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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The contents of this presentation are those of the presenter and do not necessarily reflect the views of CDC

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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

MMWR

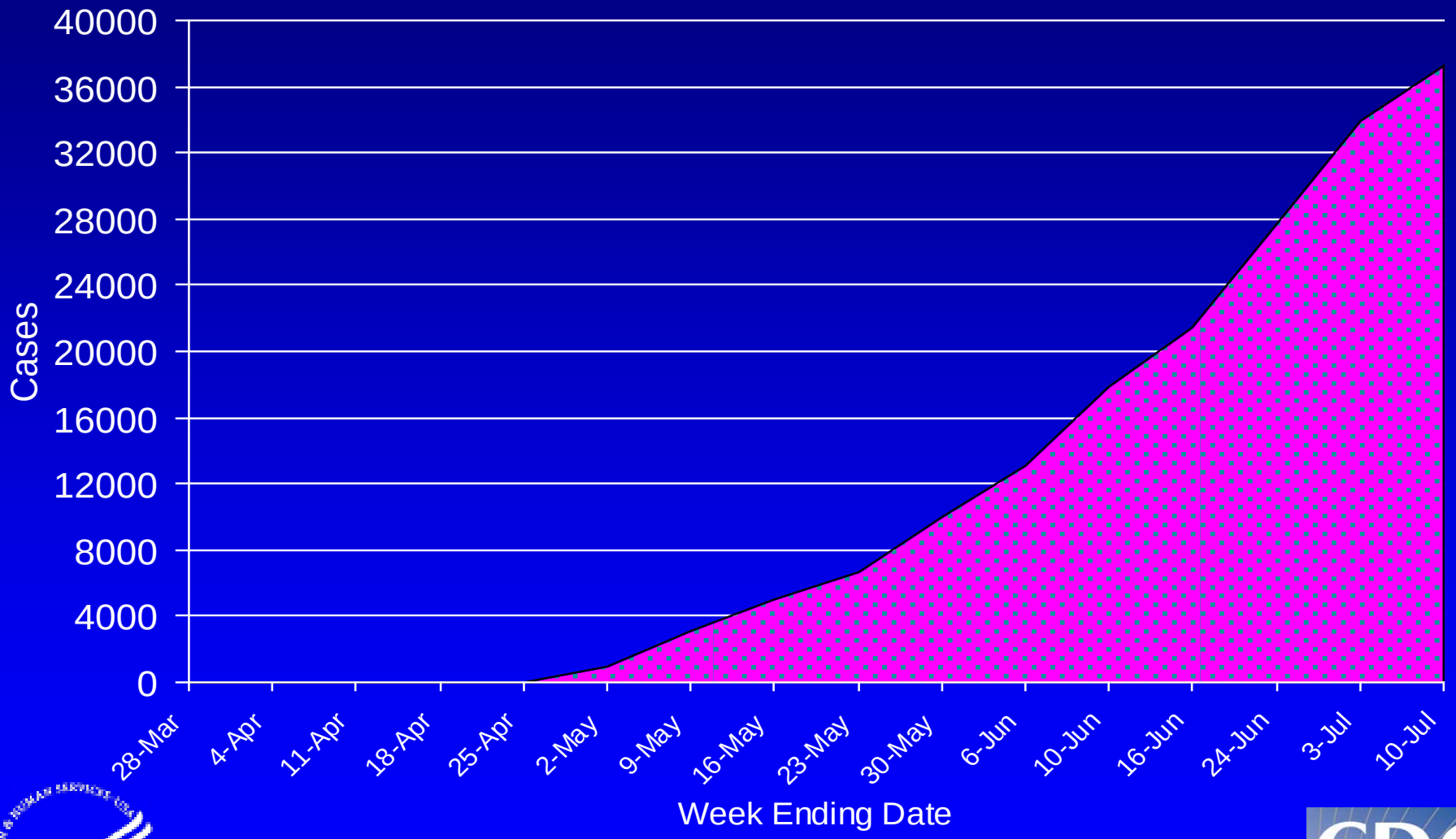
Swine Influenza A (H1N1) Infection in Two Children — Southern California, March–April 2009

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)



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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

