

2009 H1N1 Influenza Vaccine Program

Tom Shimabukuro, MD, MPH, MBA

**Pandemic Influenza Vaccine Coordinator
Immunization Services Division**

Centers for Disease Control and Prevention (CDC)

California Immunization Coalition Summit

May 4, 2010



General background



Response timeline

15 Apr 09
to
31 May 09

1 Jun 09
to
15 Aug 09

16 Aug 09
to
4 Oct 09

5 Oct 09
to
Present

Discovery

Preparation

Fall wave

Vaccination

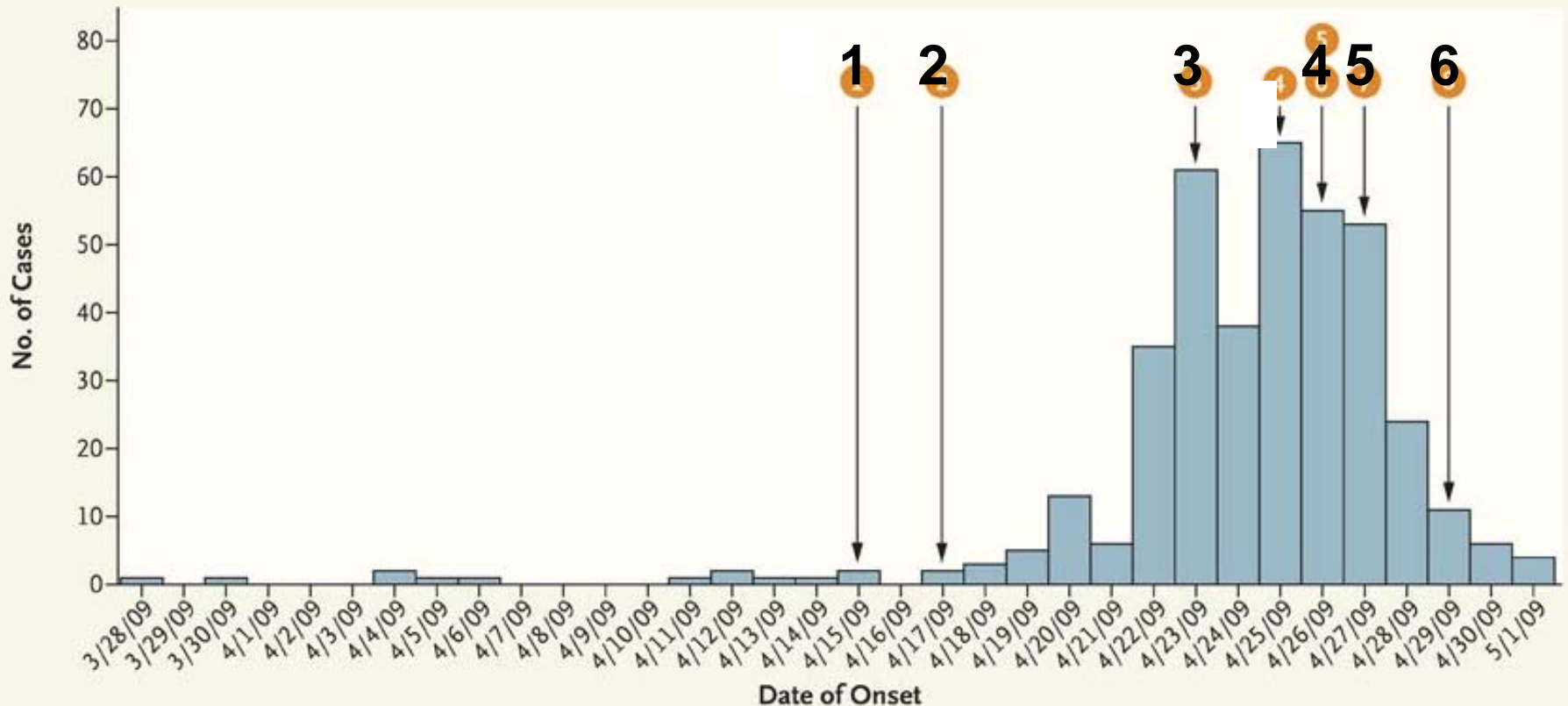


Making the diagnosis



- Mesoscale device used to diagnose influenza in 10 y/o boy during clinical trial in San Diego on April 1, 2009
- Result was influenza A positive, however, H1, H3, H5 negative

Confirmed Cases of Human Infection with Novel Influenza A (H1N1) with Known Date of Illness Onset, United States, March 28 – May 5, 2009

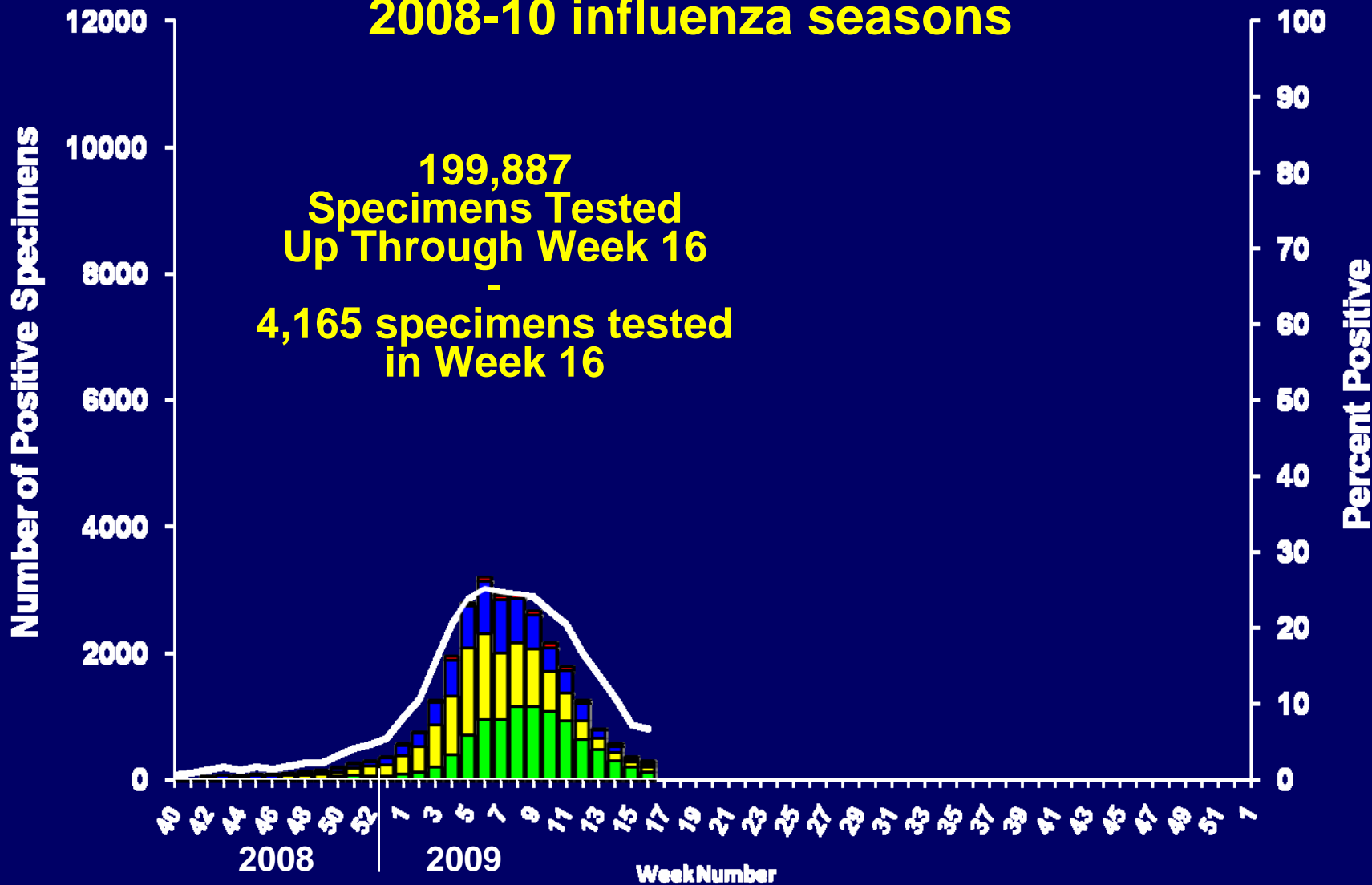


Novel Swine-Origin Influenza A (H1N1) Virus Investigation Team. *N Engl J Med* 2009;10.1056/NEJMoa0903810

1. Patient 1
2. Patient 2
3. Recognition of potential match between Mexico and US viruses
4. US declares a public health emergency
5. WHO raises to Pandemic Phase 4
6. WHO raises to Pandemic Phase 5



