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ALDO MORO

CORSO DI IGIENE

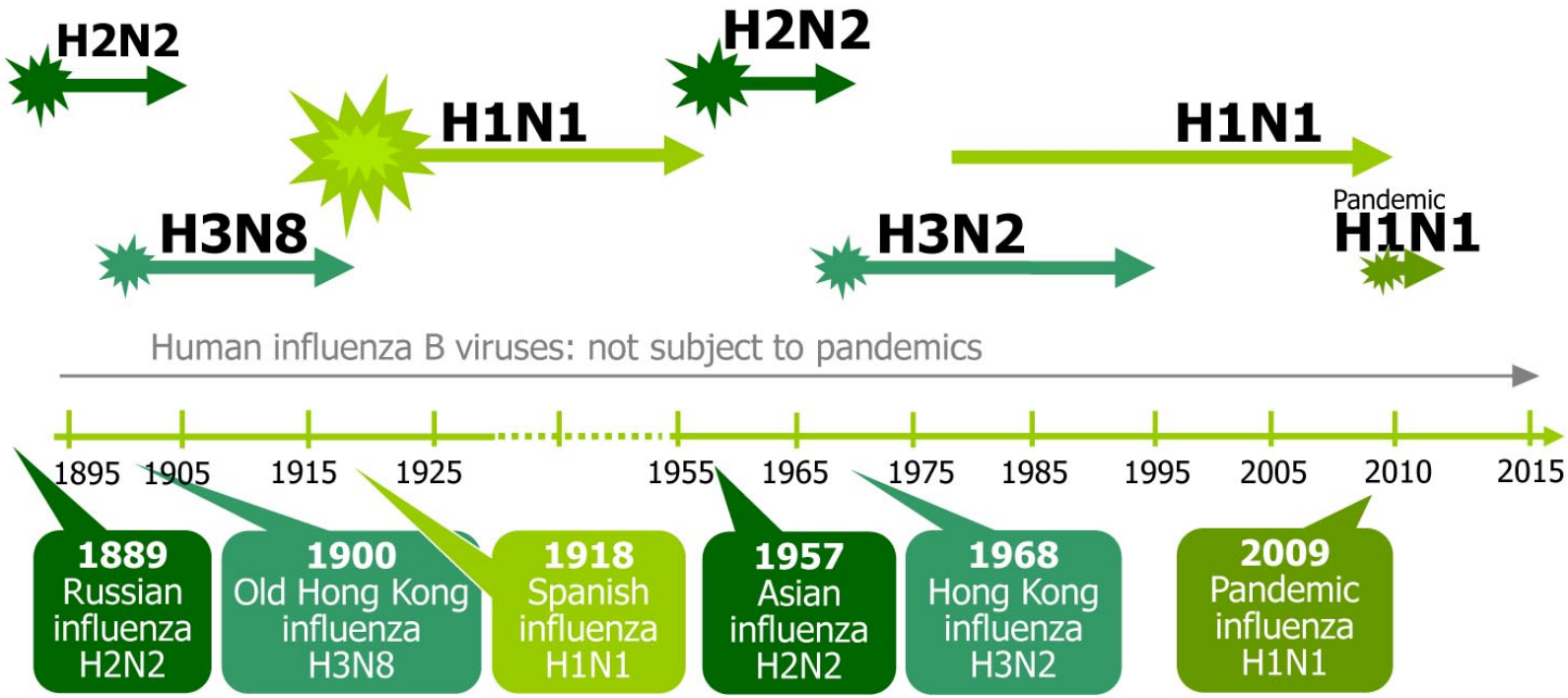
Scuola
di
Medicina

Influenza

Influenza

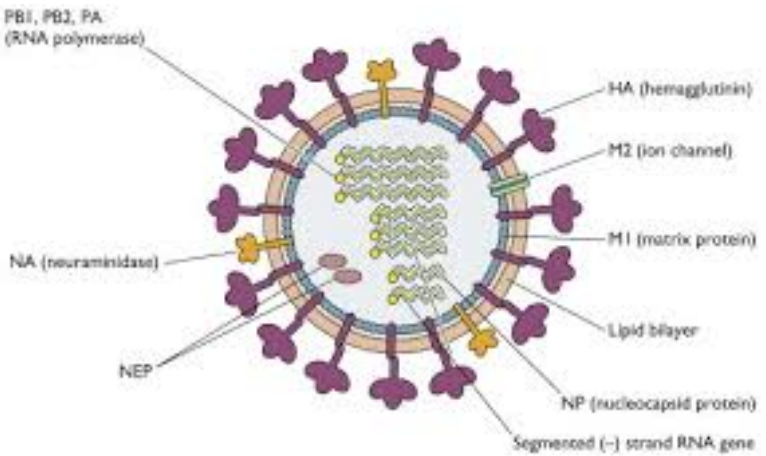
- Highly infectious viral illness
- First pandemic in 1580
- At least 4 pandemics in 19th century
- Estimated 21 million deaths worldwide in pandemic of 1918-1919
- Virus first isolated in 1933

Influenza pandemic in the recent history



Influenza Virus

- Single-stranded RNA virus
- Orthomyxoviridae family
- 3 types: A, B, C
- Subtypes of type A determined by hemagglutinin and neuraminidase



