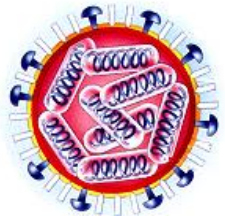
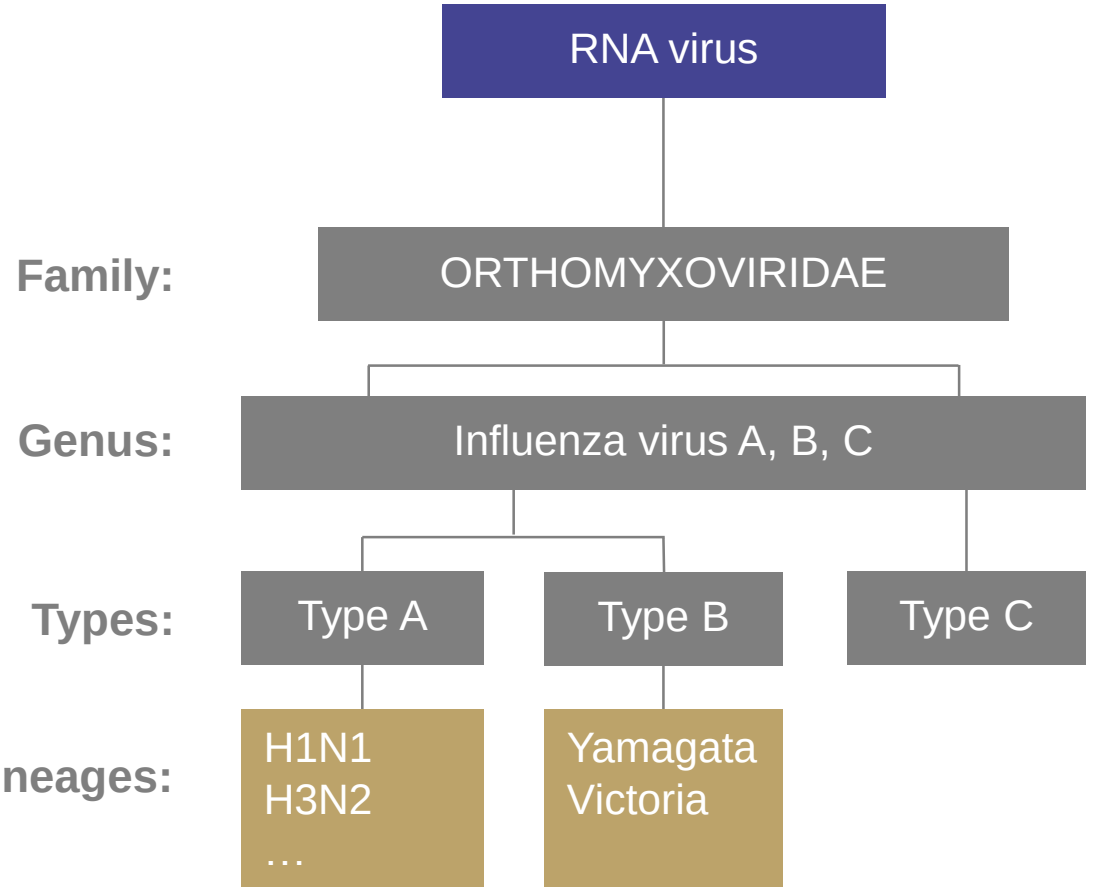
واکسن

دکتر بابک عبدی نیا
فوق تخصص عفونی کودکان ،استاد دانشگاه علوم پزشکی تبریز



Influenza Virus

Influenza virus classification[1,2]

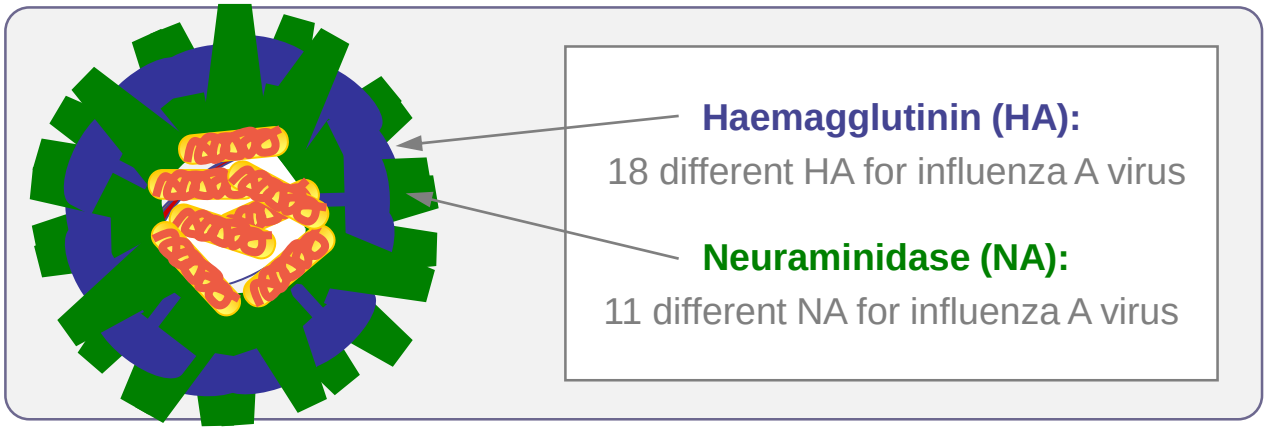


References: 1. Kingsbury DW. Virology, 2nd edition, New York; 1990. p. 1076-87 **2.** Keiji Fukuda et al, Vaccines, 2004

Constant and rapid genetic evolution of influenza[1]

