Tracking the 2009 Novel (H1N1) Influenza Pandemic: Surveillance and Epidemiology

Center for Infectious Diseases & Emergency Readiness

Tomás Aragón, MD, DrPH
UC Berkeley School of Public Health
http://www.idready.org (cider)
http://www.medepi.com (tja)
Email: aragon@berkeley.edu

November 1, 2009

Outline

How do I know I have the flu?

- fever*
- cough
- sore throat
- runny or stuffy nose
- body aches
- headache
- chills
- fatigue
- sometimes diarrhea and vomiting

*Its important to note that not everyone with flu will have a fever.

What should I do if I get sick?

If you get sick with flu-like symptoms this flu season, you should stay home and avoid contact with other people except to get medical care. Most people with 2009 H1N1 have had mild illness and have not needed medical care or antiviral drugs and the same is true of seasonal flu.

However, some people are more likely to get flu complications and they should talk to a health care provider about whether they need to be examined if they get flu symptoms this season.

Who is more likely to get flu complications?

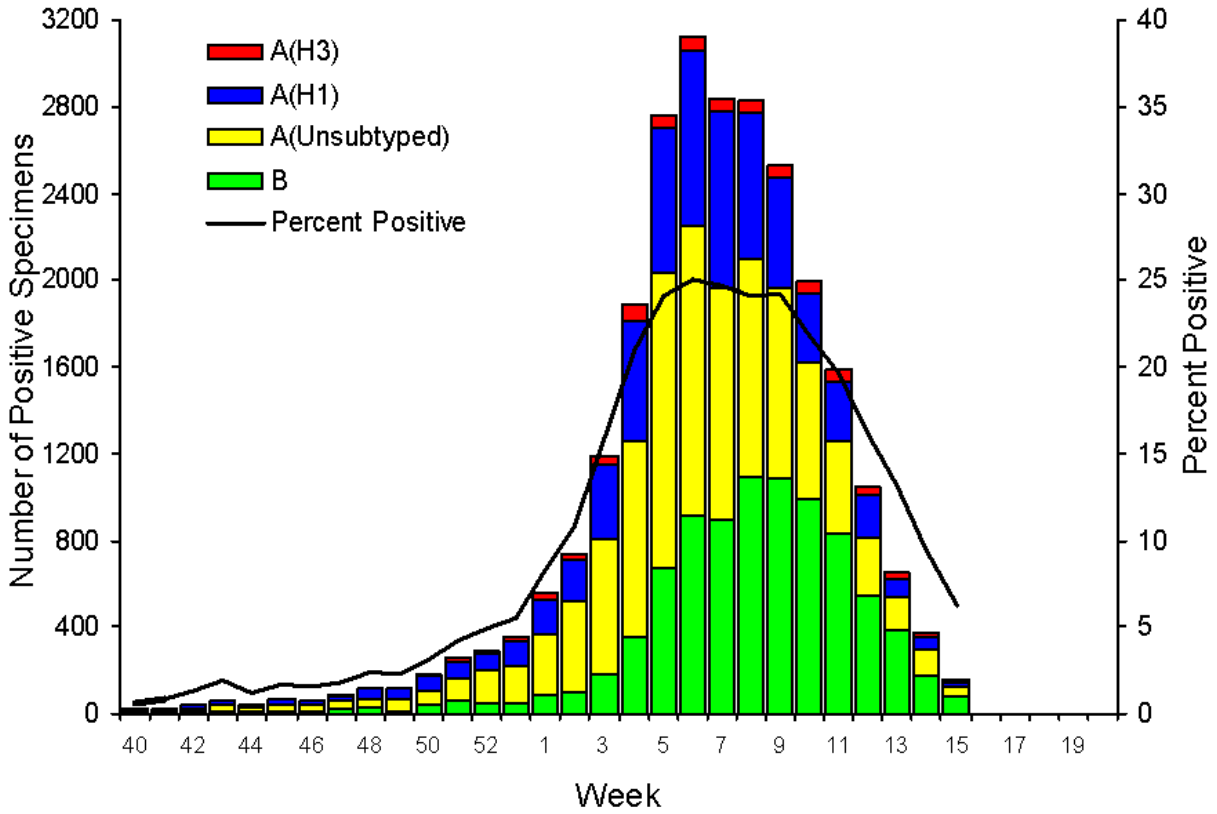
- Children younger than 5, but especially <2 years;
- People 65 and older;
- Pregnant women; and
- People with chronic medical conditions:
  - Cancer;
  - Blood disorders (including sickle cell disease);
  - Chronic lung disease (asthma, COPD);
  - Diabetes;
  - Heart disease;
  - Kidney disorders;
  - Liver disorders;
  - Neurological & neuromuscular disorders; and
  - Weakened immune systems (e.g., AIDS).

Who should get vaccinated against novel H1N1 flu?

- Pregnant women
- Household contacts and caregivers for children younger than 6 months of age
- Healthcare and emergency medical services personnel
- All people from 6 months through 24 years of age
  - Children from 6 months through 18 years of age
  - Young adults 19 through 24 years of age
- Persons aged 25 through 64 years who have health conditions associated with higher risk of medical complications from influenza.

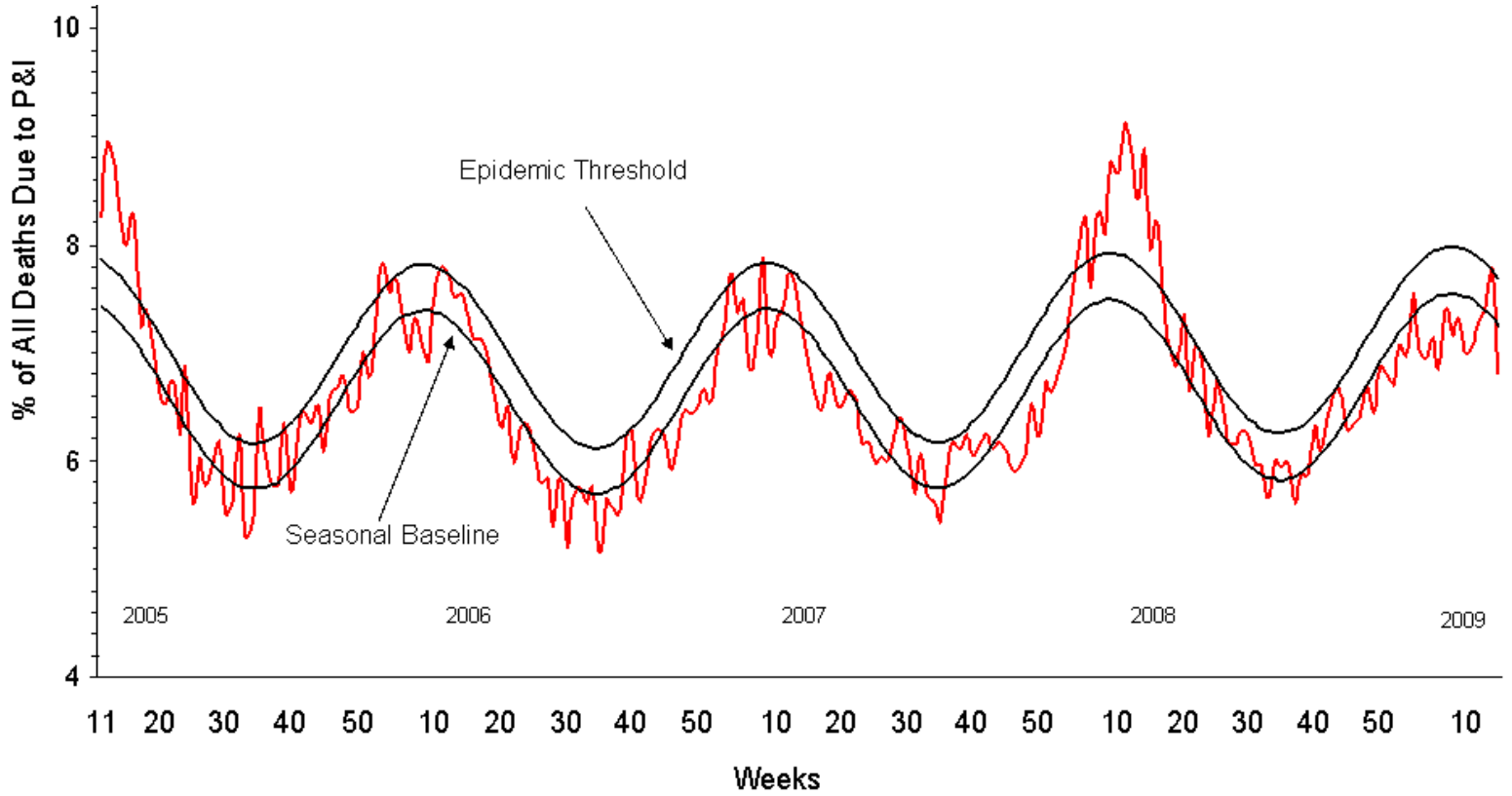
Pandemic influenza A, 1918, Camp Funston