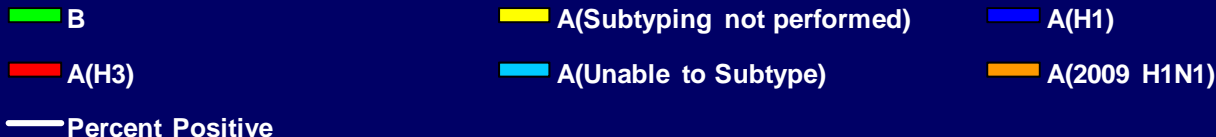
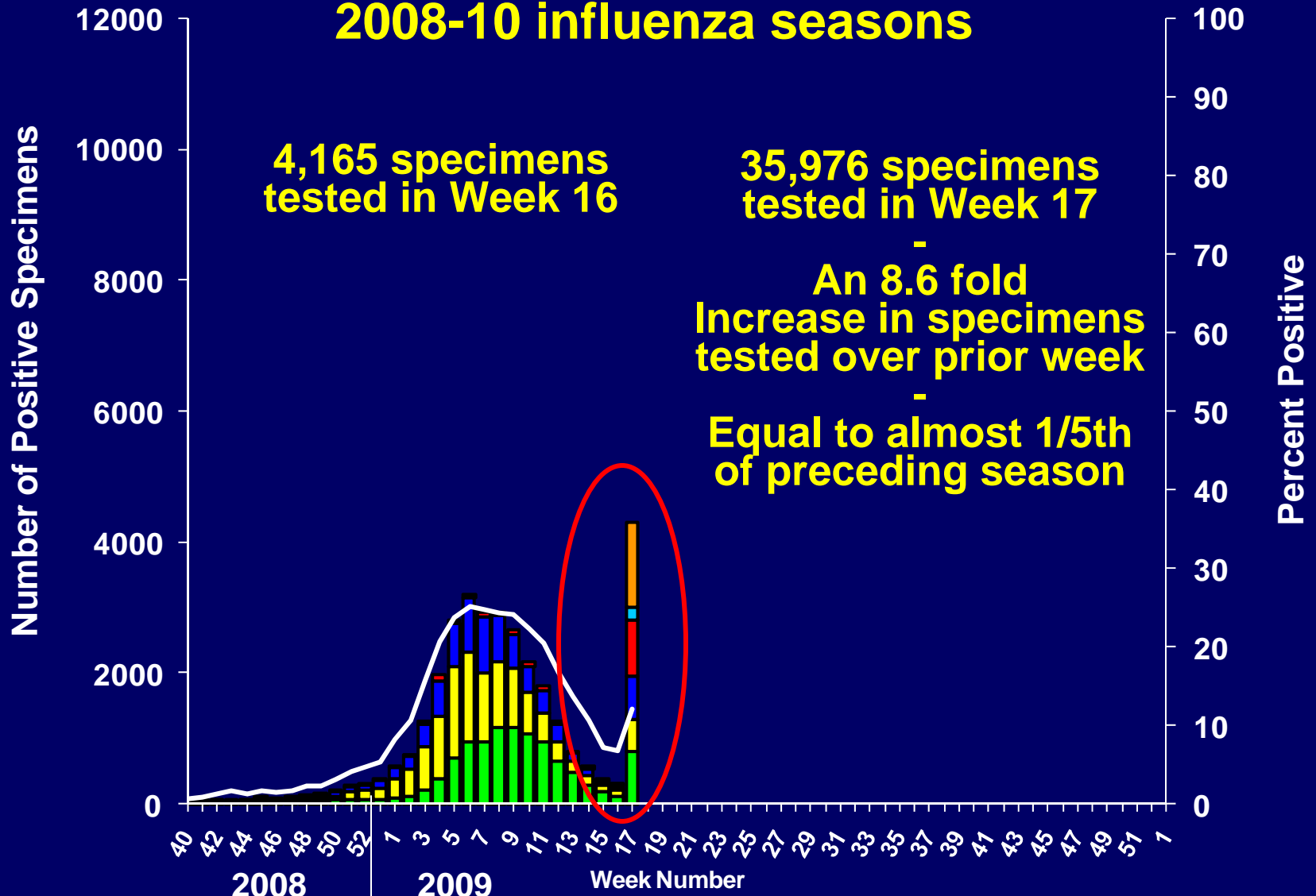
CDC virologic surveillance collaborating laboratories 2008-10 influenza seasons



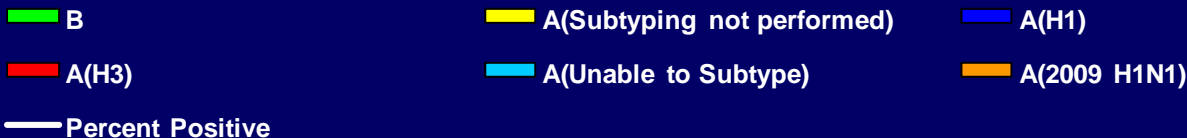
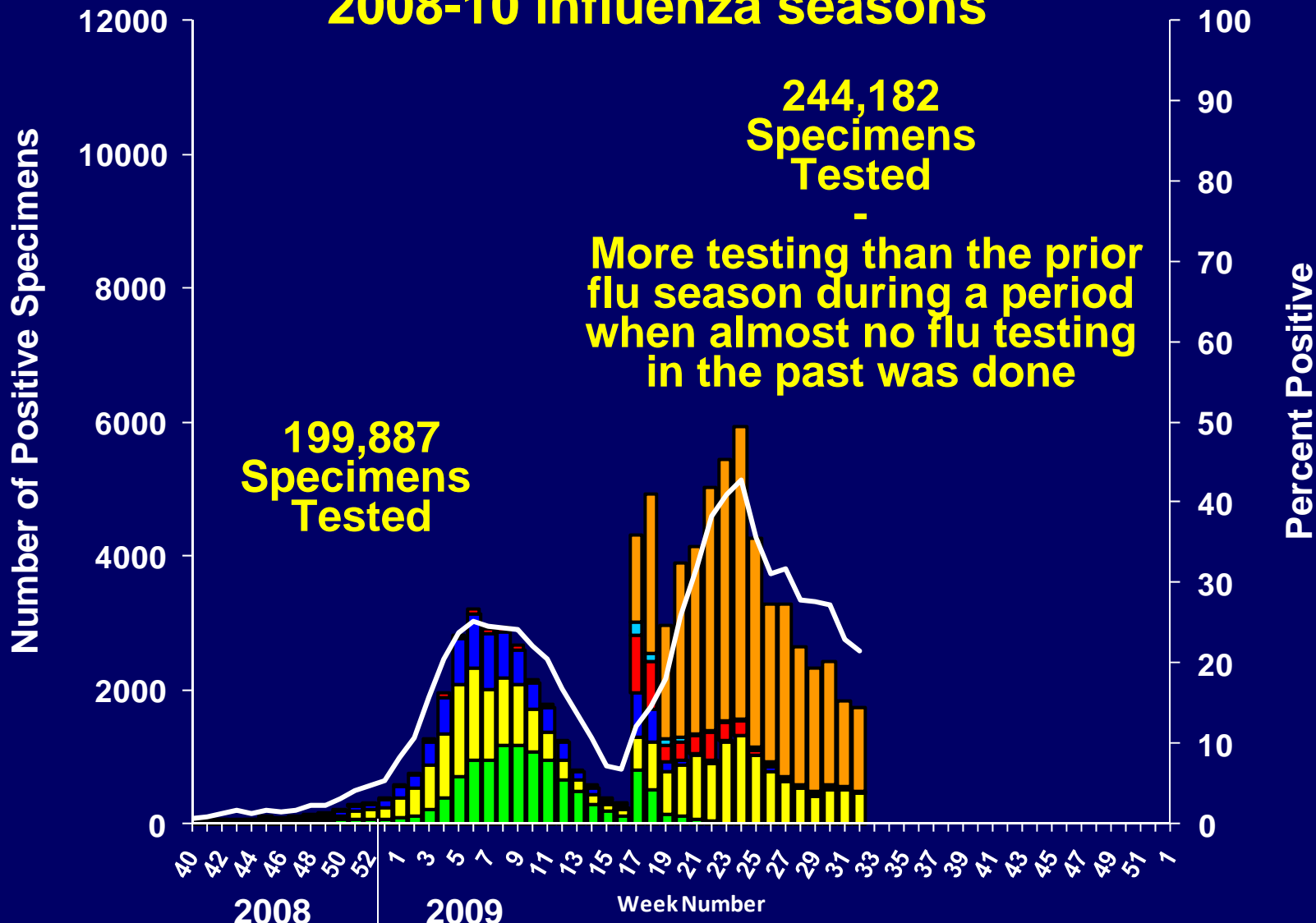
- B
- A(H3)
- A(Subtyping not performed)
- A(Unable to Subtype)
- A(H1)
- A(2009 H1N1)
- Percent Positive