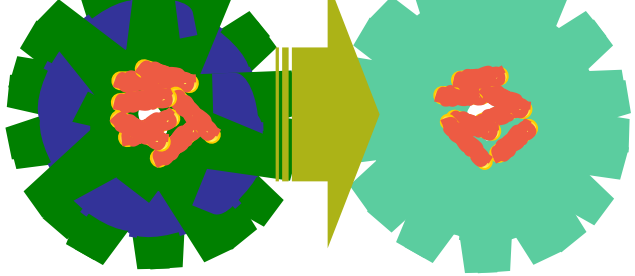
Surface antigens of influenza viruses change:

- Antigenic **drift**:
  - **Minor changes** associated with annual outbreaks or epidemics
  - Impact : updating vaccine yearly to match predicted strains that will be circulating
- Antigenic **shift**:
  - **Major changes** resulting in new subtype with a new HA protein (and sometimes NA)
  - Can lead to pandemics

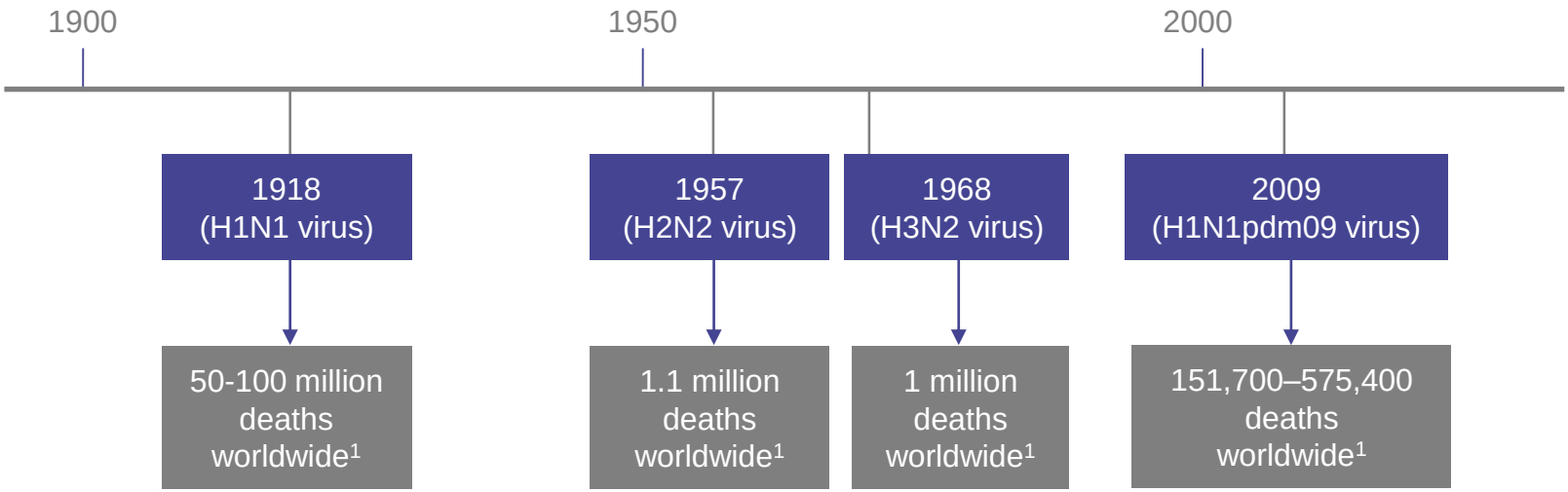


Reference: 1. ECDC Fact Sheet for Health Professionals http://ecdc.europa.eu/en/healthtopics/seasonal_influenza/basic_facts/Pages/factsheet_professionals_seasonal_influenza.aspx