Pre-pandemic influenza positive tests, 2008-2009



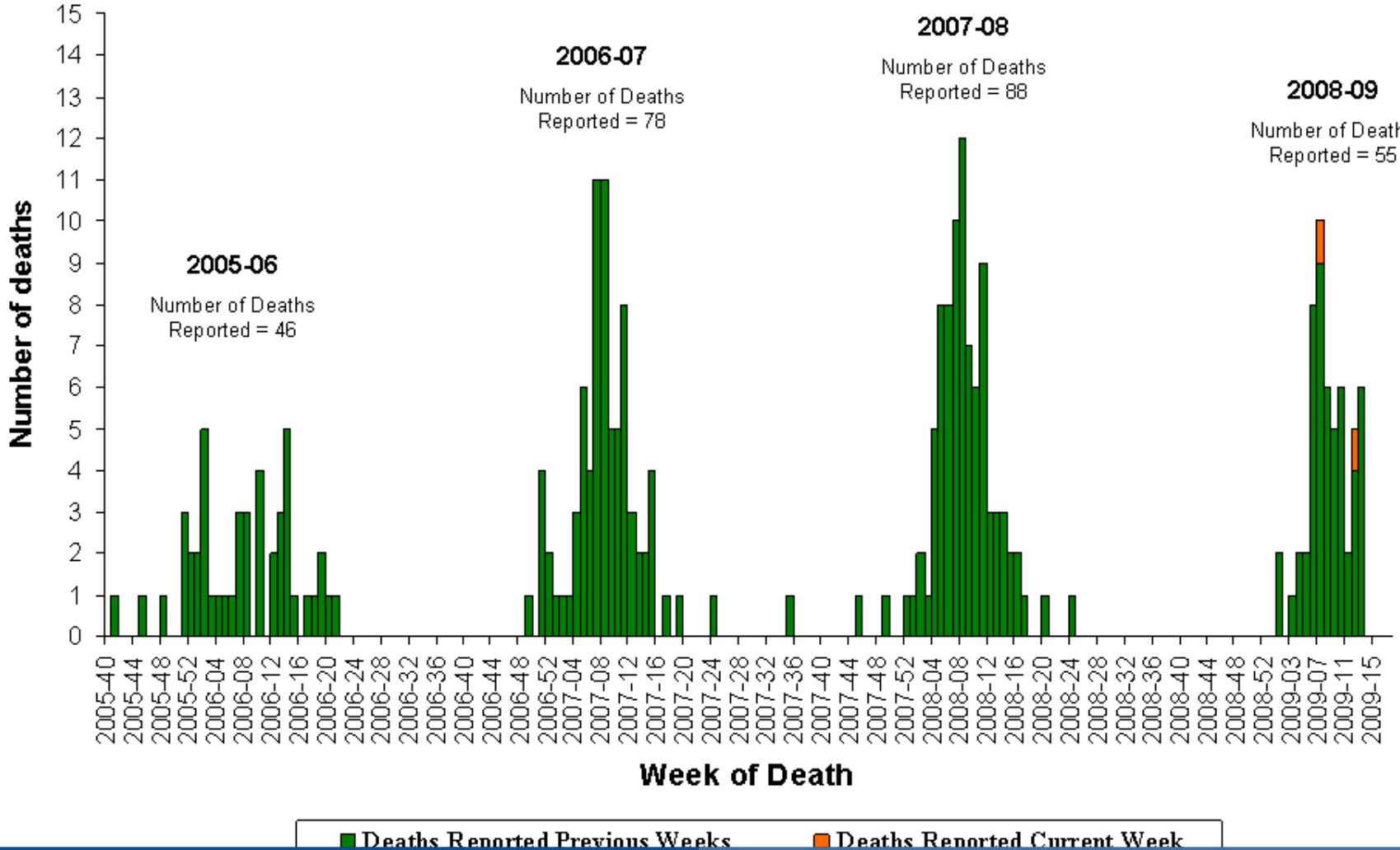
No. (N = 25,925) and % of specimens testing positive for influenza reported by WHO and National Respiratory and Enteric Virus Surveillance System collaborating labs, by type, and week - U.S., Sept. 28, 2008-April 18, 2009

Pre-pandemic pneumonia & influenza (P&I) mortality

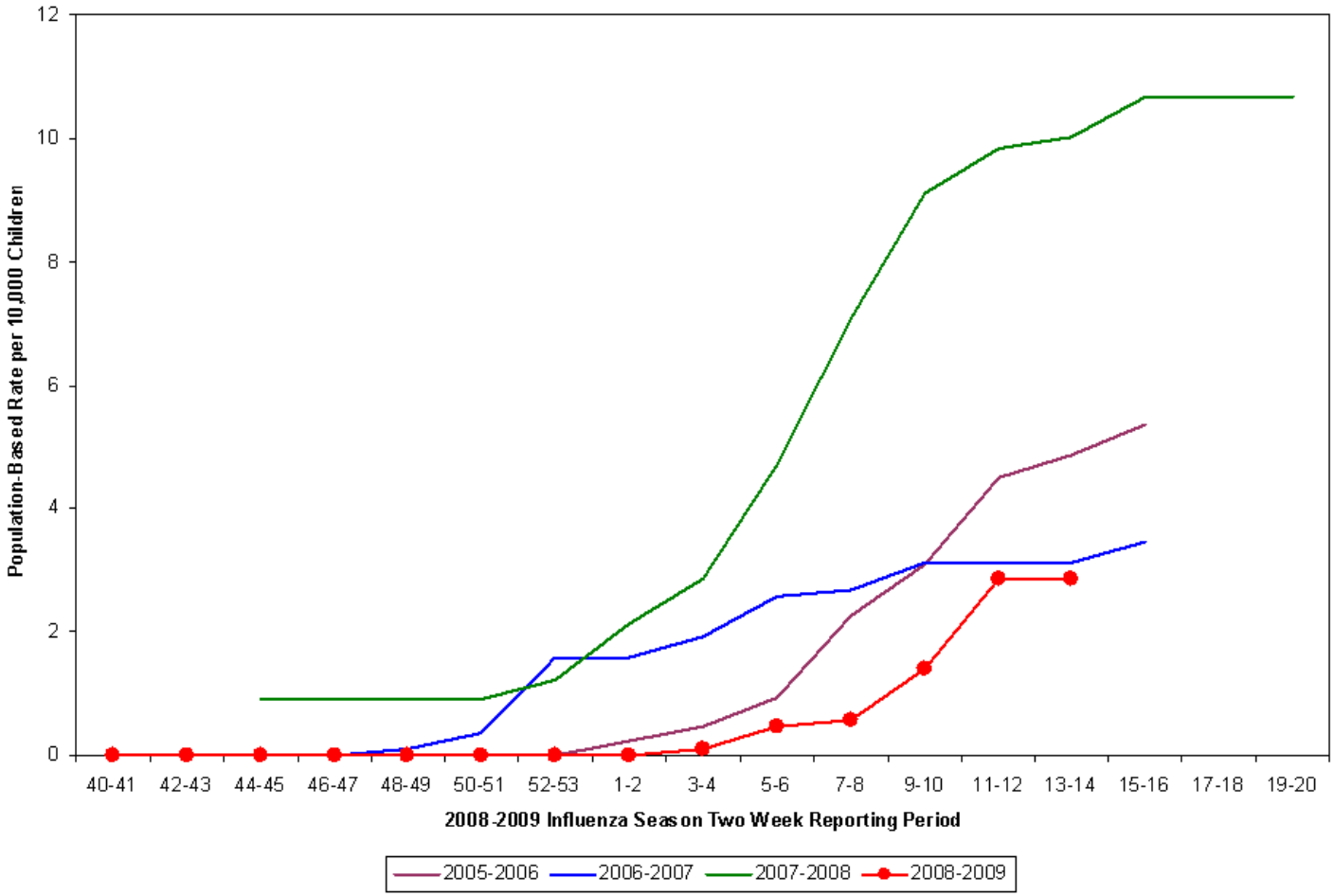


During week 15 (ending April 18, 2009), 6.8% of all deaths reported through the 122-Cities Mortality Reporting System were due to P&I. This percentage is below to the epidemic threshold of 7.7% for week 15.

Pre-pandemic influenza-associated pediatric deaths

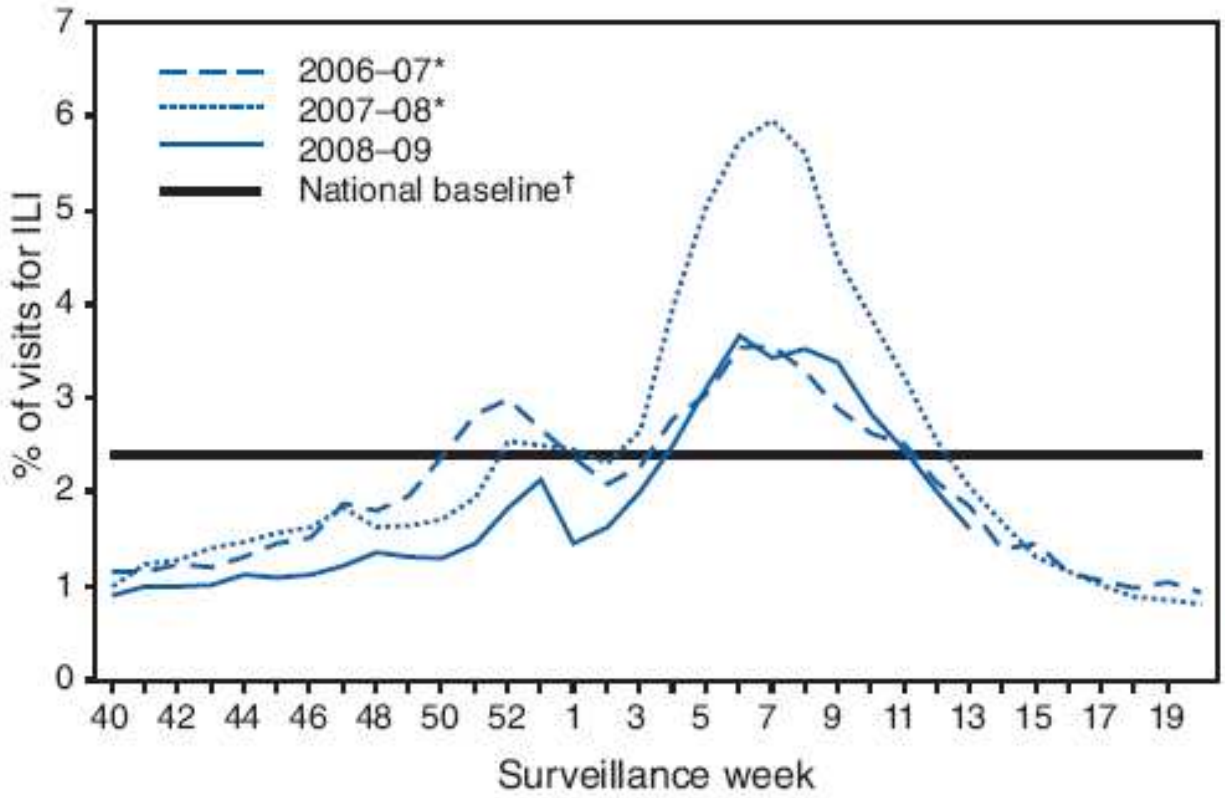


Pre-pandemic influenza pediatric hospitalizations



Laboratory-confirmed influenza-associated hospitalization rates for children 0-4

Pre-pandemic influenza surveillance (PMID: 19373198)