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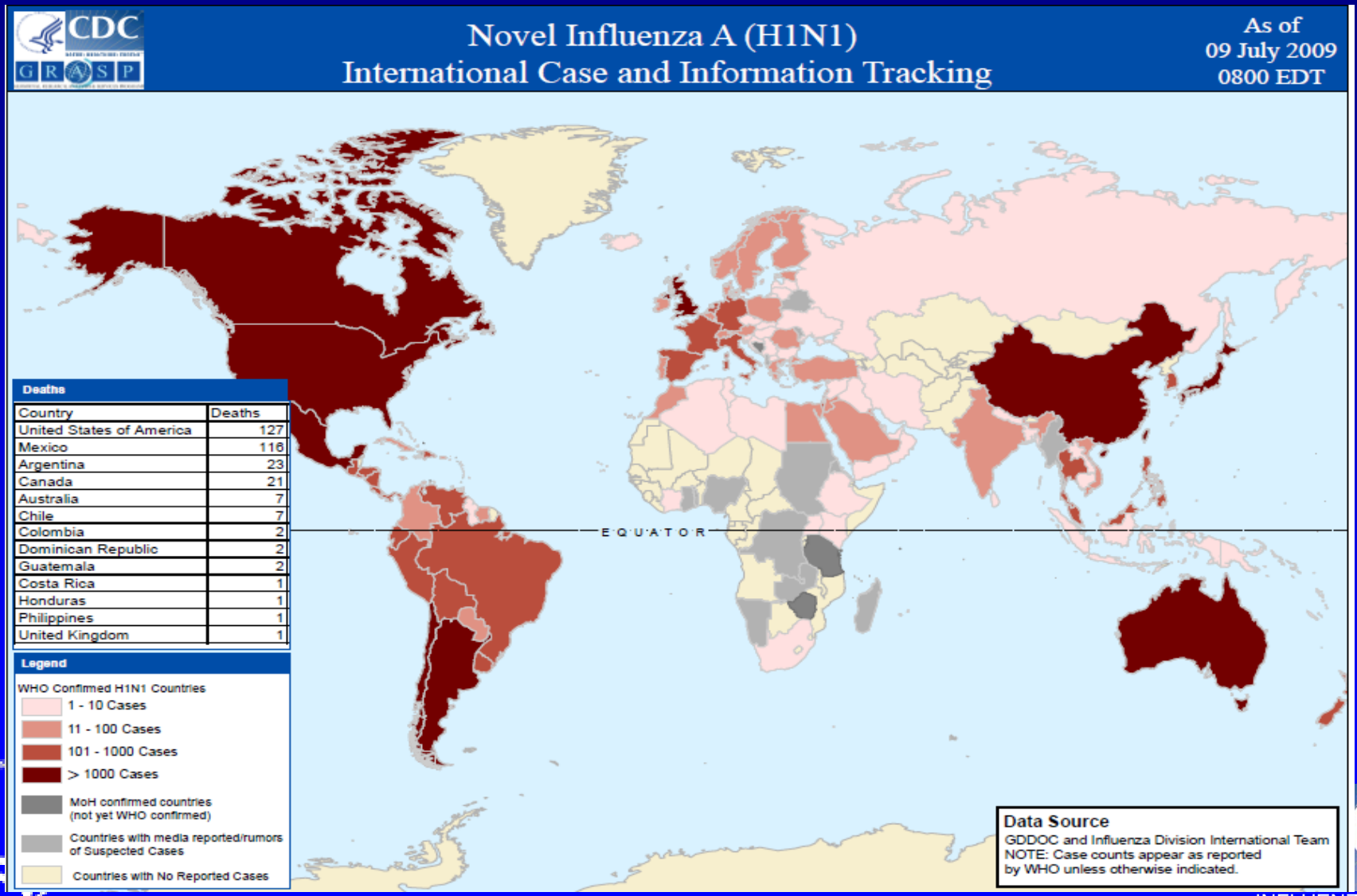