Genetic shift can lead to an influenza pandemic



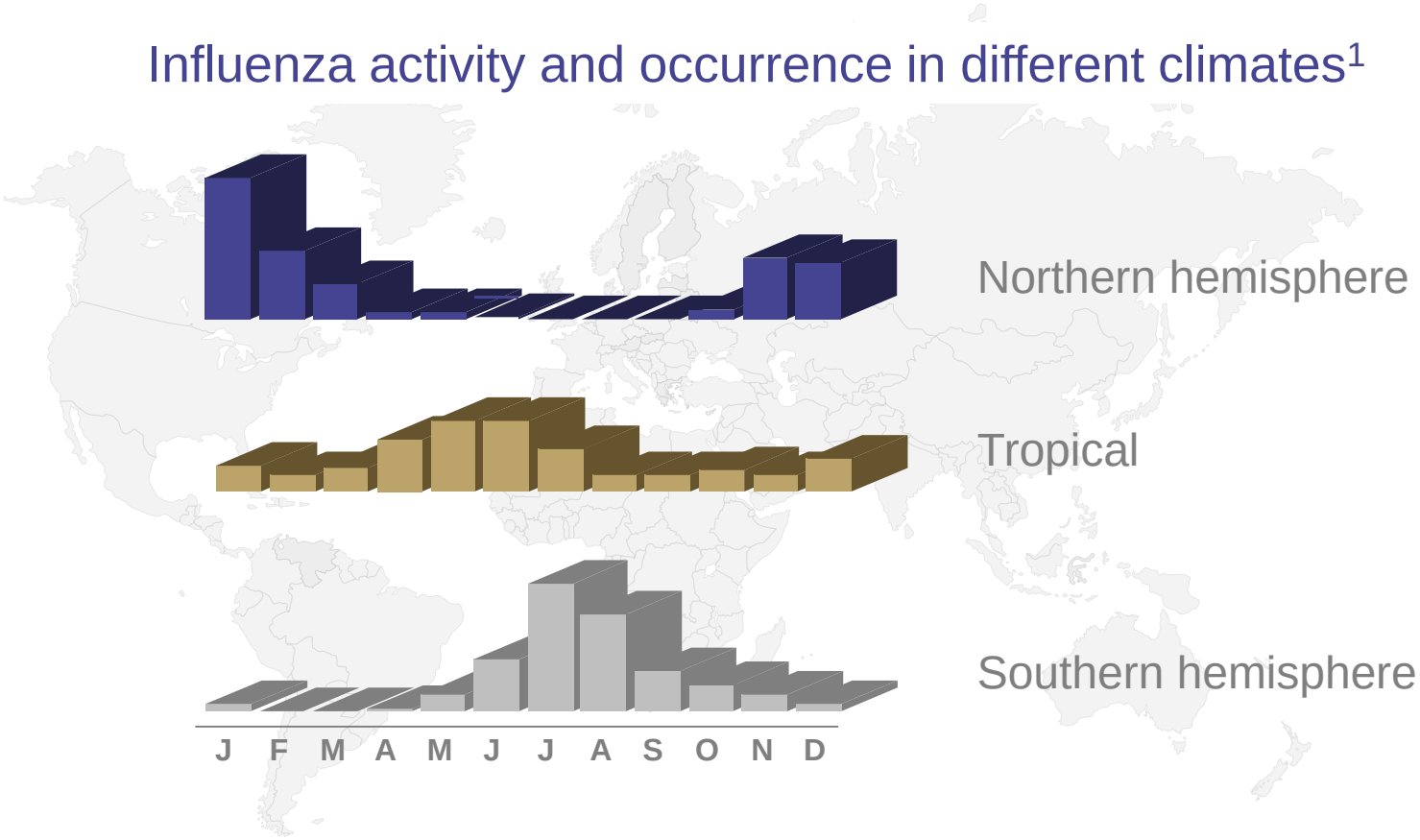
- Pandemics are rare:[1]
  - Re-assortment resulting in a viable influenza A virus with the ability to infect humans is rare
  - Only four in the last hundred years[1]



Reference: 1. CDC:Pandemic influenza (http://www.cdc.gov/flu/pandemic-resources/basics/past-pandemics.html)

Influenza seasonality

Influenza activity and occurrence in different climates[1]



Temperate climates: yearly winter epidemics

Tropical climates: year-round transmission with several peaks

Reference: 1. WHO. Influenza (Seasonal). Fact SheetNo.211 http://www.who.int/mediacentre/factsheets/fs211/en/

Influenza is a respiratory disease

Symptoms of influenza:

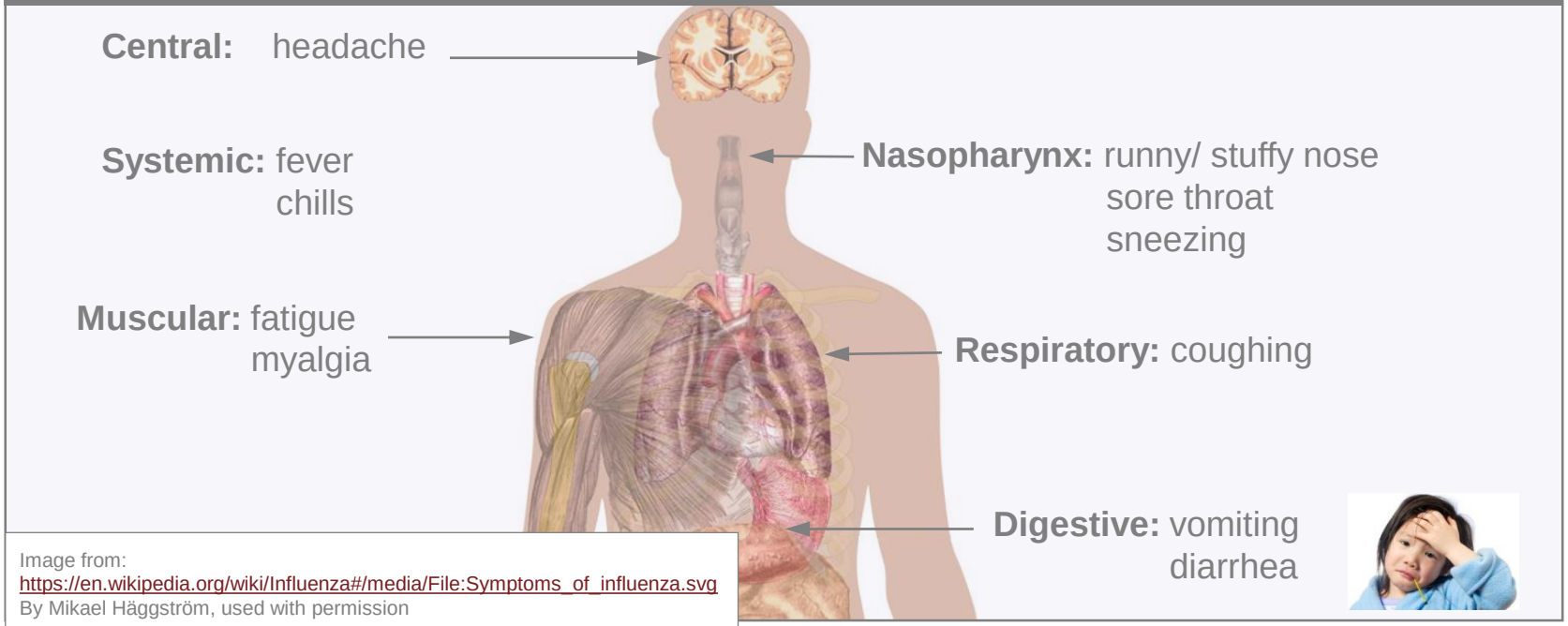


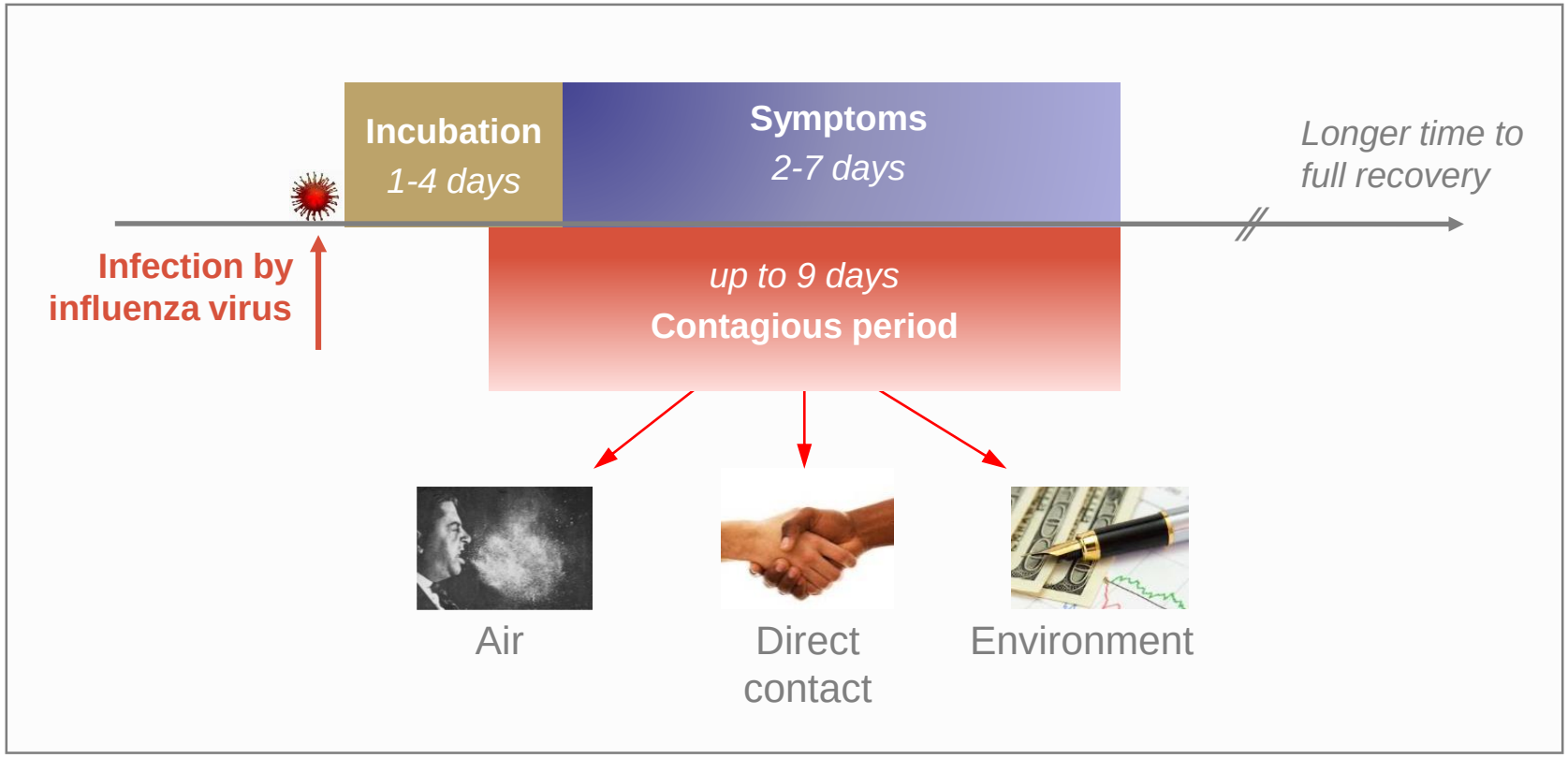
Image from:
https://en.wikipedia.org/wiki/Influenza#/media/File:Symptoms_of_influenza.svg
By Mikael Häggström, used with permission

Influenza vs common cold

Influenza and cold have similar influenza-like symptoms but in general influenza is worse than the common cold, and symptoms such as fever, body aches, extreme tiredness, and dry cough are more common and intense with more rapid onset. People with colds are more likely to have a runny or stuffy nose. Colds generally do not result in serious health problems such as pneumonia, bacterial infections, or hospitalizations.[1,2]

Reference: 1. CDC: Seasonal flu; Questions and Answers (http://www.cdc.gov/flu/about/qa/coldflu.htm) **2.** CDC: Seasonal flu: Flu & You (https://www.cdc.gov/flu/consumer/symptoms.htm)

Influenza is a highly transmissible viral disease



Reference: 1. CDC: Seasonal flu; Clinical signs and symptoms of influenza (https://www.cdc.gov/flu/professionals/acip/clinical.htm)