Percent of visits for ILI reported by U.S. Outpatient ILI Surveillance Network (ILINet), by week - U.S., Sept 28, 2008-April 4, 2009 and 2006-07 and 2007-08 influenza seasons

Pre-pandemic influenza surveillance

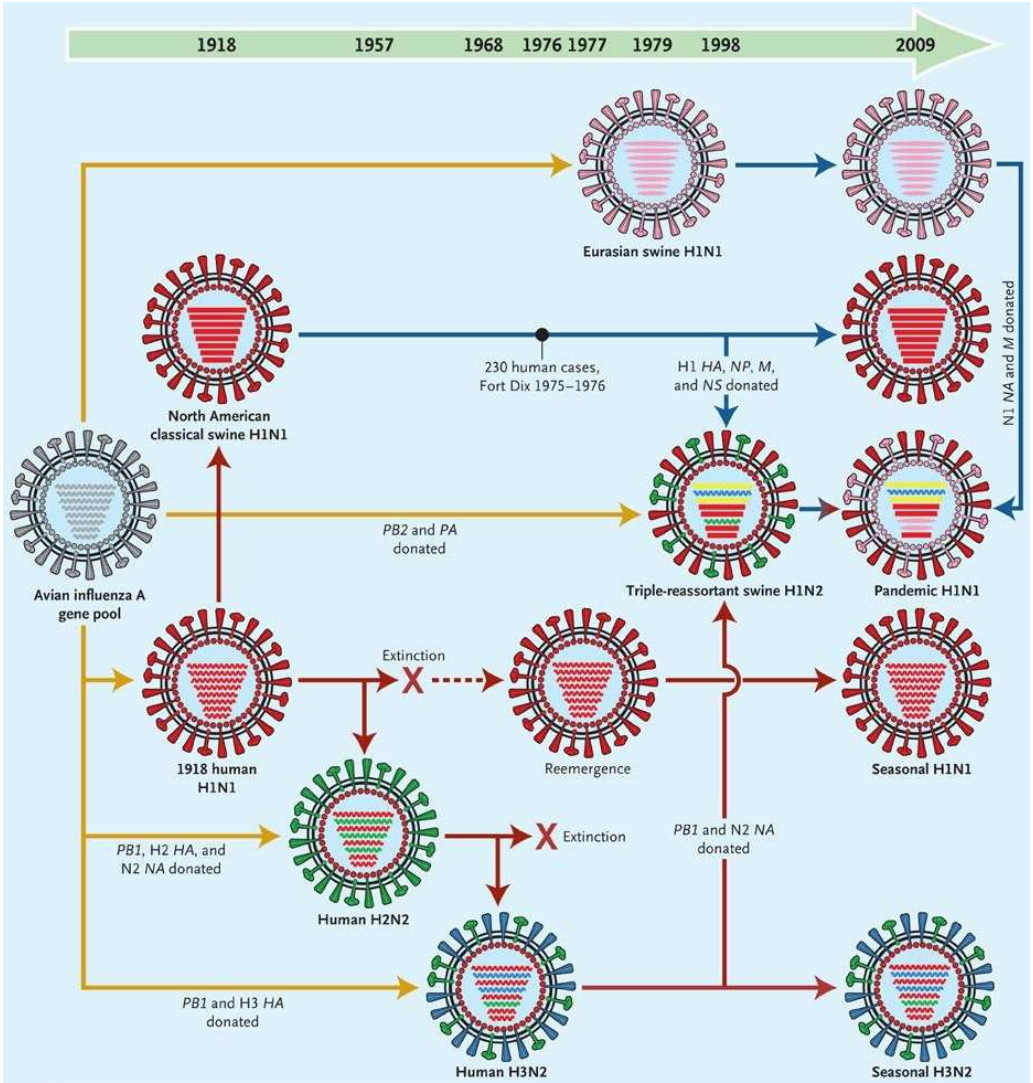
Number and percentage of influenza viruses tested for resistance to influenza antiviral medications, by virus type — United States, October 1, 2008–April 4, 2009 (CDC MMWR, PMID: 19373198)

		Resistant to oseltamivir[a]			Resistant to adamantanes	
Influenza virus	No. tested	No.	(%)	tested	No.	(%)
A (H1N1)	699	694	(99.3)	683	3	(0.4)
A (H3N2)	103	0	(0)	100	100	(100)
B	274	0	(0)	n/a[b]	n/a	n/a

[a] None of the tested isolates were resistant to zanamivir.

[b] The adamantanes (amantadine and rimantadine) are not effective against influenza B viruses.

Relationships among human & swine influenza viruses



México reports outbreak of influenza-like illness cases

Notification via WHO International Health Regulations (IHR)

On March 18, 2009, surveillance systems in México alerted authorities to an unusual number of cases of influenza-like illness. After a few days of discussion starting on April 11 between the PAHO and México authorities regarding unusual numbers of acute respiratory infections, the authorities notified PAHO according to recommendations in IHR of a potential public health emergency of international concern (PHEIC). The event was an outbreak of acute respiratory illness in the states of Veracruz and Oaxaca, México.

First U.S. case detected

Patient A, San Diego County

On March 30, 2009, 10 y.o. boy had onset of fever, cough, and vomiting. He was taken to an outpatient clinic, and NP swab was collected as part of a clinical study. He received no treatement and all his symptoms resolved uneventfully within 1 week. Initial testing at the clinic identified influenza A virus, but the test was negative for human influenza subtypes H1N1, H3N2, and H5N1. CDC notified on April 13, and received specimen on April 14. The boy and his family reported that the child had had no exposure to pigs. (Source: MMWR, PMID: 19390505)

Second U.S. case detected

Patient B, Imperial County

On March 28, 2009, 9 y.o. girl had onset of cough and fever (104.3° F). She was taken to an outpatient facility that was participating in an influenza surveillance project, treated with antibiotics, and recovered uneventfully. CDC received a specimen on April 17, forwarded as unsubtypable influenza A virus from the Naval Health Research Center in San Diego. CDC identified isolate as a swine influenza A (H1N1) virus on April 17, and notified the California Department of Public Health. The girl and her family reported that the child had had no exposure to pigs. No epidemiologic link between patients A and B had been identified

On April 18, using the IHR, the U.S. notified PAHO of these 2 cases, and assessed that they could be a potential PHEIC. (Source: MMWR, PMID: 19390505)

Case definition for novel influenza A (H1N1) virus infection

Confirmed case

A person with an ILI with lab confirmed novel influenza A (H1N1) virus infection by real-time RT-PCR or viral culture.

Probable case

A person with an ILI who is positive for influenza A, but negative for human H1 and H3 by influenza RT-PCR.

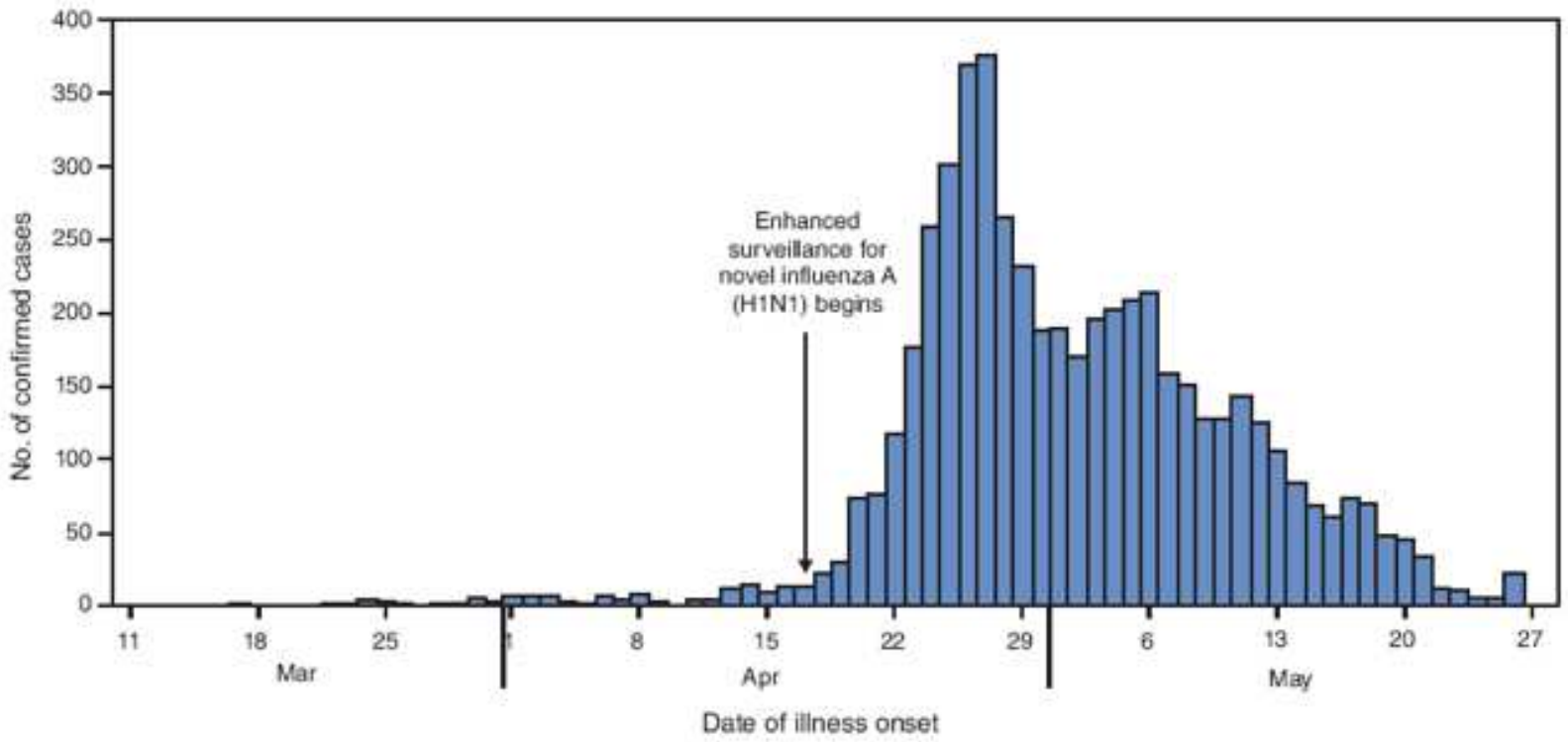
Suspected case (optional)