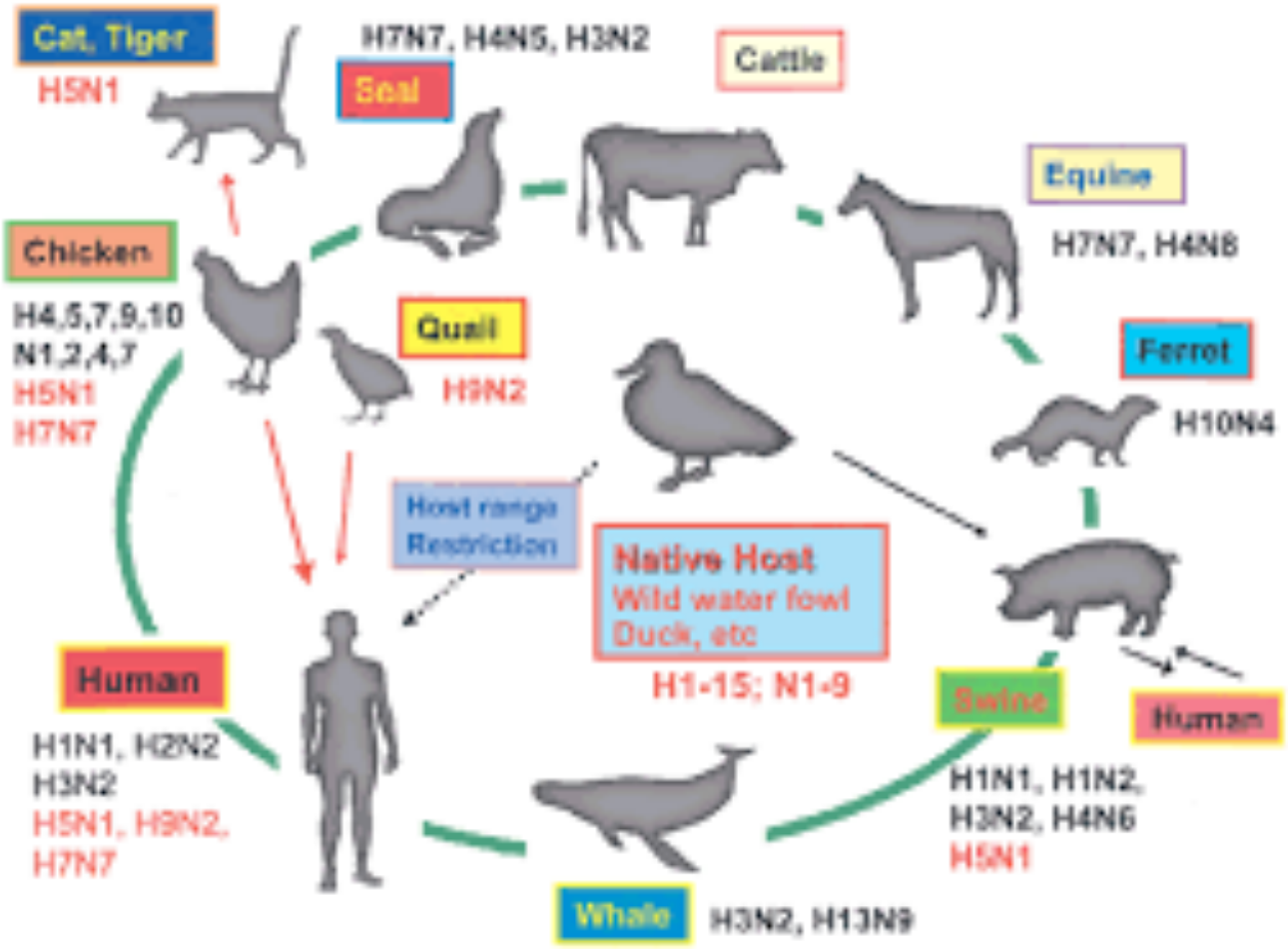
Influenza Antigenic Changes

- Antigenic Drift
  - minor change, same subtype
  - caused by point mutations in gene
  - may result in epidemic
- Antigenic Shift
  - major change, new subtype
  - caused by exchange of gene segments
  - may result in pandemic

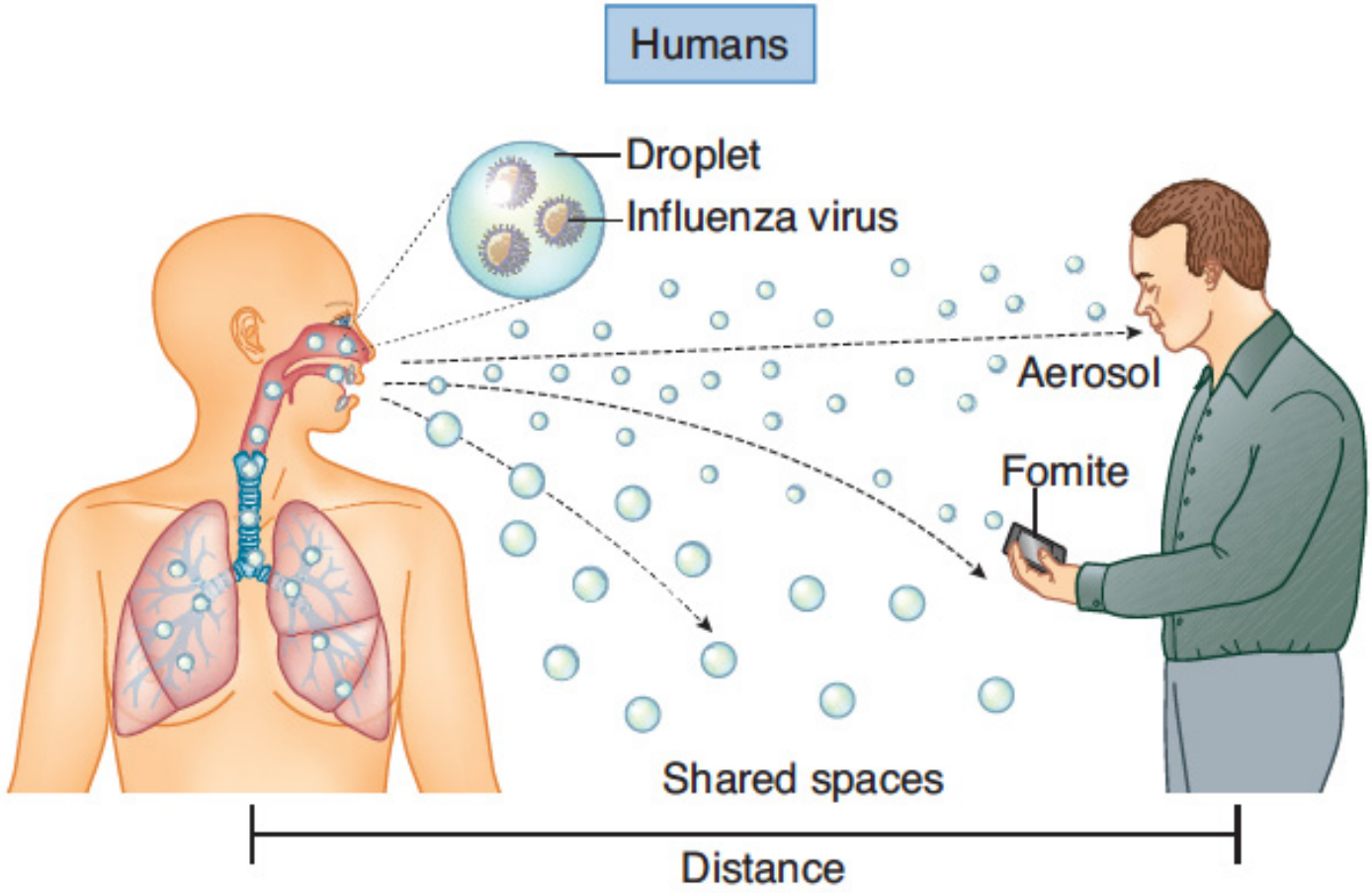
Influenza Virus Strains

- Type A-moderate to severe illness
  - all age groups
  - humans and other animals
  - **Drift and shift**
- Type B-milder disease
  - primarily affects children
  - humans only
  - **Only drift**
- Type C-rarely reported in humans
  - no epidemics
  - **Only drift**

The antigenic shift



The pandemic strains
Contagion



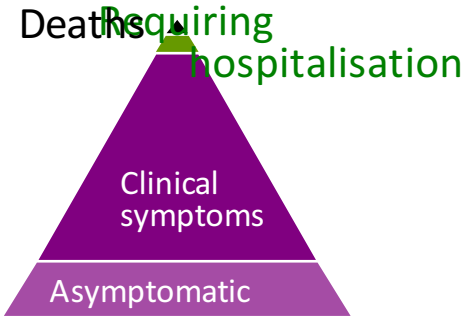
The pandemic strains
Virulence

		
Watery eyes and sinuses and swelling of the head.	Cyanosis of the shanks.	Haemorrhages of the trachea.
Larmoiement et gonflement de la tête.	Cyanose des pattes.	Hémorragies trachéales.

