococo. En: Manual de Vacunación 2008-2009. México: Secretaría de Salud; 2008. p. 106-10.
71. GlaxoSmithKline Vaccine HPV 007 Study Group; Romanowski B, de Borba PC, Naud PS, et al. Sustained efficacy and immunogenicity of human papillomavirus (HPV)-16/18-adjuvante vaccine: analysis of a randomised placebo-controlled trial up to 6.4 years. Lancet. 2009;374:1975-85.
72. Dochez C, Bogers JJ, Verhelst R, Rees H. HPV vaccines to prevent cervical cancer and genital warts: an update. Vaccine. 2014;32:1595-601.
73. Schwars TF. Clinical update of the AS04-adjuvanted human papillomavirus-16/18 cervical cancer vaccine, Cervarix. Springer Healthcare; septiembre 2009.

74. Vanegas VA, Rubio AI, Bedoya AM, Sánchez GI. Estructura molecular y antigénica de la vacuna contra el virus del papiloma humano 16 (VPH 16). Acta Biol Colomb. 2008;13:37-48.
75. Lizano-Soberón M, Carrillo-García A, Contreras Paredes A. Infección por virus del papiloma humano: epidemiología, historia natural y carcinogénesis. Cancerología. 2009;4:205-16.
76. Bathia N, Lynde C, Vender R, Bourcier M. Understanding genital warts: epidemiology, pathogenesis, and burden of disease of human papillomavirus. J Cutan Med Surg. 2013;17(Suppl 2):S47-54.
77. Draper E, Bissett SL, Howell-Jones R, et al. A randomized, observer-blinded inmunogenicity trial of Cervarix® and Gardasil® human papillomavirus vaccines in 12-15 year old girls. www.plosone.org. 2013;8:e61825.
78. Harper DM. Currently approved prophylactic HPV vaccines. Expert Rev Vaccines. 2009;8:1663-79.
79. Canada Communicable Disease Report. Update on human papillomavirus (HPV) vaccines. CCDR. 2012;38(ACS-1).
80. Dunne EF, Nielson CM, Stone KM, Markowitz LE, Giuliano AR. Prevalence of HPV infection among men: a systematic review of the literature. J Infect Dis. 2006;1994:1044-57.
81. Maleki Z. Human papilloma virus vaccination: review article and an update. World J Obst Gynecol. 2016;5:16-27.
82. Campinis Mart M, Moraga Llop FA. Nuevas perspectivas de la vacunación frente al virus del papiloma humano en la mujer adulta. p.p. 160 -166 y Taller de casos prácticos: Vacunación frente al virus del Papiloma humano en pacientes con infección por el virus de la Inmunodeficiencia humana pp. 255-260 en: Vacunas 2015. http://www.vhebron.net/es/medicina-preventiva
83. Declaración de la FIGO sobre la seguridad de la vacunación del VPH, 2 de agosto de 2013. p. 1-6. Disponible en: http://www.femecog.org.mx/cerca%20de%20ti/VI-FIGO%20Statement.pdf
84. Daron F, Samakoses R, Block SL, et.al. Long-term study of a quadrivalent human papillomavirus vaccine. Pediatrics. 2014;134:e657-65.
85. Wright TC, Huh WK, Monk BJ, Smith JS, Ault K, Herzog TJ. Age considerations when vaccinating against HPV. Gynecol Oncol. 2008;109(2 Suppl):S40-7.
86. Stanley M, Wheeler C. Primary end-points for prophylactic HPV vaccine trials. Chapter 6. HPV VLP vaccines-alternative dosage schedules and immunization in immunosuppressed subjects. Disponible en: https://www.ncbi.nlm.nih.gov/books/NBK304972/
87. Lazcano-Ponce E, Stanley M, Muñoz N, et al. Overcoming barriers to HPV vaccination: non-inferiority of antibody response to human papillomavirus 16/18 vaccine in adolescents vaccinated with a two-dose vs. a three-dose schedule at 21 months. Vaccine. 2014;32:725-32.
88. Programa de Vacunación Universal y Semanas Nacionales de Salud. México: Secretaría de Salud, Lineamientos generales; 2015.
89. Paavonen J, Naud P, Salmerón J, et al. HPV PATRICIA Study Group. Efficacy of human papillomavirus (HPV)-16/18 AS04-adjuvanted vaccine against cervical infection and precancer caused by oncogenic HPV types (PATRICIA): final analysis of a double-blind, randomised study in young women. Lancet. 2009 Jul 25;374(9686):301-14.