Does not meet the confirmed/probable case definition, and is

- a previously healthy person <65 years hospitalized for ILI;
- ILI and resides in a state without confirmed cases, but has traveled to a state or country where there are cases;
- ILI and has epidemiologic link in the past 7 days a case

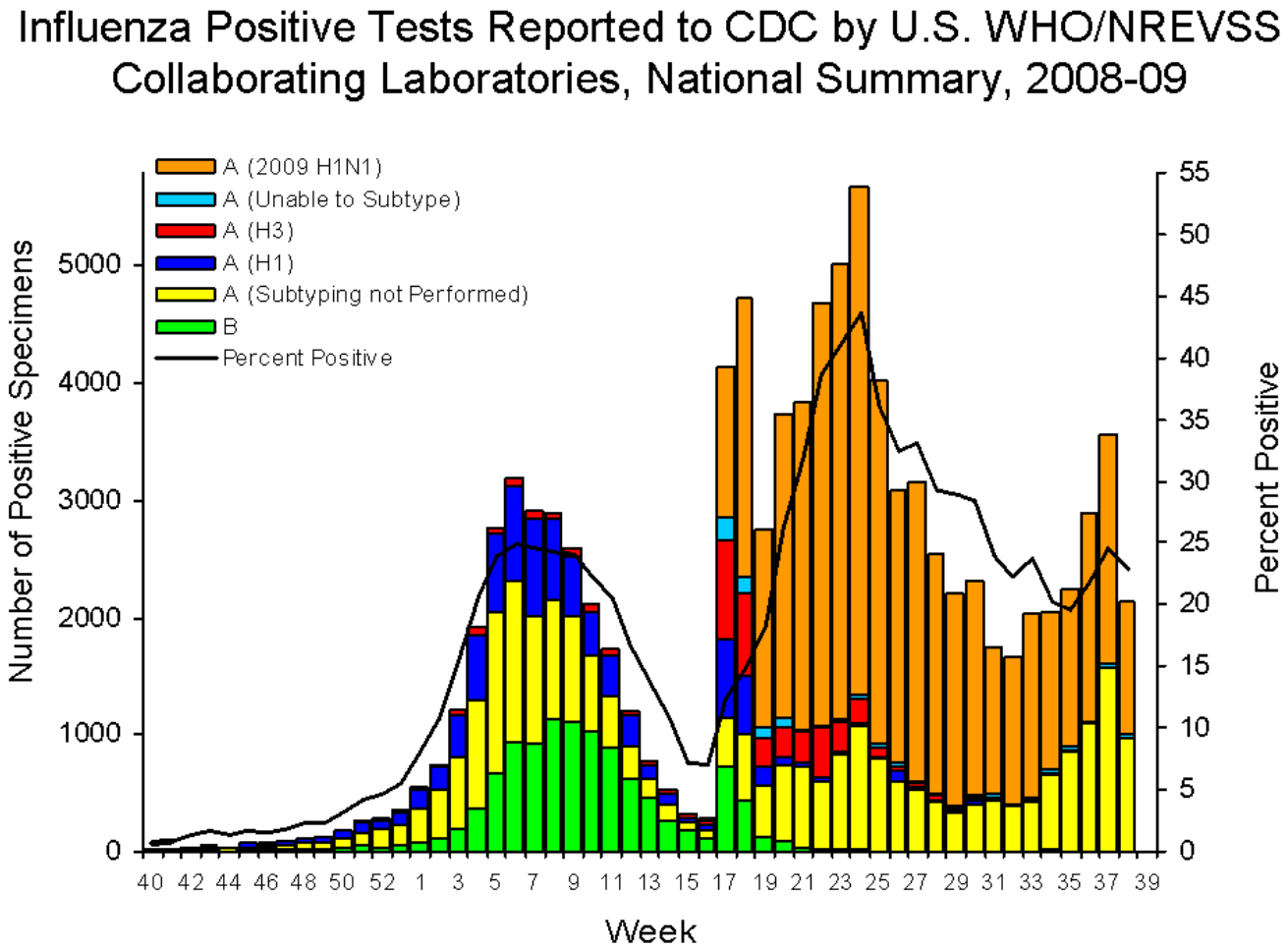
Source: `http://www.cdc.gov/h1n1flu/casedef.htm` (Posted 2009-06-01)

Novel H1N1 influenza A in México



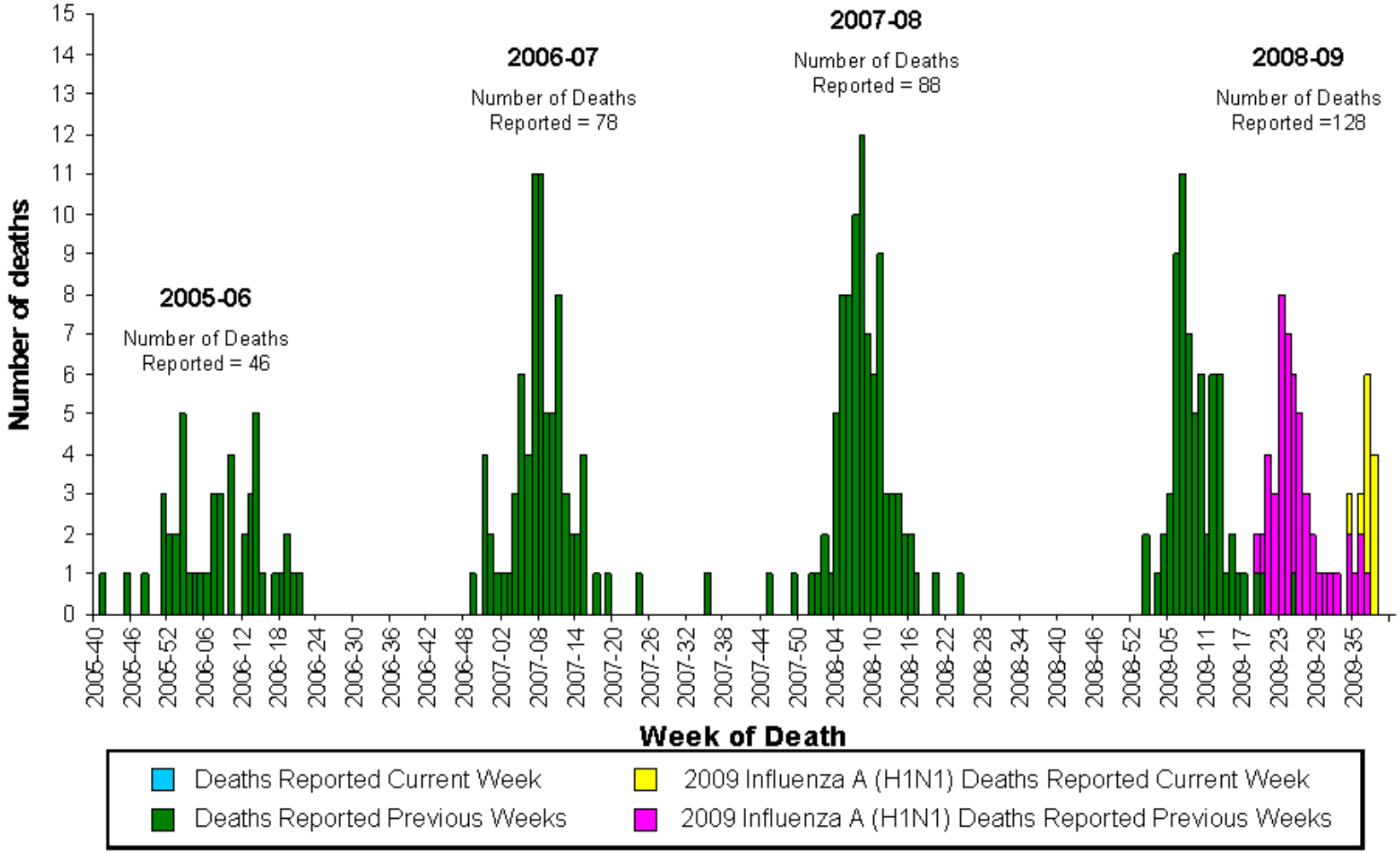
No. (N = 5,305) of lab-confirmed cases of novel influenza A (H1N1) infection, by date of illness onset — México, March–May 2009. Includes all confirmed cases with onset data reported as of May 29, 2009. Not all cases because of a backlog of untested specimens. (CDC MMWR, PMID: 19498336)

