

Update on the epidemiology and clinical features of Novel H1N1

Joseph Bresee, MD
Chief, Epidemiology and Prevention Branch
Influenza Division, NCIRD
Centers for Diseases Control and Prevention

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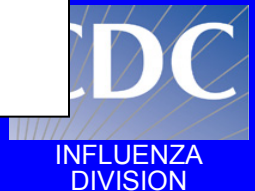
Increased swine influenza detection in humans 2005-9

- January 2007 – “Novel influenza A” made a Nationally Notifiable Disease but CSTE – part of pandemic preparedness efforts
- RT-PCR for influenza capabilities developed by public health labs in U.S.
- Increasing numbers of swine influenza infections in humans being detected from improved surveillance
- Increasing efforts at states, CDC, and USDA to investigate human cases of swine influenza

Triple-Reassortant Swine Influenza A (H1) in Humans in the United States, 2005–2009

Shinde, et al.

N Engl J Med. 2009 Jun 18;360(25):2616-25



Swine Influenza A (H1N1) Infection in Two Children – Southern California, March–April 2009

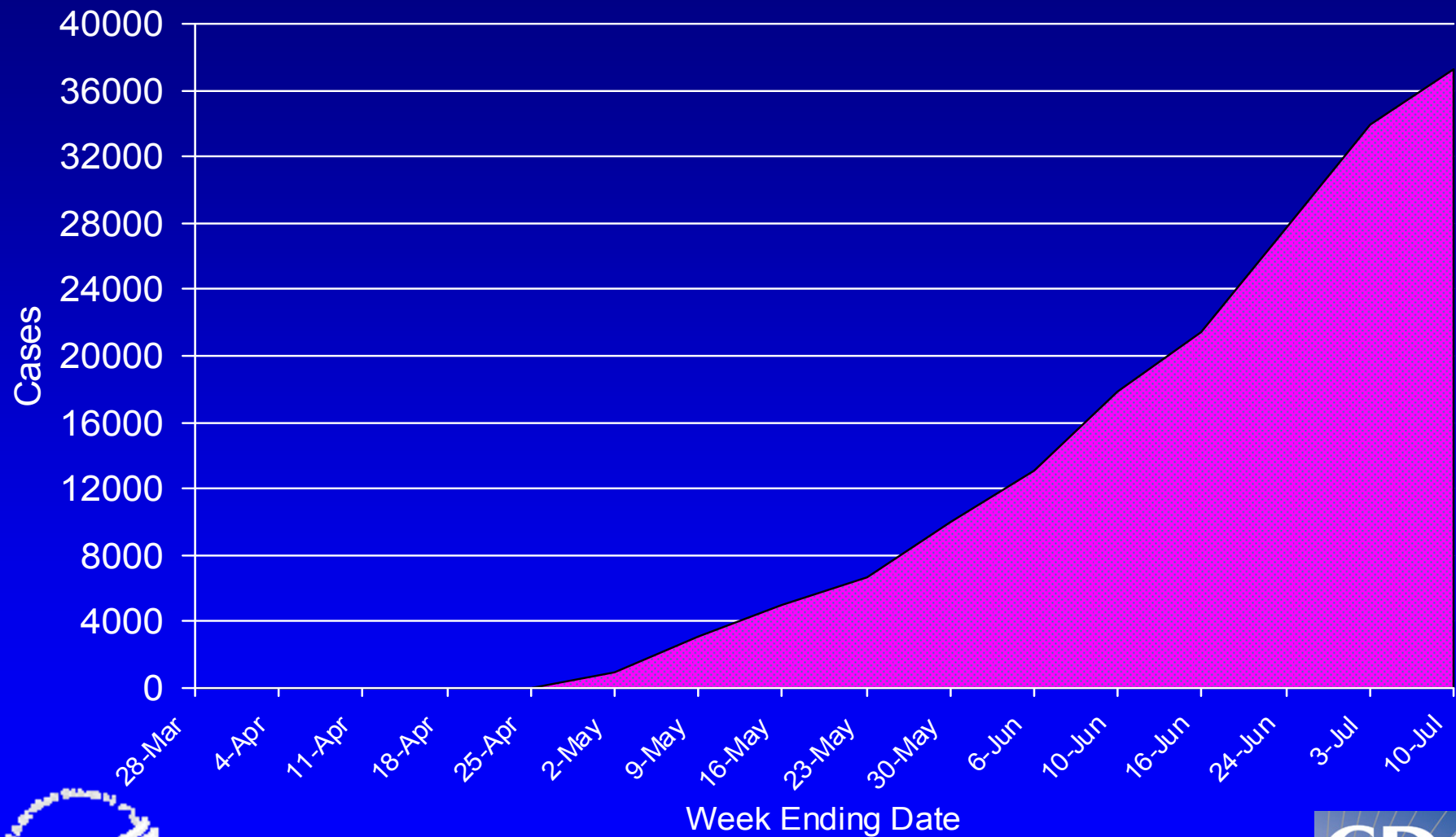
On April 21, this report was posted as an MMWR Early Release on the MMWR website (<http://www.cdc.gov/mmwr>).

Novel Influenza A (H1N1) Detected

- March 2009
 - 2 cases of febrile respiratory illness in children in late March
 - No common exposures, no pig contact
 - Uneventful recovery
 - Residents of adjacent counties in southern California
 - Tested because part of enhanced influenza surveillance



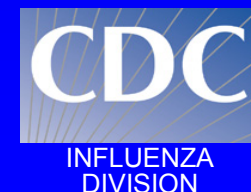
Confirmed and Probable Novel H1N1 Cases by Report Date 10 JUN 2009 (N=37,246)