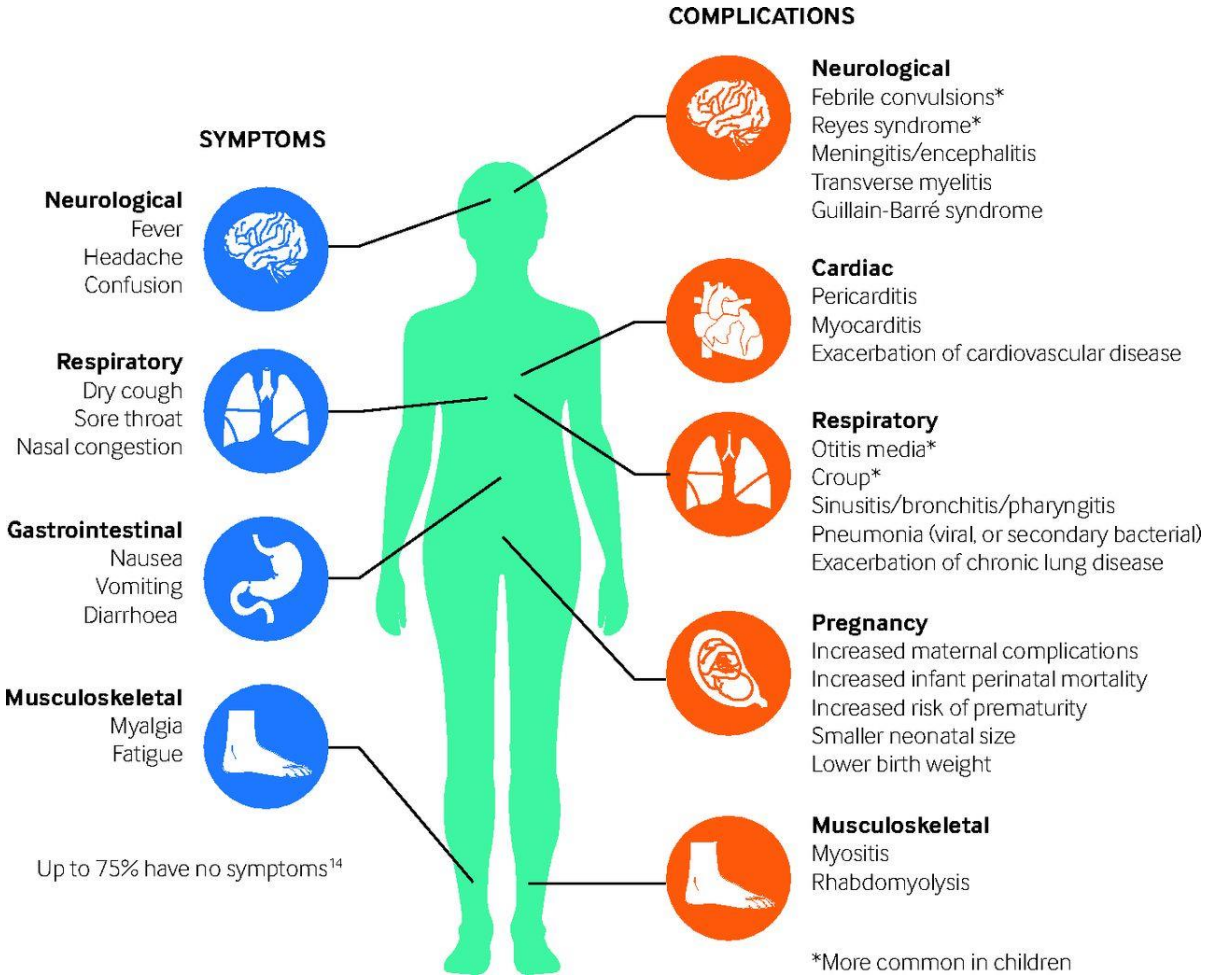
Main clinical features of influenza infections

- Not all people infected will present with all the symptoms
  - During a typical season up to ~75% of infected people are asymptomatic[1]
- The disease can be mild to very severe
  - Severity depends on the virus, host factors, and other factors, e.g. access to care[1]
- Flu is not easily distinguished from other acute respiratory influenza-like illnesses without laboratory testing
- Influenza complications
  - Bacterial superinfections (e.g. pneumonia), decompensation of chronic diseases, deaths (mainly among high-risk groups : the very young, elderly or chronically ill)
- Case management
  - Symptomatic treatment:
  - Antivirals may be used for hospitalized persons or at high risk of influenza complications[2]

References: **1.** ECDC Fact Sheet for Health Professionals http://ecdc.europa.eu/en/healthtopics/seasonal_influenza/basic_facts/Pages/factsheet_professionals_seasonal_influenza.aspx **2.** CDC: Seasonal influenza. Antiviral drugs (http://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm l)

Symptoms and complications of Influenza

- Influenza is characterized by sudden onset of fever, myalgia, headache, malaise, dry cough, sore throat, and nasal congestion Gastrointestinal symptoms including nausea, vomiting and diarrhea are also common.
- Influenza can cause severe illness or death, particularly in high risk populations



Reference: 1. S Ghebrehewet, *BMJ 2016;355:i6258* http://www.bmj.com/content/355/bmj.i625

A frequent and serious disease leading to heavy public health burden (WHO data)

ANNUAL ATTACK RATE[1]