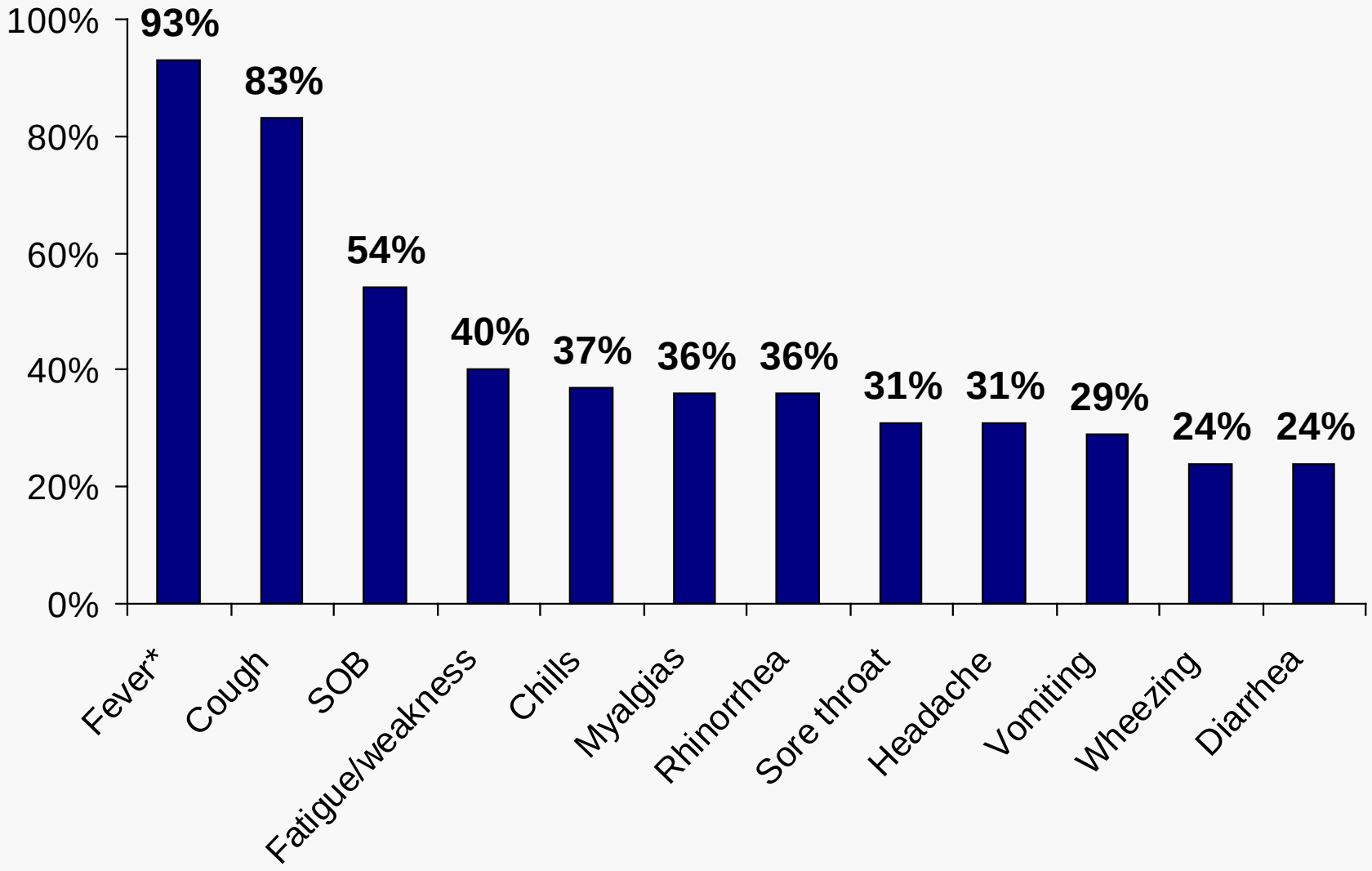
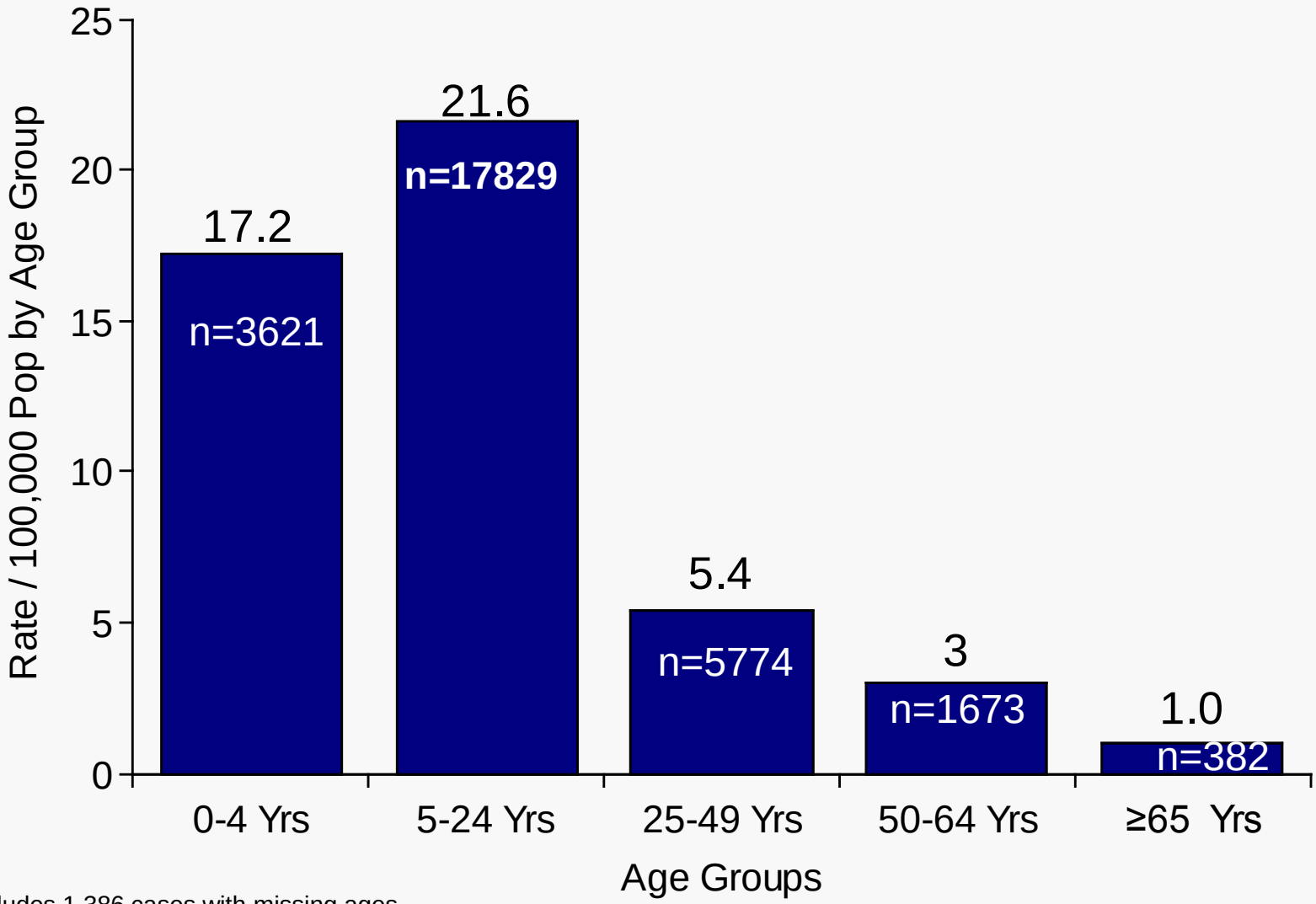
International Map
Pandemic H1N1 – 10 JUL 2009