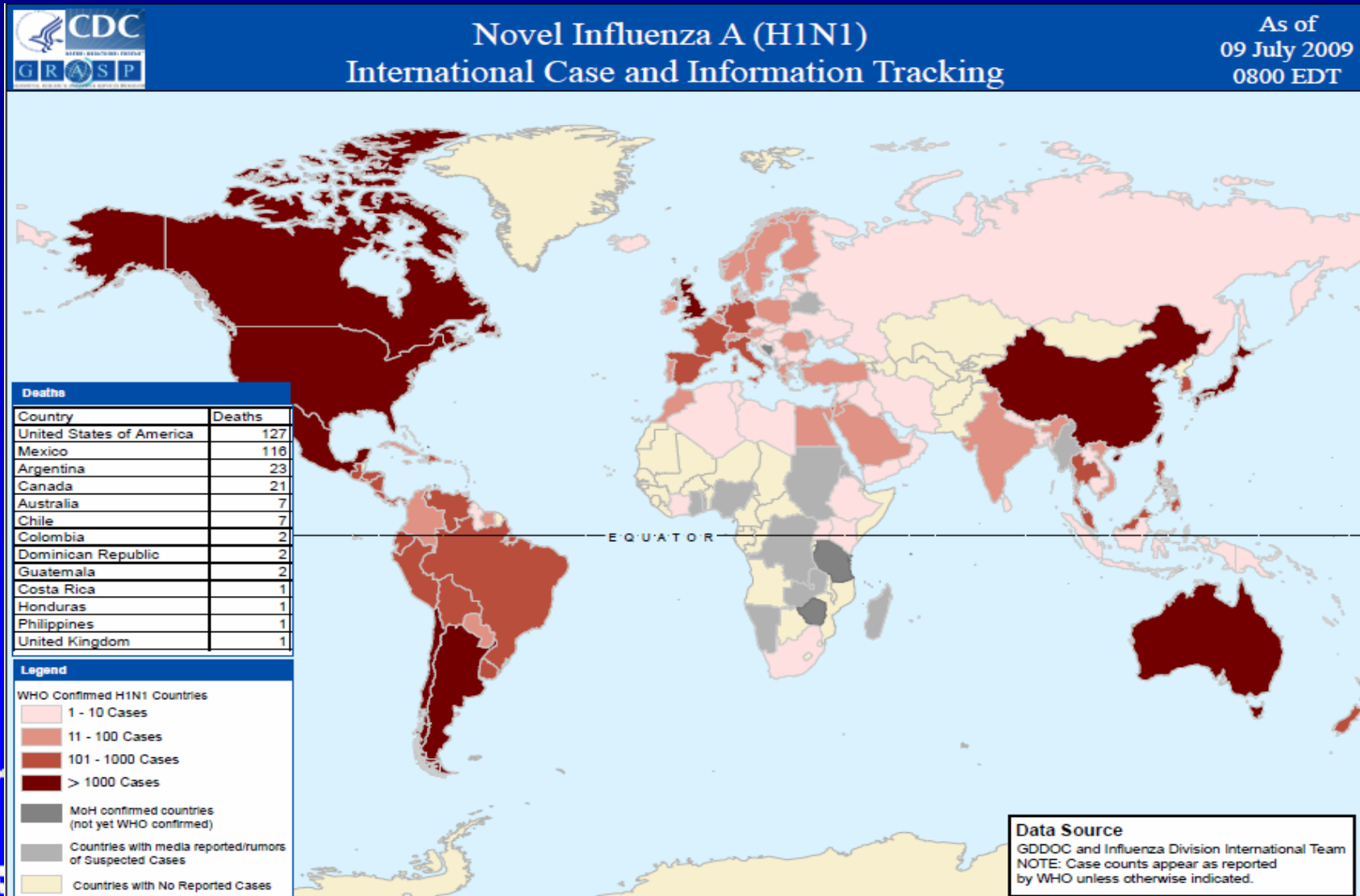
Descriptive Statistics of Novel Influenza A (H1N1) Cases Reported to CDC by States- 10 JUL 2009

US TOTALS	CASES	HOSPS	DEATHS
CASES	37,246	4,132	211
SLTTs AFFECTED	54	48	24

- Sex: 50% male/female
- Median age:
 - all cases 12 years
 - hospitalized 20 years
 - died 37 years

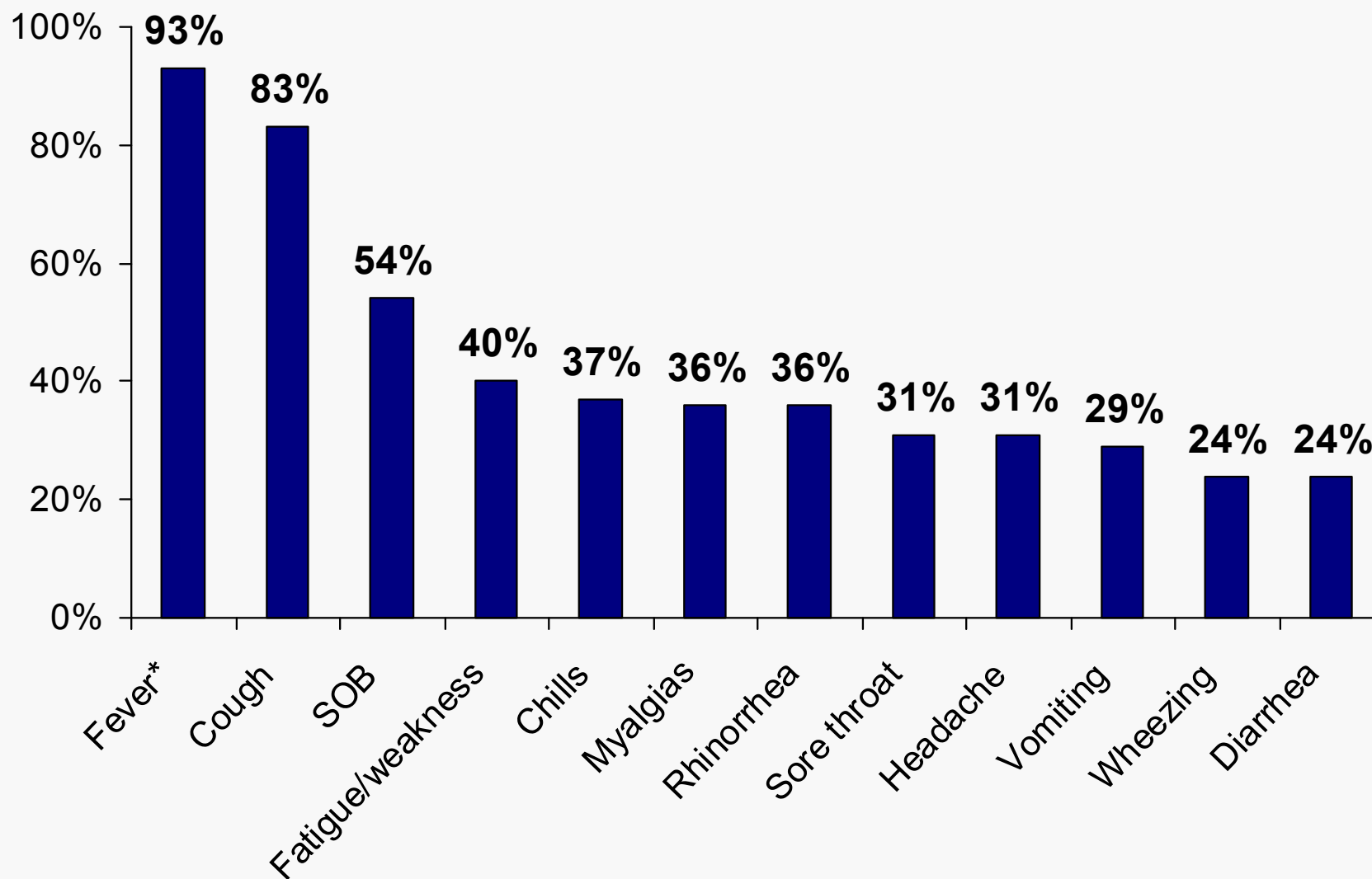


International Map Pandemic H1N1 – 10 JUL 2009





Epidemiology/Surveillance
Pandemic H1N1 Hospitalizations Reported to CDC
Clinical Characteristics as of 19 JUN 2009 (n=268)