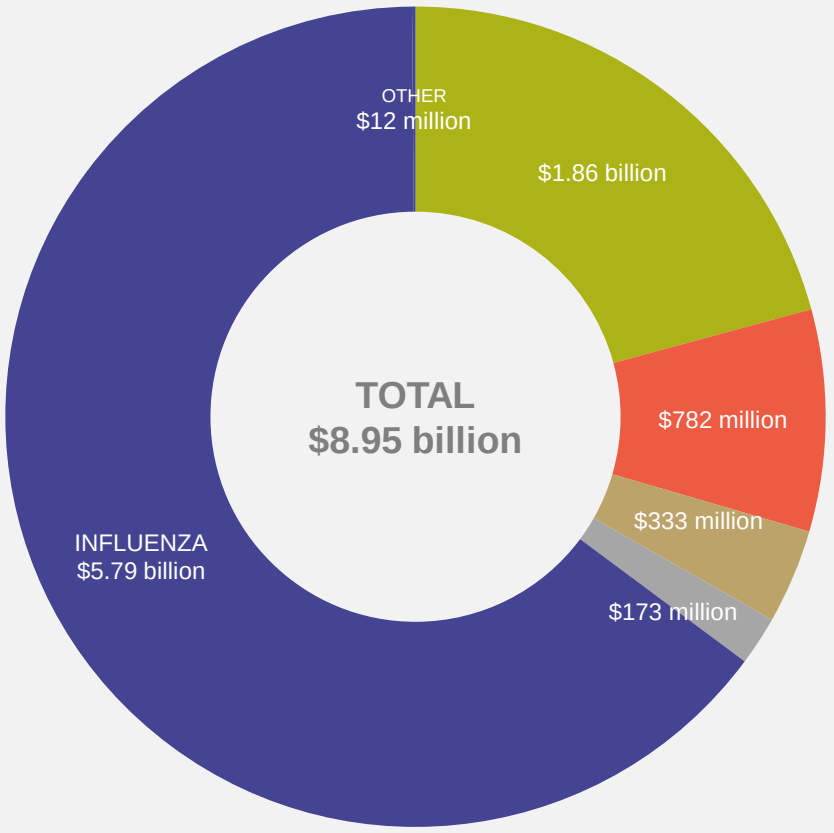
- **5–10% in adults**
- **20–30% in children**

3 TO 5 MILLION CASES OF SEVERE ILLNESS[2]

290,000TO 650,000 ESTIMATED DEATHS EVERY YEAR WORLDWIDE[2]

References: 1. WHO (http://www.who.int/biologicals/vaccines/influenza/en/) **2.** WHO Fact Sheet Nov 2016 (http://www.who.int/mediacentre/factsheets/fs211/en/)

In the US, influenza accounts for 65% of the annual economic burden of vaccine-preventable diseases[1]



Pneumococcal disease $1.86 billion

Meningitis 1%
Sepsis 4%
Pneumonia 95%

Herpes Zoster $782 million

Postherpetic neuralgia 9%
Complicated 9%
Uncomplicated 82%

HPV $333 million

Vulvar cancer 1%
Vaginal cancer 1%
Carcinoma in situ of cervix 4%
Anal cancer 4%
Cervical cancer 27%
Genital warts 63%

Hepatitis B $173 million

Chronic hepatitis1%
Cirrhosis 3%
Acute hepatitis B 12%
Liver cancer 84%

Image from: Ozawa S, et al. Health Aff (Millwood). 2016;35(11):2124

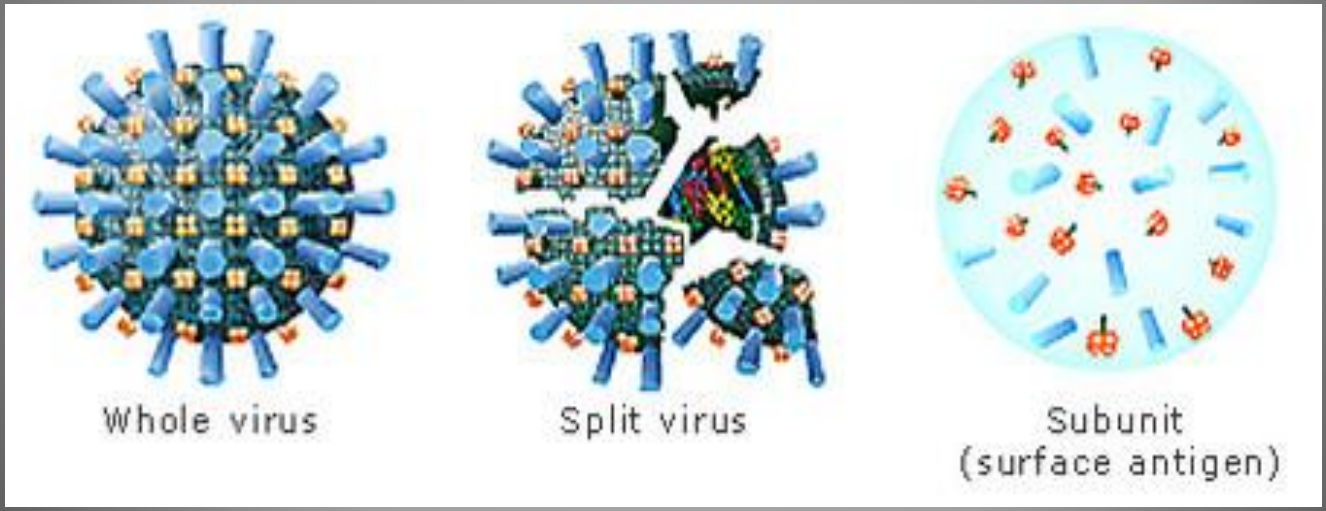
Reference: 1. Ozawa S, *et al. Health Aff (Millwood)* 2016; 35(11):2124

Children are recommended by WHO for influenza vaccination (1/2)

- Influenza infection is highest in children, affecting 20–30% of the total pediatric population[1]
- Influenza is a burdensome disease in children
  - Considerable number of children need hospitalization
  - Up to 10% of all admitted children need management in the intensive care unit (especially children <2 years of age)[3]
- Children may die from influenza
  - At least 28,000 to 111,500 deaths in children younger than 5 years attributable to influenza-associated acute lower respiratory infections per year in the world[2]

References: 1. . WHO. Weekly epidemiological record No. 47, 2012, 87(47):461 (http://www.who.int/wer/2012/wer8747.pdf.) **2**. Nair H, *et al. Lancet.* 2011;378(9807):1917 **3.** Kobbe R.. Vaccine. 2015;33(49):6967