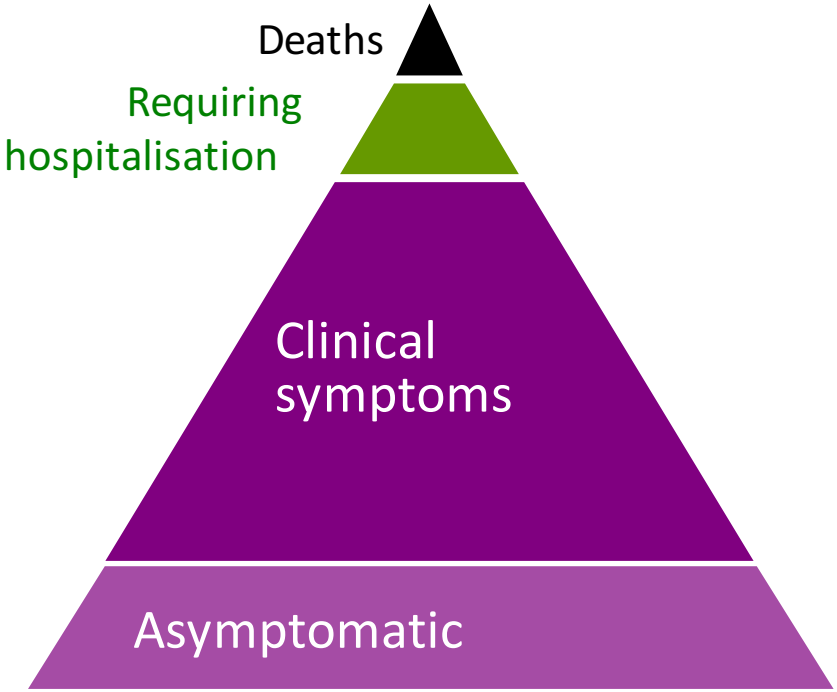
2009 Influenza A(H1N1)

- In April 2009 a novel influenza A(H1N1) virus appeared and quickly spread across North America
- By May 2009 the virus had spread to many areas of the world
- Cause of the first influenza pandemic since 1968
- Pandemic monovalent influenza vaccine produced and deployed in nationwide vaccination campaign

Seasonal influenza compared to pandemic — proportions of types of cases



Seasonal influenza



Pandemic

ECDC

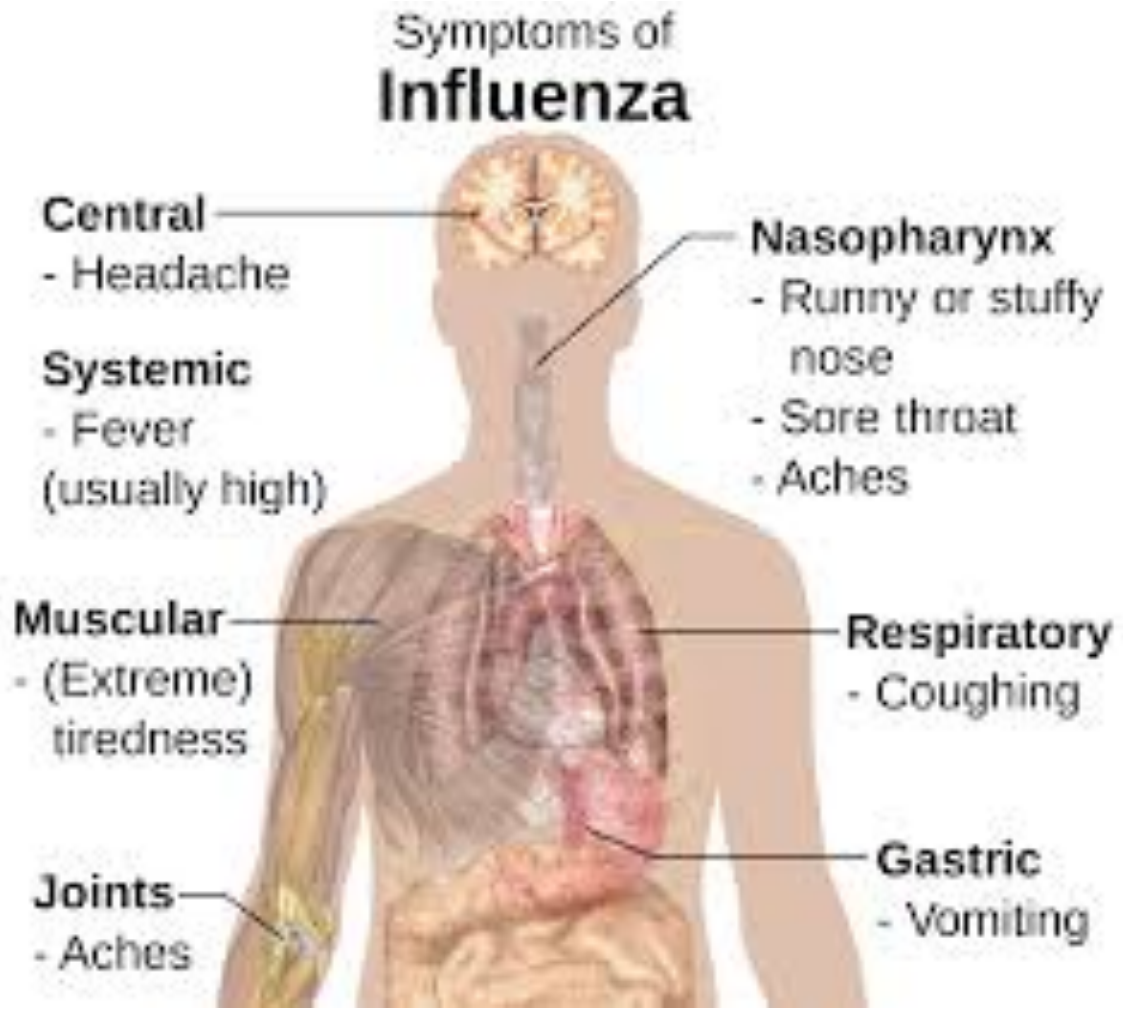
Influenza Pathogenesis

- Respiratory transmission of virus
- Replication in respiratory epithelium with subsequent destruction of cells
- Viremia rarely documented
- Virus shed in respiratory secretions for 5-10 days

Influenza Clinical Features

- Incubation period 2 days (range 1-4 days)
- 50% of infected persons develop classic symptoms
- Abrupt onset of
  - fever
  - myalgia
  - sore throat
  - nonproductive cough
  - headache