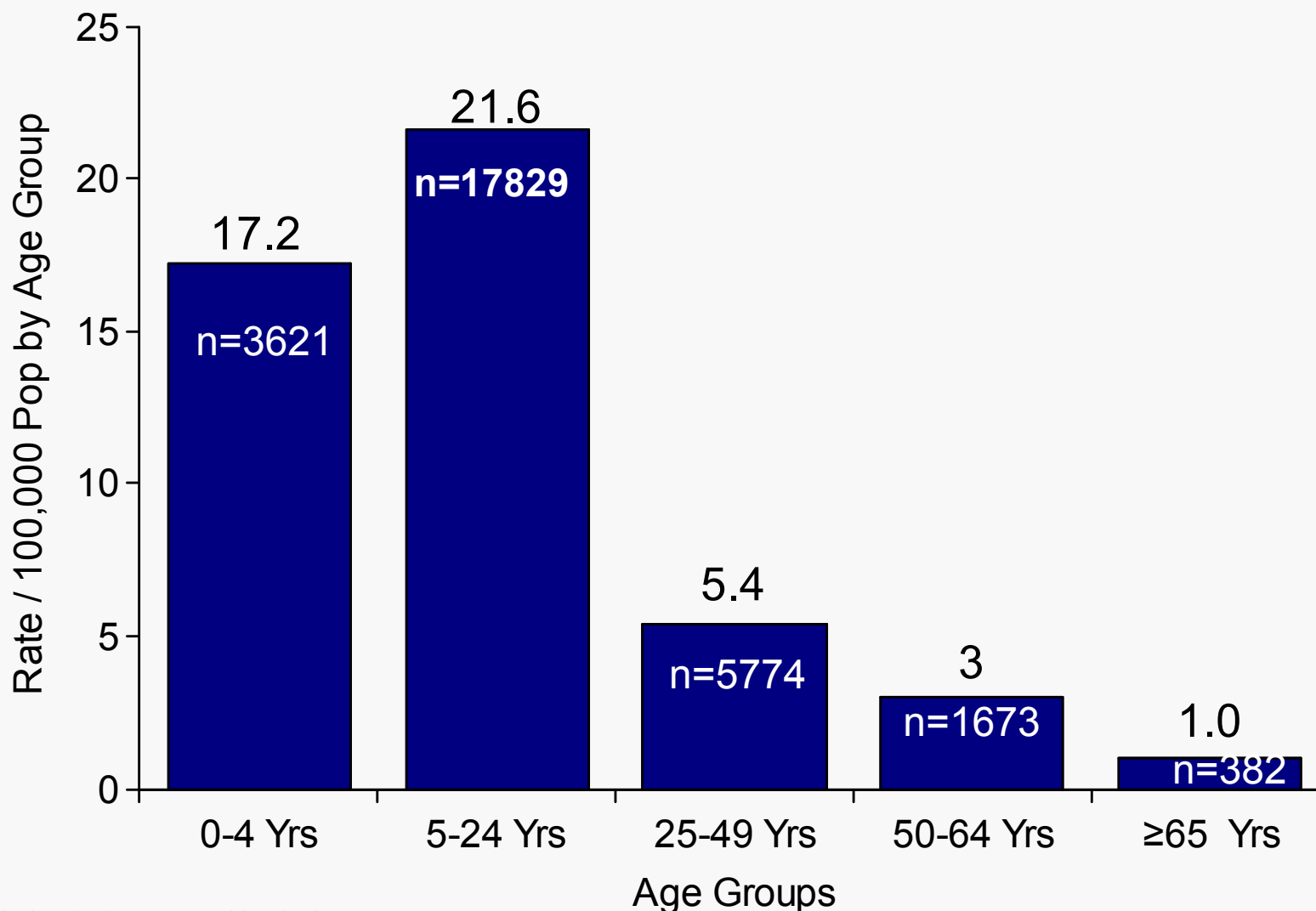




Epidemiology/Surveillance

Pandemic H1N1 Cases Rate per 100,000 Population by Age Group

As of 09 JULY 2009 (n=35,860*)



*Excludes 1,386 cases with missing ages.

Rate / 100,000 by Single Year Age Groups: Denominator source: 2008 Census Estimates, U.S. Census Bureau at:
<http://www.census.gov/popest/national/asrh/files/NC-EST2007-ALLDATA-R-File24.csv>

Data are provisional and will not be officially released by the CDC until 1100 EDT

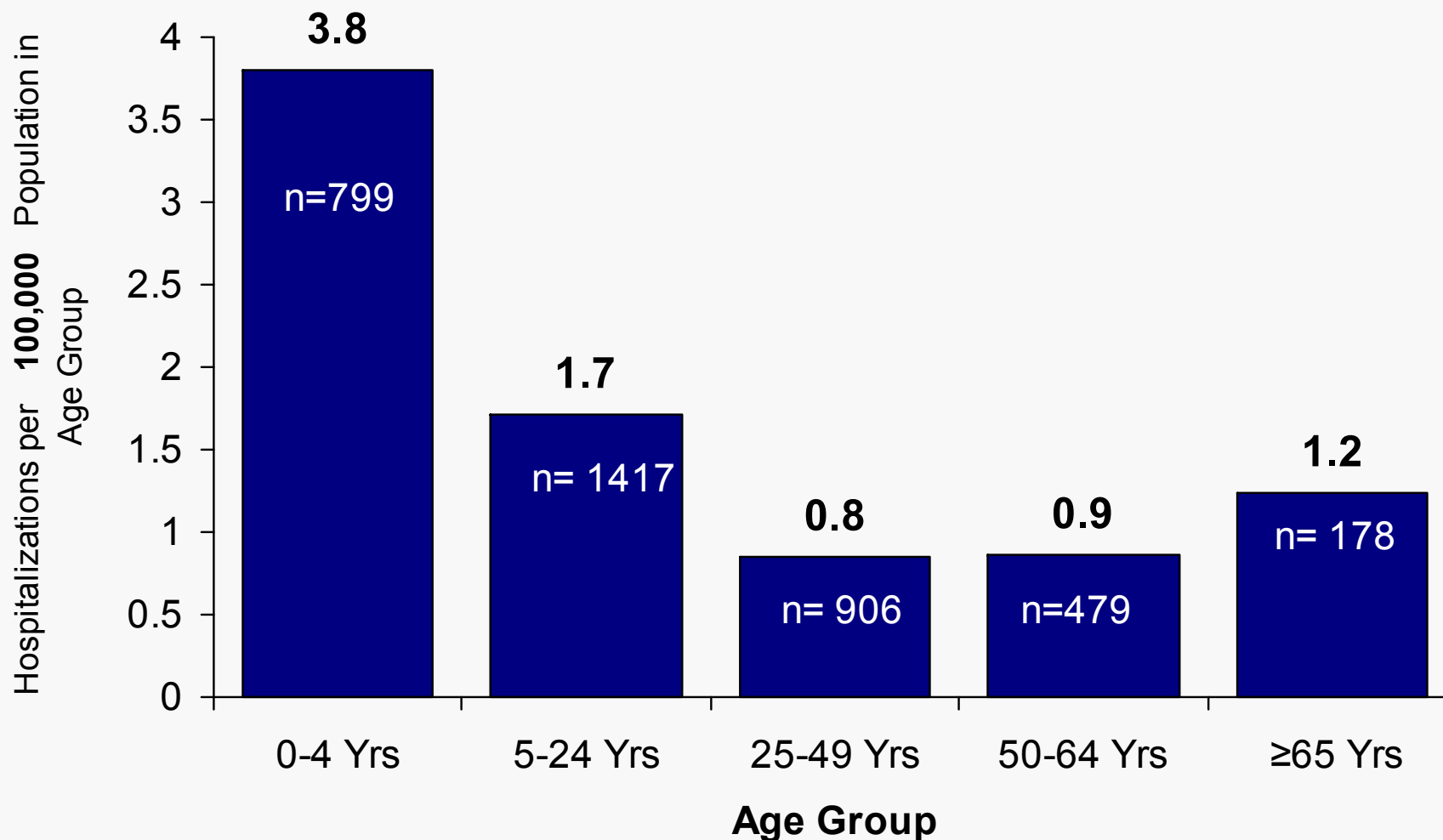
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Epidemiology/Surveillance Pandemic H1N1