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



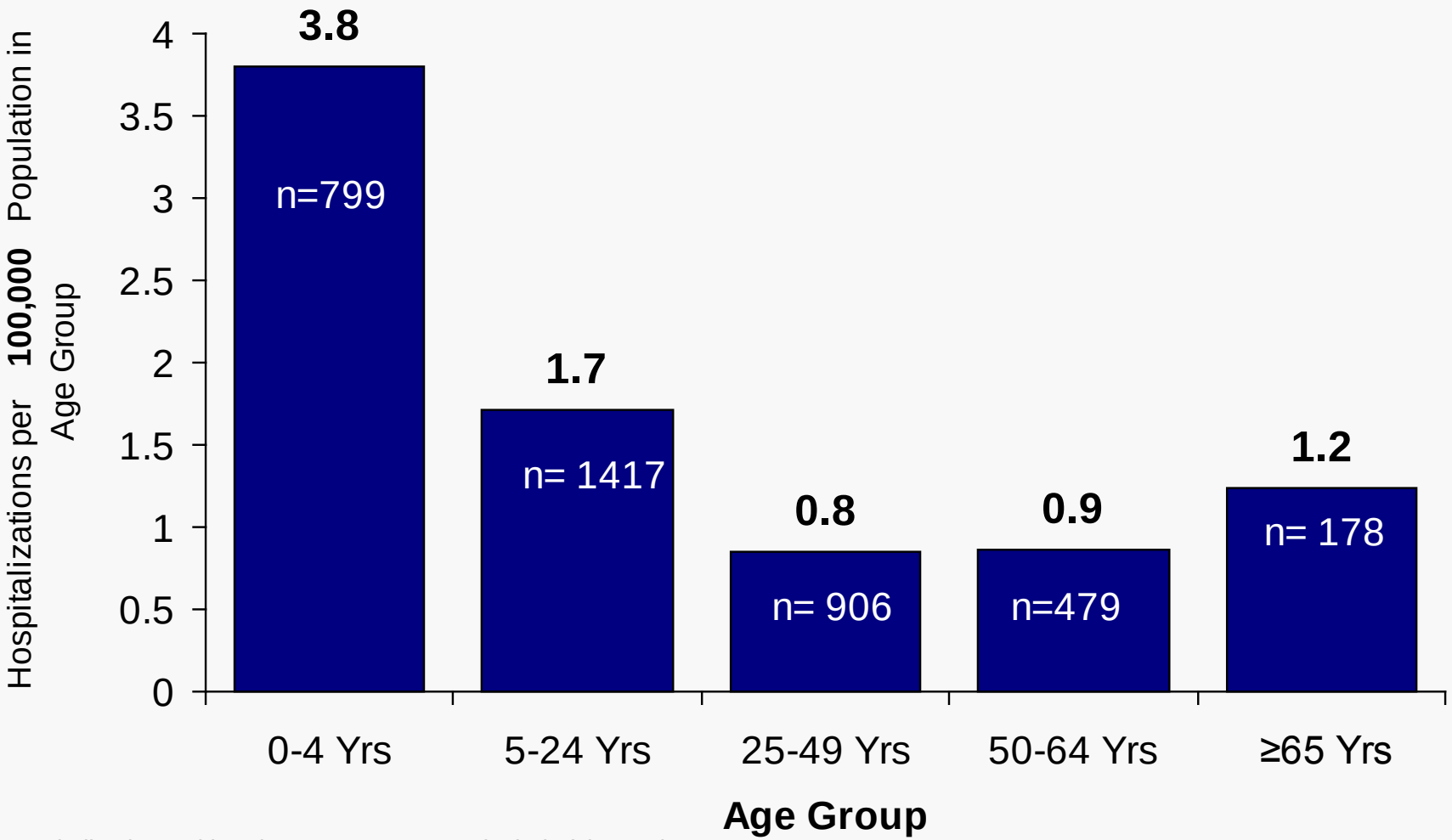
Epidemiology/Surveillance
Pandemic H1N1 Cases Rate per 100,000 Population by Age Group
As of 09 JULY 2009 (n=35,860*)