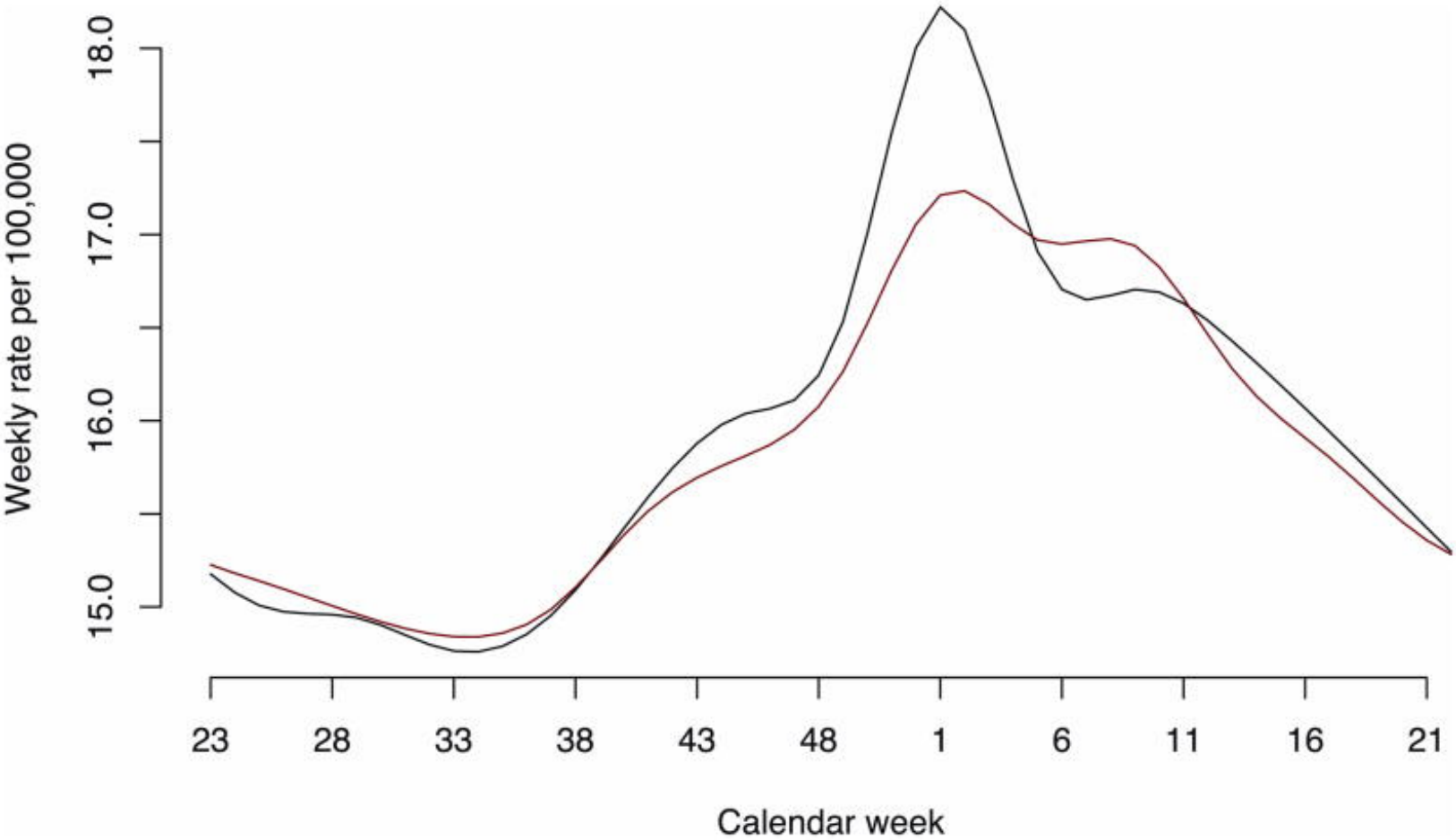
Influenza Clinical Features



Influenza Complications

- Pneumonia
  - secondary bacterial
  - primary influenza viral
- Reye syndrome
- Myocarditis
- Death is reported than less than 1 per 1,000 cases

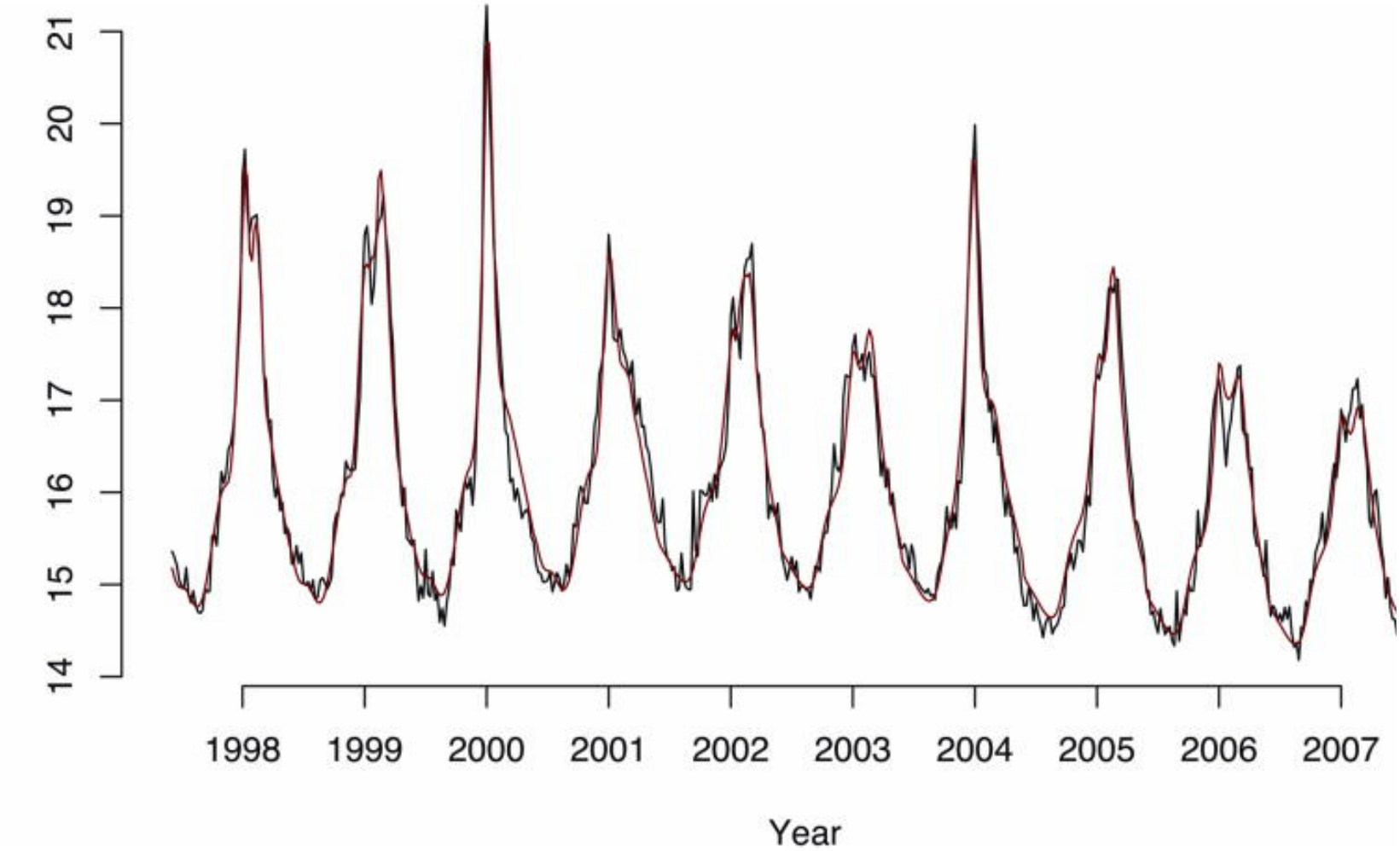
Annual all-cause mortality baselines



Base1: seasons 1997–1998 through 2000–2001; Base2: seasons 2001–2002 through 2006–2007.