Hospitalization Rate per 100,000 Population by Age Group (n=3,779) As of 09 JULY 2009



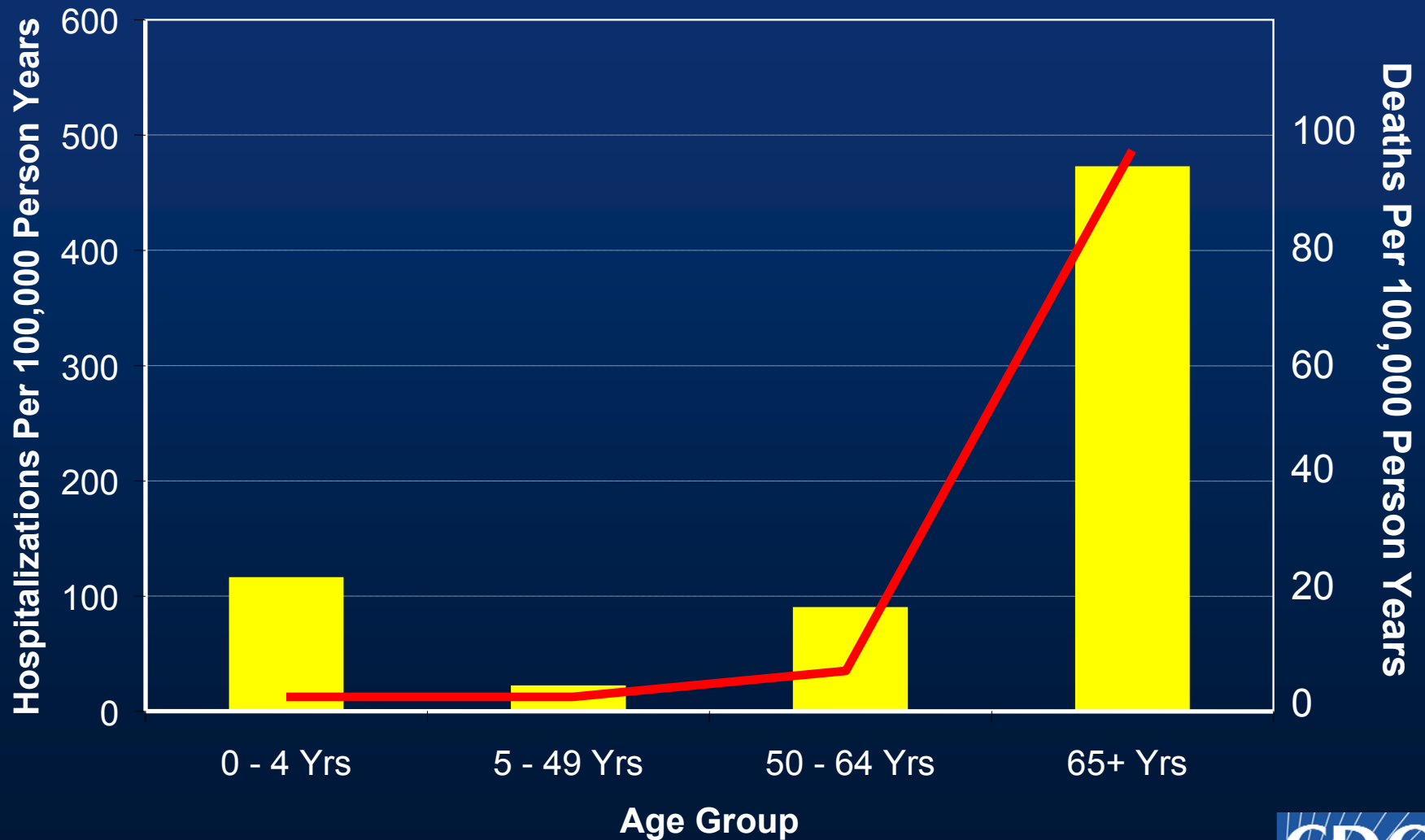
*Hospitalizations with unknown ages are not included (n=353)

*Rate / 100,000 by Single Year Age Groups: Denominator source: 2008 Census Estimates, U.S. Census Bureau at:
<http://www.census.gov/popest/national/asrh/files/NC-EST2007-ALLDATA-R-File24.csv>

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Influenza-Associated Hospitalizations Deaths By Age Group