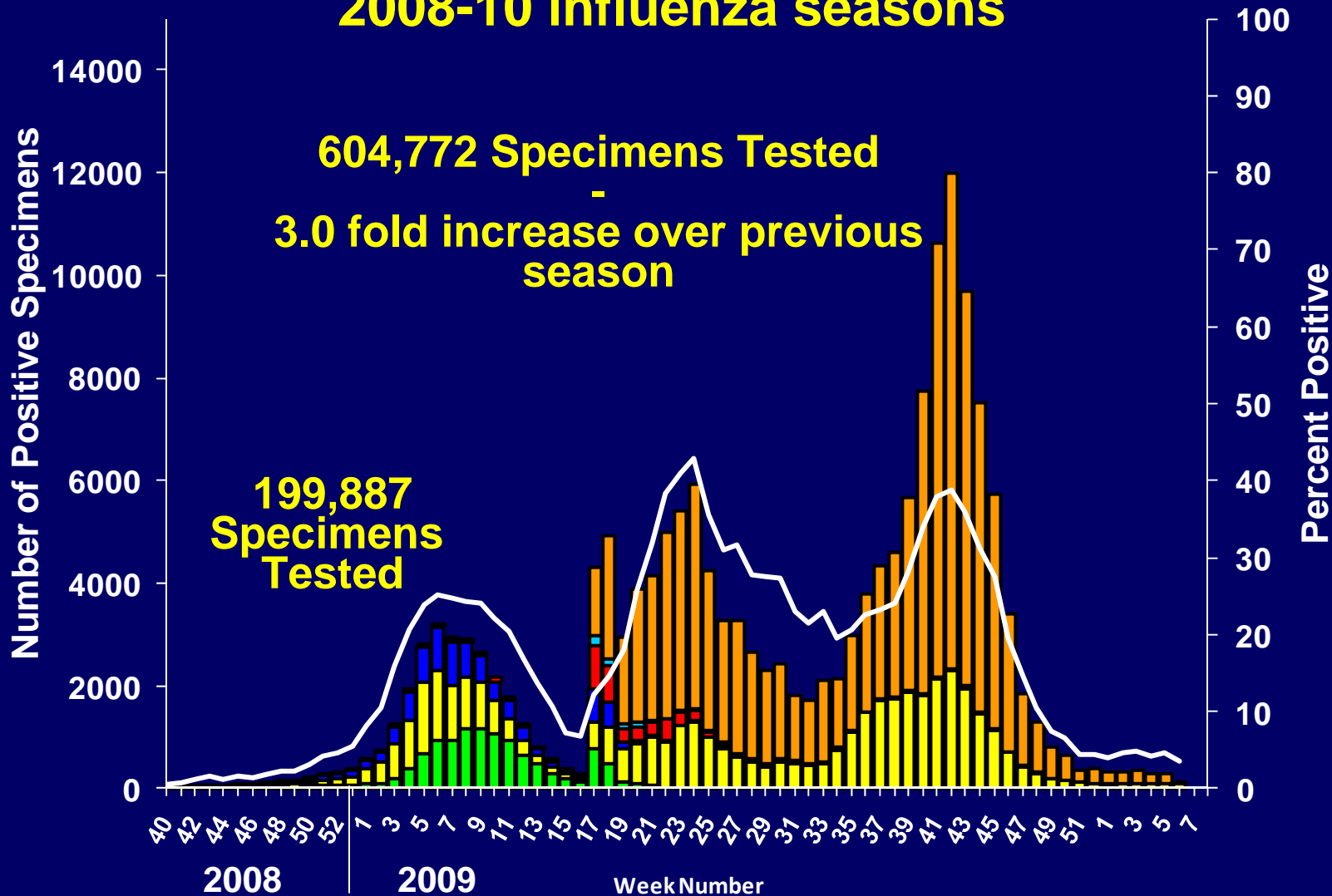
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CDC virologic surveillance collaborating laboratories 2008-10 influenza seasons



- B
- A(H1)
- A(Unable to Subtype)
- Percent Positive
- A(Subtyping not performed)
- A(H3)
- A(2009 H1N1)



National summary percentage of visits for influenza-like illness (ILI) reported by *ILINet*

October 1, 2006 – February 6, 2010



H1N1 influenza disease burden

Estimates for April 2009 through February 13, 2010

2009 H1N1	Mid-Level	Estimated Range
Cases	~59 million persons	~42M to ~86 million persons
Hospitalizations	~265,000 persons	~188,000 to ~389,000 persons
Deaths	~ 12,000 persons	~8,520 to ~17,620 persons

http://www.cdc.gov/h1n1flu/estimates_2009_h1n1.htm



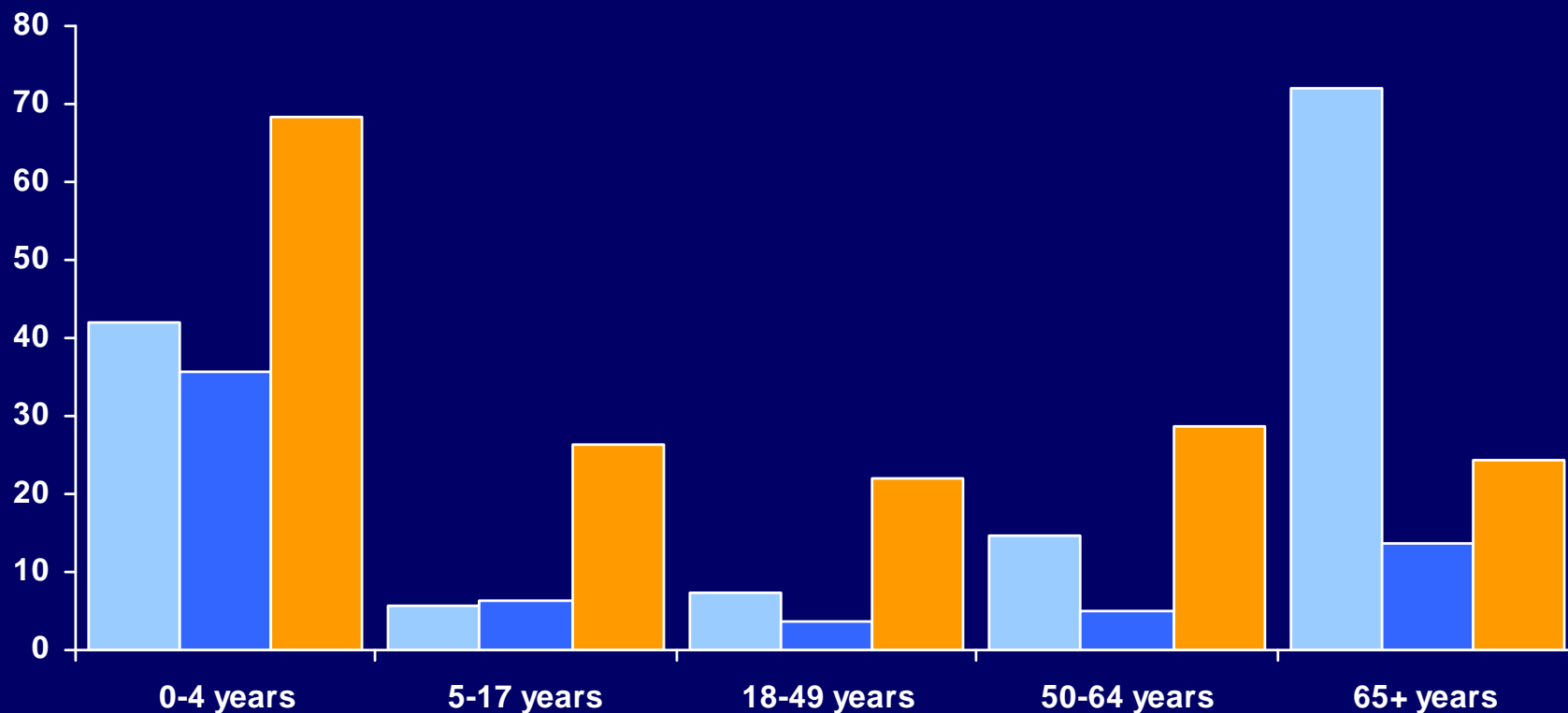
Cumulative influenza hospitalization rates by age group

Emerging Infections Program (EIP) Network

Influenza Week 5 – 12 FEB 2010

Hospitalizations per 100,000 Population

- October 2007 to April 2008 (2007-2008 full season, H3N2 virus predominant)*
- October 2008 to April 2009 (2008-2009 full season, H1N1 virus predominant)*
- September 2009 to February 2010 (2009 - 2010 partial season, 2009 H1N1 predominant)*†



Laboratory-confirmed influenza-associated hospitalizations are monitored using a population-based surveillance network that includes 10 EIP sites* in CA, CO, CT, GA, MD, MN, NM, NY, OR and TN, and 6 new sites† in IA, ID, MI, ND, OK and SD.