Types of Inactivated Influenza Vaccines



http://www.ifpma.org/resources/influenza-vaccines/influenza-vaccines/about-influenza-vaccine.html

Trivalent versus Quadrivalent Influenza Vaccines

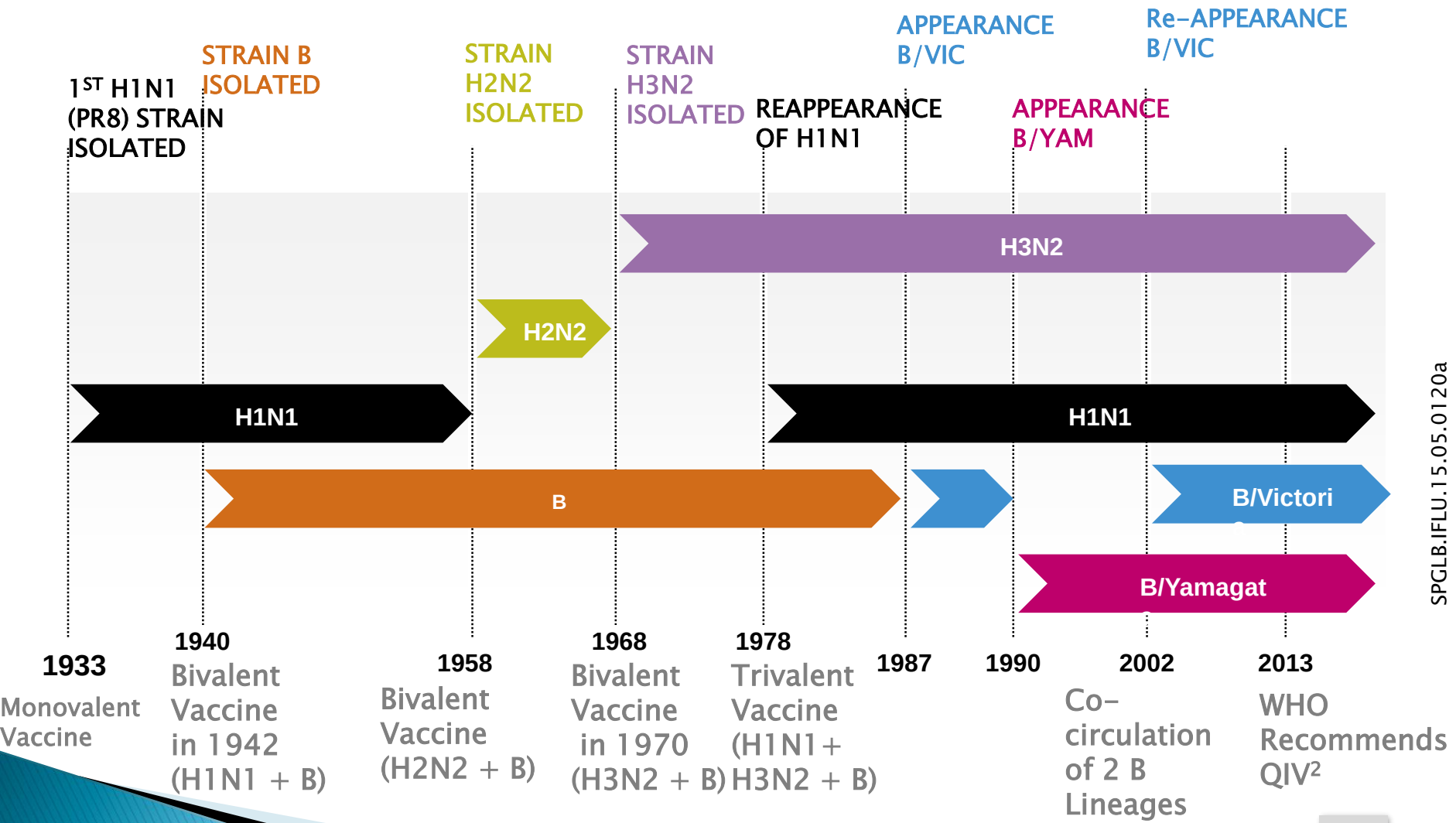
TIV

1. A(H3N2)
2. A(H1N1)pdm09
3. B/Yamagata or B/Victoria

QIV

1. A(H3N2)
2. A(H1N1)pdm09
3. B/Yamagata
4. B/Victoria

Vaccine Composition and Influenza Virus Evolution



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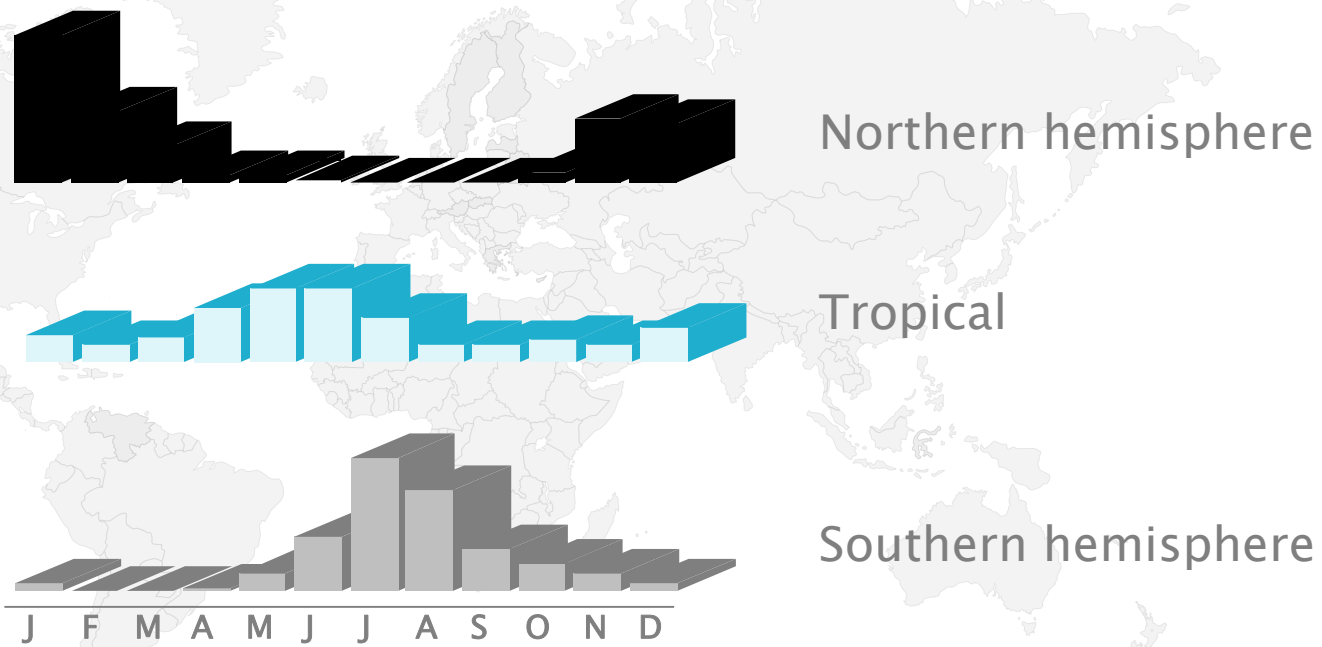
1) Hannoun, Expert rev. Vaccines 12(9), 1085-1094 (2013)
2) http://www.who.int/influenza/vaccines/virus/recommendations/2013_14_north/en/

BACK

Influenza seasonality

Influenza activity and occurrence in different climates[1]



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Tropical climates: year-round transmission with several peaks

Reference: 1. WHO. Influenza (Seasonal). Fact Sheet No. 211 http://www.who.int/mediacentre/factsheets/fs211/en/

WHO position

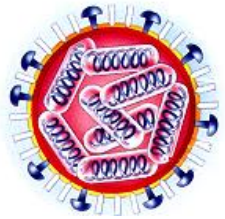
"The most effective way to prevent the disease is vaccination.

Safe and effective vaccines are available
and have been used for more than 60 years.

Among healthy adults, influenza vaccine provides
protection, even when circulating viruses may
not exactly match the vaccine viruses."

– *WHO, Nov. 2016*[1]

Reference: 1. WHO Media Center Fact Sheet Nov. 2016 (http://www.who.int/mediacentre/factsheets/fs211/en/)



Who should be vaccinated?

WHO recommendations for influenza vaccination

WHO Recommends[1]

- People at high risk of complications:
  - Pregnant women (highest priority)
  - Children aged 6 months to 5 years:
    - Children aged 6–23 months of age
    - Children aged 2–5 years of age
  - Elderly people (≥65 years of age)
  - People with underlying health conditions (diabetes, asthma, chronic heart or lung diseases, HIV/AIDS)
  - International travelers with any of the above
- People at high risk of exposure and/or capable of transmitting influenza to those at high risk of influenza related complications:
  - Healthcare workers

Reference: 1. WHO. Weekly epidemiological record No. 47, 2012, 87(47):461 (http://www.who.int/wer/2012/wer8747.pdf.)

Overall conclusion

- Seasonal influenza
  - A significant disease causing considerable morbidity in all age groups and mortality in WHO recommended groups
  - A public health problem with significant socioeconomic implications