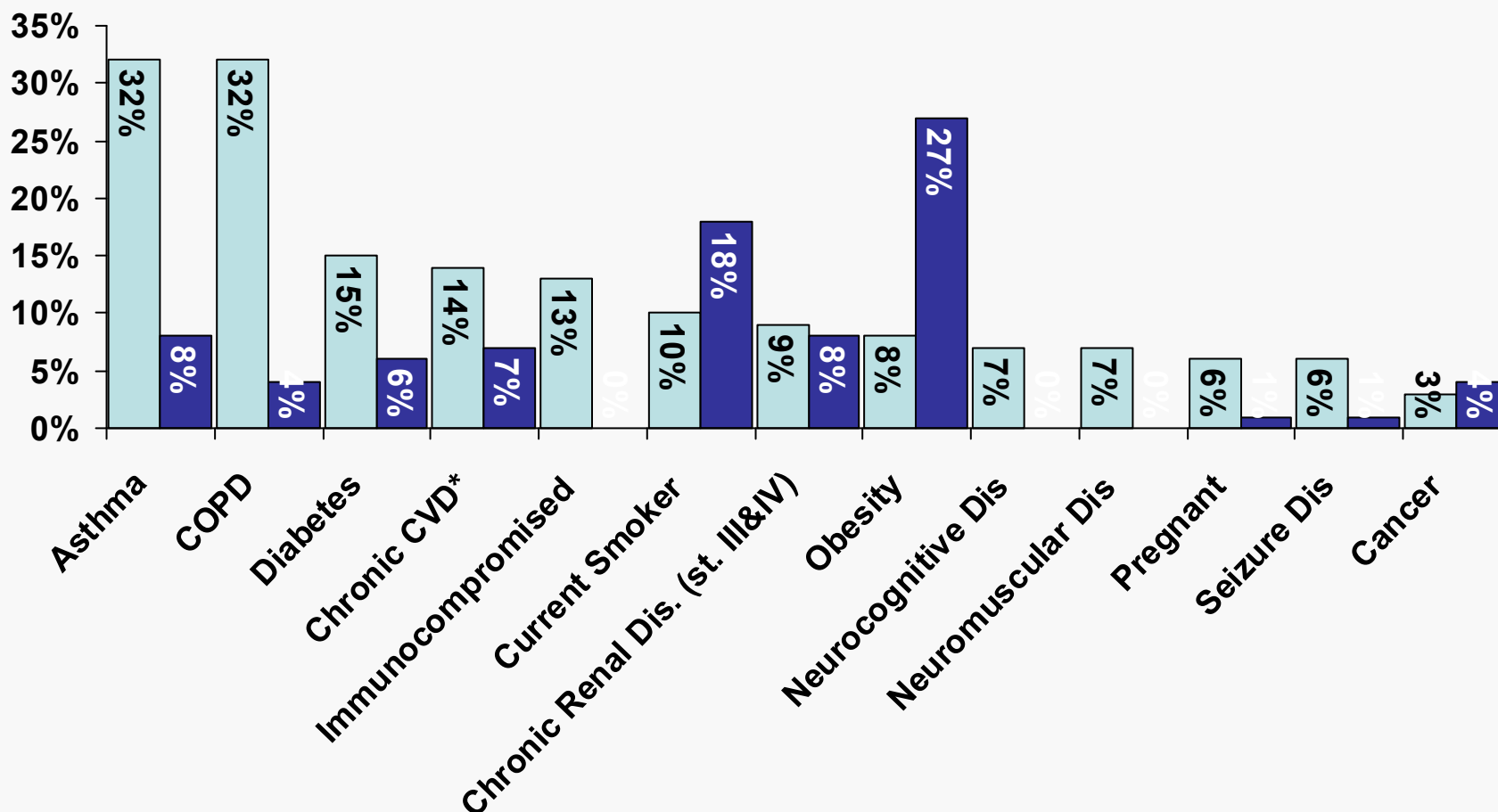
*Thompson WW, JAMA, 2004



Epidemiology/Surveillance

Pandemic H1N1 Hospitalizations Reported to CDC

Underlying Conditions as of 19 JUN 2009 (n=268)



■ Prevalence, Hospitalized H1N1 Patients ■ Prevalence, General US Pop

*Excludes hypertension

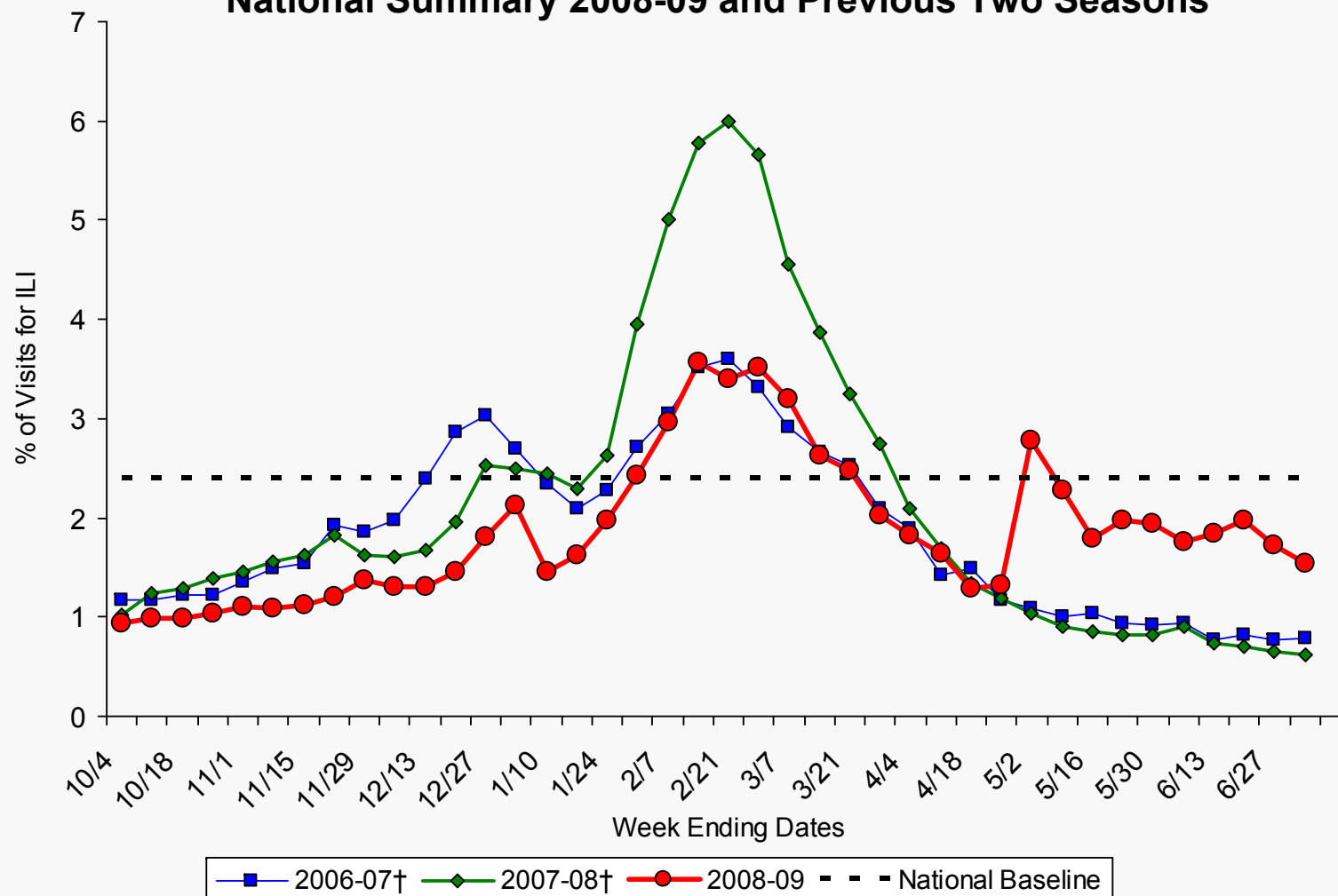
$D = 1 / (100,000 - 0.1) = 10^{-5}$





Epidemiology/Surveillance Pandemic H1N1 – 9 JUL 2009 EDT

Percentage of Visits for Influenza-like Illness (ILI) Reported by the *US Outpatient Influenza-like Illness Surveillance Network (ILINet)*, National Summary 2008-09 and Previous Two Seasons



† 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.