2009 H1N1 influenza vaccine program

- **Program overview**
 - Vaccine development, production and evaluation (clinical trials)
 - Planning and preparation
 - Program implementation
 - Coverage monitoring
 - Safety monitoring
 - Vaccine effectiveness monitoring
- **Next steps and lessons learned**



Vaccine development

- **Vaccine reference strain development**
 - Reference strains provided to manufacturers in May 2009
- **Master seed strain preparation**
- **Clinical investigational lot manufacturing**

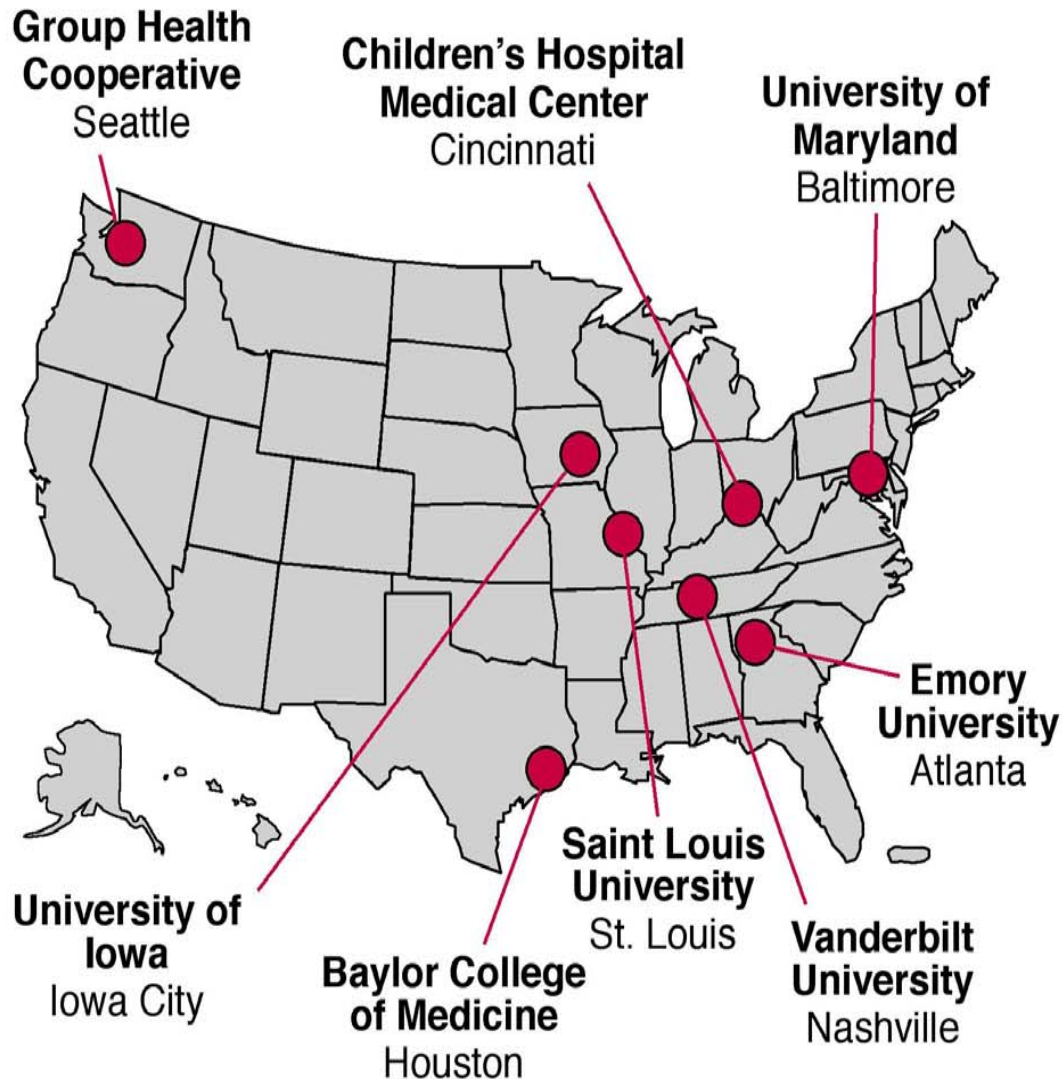


Vaccine production

- Potency assay reagents preparation and calibration
- Commercial scale bulk antigen manufacturing
 - Can occur simultaneously with clinical investigational lot manufacturing
- (Clinical trials)
- Formulation
- Fill and finish



NIH's Network of Vaccine and Treatment Evaluation Units (VTEUs)



- Established in 1962
- >160 Phase I, II, and III clinical trials since 1995
- Trials of
 - Seasonal vaccines
 - Pre-pandemic vaccines
 - Antivirals
- \$189M over 7 years, avg \approx 27M/yr (FY08-FY14)

Conclusions from trials

- One 15 μ g dose of unadjuvanted 2009 H1N1 influenza A vaccine is immunogenic for most adults
- Reactogenicity profile similar to seasonal vaccine
 - More local reactions with adjuvanted vaccine
- Immune response for most products licensed in the U.S. less robust in children age <10 years
 - Good immune response after 2nd dose
- Final formulation
 - 15 μ g for 3+ y/o (multi-dose vials and pre-filled syringes)
 - 7.5 μ g for pediatric pre-filled syringes (6-35 m/o)



Licensure

- **FDA licensure (all H1N1 vaccines used in the U.S. are licensed products)**
 - **Strain change to an existing biologic license application (like seasonal flu vaccine each year)**
 - **All manufacturers are U.S. licensed manufacturers of influenza vaccines**
 - **Manufacturers are using the same licensed production processes for H1N1 vaccines as for seasonal flu vaccines**



Vaccine products

- **Novartis**
 - Multi-dose vial and pre-filled syringe (PFS has trace thimerosal)
- **Sanofi Pasteur**
 - Multi-dose vial, p-free pre-filled syringe, p-free pediatric pre-filled syringe
- **Commonwealth Serum Laboratories (CSL)**
 - Multi-dose vial, p-free pre-filled syringe
- **MedImmune**
 - Live attenuated influenza vaccine (p-free nasal spray)



Why adjust the 2008 priority groups for the H1N1 flu pandemic?

- 2008 “Guidance” focused primarily on a severe pandemic (1918-like, $\geq 2\%$ mortality)
- Contained “tiered” prioritization recommendations
- Contained the provision
 - “At the time of the pandemic, national leaders will obtain advice from scientific and public health experts to determine whether the guidance should be modified based on the characteristics of the emerging pandemic.”





GUIDANCE ON ALLOCATING AND TARGETING PANDEMIC INFLUENZA VACCINE



U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
U.S. DEPARTMENT OF HOMELAND SECURITY



Previous pan flu planning assumptions

- Focused primarily on response to severe disease (H5N1 model, $\geq 2\%$ mortality)
- Anticipated the pandemic influenza virus emerging in Asia
- Anticipated limited quantities of pre-pandemic influenza vaccine (H5N1 flu vaccine) would be available
- Assumed the potential for severe economic and social disruption, possibly a threat to national security
- Assumed initial limited supply would necessitate prioritization of vaccine for the critical workforce and selected general population priority groups



How was 2009 H1N1 different?

- Virus emerged in North America
- Epidemiology demonstrated an age distribution quite different from seasonal flu
- No pre-pandemic influenza vaccine was available
- Larger amounts of pandemic vaccine were anticipated earlier on than in previous planning scenarios
- Confluence of seasonal and pandemic vaccination
- Overall disease has not been severe relative to seasonal flu



How was 2009 H1N1 different?

- **Based on the spring 2009 wave, did not anticipate**
 - Severe economic/social disruption
 - Degradation of key government services
 - Disruption of critical infrastructure
 - Threat to national security
- **There was the need for the U.S. government to weigh the infrastructure and security goals and public health goals in the context of the epidemiology**



Role of ACIP

- The Advisory Committee on Immunization Practices (ACIP) is the chief scientific advisory body to CDC and HHS on vaccine use
 - Advises the CDC Director and the HHS Secretary
- ACIP activities in spring/summer 2009
 - Reviewed the epidemiology of H1N1
 - Evaluated projected vaccine supply and availability data
 - Issued recommendations, August 21, 2009
<http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5810a1.htm>



Clinical/epidemiological findings considered by ACIP in July 2009

- **Distribution of cases/hospitalizations/deaths**
 - Highest incidence lab confirmed infections in school age children
 - Highest hospitalization rates among 0 through 4 year olds
 - Pregnant women disproportionately represented
 - Highest case-fatality ratio but lowest disease rates in older adults
- **Distribution of cases by age group was markedly different compared to seasonal influenza**
 - Higher proportion of hospitalized cases in children and young adults
 - Few cases in older adults
 - No outbreaks among elderly in long term care facilities
- **70% of hospitalized patients with H1N1 have an underlying medical condition that confers higher risk for complications**