*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

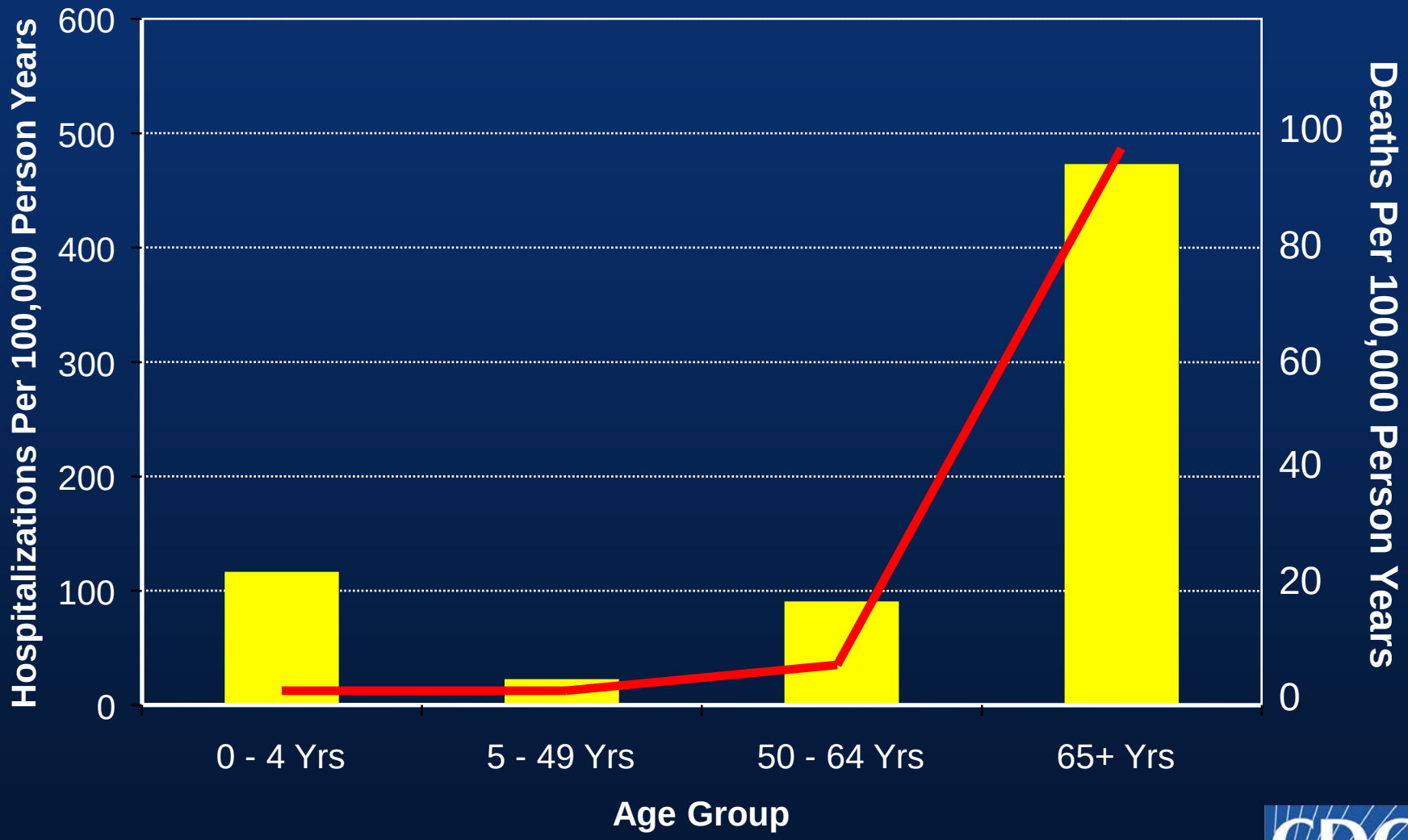
Epidemiology/Surveillance
Pandemic H1N1
Hospitalization Rate per 100,000 Population by Age Group (n=3,779)
As of 09 JULY 2009