Pandemic influenza positive tests, 2008-2009

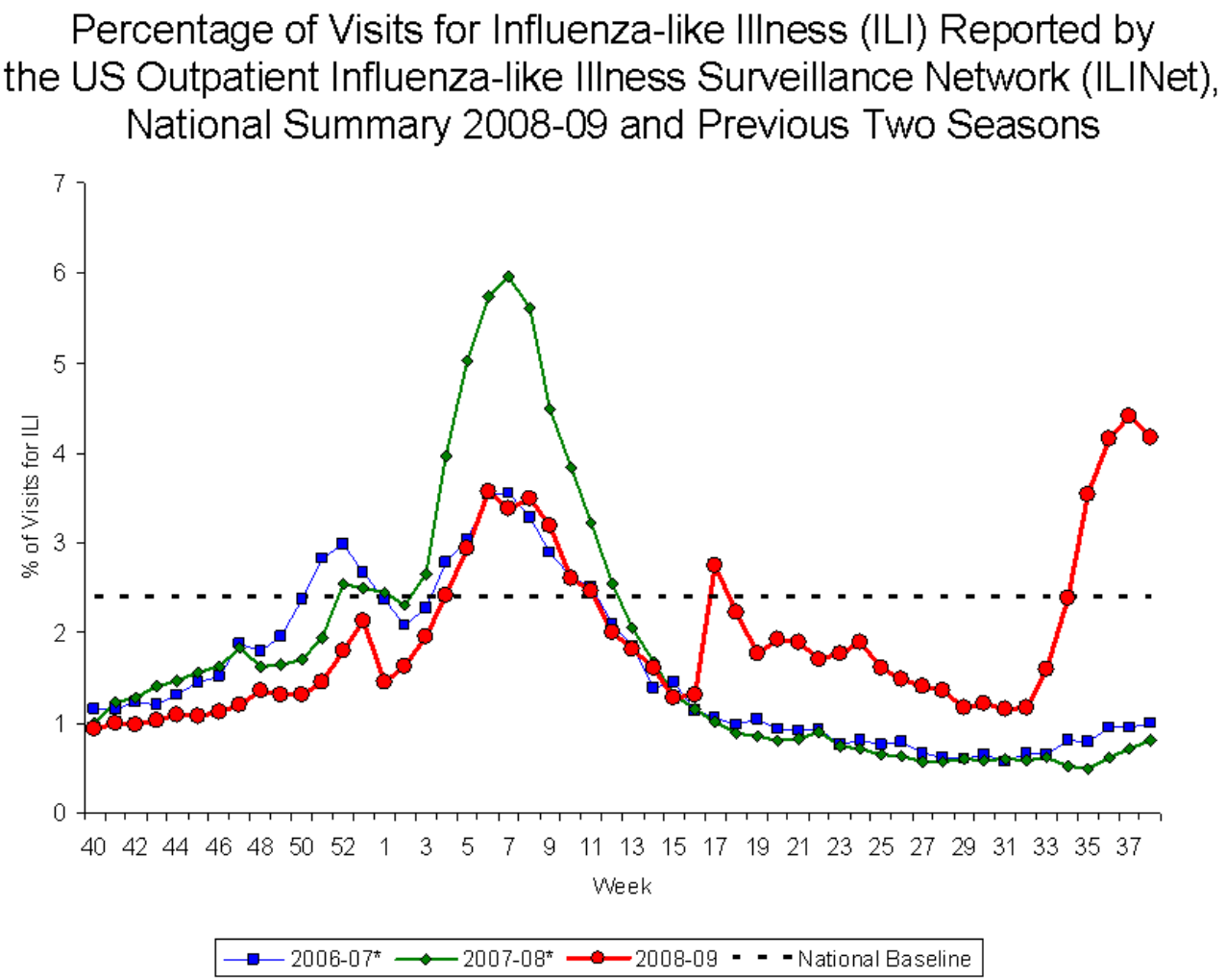


CDC Flu Weekly; Week 38 ending September 26, 2009

Pandemic H1N1 influenza-associated pediatric deaths

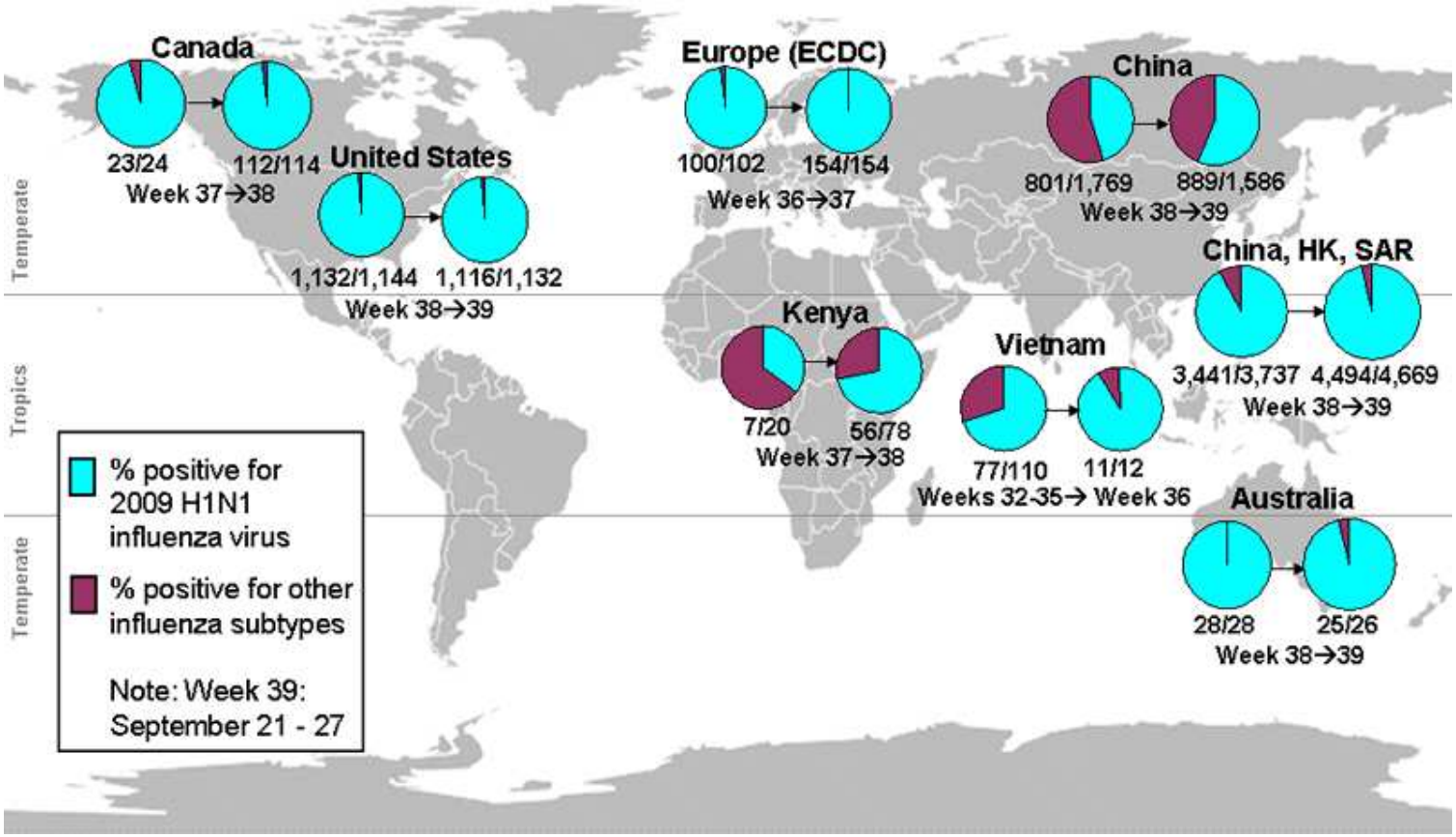


Pandemic period outpatient ILI surveillance



*There was no week 53 during the 2006-07 and 2007-08 seasons, therefore the week 53 data point for those seasons is an average of weeks 52 and 1.

International co-circulation of novel & seasonal influenza



Source : `http://www.cdc.gov/h1n1flu/updates/international/map.htm`.

Pandemic influenza surveillance

No. and % of influenza viruses tested for resistance to antiviral medications, by virus type—U.S. (Oct 1, 2008 – Jul 28, 2009)

		Resistant to oseltamivir			Resistant to adamantanes	
Influenza virus	No. tested	No.	(%)	tested	No.	(%)
A (H1N1)	1099	1094	(99.5)	1100	6	(0.5)
A (H3N2)	213	0	(0)	216	216	(100)
B	620	0	(0)	n/a[a]	n/a	n/a
Novel A (H1N1)	274	0[b]	(0)	312	312	(100)

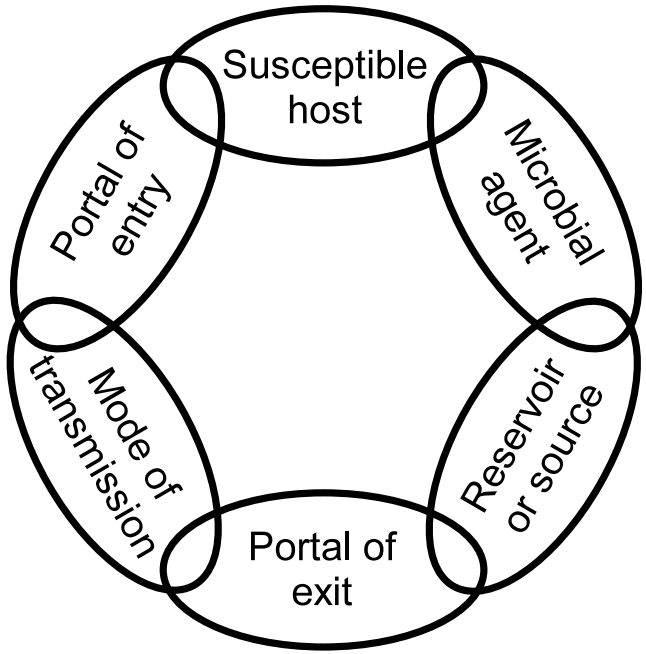
[a] The adamantanes (amantadine and rimantadine) are not effective against influenza B viruses.

[b] Five cases of oseltamivir resistant novel influenza A (H1N1) viruses have been detected worldwide, none of which were detected in the United States.

Source: CDC FluView: http://www.cdc.gov/flu/weekly/.