Data are provisional and will not be officially released by the CDC until 1100 EDT

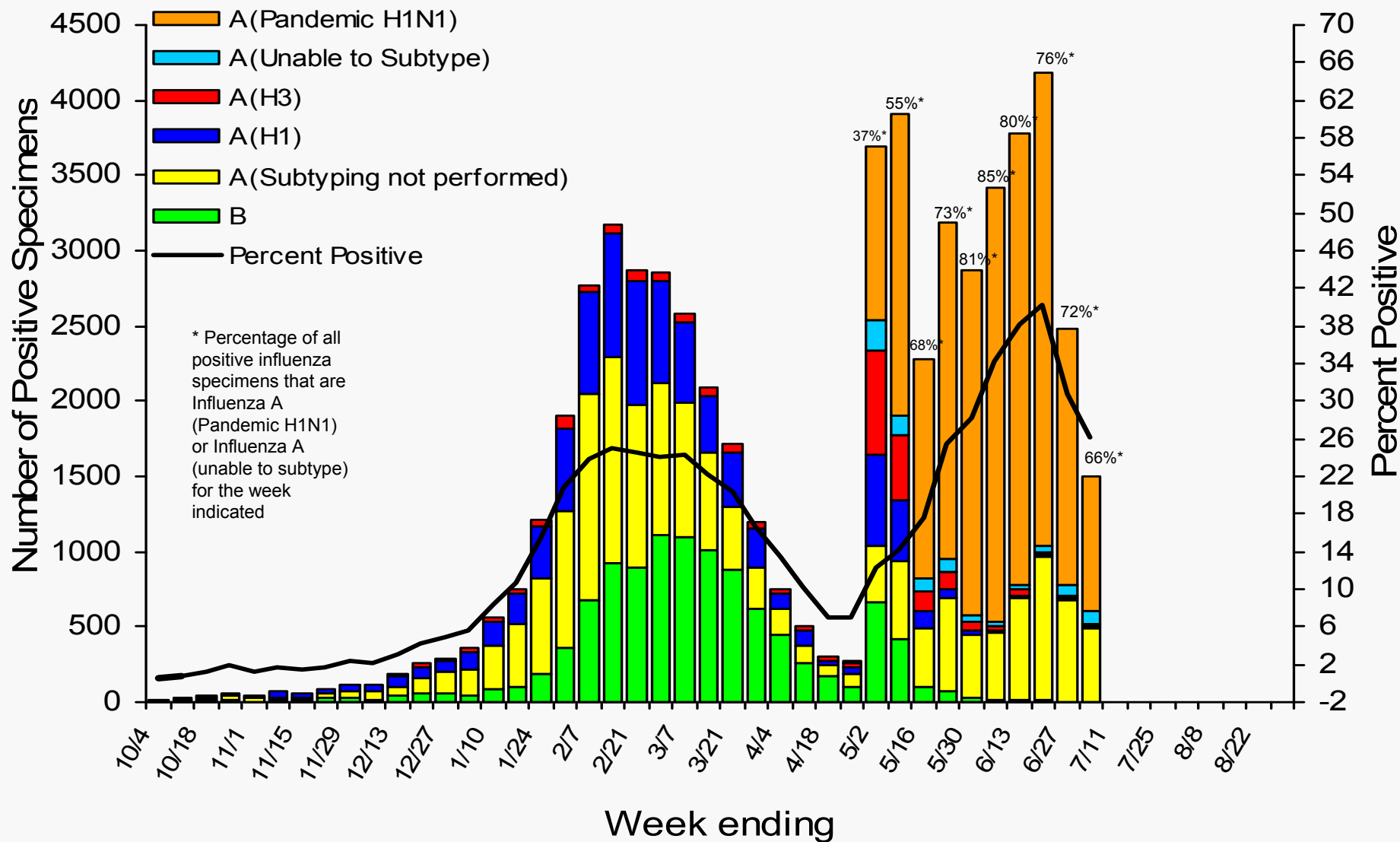
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Epidemiology/Surveillance Pandemic (H1N1) – 9 JUL 2009



U.S. WHO/NREVSS Collaborating Laboratories Summary, 2008-09



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Summary of Antiviral Resistance, U.S. 2008-09

	Influenza viruses			
Antiviral	Seasonal A (H1N1)	Seasonal A (H3N2)	Seasonal B	Pandemic H1N1
Adamantanes	Susceptible	Resistant	No activity	Resistant
Oseltamivir	Resistant	Susceptible	Susceptible	Susceptible
Zanamivir	Susceptible	Susceptible	Susceptible	Susceptible

Oseltamivir-resistance among Pandemic H1N1 viruses

3 oseltamivir-resistant isolates of Pandemic H1N1 detected

- 2 cases found to have resistant strain while on oseltamivir chemoprophylaxis
 - Japan and Denmark
- 1 case detected by Hong Kong Department of Health reported a resistant virus isolated from a 16 year-old girl who had a fever upon arrival at the Hong Kong International airport
 - Illness began prior to boarding the plane in San Francisco
 - No exposure to
 - No illness among close contacts
 - No sign of community transmission



Antiviral Treatment Recommendations

➤ **Priority: Hospitalized Patients with suspected or confirmed pandemic H1N1 virus infection**

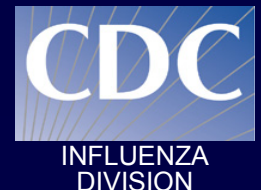
- Treatment recommended with Oseltamivir or Zanamivir
- Treat patients as soon as possible (duration: 5 days)

➤ **Outpatients with suspected or confirmed pandemic H1N1 virus infection who are at high risk for complications**

- Persons with chronic pulmonary, cardiac, renal, hepatic, metabolic, hematological disorders; immunosuppression, pregnant women, children <5 years; adults ≥65 years
- Treatment recommended with Oseltamivir or Zanamivir
- Treat patients as soon as possible (duration: 5 days)



<http://www.cdc.gov/h1n1flu/recommendations.htm>

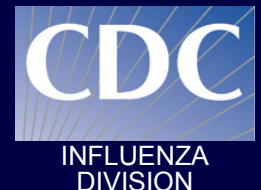


Antiviral Chemoprophylaxis

- **Post-exposure chemoprophylaxis with Oseltamivir or Zanamivir can be considered:**
 - **Close contacts of cases who are at high risk for complications of influenza**
 - **Health care personnel, public health workers, first responders with unprotected close contact exposure to an ill person with pandemic H1N1 virus infection while in the infectious period**
 - **Chemoprophylaxis: 7-10 days after last known exposure**