Salmerón D, J Public Health (Oxf). 2013

All-cause mortality trend



Salmerón D, J Public Health (Oxf). 2013

JAMA. 2000 Jan 26;283(4):499-505.

Impact of respiratory virus infections on persons with chronic underlying conditions.

Glezen WP[1], Greenberg SB, Atmar RL, Piedra PA, Couch RB.

Author information

Abstract

CONTEXT: While hospitalization rates have declined overall, hospitalizations for acute lower respiratory tract infections have increased steadily since 1980. Development of new approaches for prevention of acute respiratory tract conditions requires studies of the etiologies of infections and quantification of the risk of hospitalization for vulnerable patients.

OBJECTIVE: To determine the frequency of specific virus infections associated with acute respiratory tract conditions leading to hospitalization of chronically ill patients.

DESIGN: Analysis of viral etiology of patients hospitalized with acute respiratory tract conditions between July 1991 and June 1995.

SETTING: Four large clinics and related hospitals serving diverse populations representative of Harris County, Texas.

PATIENTS: A total of 1029 patients who were hospitalized for pneumonia, tracheobronchitis, bronchiolitis, croup, exacerbations of asthma or chronic obstructive pulmonary disease, and/or congestive heart failure.

MAIN OUTCOME MEASURE: Virus infection, defined by culture, antigen detection, and significant rise in serum antibodies, by underlying condition; hospitalization rates by low- vs middle-income status.

RESULTS: Ninety-three percent of patients older than 5 years had a chronic underlying condition; a chronic pulmonary condition was most common. Patients with chronic pulmonary disease from low-income populations were hospitalized at a rate of 398.6 per 10000, almost 8 times higher than the rate for patients from middle-income groups (52.2 per 10000; P<.001). Of the 403 patients (44.4% of adults and 32.3% of children) who submitted convalescent serum specimens for antibody testing, respiratory tract virus infections were detected in 181 (44.9%). Influenza, parainfluenza, and respiratory syncytial virus (RSV) infections accounted for 75% of all virus infections.

CONCLUSIONS: Our study suggests that respiratory virus infections commonly trigger serious acute respiratory conditions that result in hospitalization of patients with chronic underlying conditions, highlighting the need for development of effective vaccines for these viruses, especially for parainfluenza and RSV.

Impact of Influenza-United States, 1976-2007

- The number of influenza associated deaths varies substantially by year, influenza virus type and subtype, and age group
- Annual influenza-associated deaths ranged from 3,349 (1985-86 season) to 48,614 (2003-04 season), with an average of **23,607 annual deaths**
- Persons **65 years of age and older** account for approximately 90% of deaths
- 2.7 times more deaths occurred during seasons when A(H3N2) viruses were prominent

Impact of Influenza-United States

- Highest rates of complications and hospitalization among persons 65 years and older, young children, and persons of any age with certain underlying **medical conditions**
- Average of more than **200,000 influenza-related excess hospitalizations**
- 37% of hospitalizations among persons younger than 65 years of age
- Greater number of hospitalizations during years that A(H3N2) is predominant

Risk factors for influenza A (H1N1)-associated pneumonia on hospitalized people

Asthma	12.19	5.18-28.72
Cardiovascular disease	5.19	1.94-13.90
Chronic renal disease	2.14	1.02-4.53
Chronic hepatic diseases	5.26	1.40-19.81
Allergy	2.54	1.64-3.93

Xu CL et al, 2012

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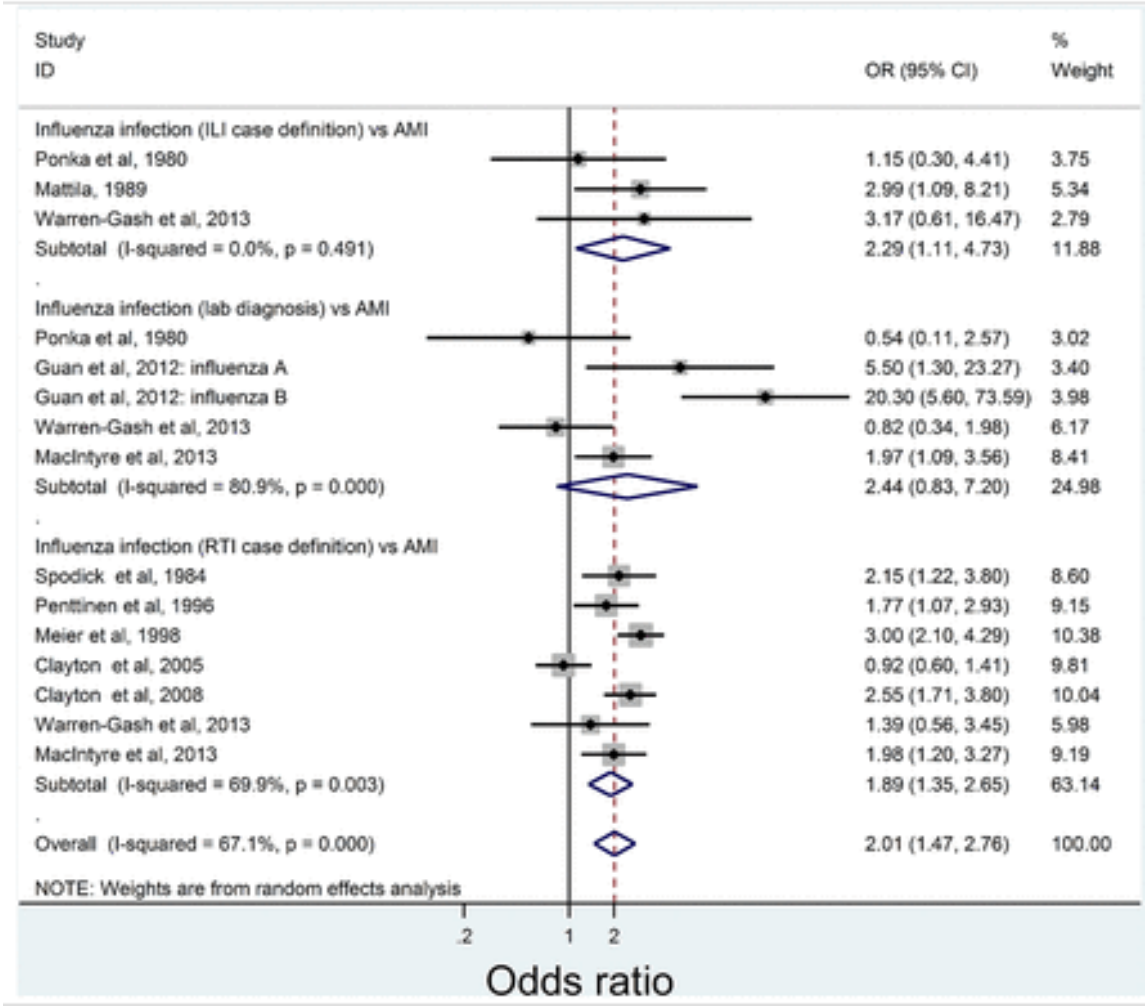
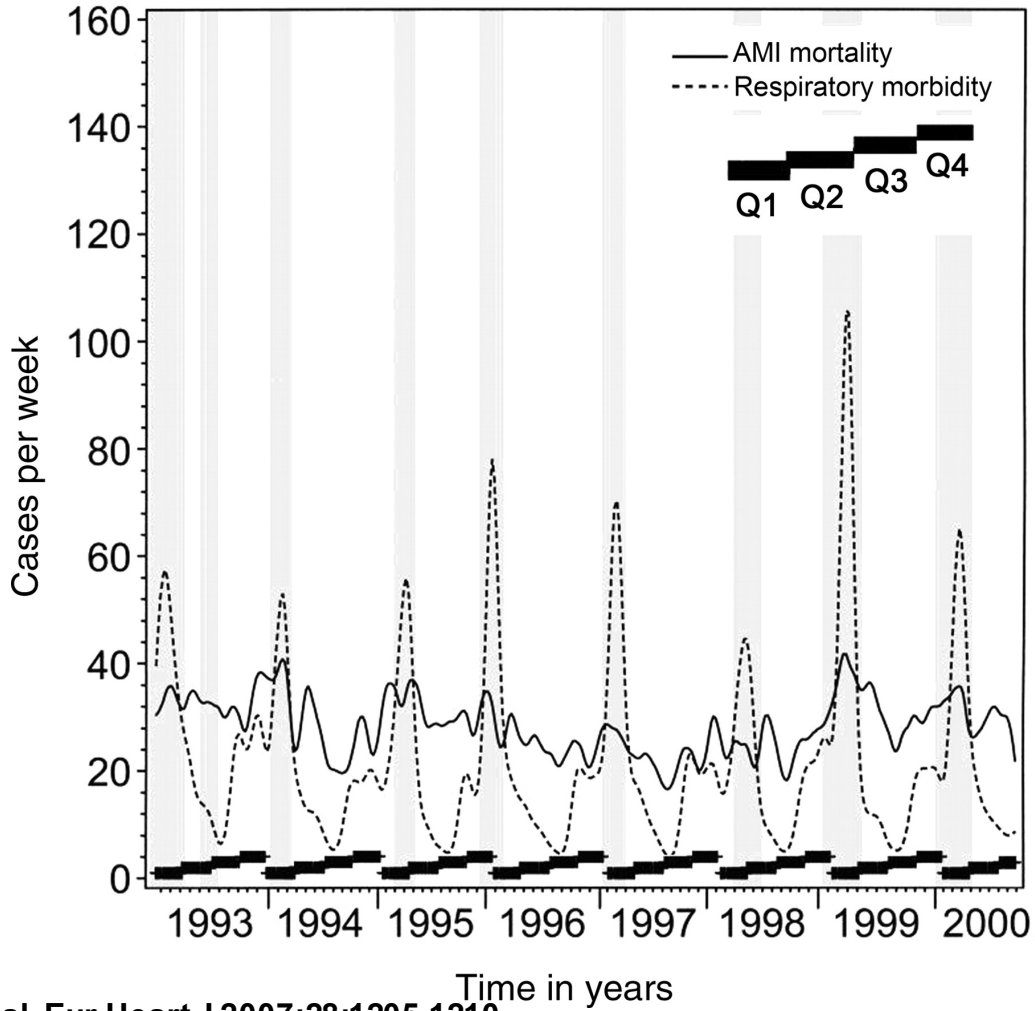
Acute myocardial infarction and influenza: a meta-analysis of case–control studies