MMWR™

Morbidity and Mortality Weekly Report

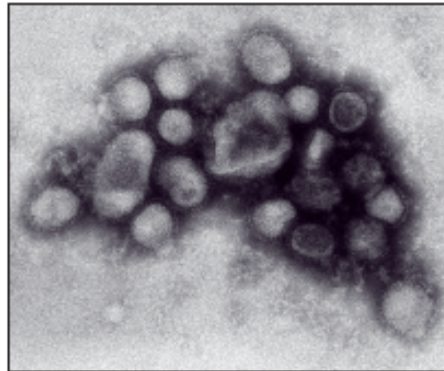
www.cdc.gov/mmwr

Recommendations and Reports

August 28, 2009 / Vol. 58 / No. RR-10

Use of Influenza A (H1N1) 2009 Monovalent Vaccine

Recommendations of the Advisory Committee
on Immunization Practices (ACIP), 2009



DEPARTMENT OF HEALTH AND HUMAN SERVICES
CENTERS FOR DISEASE CONTROL AND PREVENTION



ACIP: Initial target groups (159M)

- Pregnant women
- Persons who live with or provide care for infants <6 months (e.g., parents, siblings, and daycare providers)
- Healthcare and emergency medical services personnel
- Persons aged 6 months–24 years
- Persons aged 25–64 years who have medical conditions that put them at higher risk for influenza-related complications



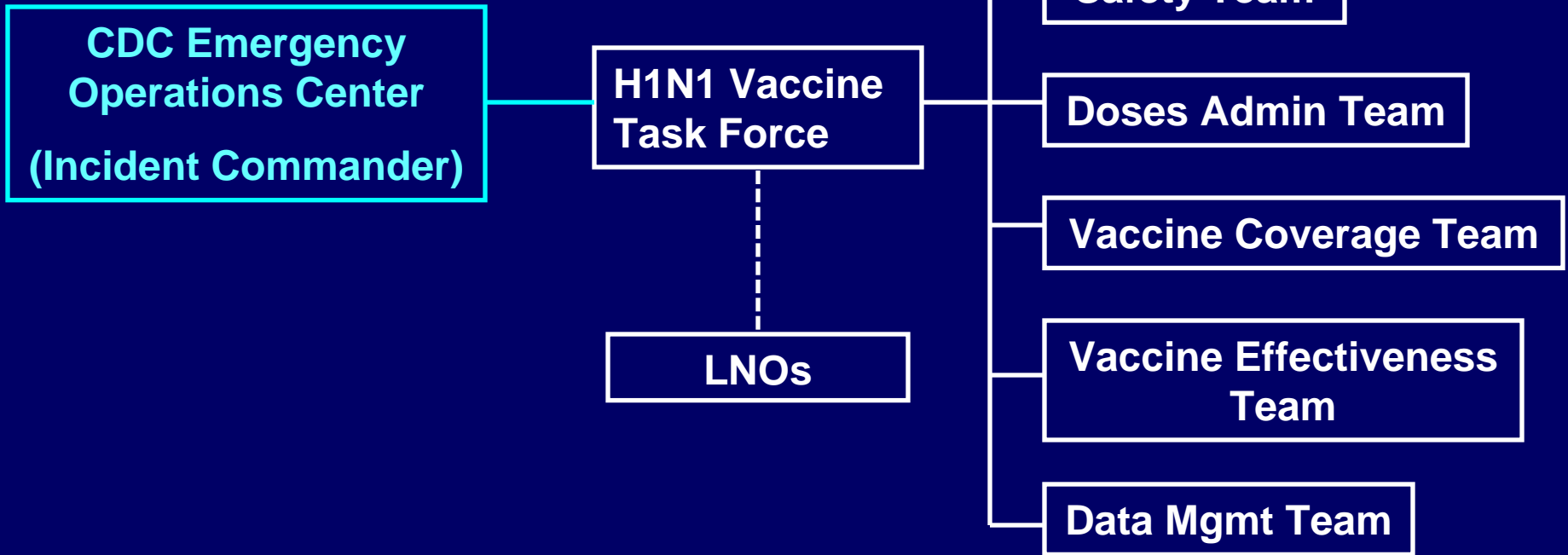
ACIP: Subset of initial target groups

(42M – limited availability scenario)

- **Pregnant women**
- **Persons who live with or provide care for infants <6 months (e.g., parents, siblings, and daycare providers)**
- **Healthcare and emergency medical services personnel who have direct contact with patients or infectious material**
- **Children aged 6 months–4 years, and**
- **Children and adolescents aged 5–18 years who have medical conditions that put them at higher risk for influenza-related complications**



CDC's H1N1 vaccine response organizational structure



H1N1 vaccine distribution

- Modeled after CDC's Vaccines for Children Program (VFC) – centralized distribution
- Uses a single contractor to distribute H1N1 vaccine and prefabricated ancillary supply kits
- Vaccine is allocated to CDC PHEP grantees pro rata according to population
- Vaccine ordering is managed at the state health department level
- Allocation and distribution within a state is a state health department managed process



H1N1 vaccine distribution

- **Vaccine ordering and shipping***
 - Contractor stood up four regional vaccine distribution centers and two ancillary kit distribution centers
 - Vaccine is inventoried at a distribution center and entered into the electronic system and can then be allocated to the states for ordering
 - States receive a daily allocation report every morning Monday through Friday and can begin ordering against their allocation (via an electronic transmission to CDC)
 - CDC electronically transmits orders to contractor for 24 hour turnaround shipping Sunday through Thursday for receipt at the state Monday through Friday
 - Contractor ships directly to “provider” (up to 150K sites)

*Ordering/shipping ops scaled back starting April 1, 2010 to match demand



H1N1 vaccine distribution

- **Variety of products and configurations available**
 - Multi-dose vials (MDVs): 5 mL vials (formulated at 15 μ g per 0.5 mL dose)
 - Pre-filled syringes (formulated at 15 μ g)
 - Pediatric pre-filled syringes (formulated at 7.5 μ g)
 - nasal sprayers (LAIV)
- **Ancillary kits**
 - needles, syringes (for MDVs), alcohol pads, vaccination record cards
 - Sharps container(s)
 - Vaccination record cards only for nasal sprayers



H1N1 vaccine distribution

- **Distribution limitations**
 - Minimum order is 100 vaccine doses and one ancillary supply kit
 - Orders in increments of 100 vaccine doses only
- **If facilities or providers require smaller orders than 100 doses or want to customize orders**
 - State/local health departments may use internal resources to repackage and sub-distribute
 - State/local health departments may contract with 3rd party distributors to repackage and sub-distribute