<http://www.cdc.gov/h1n1flu/recommendations.htm>



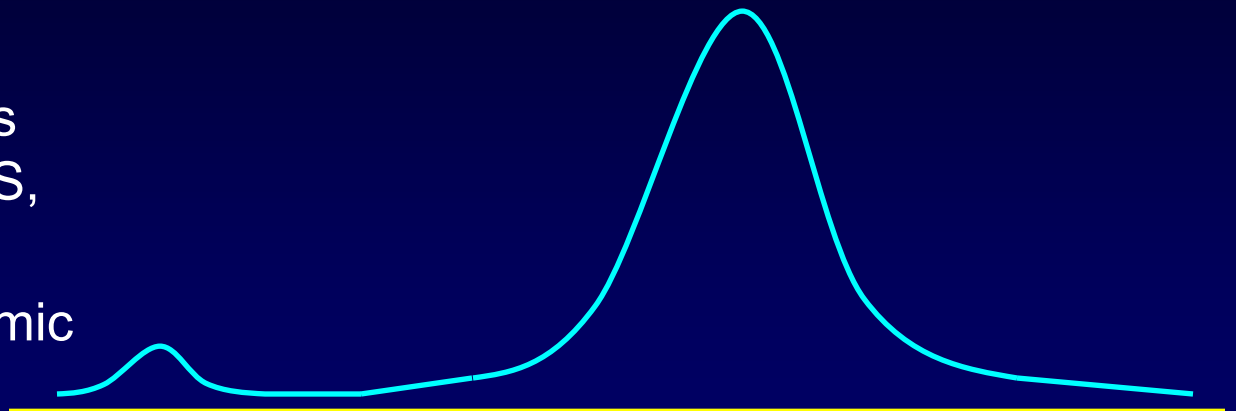
Summary of key points

- Once emerged, pandemic H1N1 virus spread to all 5 states and globally quickly
- Some areas more affected than others
- Expect continued summertime circulation with focal outbreaks
- Elderly seemingly relatively spared
- Capable of causing severe disease and death
 - Most severe outcomes among people with underlying health problems that are associated with high risk of influenza complications
- Virus remains sensitive to oseltamivir and zanamivir

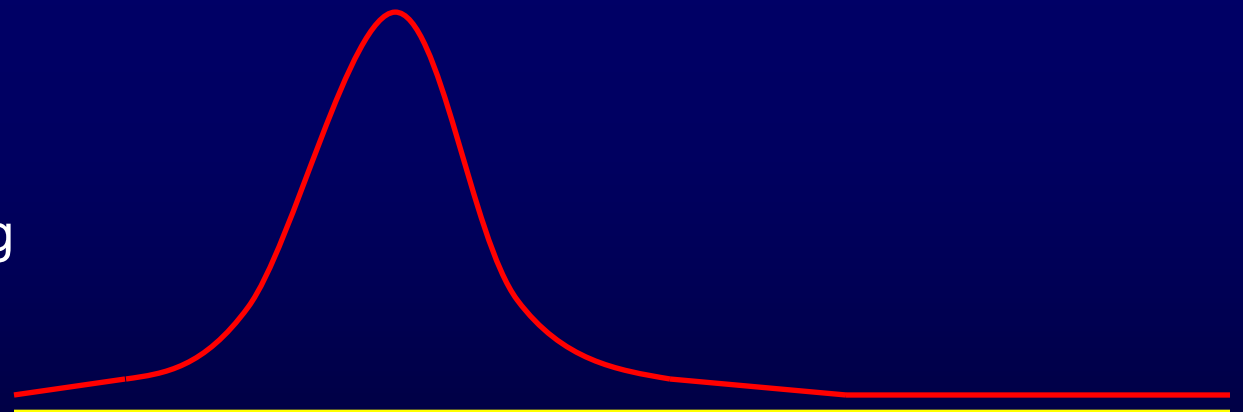


What's Next

- Disease likely persists through summer in US, expected surge in fall
- Severity of Fall epidemic difficult to predict
- Southern Hemisphere being monitored for subtypes, spread, and severity
- Vaccine being readied
- Surveillance continuing



Northern Hemisphere



Southern Hemisphere



Pandemic H1N1 Vaccine: Development and Manufacturing

Tom Shimabukuro, MD, MPH, MBA

**Immunization Services Division
Centers for Disease Control and Prevention**

July 15 & 16, 2009



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- *National Strategy for Pandemic Influenza* (Nov. 2005) goal is to provide vaccine to everyone in U.S. w/in 6 mo. of pandemic onset
- H1N1 Vaccine Strategy follows pandemic playbook for vaccine development, production, and administration
- Clinical studies will inform vaccine formulation and safety profile
- Key decision issues:
 - ✓ Vaccine product type
 - ✓ Use of thimerosal preservative
 - ✓ Use of oil in water emulsion

H1N1 Vaccines



Courtesy Robin Robinson, PhD, HHS/ASPR/BARDA Director

www.cdc.gov/H1N1flu



Phases of a vaccination program

- Vaccine development
- Commercial scale manufacturing
- Distribution and administration
- Post-launch effectiveness, safety and utilization monitoring



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Vaccine development

- Vaccine reference strain development
- Master seed strain preparation
- Clinical investigational lot manufacturing
- Clinical studies
 - ✓ To assess immunologic response and safety
 - ✓ Will inform formulation decisions



Commercial scale production

- Potency assay reagents preparation and calibration
- Commercial scale bulk antigen manufacturing without adjuvant
- Commercial bulk antigen manufacturing with adjuvant
- Bulk adjuvant manufacturing
- Commercial scale syringe/needle manufacturing
- Vaccine formulation fill-finish

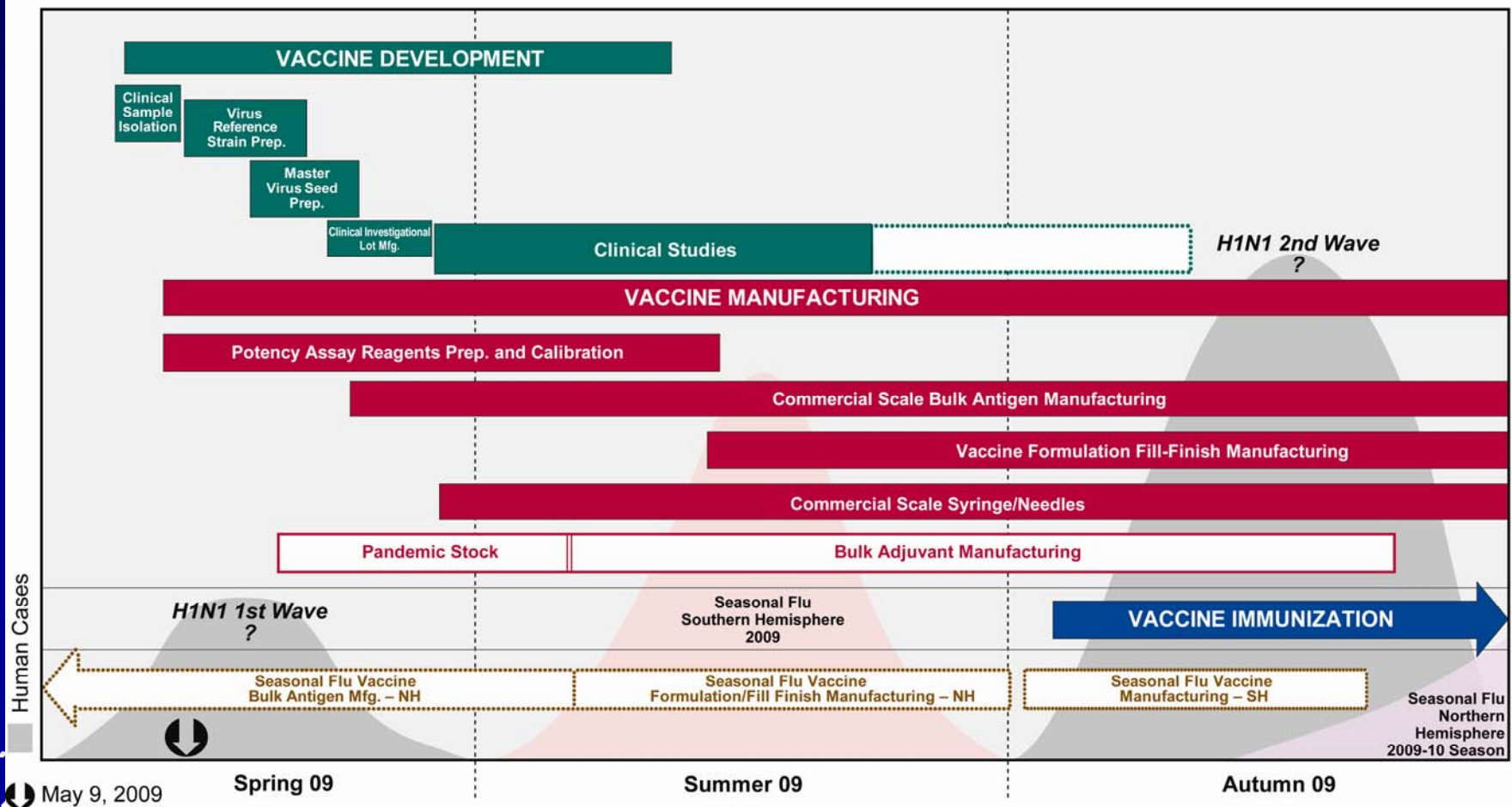
Note: Decisions on using adjuvanted vaccine are pending and will depend on multiple factors to include vaccine supply, clinical trial results and disease severity