*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

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

Influenza-Associated Hospitalizations Deaths By Age Group



*Thompson WW, JAMA, 2004

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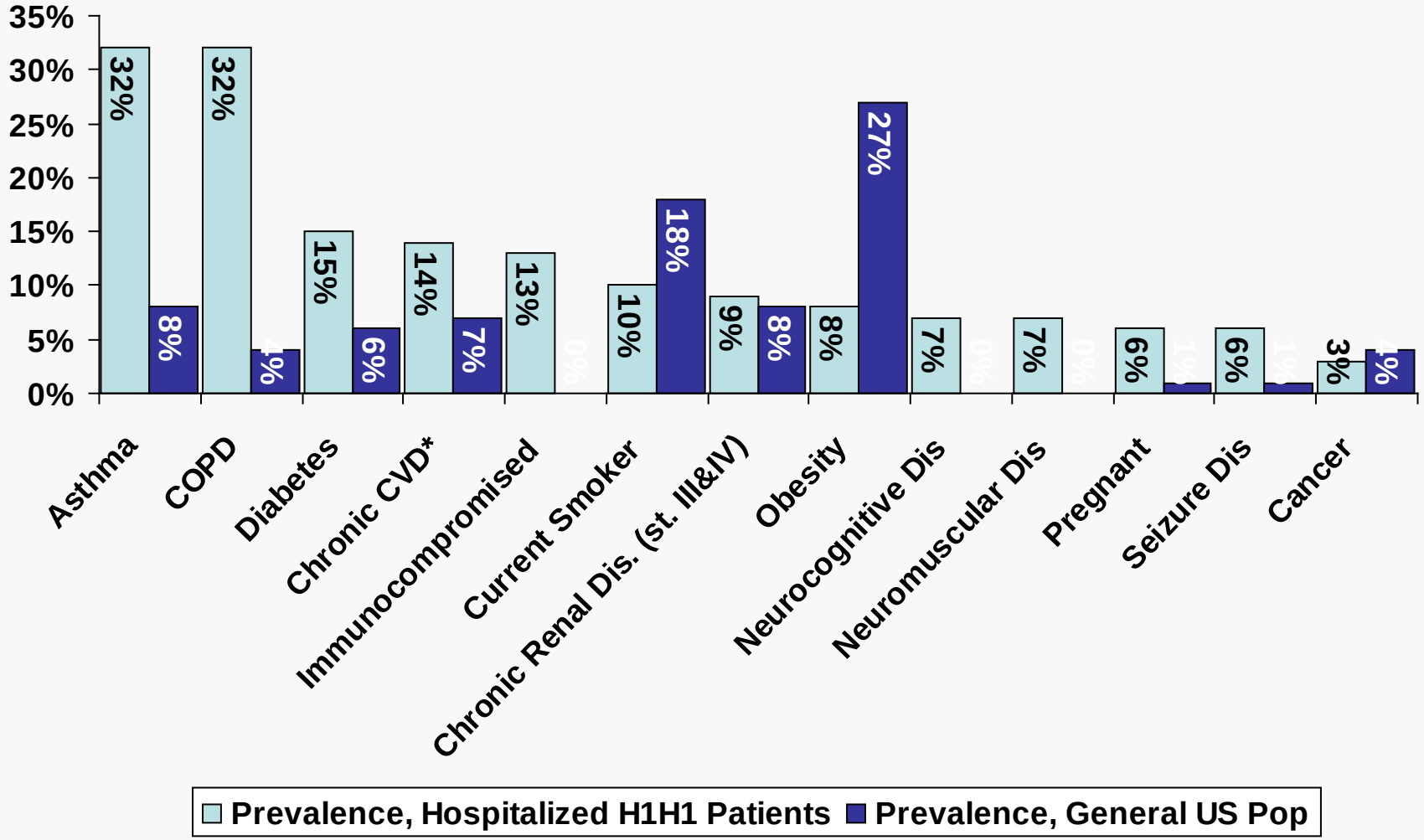
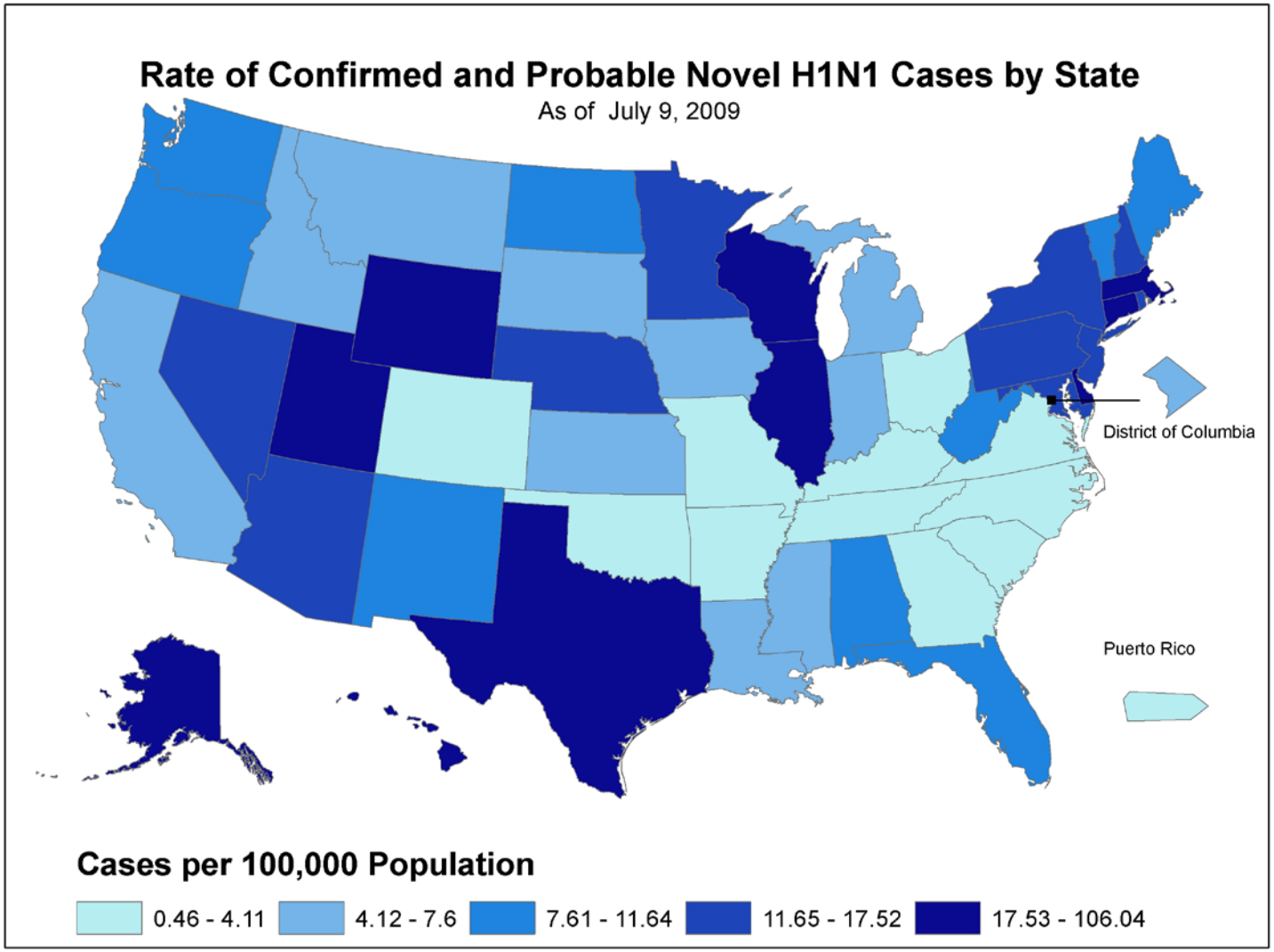
Epidemiology/Surveillance
Pandemic H1N1 Hospitalizations Reported to CDC
Underlying Conditions as of 19 JUN 2009 (n=268)