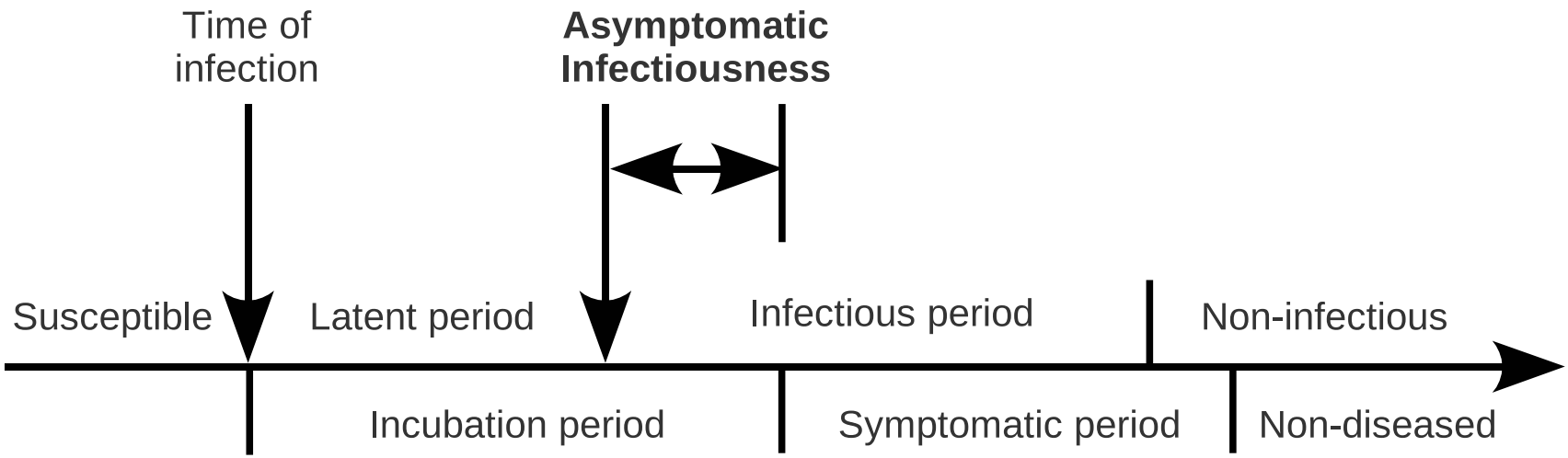
Mechanisms: Chain model of infectious diseases

- Microbial agent(s)
- **Reservoirs and/or source**
- Portal(s) of exit
- **Modes of transmission**
- Portal(s) of entry
- **Susceptible hosts**



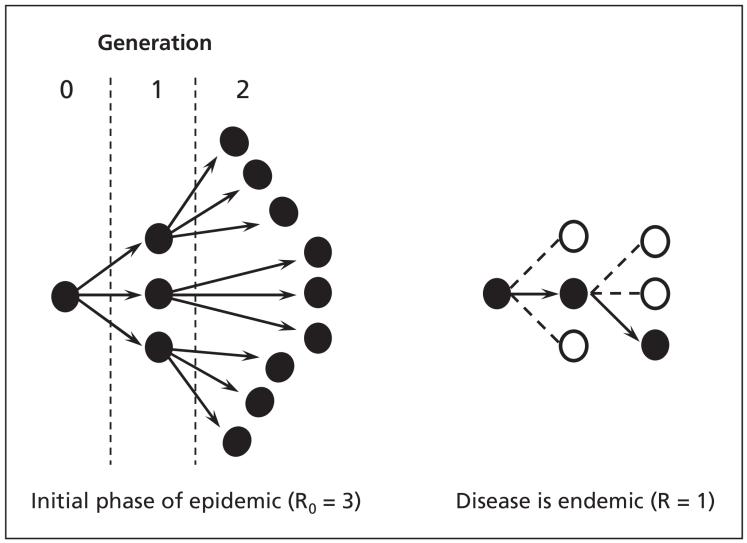
Source: Epidemiologic Methods for the Study of Infectious Diseases, Oxford University Press 2001

Mechanisms: Natural history of infection & infectiousness



When the latent period is *shorter* than the incubation period, an infected person becomes infectious *before* symptom onset.

Dynamics: Reproductive number and infection rate



Source (figure): PMID: 19620267

Basic reproductive number

$$R_0 = d \times c \times p$$

Transmission probability (p)

- Biologic infectiousness
- Biologic susceptibility
- Interruptors (e.g., PPE)

Effective reproductive number

$$R(t) = R_0 x(t)$$

Infection rate among susceptibles

$$I(t) = c \times p \times P(t)$$

Signature features of influenza pandemics

Past pandemics characterized by . . .

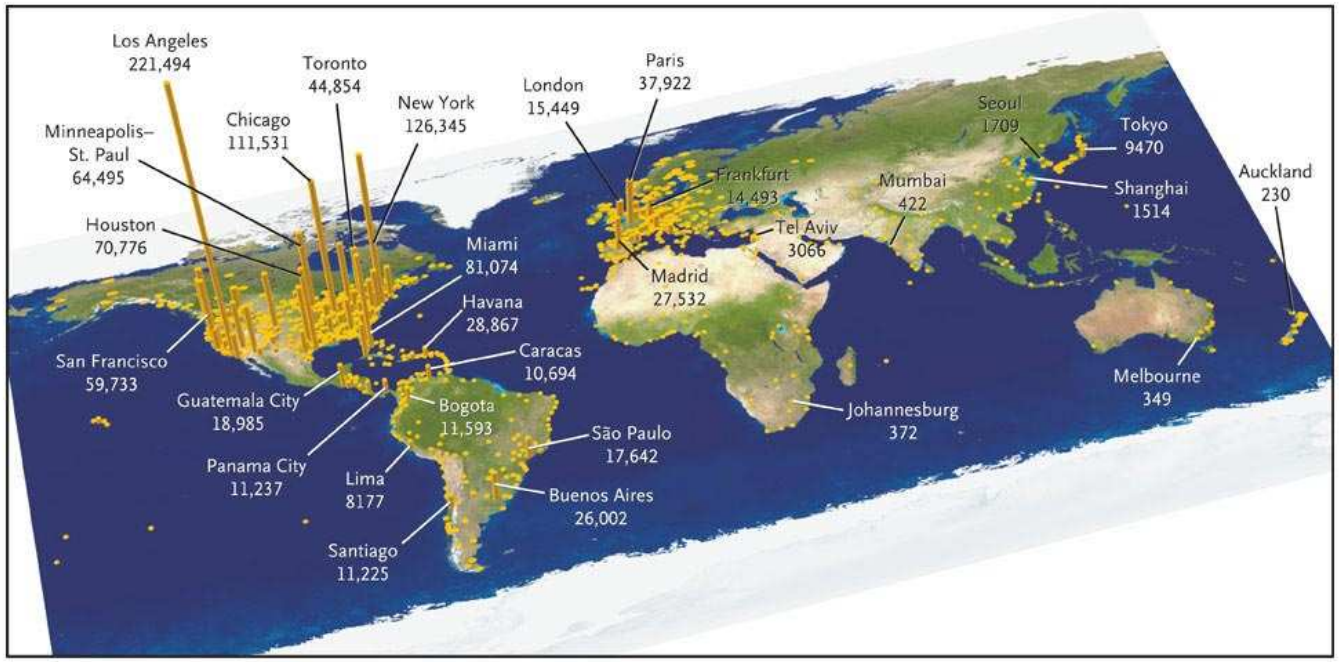
- Shift in virus subtype;
- Higher transmissibility compared to seasonal influenza;
- Shifts of the highest death rates to the youngest populations (antigen recycling, immune potentiation, bacterial superinfection due to asymmetric carriage); and
- Geographic differences in impact

Reasons for multiple waves

- Adaptation of virus to host population
- Susceptibility of host population
- Seasonality
- Demographic and geographic variations

Source: Miller et al. (2009), PMID: 19423872

Spread of novel influenza A (H1N1) via global air travel

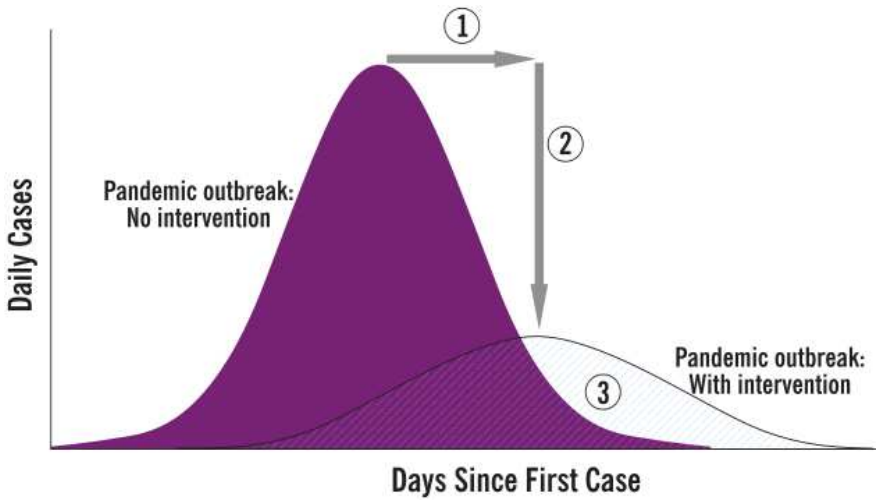


Destination cities and corresponding volumes of international passengers arriving from México between March 1 and April 30, 2008. A total of 2.35 million passengers flew from México to 1018 cities in 164 countries. Source: Khan et al. (2009), PMID 19564630

CDC community mitigation strategy (Feb, 2007)

Goals of community mitigation

1. Delay outbreak peak
2. Decompress peak burden
3. Diminish overall health impacts

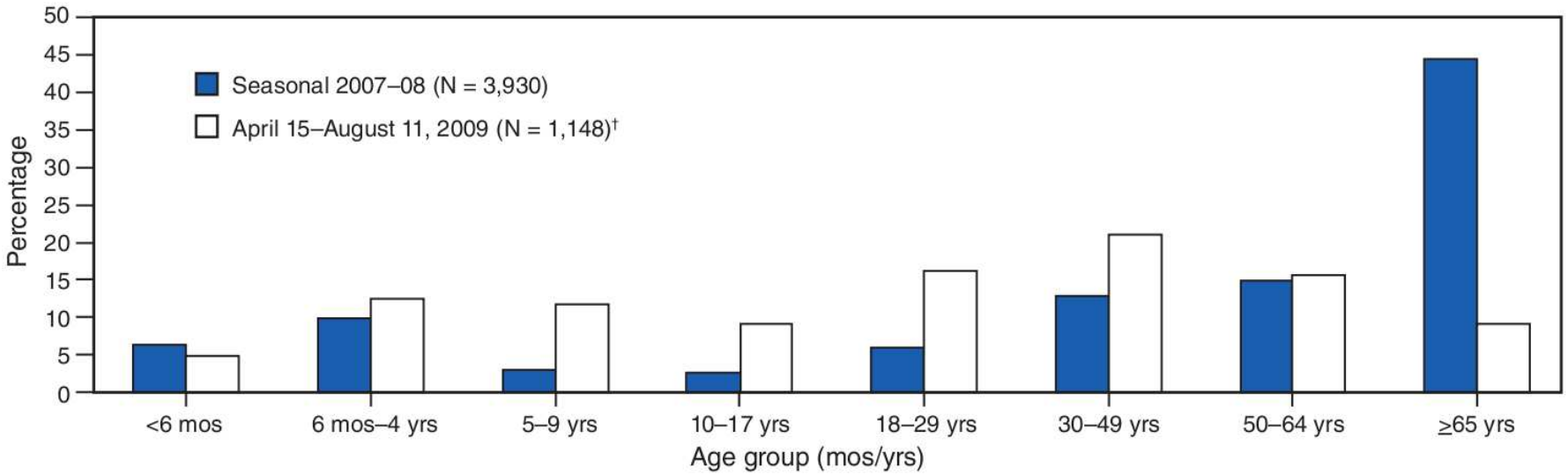


Community mitigation

- Isolation (case)
- Quarantine (exposed)
- Social distancing (mixing)
  - School dismissals
  - Travel restrictions
  - Mass gathering restrictions
- Sheltering in place (non-exposed)