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U.S. 2009-H1N1 Vaccine Strategy



Courtesy Robin Robinson, PhD, HHS/ASPR/BARDA Director

Ver 10a_05-08-09
TW_DWC

Vaccine manufacturers

- Novartis (45.7%)
 - ✓ Also manufactures MF59 adjuvant for potential pre-formulation with vaccine
- Sanofi Pasteur (26.4%)
- CSL (18.7%)
- MedImmune (5.8%)
- GSK (3.4%)
 - ✓ Also manufactures ASO3 adjuvant in a separate vial for potential mixing at the place of administration



Vaccine products (general)

- Unadjuvanted multidose vials*
- Unadjuvanted p-free pre-loaded syringes†
- Nasal sprayers (live attenuated)†

Potentially

- Multidose vials pre-formulated with adjuvant
- Multidose vials formulated for adjuvant to be mixed at the place of administration (separate antigen and adjuvant vials)

*All multidose vials will contain thimerosal preservative

†Up to 20% of vaccine may be p-free pediatric formulation



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Vaccine ancillary supplies

- Needle/syringe units for multidose vials
- Sharps containers
- Alcohol pads
- Mixing syringes if adjuvanted vaccine is used



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Vaccine products

- Novartis (45.7%)
 - ✓ Multidose vials: standard unadjuvanted
 - ✓ Multidose vials pre-formulated with Novartis MF59 adjuvant*
- Sanofi Pasteur (26.4%)
 - ✓ Multidose vials: standard unadjuvanted and formulated for GSK ASO3 adjuvant (separate antigen and adjuvant)*
- ✓ P-free pre-loaded syringes

*Decision to use an adjuvanted vaccine is TBD



Vaccine products cont.

- CSL (18.7%)
 - ✓ Multidose vials: standard unadjuvanted and formulated for GSK ASO3 adjuvant (separate antigen and adjuvant)*
 - ✓ P-free pre-loaded syringes
- MedImmune (5.8%)
 - ✓ Nasal sprayers, p-free
- GSK (3.4%)
 - ✓ Multidose vials: standard unadjuvanted and formulated for GSK ASO3 adjuvant (separate antigen and adjuvant)*

*Decision to use an adjuvanted vaccine is TBD



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✓ www.cdc.gov/H1N1flu



Storage and handling

- Inactivated vaccine
 - ✓ 2-8°C
- Live attenuated
 - ✓ 2-8°C
- Oil-in-water adjuvant
 - ✓ 2-8°C, 2-5 year shelf life
- Inactivated vaccine mixed with adjuvant
 - ✓ Stable up to 8 hours after mixing



Emergency Use Authorization

- “... use of an unapproved medical product or an unapproved use of an approved medical product during a declared emergency ...”
 - ✓ Unadjuvanted pandemic H1N1 vaccine may be licensed in a manner similar to a seasonal flu vaccine strain change and therefore would not need an EUA
 - ✓ Adjuvanted vaccines, if used (for the 2009-10 flu season), will be administered under an EUA





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Pandemic H1N1 Vaccine: Program Implementation

Pascale Wortley, MD, MPH

**Immunization Services Division
Centers for Disease Control and Prevention**

July 15 & 16, 2009



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Vaccine purchase, allocation, and distribution

- Vaccine procured and purchased by US government
- Vaccine will be allocated across states proportional to population
- Vaccine will be sent to state-designated receiving sites: mix of local health departments and private settings



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Vaccine planning assumptions:

- Vaccine available starting mid-October
- Initial amount: 40, 80, or 160 million doses over one month period
- Subsequent weekly production: 10, 20 or 30 million doses
- 2 doses required
- Preservative free single dose syringes for young children and pregnant women



Vaccine planning assumptions:

Populations to plan for:

Students and staff (all ages) associated with schools (K-12) and children (age >6 m) and staff (all ages) in child care centers

- Pregnant women, children 6m-4yrs, new parents and household contacts of children <6 months of age
- Non-elderly adults (age <65) with medical conditions that increase risk of influenza
- Health care workers and emergency services personnel



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Delivery model

Public health-coordinated effort that blends vaccination in public health-organized clinics and in the private sector (provider offices, workplaces, retail settings)



Private sector providers who wish to administer H1N1 vaccine will need to enter into an agreement with public health in order to receive vaccine



Public Health planning efforts

- Reaching out to private providers (defined broadly) to assess interest in providing H1N1 vaccine
- Retail sector, pharmacists may be involved
- Planning large scale clinics
 - Especially important for school-age children given limited private sector capacity



Issues for administration in provider offices

- Storage capacity
- Administering according to recommended age groups
- Reporting doses administered early on
- Insurance reimbursement for administration



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Monitoring vaccine coverage

- Initially, states will be required to report doses administered on a weekly basis
- Transition to assessment via population surveys (BRFSS, NIS)



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Monitoring vaccine safety

- Vaccine Adverse Event Reporting System (1-800-822-7967, <http://vaers.hhs.gov/contact.htm>) for signal detection
- Network of managed care organizations representing approximately 3% of the U.S. population, the Vaccine Safety Datalink (VSD) to test signals.
- Active surveillance for Guillain Barre Syndrome through states participating in Emerging Infections Program.



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Monitoring vaccine effectiveness (VE)

- VE for prevention of PCR-confirmed medically attended influenza at 4 community-based sites
- VE for prevention of influenza hospitalizations diagnosed by provider-ordered clinically available tests at 10 sites nationwide through the Emerging Infections Program
- DoD will be assessing VE in active duty service members



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