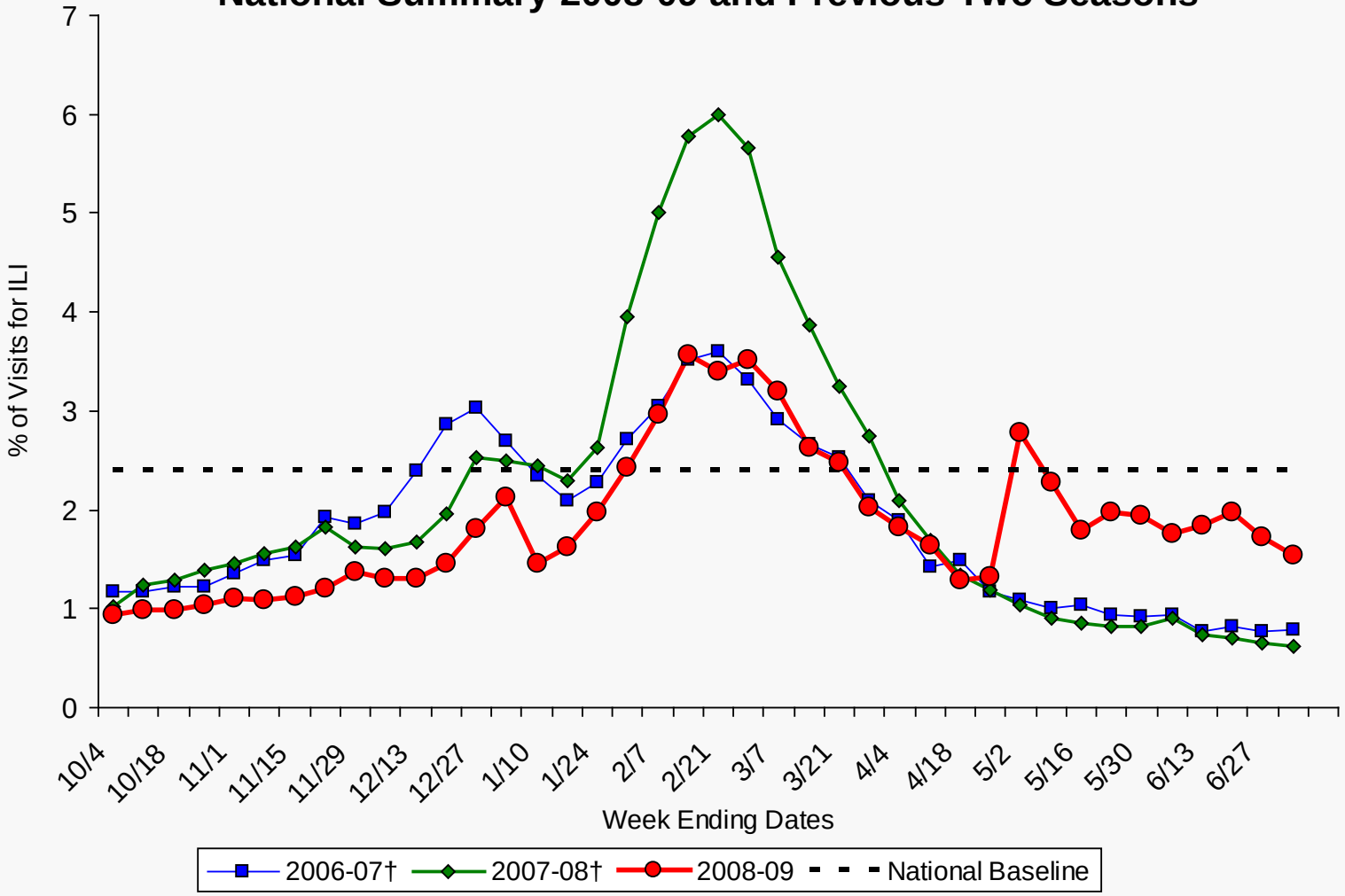


*Excludes hypertension

Pandemic H1N1 Cases by State

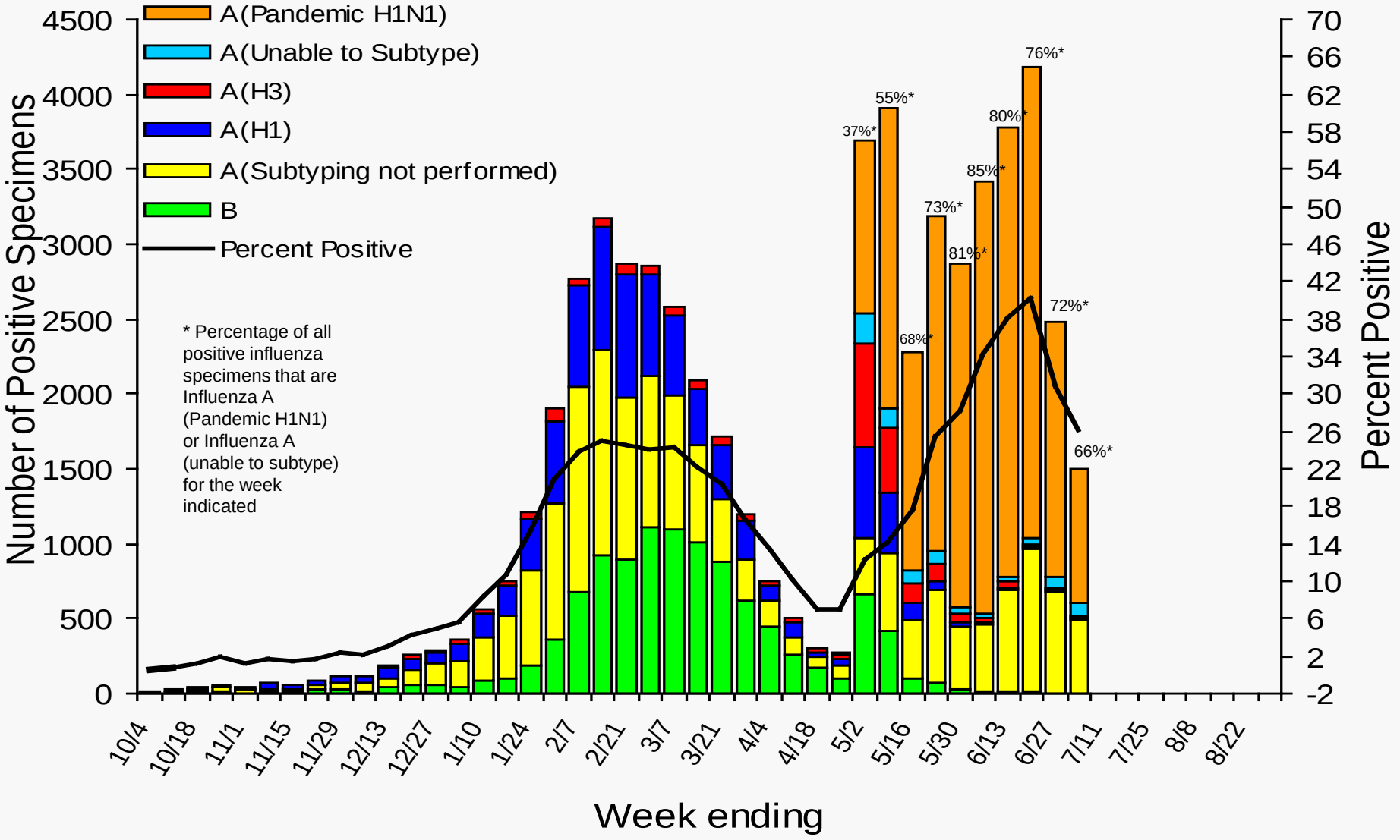


Epidemiology/Surveillance
Pandemic H1N1 – 9 JUL 2009 EDT
Percentage of Visits for Influenza-like Illness (ILI) Reported by the *US Outpatient Influenza-like Illness Surveillance Network (ILINet)*, National Summary 2008-09 and Previous Two Seasons



† 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.

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**

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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

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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

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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

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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 heath problems that are associated with high risk of influenza complications
- Virus remains sensitive to oseltamivir and zanamvir

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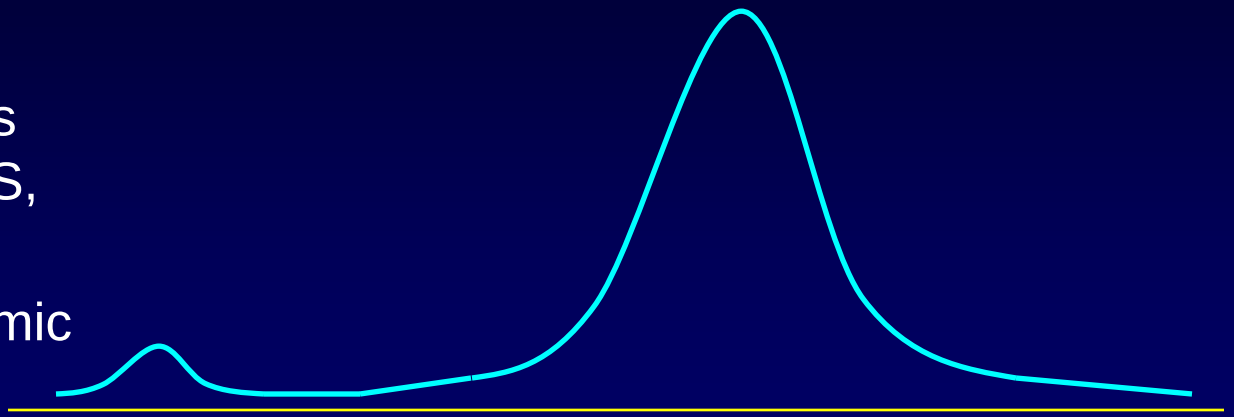
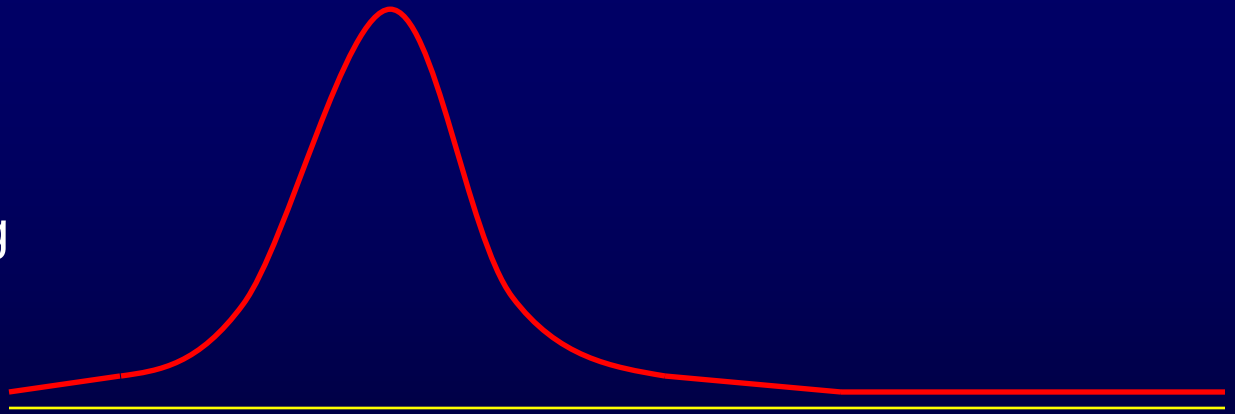
What's Next