Source: `http://www.pandemicflu.gov/plan/community/community_mitigation.pdf`

Percentage of H1N1 hospitalizations by age



Distribution by age group of persons hospitalized with laboratory-confirmed influenza,* — United States, 2007–08 winter influenza season and April 15–August 11, 2009 (CDC RR, PMID: 19713882)

Case rate and hospitalization rate per 100,000

Table: Case Rate and Hospitalization Rate per 100,000 Population by Age Group of Laboratory-Confirmed nH1N1 in the United States

Age (years)	Case Rate	Hospitalization Rate
0–4	22.9	4.5
5–24	26.7	2.1
25–49	6.97	1.1
50–64	3.92	1.2
$\geq$ 65	1.3	1.7

IOM 2009 (ISBN: 0-309-14428-0)

Novel influenza A (H1N1) characteristics (642 cases)

Characteristic	Value (%)
Male sex	302/592 (51)
Median age (range)	20 (3 mo–81 yr)
Clinical symptoms	
Fever	371/394 (94)
Cough	365/397 (92)
Sore throat	242/367 (66)
Diarrhea	82/323 (25)
Vomiting	74/295 (25)
Hospitalization	
Total	36/399 (9)
Infiltrate on CXR	11/22 (50)
Admitted to ICU	8/22 (36)
Respiratory failure	4/22 (18)
Full recovery	18/22 (82)
Died	2/36 (6)

Source: NEJM 2009; PMID: 19423860

Complications

- Primary viral pneumonia
- Secondary bacterial pneumonia (esp. group A streptococcus, *Staphylococcus aureus*, and *Streptococcus pneumoniae*
- Primary neurological
- Exacerbation of underlying chronic condition
- Pulmonary emboli?
- Death

Sources: PMIDs: 17366454, 19423871, 19498336, 19564631, 19564633, 19609249, 19629027

Comparison of Respiratory Viral Signs and Symptoms

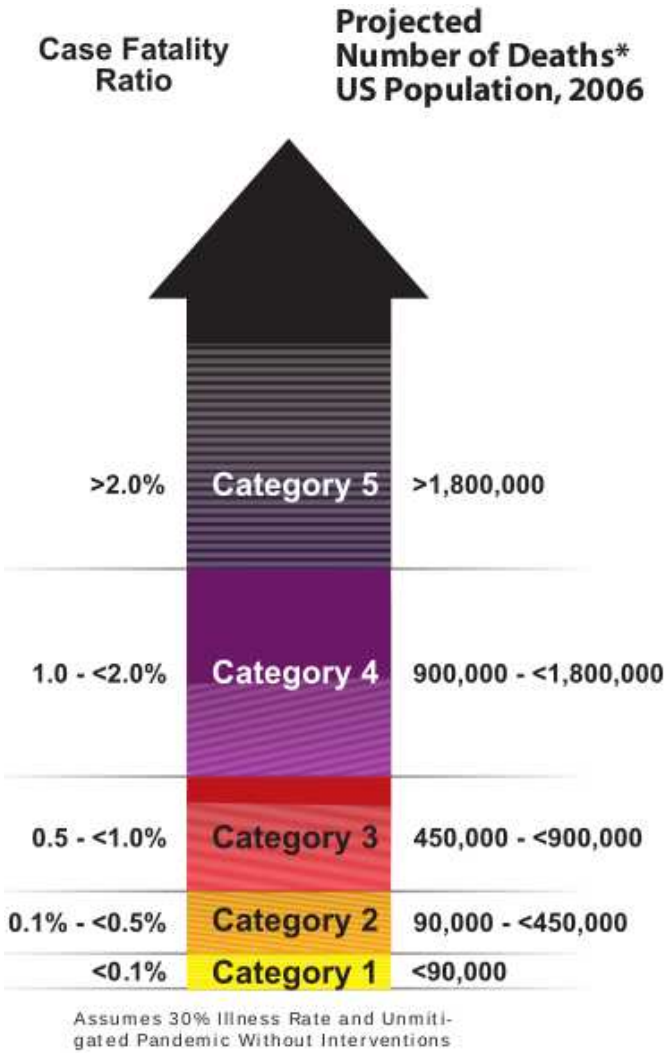
	Common Cold (coryza)	Seasonal Influenza (e.g., H3N2)	Avian Influenza (e.g., H5N1)	nH1N1
Fever	No/rare	Common/high	Common/high	Common/high
Malaise	No	Yes	Yes	Yes
Myalgias	No	Yes	Yes	Yes
Rhinorrhea	Copious	Mild	Mild	Mild
Cough	No	Common	Common	Common
Sore throat	Mild	Moderate to severe	Moderate to severe	Moderate to severe
Diarrhea	No	Uncommon	Common	Common
Morbidity (bed rest)	Rarely	Common	Common	Common
Fatalities	No	Elderly, very young, those with underlying illness	All groups but predominance in < 50 years	Ages 25–49

IOM 2009 (ISBN: 0-309-14428-0)

Risk factors for complications/death

- Comorbid conditions (MMWR, PMID: 19478723)
- Children & young adults (MMWR RR, PMID: 19713882)
- Pregnancy (PMID: 19444154, 19643469)
- Obesity? (MMWR, PMID: 19609249)

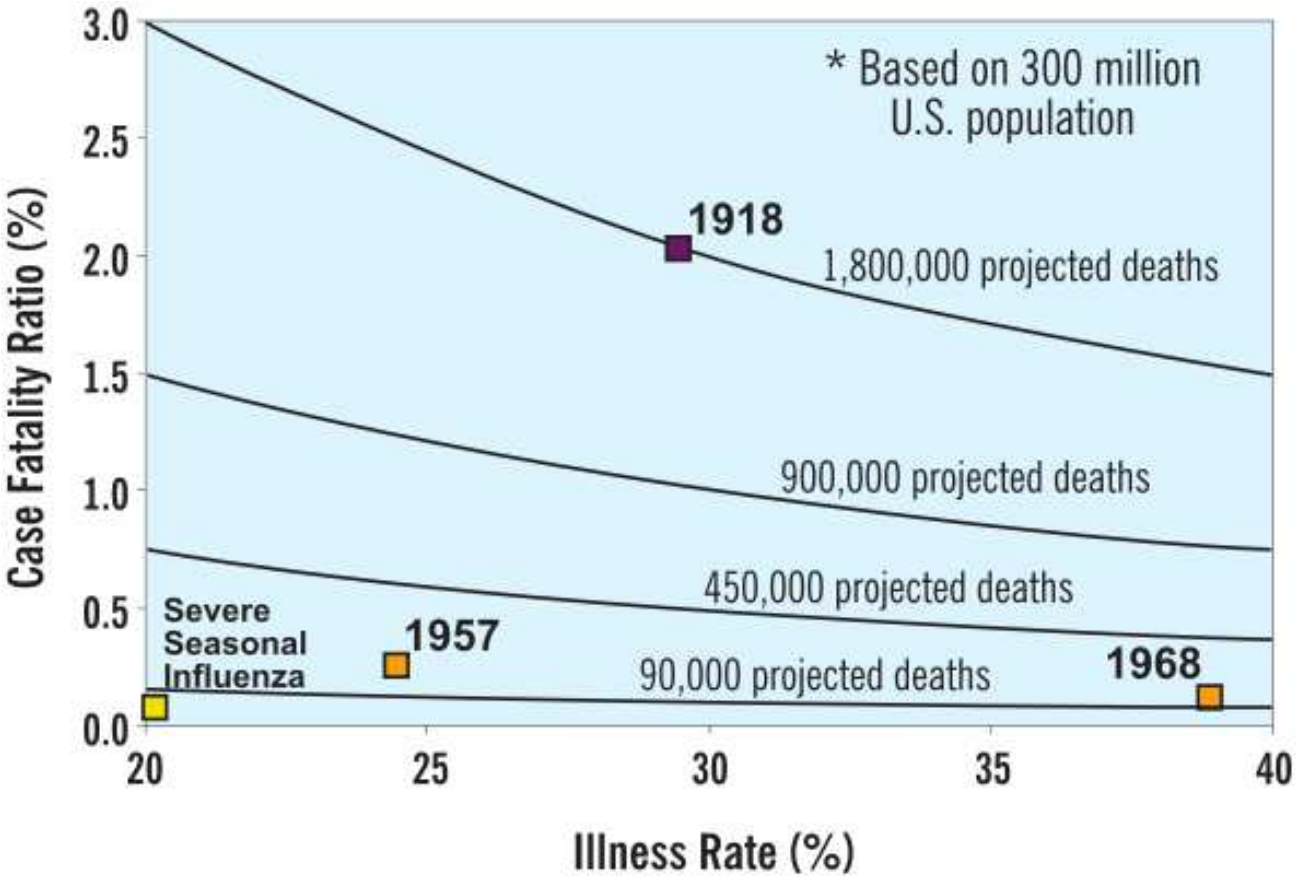
CDC Pandemic Influenza Severity Index (Feb, 2007)