Barnes M et al, Hearth 2015

Smoothed data plot of deaths due to acute myocardial infarction and morbidity from acute respiratory disease from 1993 to 2000 in the whole study population.



Mohammad Madjid et al. Eur Heart J 2007;28:1205-1210

European Heart Journal

Case Rep Cardiol. 2015;2015:738146. Epub 2015 Nov 5.

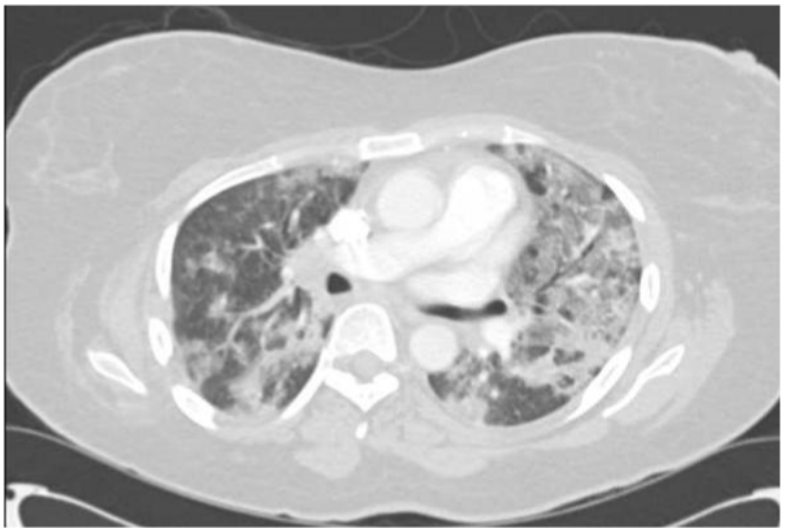
Influenza Induced Cardiomyopathy: An Unusual Cause of Hypoxemia.

Quddus A[1], Afari ME[1], Minami T[2].

⊕ Author information

Abstract

Influenza has considerable burden on public health funds. The complications of influenza can be devastating. We present a case of a 42-year-old woman with history of asthma who presented to the emergency room in winter with shortness of breath and general malaise and was found to be in hypoxemic respiratory failure. She was diagnosed with influenza and workup revealed severely depressed systolic cardiac function (ejection fraction of 25%). She was treated with oseltamivir and diuresis and regained cardiac function within a week. We review the pathophysiology and management of influenza induced cardiomyopathy.



Influenza Among School-Aged Children

- School-aged children
  - typically have the highest attack rates during community outbreaks of influenza
  - serve as a major source of transmission of influenza within communities

Influenza Diagnosis

- Clinical and epidemiological characteristics
- Isolation of influenza virus from clinical specimen (e.g., throat, nasopharynx, sputum)
- Significant rise in influenza IgG by serologic assay