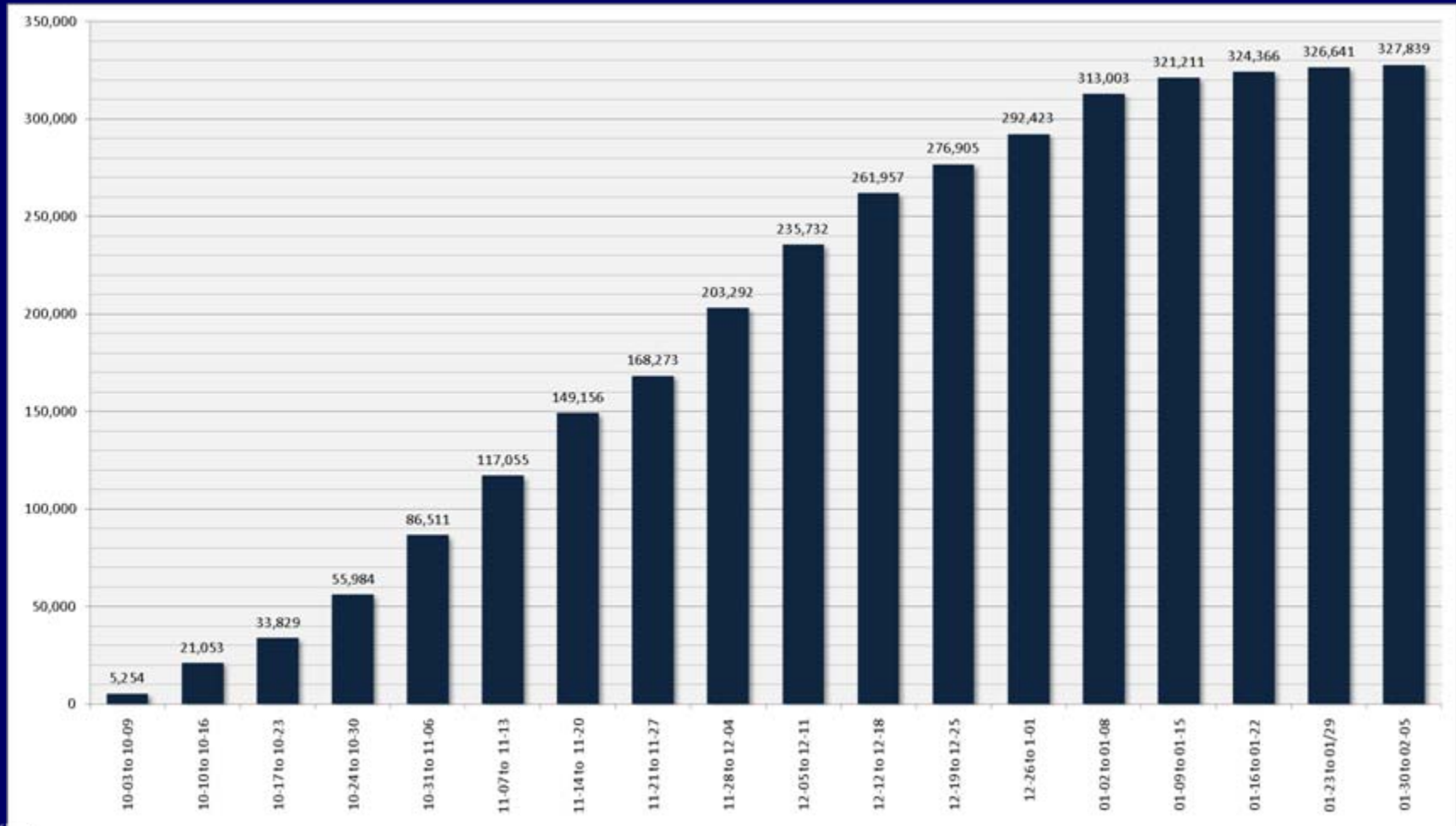


H1N1 vaccine distribution

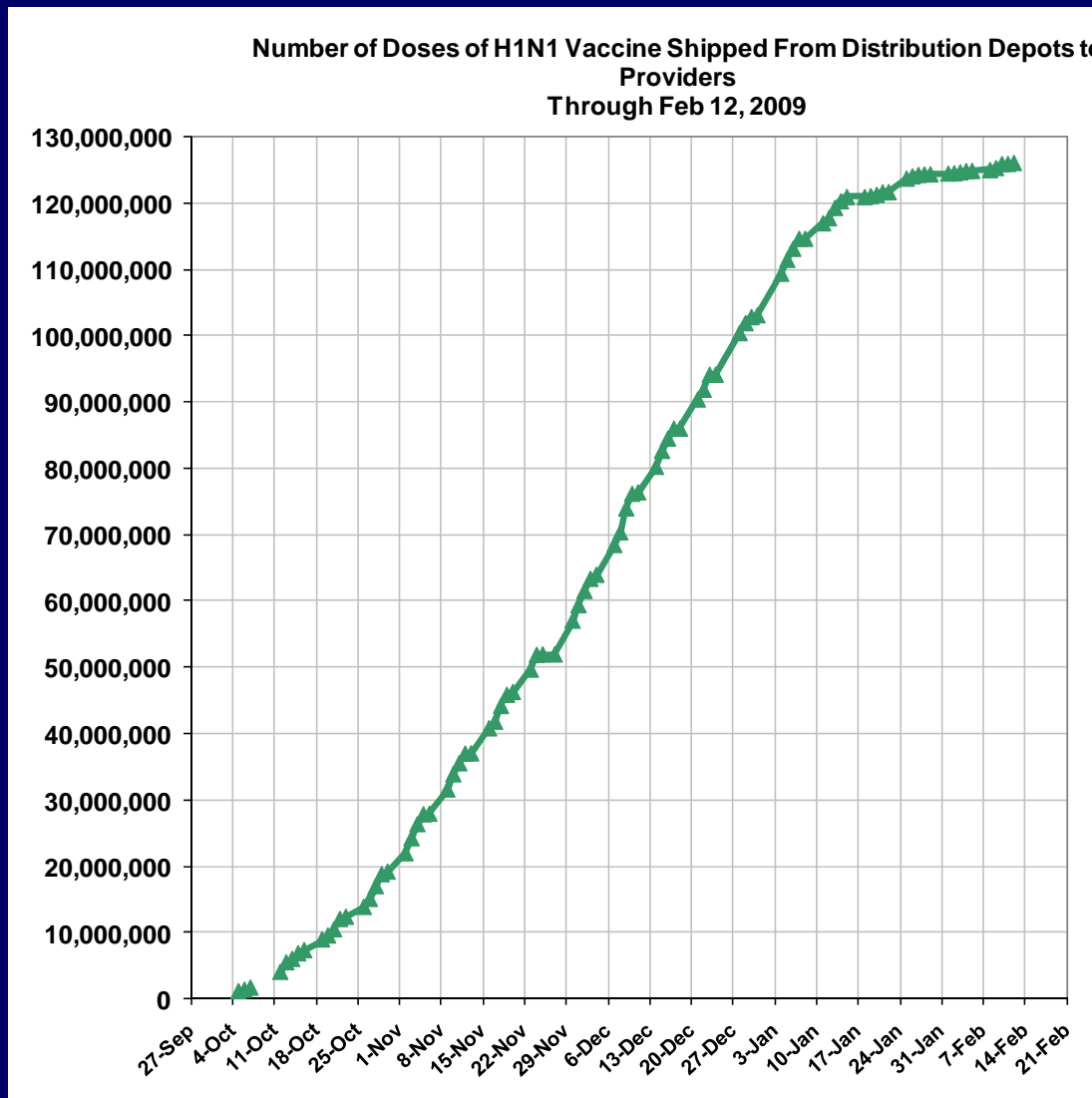
- Allocation and ordering began September 30, 2009
- Shipping began the first week in October, 2009
- As of April 16, 2010
 - 126 million doses shipped



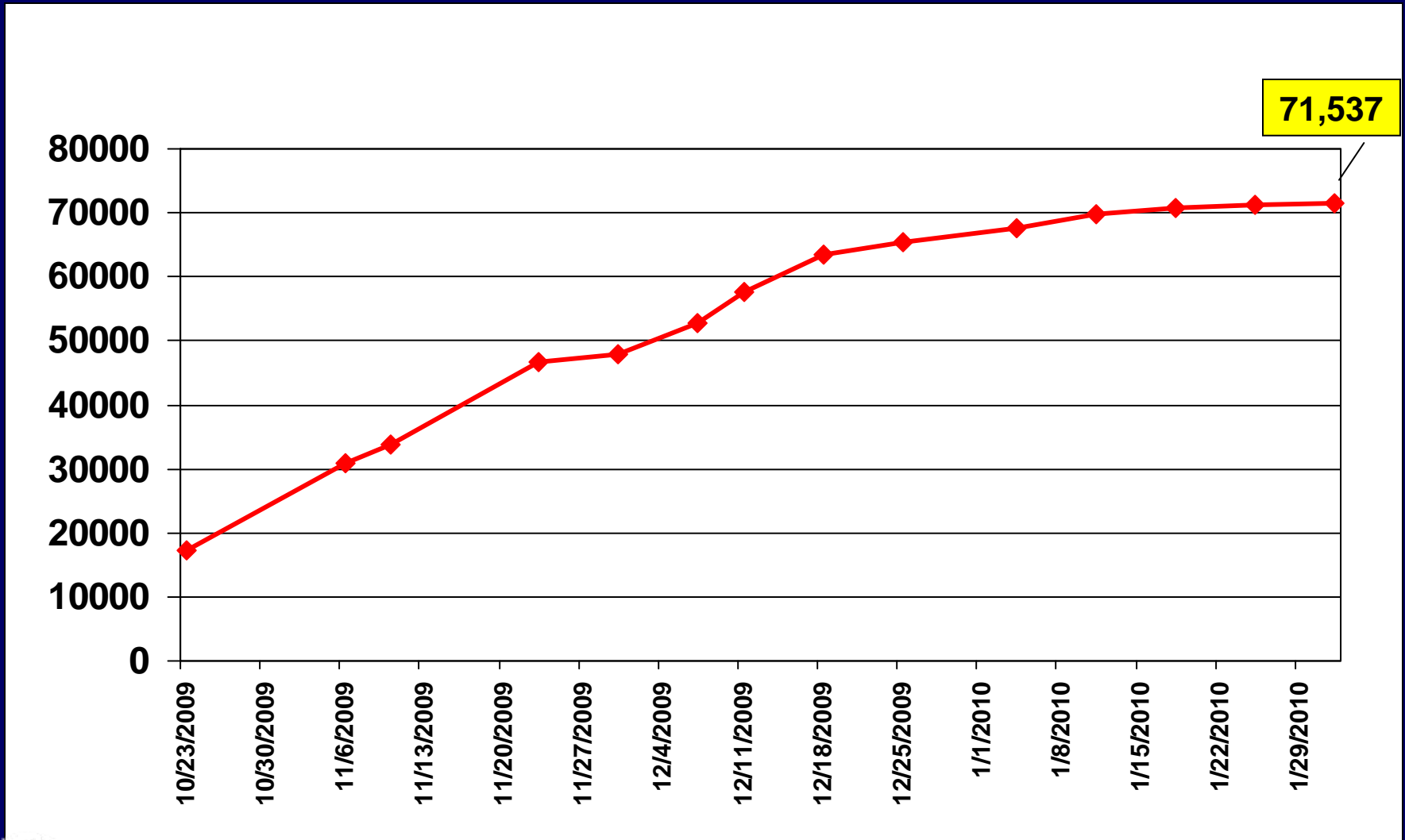
Cumulative number of weekly H1N1 vaccine shipments Oct 3, 2009 to Feb 5, 2010