This guidance introduced, for the first time, a Pandemic Severity Index (PSI), which used case fatality risk as the critical driver for categorizing the severity of a pandemic. The PSI was designed to allow better forecasting of the impact of a pandemic and to enable recommendations to be made on the use of mitigation interventions

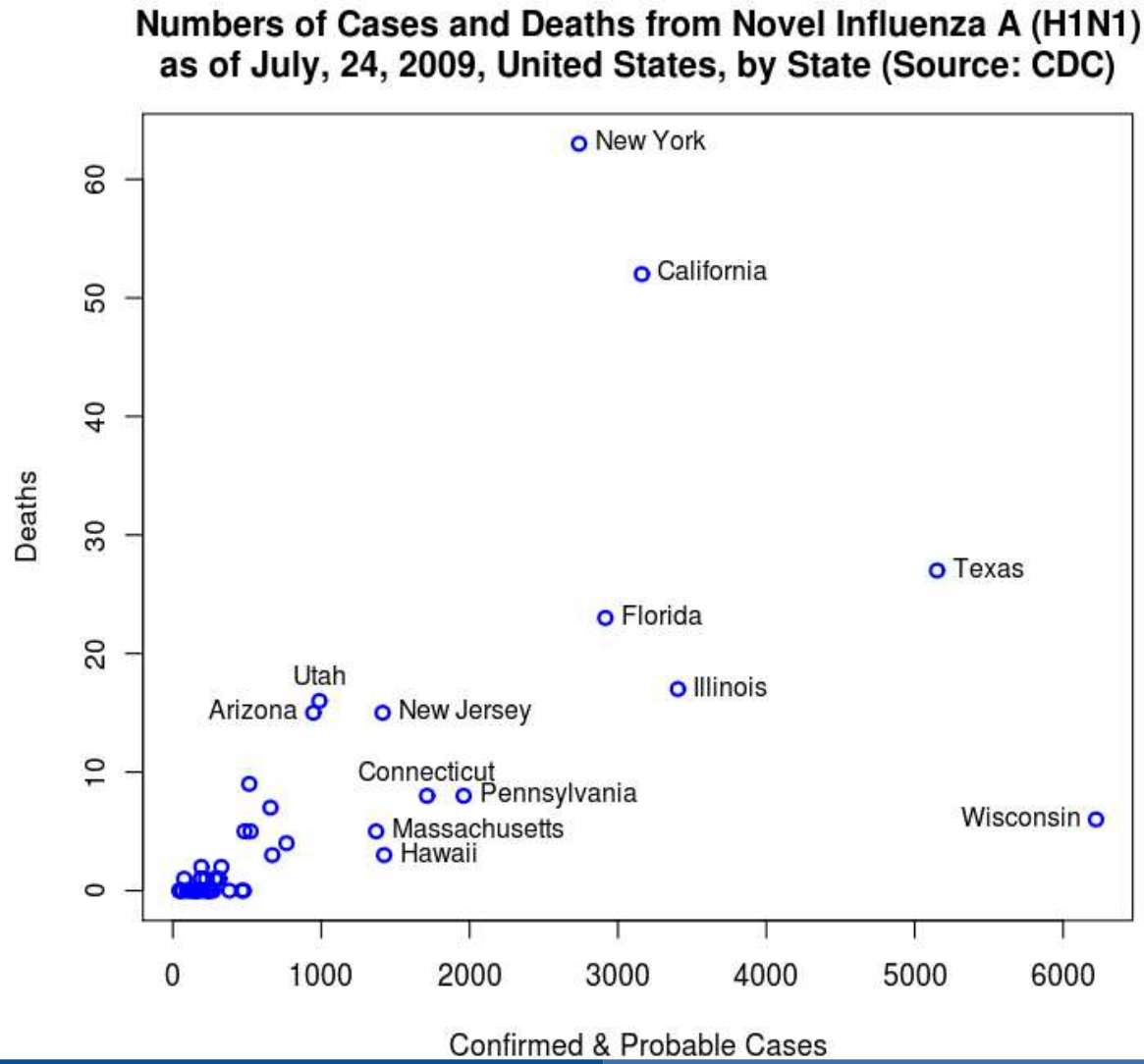
Available from `http://www.pandemicflu.gov/plan/community/community_mitigation.pdf`

Projected mortality of a modern influenza pandemic



CDC 2007 (http://www.pandemicflu.gov/plan/community/community_mitigation.pdf)

U.S. novel influenza A (H1N1) cases and deaths



U.S. novel influenza A (H1N1) cases and deaths

Number of cases, deaths, and informal CFR calculations of novel influenza A (H1N1) infections as of July, 24, 2009, Unites States (states with most cases shown)

State	Population[a]	Cases	Deaths	CFR[b] (%)
Wisconsin	5,627,967	6,222	6	0.10
Texas	24,326,974	5,151	27	0.52
Illinois	12,901,563	3,404	17	0.50
California	36,756,666	3,161	52	1.65
Florida	18,328,340	2,915	23	0.79
New York	19,490,297	2,738	63	2.30

[a] U.S. Census 2008 population projections

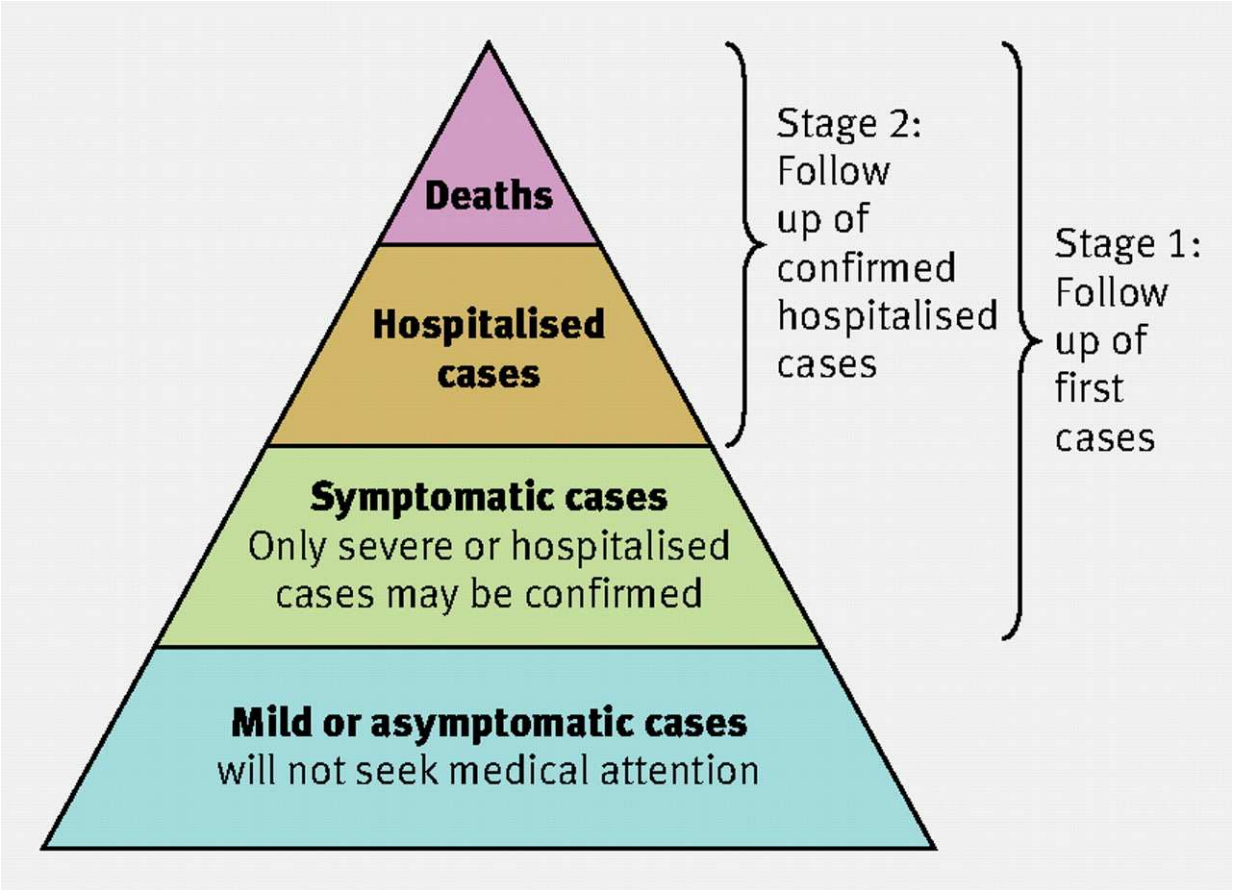
[b] These are "back of the envelope" calculations and are not recommended.

Estimating novel influenza A (H1N1) case fatality risk

Method used	CFR (%)
Extrapolating from seasonal influenza mortality method (US data: age <65)	0.004% – 0.06%
Multiplier method (10x to 30x WHO-reported cases)	0.01% – 0.03%
Community survey method (New York City data)	0.002% – 0.003%
Extrapolating from a "mature" epidemic method (Canadian data)	0.0004% – 0.003%

Source: Wilson & Baker (2009), PMID: 19573509

Spectrum of influenza cases and "case" fatality risk



CFR estimates depend on how these deaths change as a proportion of total "case" numbers as the pandemic progresses. (Source: Garske et. al (2009), PMID: 19620267)

Sources of bias in measuring CFR

Shifts in case ascertainment over time

- In general, most serious cases seek medical care (overestimation)
- Over time, efforts may become more focused on the most severe cases (overestimation) .

Delay between symptom onset and death . . .

which in the early phase of an epidemic can lead to underestimation of the case fatality risk if it has not been adjusted.

Influenza deaths not attributed to influenza

Influenza can precipate cardiopulmonary, vasular deaths that may not be attributed to influenza (underestimation).

Source: Garske et. al. PMID: 19602714

Summary

1. Background
2. Transmission
   - Pandemic detection
   - Mechanisms & dynamics
   - Containment vs. mitigation
3. Burden of illness
   - Clinical syndrome
   - Complications
   - Risk factors
4. Burden of deaths
   - Case fatality risk (CFR)
   - Measurement bias

What's next? Prairie dogs?