- 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

www.cdc.gov/H1N1flu

Pandemic H1N1 Vaccine: Development and Manufacturing

Tom Shimabukuro, MD, MPH, MBA

Immunization Services Division
Centers for Disease Control and Prevention

July 15 & 16, 2009

H1N1 Vaccines

- *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 adjuvant

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

Vaccine development

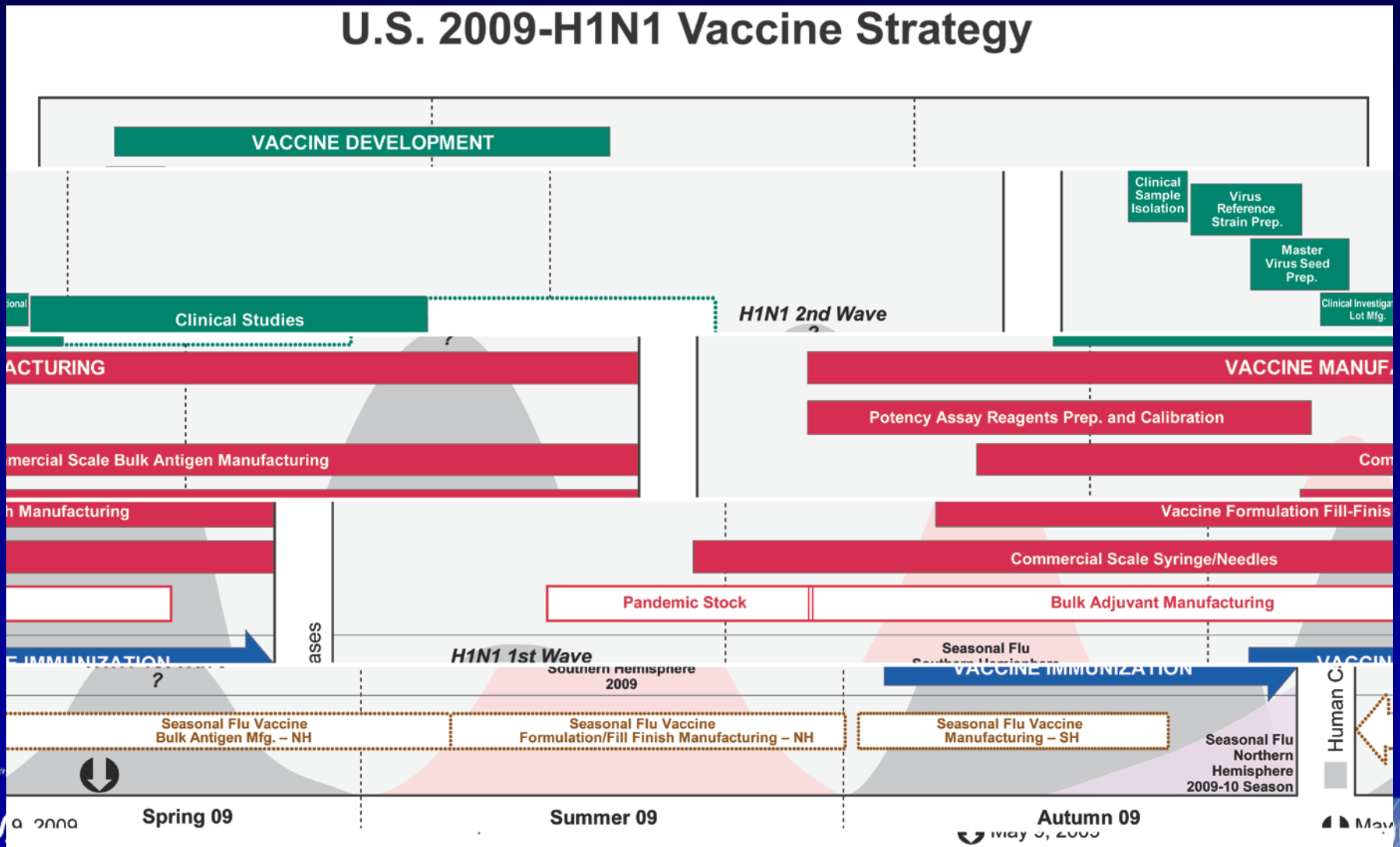
- Vaccine reference strain development
- Master seed strain preparation
- Clinical investigational lot manufacturing
- Clinical studies
  - ✓To assess immunologic response and safety
  - ✓Will inform formulation decisions

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

U.S. 2009-H1N1 Vaccine Strategy



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

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)†**

<u>Potentially</u>

- **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

Vaccine ancillary supplies

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

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)***

*Decision to use an adjuvanted vaccine is TBD

- ✓**P-free pre-loaded syringes**

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)*
  - ✓ASO3 adjuvant

*Decision to use an adjuvanted vaccine is TBD

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**

Pandemic H1N1 Vaccine: Program Implementation

Pascale Wortley, MD, MPH

Immunization Services Division
Centers for Disease Control and Prevention

July 15 & 16, 2009

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

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

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

Monitoring vaccine coverage

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

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.

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