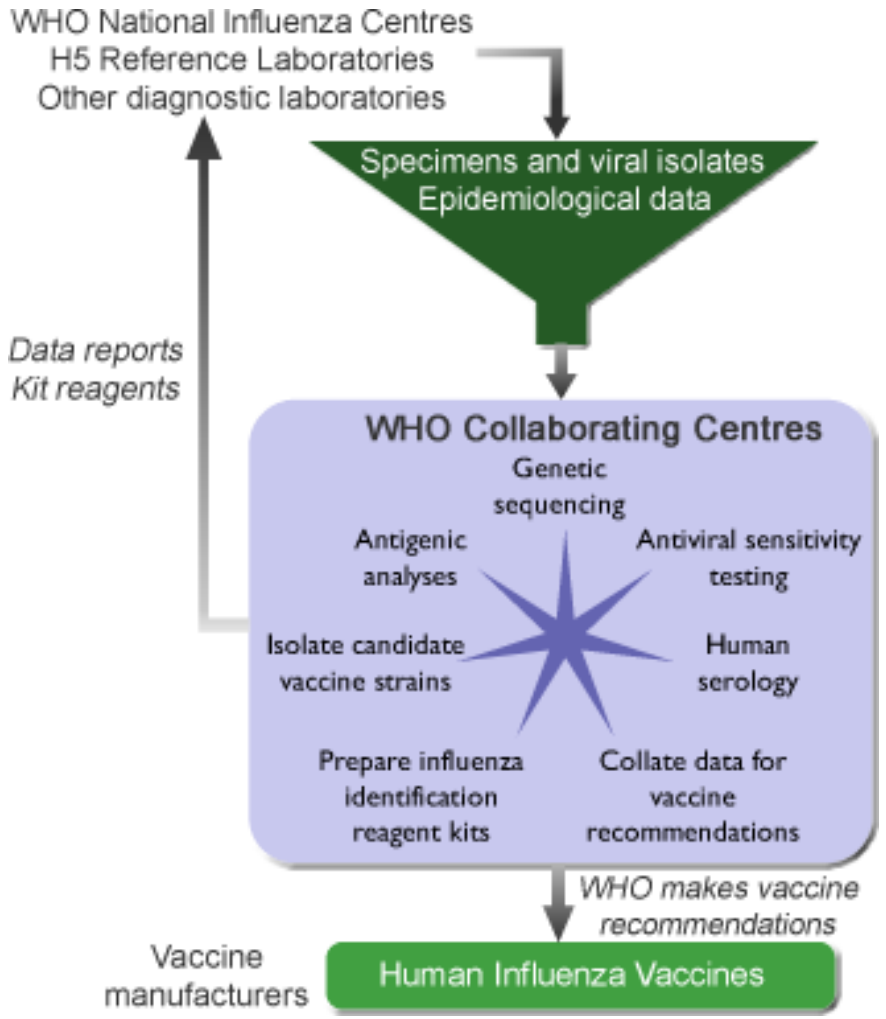
Influenza Epidemiology

- Reservoir
  - human, animals (type A only)
- Transmission
  - Respiratory
  - probably airborne
- Temporal pattern
  - peak December – March in temperate climate
  - may occur earlier or later
- Communicability
  - 1 day before to 5 days after onset (adults)

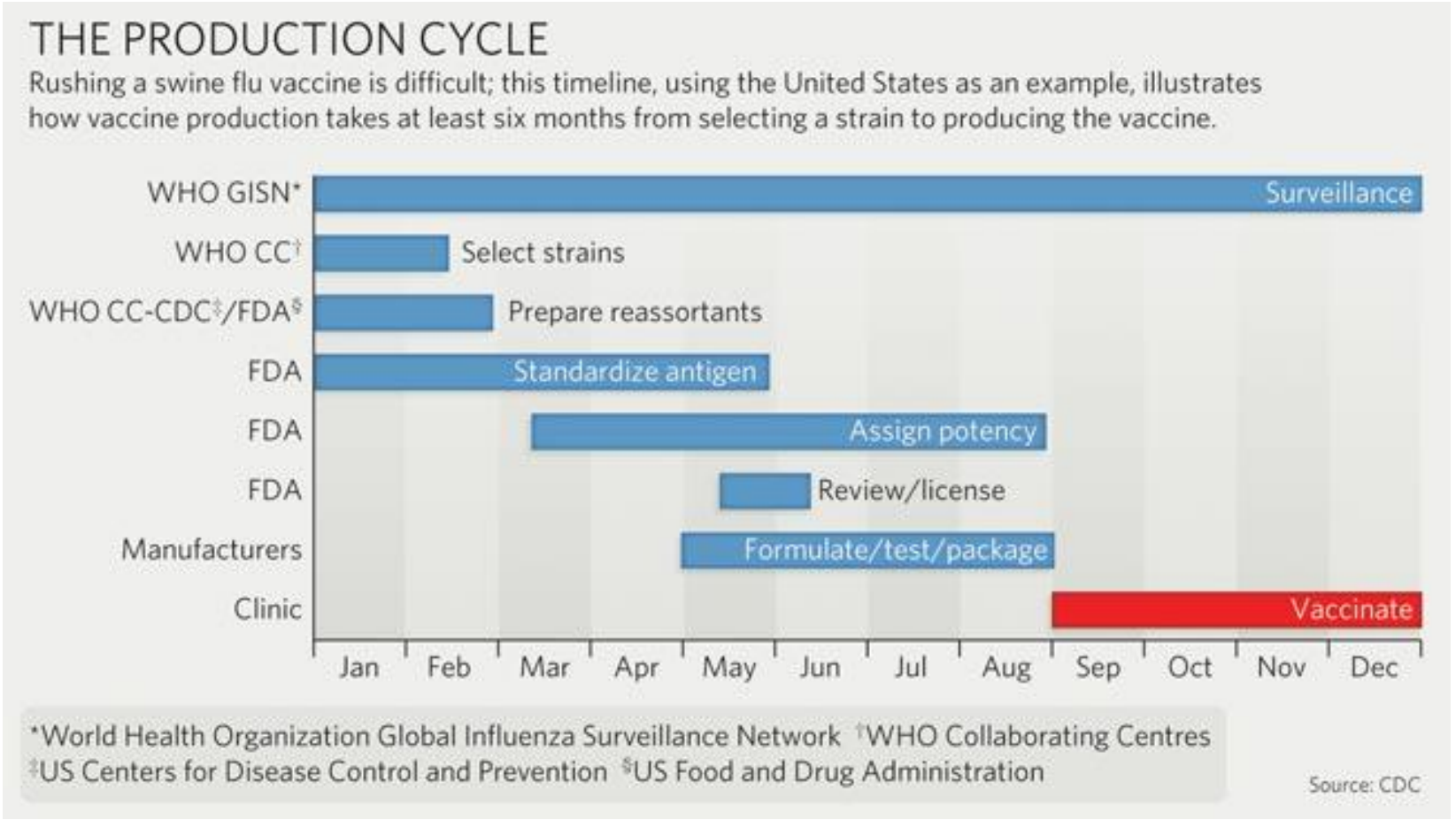
Influenza Vaccines

- Inactivated subunit (IIV)
  - intramuscular or intradermal
- Live attenuated vaccine (LAIV)
  - intranasal

Influenza vaccine production



Influenza vaccine production



Influenza official recommendations WHO

Influenza

Recommended composition of influenza virus vaccines for use in the 2016-2017 northern hemisphere influenza season

25 February 2016

It is recommended that trivalent vaccines for use in the 2016-2017 influenza season (northern hemisphere winter) contain the following:

- an A/California/7/2009 (H1N1)pdm09-like virus;
- an A/Hong Kong/4801/2014 (H3N2)-like virus;
- a B/Brisbane/60/2008-like virus.

It is recommended that quadrivalent vaccines containing two influenza B viruses contain the above three viruses and a B/Phuket/3073/2013-like virus.