- Vaccination
  - The most effective way to prevent influenza infection and severe outcomes
  - Composition updated twice yearly due to rapid evolution of the influenza viruses
- The main challenges are to improve vaccine coverage rate and performance
- Influenza vaccine performance is under constant improvement
  - QIV: New standard of care for all age groups to match influenza virus evolution
  - HD: Proposing a proven solution adapted to the elderly population

واکسن پنوموکوک کونژوگه

Conjugated Pneumococcal vaccine

- Active immunisation for the prevention of invasive disease, pneumonia and acute otitis media caused by Streptococcus pneumoniae in infants
- and children from 6 weeks to 17 years of age.

- The use of Prevenar 13 should be determined on the basis of official recommendations taking into consideration the impact of invasive disease and pneumonia in different age groups as well as the variability of serotype epidemiology in different geographical areas.

- The recommended immunisation series consists of four doses. The primary infant series consists of three doses, with the first dose usually given at 2 months of age and with an interval of at least 1 month between doses. The first dose may be given as early as six weeks of age. The fourth (booster) dose is recommended between 11 and 15 months of age.

Preterm infants (< 37 weeks gestation)

- In preterm infants, the recommended immunisation series consists of four doses, each of 0.5 ml. The primary infant series consists of three doses, with the first dose given at 2 months of age and with an interval of at least 1 month between doses. The first dose may be given as early as six weeks of age. The fourth (booster) dose is recommended between 11 and 15 months of age.

Unvaccinated infants and children ≥ 7 months of age

- Two doses, with an interval of at least 1 month between doses. A third dose is recommended in the second year of life.
- Children aged 12-23 months: Two doses, with an interval of at least 2
- months between doses.

  Children and adolescents aged 2-17 years: One single dose.

Children aged 12-59 months

- Children who are considered completely immunised with Prevenar (7-valent) should received one dose of 0.5ml of Prevenar 13 to elicit immune responses to the additional 6 serotypes. This dose of Prevenar 13 should be administered at least 8 weeks after the final dose of Prevenar (7-valent)