Number of doses of H1N1 vaccine shipped from distribution depots to providers through Feb 12, 2009



Cumulative number of ship-to sites, H1N1 vaccine program Oct 2009-Jan 2010



Program implementation

- **During the initial roll out many states targeted vaccine to**
 - Hospitals and healthcare facilities
 - Pediatricians, obstetricians and family practitioners
 - Public health clinics
- **As vaccine supply increased some state/local health departments coordinated with school systems to conduct school-located clinics**
- **As supply permitted, states opened up vaccination to high risk adults, all adults 25-64 y/o and then to 65+ y/o**
- **Adult vaccinators include**
 - Internists
 - Occupational health clinics
 - Community vaccinators and retail pharmacies
 - Nursing homes



Special programs and inventory management

- Federal civilian employee vaccination program
- Voluntary transfers from one state to another
- Advanced allocations (implemented Dec 2009)
- Retail pharmacy chain program (implemented late Dec 2009)
- Transition to replenishment ordering for regional distribution centers (implemented early Jan 2010)



Retail pharmacy chain and clinic H1N1 vaccine initiative

- Launched December 21, 2009
- 11 retail chains are participating (representing 51% US pharmacy market share, >31,000 stores)
- All but 3 states opted in (GA, HI, WV)
- Reporting doses shipped to states weekly
- First shipment of vaccine Dec 24, 2009
- Initial order minimum: 100,000 doses
- Total shipped to retailers: 5,466,300 doses
- No orders received since Jan 15, 2010
- Will evaluate program and include lessons learned in next seasonal flu campaign



Retail pharmacy marketing efforts

**H1N1
FLU SHOTS
ARE HERE!**

Find a location near you >

SAFeway
Ingredients for life.™

**H1N1
Flu Shot
Available**
(swine flu)

At select locations for a limited time.

Find a Pharmacy for Details >

Protect yourself this flu season.
H1N1 VACCINATIONS
available at select locations!

Learn more. >>

H1N1 Facts Web Refills Kroger Pharmacy

**Mollen
Immunization Clinics**

**H1N1/FLU SHOT
LOCATOR**

Zip Code:

**Walmart
Flu Shot Clinics**

Walgreens

H1N1 Vaccinations
are now available at all locations
nationwide for \$18. [→ Find a location](#)

Fight off the flu.
Protect your family this flu season with the help of a flu vaccination.

- 1 Get checked in.
- 2 Pay at the pharmacy counter.
- 3 **Get vaccinated.**

Costco
WHOLESALE

**Protect Your Health
with Costco
Flu Clinics**

Stop & Shop

Adult H1N1 Vaccinations

Stop & Shop Pharmacists in Connecticut, Massachusetts, New Jersey, New York and Rhode Island are able to administer H1N1 flu vaccinations.

Available in select Stop & Shop locations, these pharmacists have been specially trained by the American Pharmaceutical Association. To schedule an appointment, simply call one of the Stop & Shop pharmacies listed below, or stop by the pharmacy while you're shopping. Available while supplies last.

To help protect you and your family during the flu season, our pharmacist immunizers listed below will be offering H1N1 flu shots in our pharmacies for \$15.

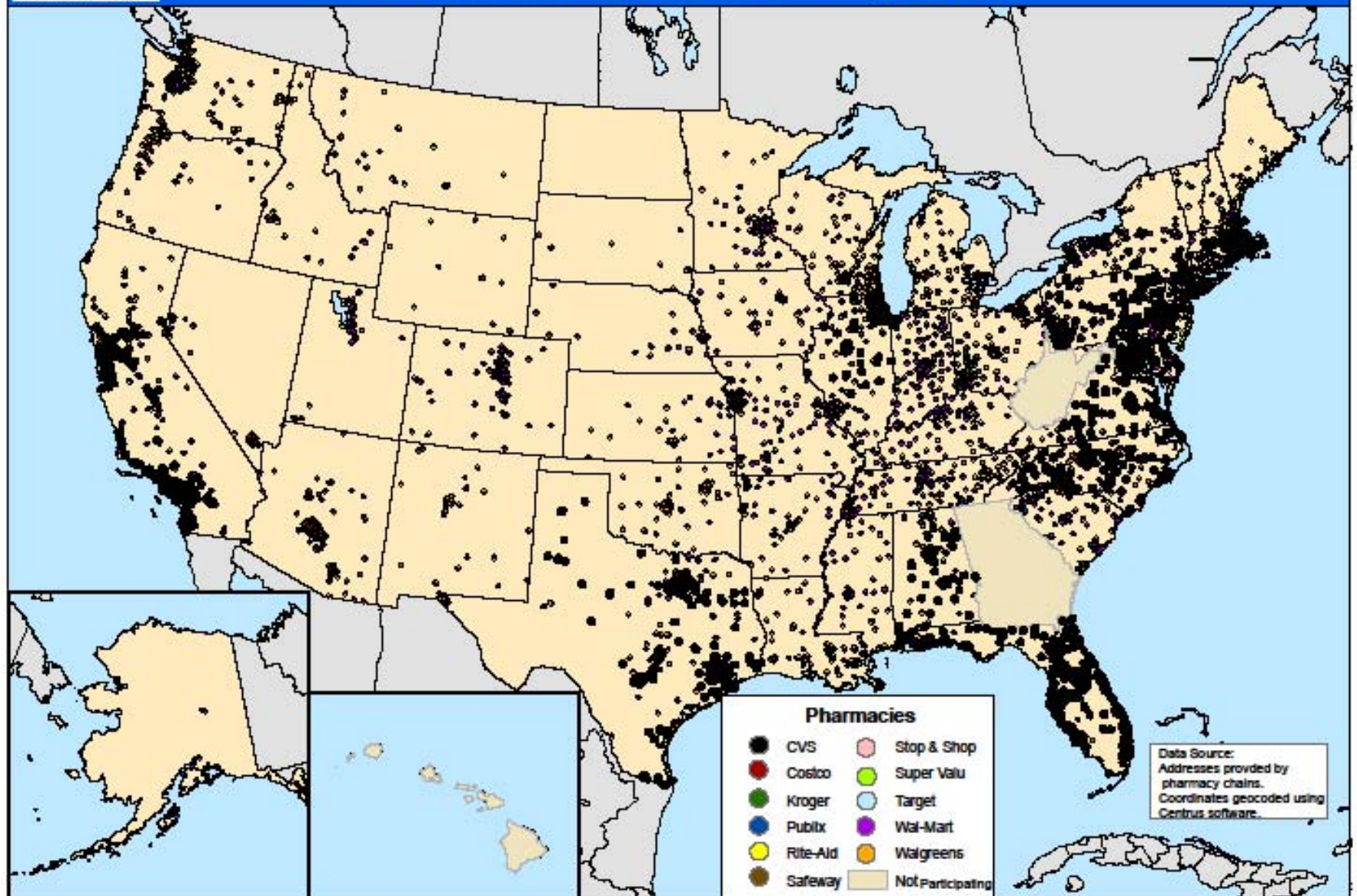
If your store does not have a pharmacist immunizer, [click here](#) for our H1N1 flu clinic schedule.

For answers to your most frequently asked questions about H1N1, [click here](#).

get H1N1 flu shots

Protect yourself with immunizations. H1N1 Flu shots are available at select Rite Aid Pharmacies.

*Certain limitations apply.