90. Einstein MH, Baron M, Levin MJ, et al. Comparison of the immnunogenicity and safety of Cervarix and Gardasil human papillomavirus (HPV) cervical cancer vaccines in healthy women aged 18-45 years. Hum Vaccin. 2009;5:705-19.
91. FDA News Relase. FDA licenses new vaccine for prevention of cervical cancer and other diseases in females by human papillomavirus. June 8, 2006. Disponible en: http://www.fda-gov/bbs/topics/NEWS/2006/NEW01385.
92. Giuliano AR, Isaacs-Soriano K, Torres BN, et al. Immunogenicity and safety of Gardasil among mid-adult aged men (24-45 years) – The MAM Study. Vaccine. 2015;33:5640-6.
93. Dantés HG, Farfán-Ale JA, Sarti E. Epidemiological trends of dengue disease in Mexico (2000-2011): a systematic literature search and analysis. PLoS Negl Trop Dis. 2014;8:e3158.
94. World Health Organization. Global strategy for dengue prevention and control. 2012-2020. Disponible en: http://apps.who.int/iris/bitstream/10665/75303/1/9789241504034_eng.pdf
95. Liu Y, Zhou J, Yu Z, et al. Tetravalent recombinant dengue virus-like particles as potential vaccine candidates: immunological properties. BMC Microbiol. 2014;14:233.
96. Arellano C, Castro L, Díaz-Caravantes RE, et al. Knowledge and beliefs about dengue transmission and their relationship with prevention practices in Hermosillo, Sonora. Front Public Health. 2015;3:142.
97. Secretaría de Salud. Dirección General de Epidemiología – Panorama epidemiológico de fiebre por dengue y fiebre hemorrágica por dengue – Semana epidemiológica 52. 4 de enero de 2016. Disponible en: http://www.epidemiologia.salud.gob.mx/doctos/panodengue/PANORAMAS_2015/Pano_dengue_sem_52_2015.pdf
98. Secretaría de Salud. Guías prácticas clínicas. Manejo del dengue no grave y el dengue grave. 11 de diciembre de 2015. Disponible en: http://www.gob.mx/cms/uploads/attachment/file/37875/SSA_151_08_EyR_Dengue_170310.pdf
99. Valencia-Mendoza A, Danese-dlSantos LG, Sosa-Rubí SG, Aracena-Genao B. Costo-efectividad de prácticas en salud pública: revisión bibliográfica de las intervenciones de la Iniciativa Mesoamericana de Salud. Salud Publica Mex. 2011;53(Supl 3):S375-85.
100. Jelitha R, Nirmalatiban P, Nyanamalar S, Cabriz MG. Descriptive review of safety, reactogenicity and immunogenicity of dengue vaccine clinical trials, 2003-2013. Med J Malaysia. 2015;70:67-75.
101. McArthur MA, Sztein MB, Edelman R. Dengue vaccines: recent developments, ongoing challenges and current candidates. Expert Rev Vaccines. 2013;12:933-53.
102. Capeding MR, Tran NH, Hadinegoro SR, et al. Clinical efficacy and safety of a novel tetravalent dengue vaccine in healthy children in Asia: a phase 3, randomised, observer-masked, placebo-controlled trial. Lancet. 2014;384:1358-65.
103. Hernández-Ávila M, Lazcano-Ponce E, Hernández-Ávila JE, et al. Análisis de la evidencia sobre eficacia y seguridad de la vacuna de dengue CYD-TDV y su potencial registro e implementación en el Programa de Vacunación Universal de México. Salud Publica Mex. 2016;58:71-83.
104. Comisión Federal para la Protección contra Riesgos Sanitarios. México aprueba la primera vacuna contra el virus del dengue a nivel mundial. Comunicado de prensa 106/15. 9 de diciembre de 2015. Disponible en: http://www.cofepris.gob.mx/Documents/NotasPrincipales/09122015.pdf
105. Summary of the April 2016 Meeting of the Strategic Advisory Group of Experts on Immunization (SAGE). Ginebra, Suiza. Disponible en: http://www.who.int/immunization/sage/meetings/2016/april/SAGE_April_2016_Meeting_Web_summary.pdf?ua=1
106. Hadinegoro SR, Arredondo-García JL, Capeding MR, et al. Efficacy and long-term safety of a dengue vaccine in regions of endemic disease. N Engl J Med. 2015;373:1195-206.
107. Villar L, Dayan GH, Arredondo-García JL. Tornieporth N, Saville M, Noriega F; CYD15 Study Group. Efficacy of a tetravalent dengue vaccine in children in Latin America. N Engl J Med. 2015 Jan 8;372(2):113-23. doi: 10.1056/NEJMoa1411037. Epub 2014 Nov 3.