Transmission of LAIV Virus

- LAIV replicates in the nasopharyngeal mucosa
- Vaccinated children can shed vaccine viruses in nasopharyngeal secretions for up to 3 weeks
- One instance of transmission of vaccine virus to a contact has been documented

Inactivated Influenza Vaccine Efficacy

- About **60%** effective among healthy persons younger than 65 years of age
- 50-60% effective in preventing hospitalization among elderly persons
- **80% effective in preventing death among elderly persons**

LAIV Efficacy in Healthy Children

- 87% effective against culture-confirmed influenza in children 60 – 84 months old
- 27% reduction in febrile otitis media (OM)
- 28% reduction in OM with accompanying antibiotic use
- Decreased fever and OM in vaccine recipients who developed influenza

Inactivated Influenza Vaccine Recommendations

- Advisory Committee on Immunization Practices recommends annual influenza vaccination for all persons 6 months of age and older
- Protection of **persons at higher risk** for influenza related complications should continue to be a focus of vaccination efforts as providers and programs transition to routine vaccination of all persons aged 6 months and older

Inactivated Influenza Vaccine Recommendations

When vaccine supply is limited, vaccination efforts should focus on delivering vaccination to the following groups of persons:

- children 6 months through 4 years (59 months) of age
- persons 50 years and older
- **persons with chronic pulmonary (including asthma), cardiovascular (except hypertension), renal, hepatic, neurologic, hematologic, or metabolic disorders (including diabetes mellitus)**
- persons who are **immunosuppressed** (including immunosuppression caused by medications or by human immunodeficiency virus)
- women who are or will be **pregnant during the influenza season**

Inactivated Influenza Vaccine Recommendations

- children 6 months through 18 years of age and receiving long-term aspirin therapy and who therefore might be at risk for experiencing Reye syndrome after influenza virus infection
- **residents of nursing homes and other chronic-care facilities**
- American Indians/Alaska Natives
- persons who are morbidly obese (body-mass index is 40 or greater)
- **healthcare personnel**
- household contacts and caregivers of children younger than 5 years of age and adults 50 years of age or older, with particular emphasis on vaccinating contacts of children aged younger than 6 months
- household contacts and caregivers of persons with medical conditions that put them at higher risk for severe complications from influenza

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Pregnancy and Inactivated Influenza Vaccine

- Risk of hospitalization 4 times higher than non-pregnant women
- Risk of complications comparable to nonpregnant women with high-risk medical conditions
- **Vaccination (with IIV) recommended if pregnant during influenza season**
- **Vaccination can occur during any trimester**

THE LANCET

Volume 355, Issue 9198, 8 January 2000, Pages 93–97

Effects of influenza vaccination of health-care workers on mortality of elderly people in long-term care: a randomised controlled trial

Influenza vaccine uptake in health-care workers was 50·9% in hospitals in which they were routinely offered vaccine, compared with 4·9% in those in which they were not. The uncorrected rate of mortality in patients was 102 (13·6%) of 749 in vaccine hospitals compared with 154 (22·4%) of 688 in no-vaccine hospitals (odds ratio 0·58 [95% CI 0·40–0·84], p=0·014). The two groups did not differ for proportions of patients positive for influenza infection (5·4% and 6·7%, respectively); at necropsy, PCR was positive in none of 17 patients from vaccine hospitals and six (20%) of 30 from novaccine hospitals (p=0·055).

Carman et al, Lancet 2000

thebmj

Effectiveness of an influenza vaccine programme for care home staff to prevent death, morbidity, and health service use among residents: cluster randomised controlled trial

Conclusions Vaccinating care home staff against influenza can prevent deaths, health service use, and influenza-like illness in residents during periods of moderate influenza activity.

Hayward et al, 2006

Influenza vaccination of health care workers in long-term-care hospitals reduces the mortality of elderly patients.

Vaccination of HCWs was associated with ***reductions*** *in* ***total patient mortality*** *from 17% to 10% (odds ratio [OR], 0.56; 95% confidence interval [CI], 0.40-0.80) and* ***in influenza-like illness*** *(OR, 0.57; 95% CI, 0.34-0.94).*

Potter J et al, J Infect Dis 1997

HIV Infection and Inactivated Influenza Vaccine

- Persons with HIV at increased risk of complications of influenza
- IIV induces protective antibody titers in many HIV-infected persons
- IIV will benefit many HIV-infected person

Simultaneous Administration of LAIV and Other Vaccines

- Inactivated vaccines can be administered either simultaneously or at any time before or after LAIV
- Other live vaccines can be administered on the same day as LAIV
- Live vaccines not administered on the same day should be administered at least 4 weeks apart

Inactivated Influenza Vaccine Contraindications and Precautions

- Severe allergic reaction (e.g., anaphylaxis) to a vaccine component or following a prior dose of inactivated influenza
- Moderate or severe acute illness
- History of Guillain-Barré syndrome (GBS) within 6 weeks following a previous dose of influenza vaccine

Relationship between Guillain-Barré syndrome, influenza-related hospitalizations, and influenza vaccine coverage

- GBS hospitalizations demonstrated a seasonal pattern with winter months having higher rates compared to the month of June.
- **P&I hospitalization rates** were significantly correlated with **hospitalization rates for GBS.**
- **Vaccine coverage did not significantly affect the rates of GBS hospitalization at the population level.**

Iqbal S et al, Vaccine 2015

Live Attenuated Influenza Vaccine Contraindications and Precautions

- Children younger than 2 years of age, or 50 years of age and older*
- Persons with chronic medical conditions*
- Children and adolescents receiving long-term aspirin or aspirin-containing therapy*
- Immunosuppression from any cause*
- Pregnant women*
- History of egg allergy*
- History of severe allergic reaction following dose of influenza vaccine

Live Attenuated Influenza Vaccine Contraindications and Precautions

- Severe allergy to vaccine component
- History of Guillain Barré syndrome (GBS) within 6 weeks following a previous dose of influenza vaccine
- Children younger than 5 years with recurrent
- wheezing*
- Recent wheezing
- Persons with asthma*
- Persons who care for severely immunosuppressed persons requiring protective environment for 7 days after receipt
- Persons who have taken influenza antiviral medications within previous 48 hours
- Moderate or severe acute illness

Influenza Vaccine Adverse Events

- IIV
  - local reactions – common
  - Guillain-Barré syndrome – expected to be greater among persons with a history of GBS than among persons with no history of GBS
- LAIV
  - nonspecific systemic symptoms – common

Inactivated Influenza Vaccine Adverse Reactions

- Local reactions (soreness, redness)
  - 15%-20%
- Fever, malaise, myalgia
  - less than 1%
- Allergic reactions (hives, angioedema, anaphylaxis)
  - rare

Live Attenuated Influenza Vaccine Adverse Reactions

- Children
  - no significant increase in URI symptoms, fever, or other systemic symptoms
  - increased risk of wheezing in children 6-23 months of age
- Adults
  - significantly increased rate of cough, runny nose, nasal congestion, sore throat, and chills reported among vaccine recipients
  - no increase in the occurrence of fever
- No serious adverse reactions identifie

Influenza Antiviral Agents

- Amantadine and rimantadine
  - Not recommended because of documented resistance in U.S. influenza isolates
- **Zanamivir and oseltamivir**
  - neuraminidase inhibitors
  - effective against influenza A and B
- **oseltamavir and zanamavir approved for prophylaxis**

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Influenza Surveillance

- Monitor prevalence of circulating strains and detect new strains
- Estimate influenza-related morbidity, mortality and economic loss
- Rapidly detect outbreaks
- Assist disease control through rapid preventive action