Financing/reimbursement

- Vaccine is available at no-cost for providers
- Providers cannot charge for vaccine since it is being provided free by the federal government
- Providers can bill insurance or charge the patient a vaccine administration fee
- Providers are encouraged to vaccinate under- or uninsured patients; however, if unable, providers should refer these patients to public health



Coverage monitoring systems

- **Behavioral Risk Factor Surveillance System (BRFSS)**
 - State-level estimates of coverage
- **National 2009 H1N1 Flu Survey (NHFS)**
 - National estimates of coverage and behavioral factors
- **SDI provider office claims data**
 - Data from 75% of private physicians offices
- **RAND internet panel survey of healthcare personnel**

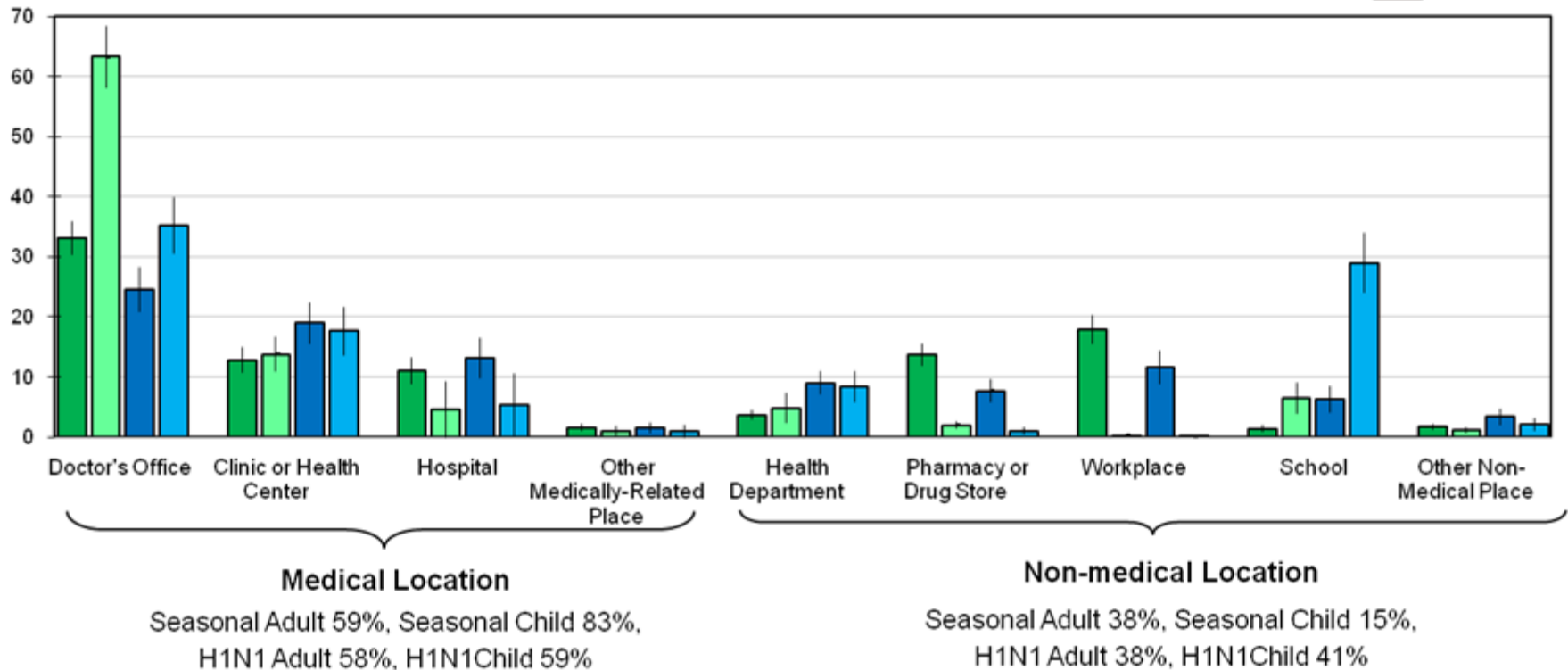


H1N1 vaccine coverage

- **National vaccination coverage**
 - 24.1% overall (National H1N1 Flu Survey, 2/21/10–2/27/10)
 - 21.2% adults, 33.8% children, 41% of est. doses to children
 - 39.5% healthcare and emergency medical service personnel
 - 16.3% adults living or caring for infants age <6 mo (not HCP)
 - 71% of doses to persons in ACIP initial target groups
 - 17% of doses by spray (7% of seasonal doses by spray)
- **Estimated cumulative doses administered by 2/27/10 (126 million doses shipped by 2/18/10)**
 - ~70-80 million total



Place of Vaccination for Adults and Children NHFS, Interviews Conducted January 2010

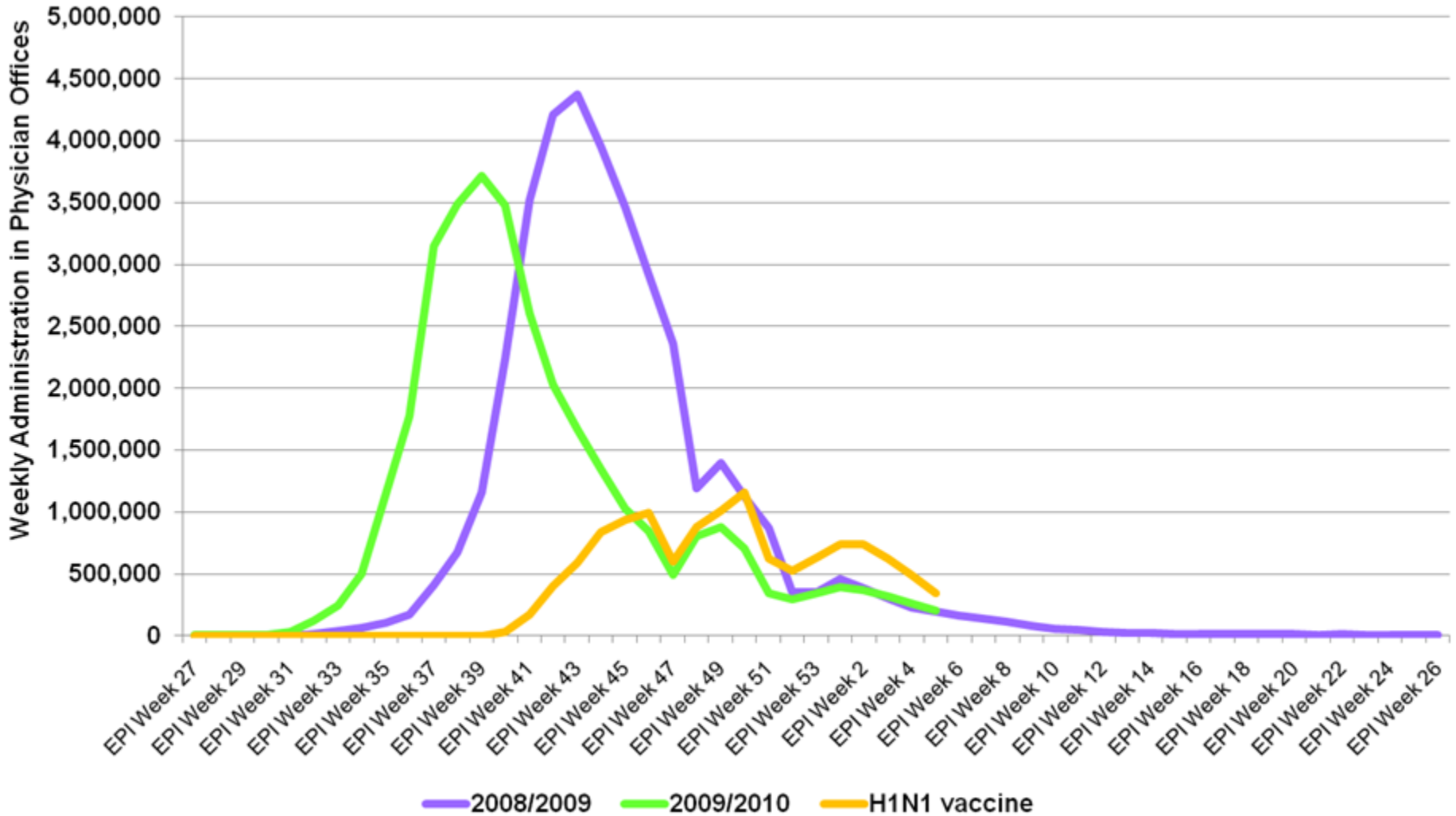


* Totals do not equal 100% due to “don’t know”

NOTE: Children are more likely than adults to receive seasonal vaccinations in a medical location. School location was a prominent place of vaccination of H1N1 for children.



Weekly administration of influenza vaccines in private providers' offices based on claims data, Feb 6, 2010, SDI



H1N1 vaccine safety monitoring

- **Components**
 - **Signal detection**
 - **Signal investigation and verification**
 - **Causality assessment**
 - **Vaccine Safety Risk Assessment Working Group of the National Vaccine Advisory Committee**
 - **Response and program modification**



H1N1 vaccine safety monitoring

- **Vaccine Adverse Event Reporting System – VAERS (signal detection)**
 - Pros: national in scope; able to detect rare events
 - Cons: passive; no denominator
- **VAERS**
 - Reports of serious adverse events for H1N1 vaccine are not proportionally greater than for seasonal flu vaccine
 - No signals detected (data mining with comparison to similar vaccines)
 - Data to date indicates that H1N1 vaccine has a similar safety profile to seasonal flu vaccine



H1N1 vaccine safety monitoring

- **Vaccine Safety Datalink – VSD (signal investigation and verification)**
 - **Pros: population-based (9M members of 8 managed care organizations, represent ~3% of US population); rapid cycle analysis**
 - **Cons: inadequate power for rare adverse events; not representative of entire US population**
- **VSD**
 - **Weak signal for Bell's palsy detected**
 - **Additional review and analysis underway**



H1N1 vaccine safety monitoring

- **Defense Medical Surveillance System**
 - DoD/FDA collaboration
 - Linking vaccination history and interaction with military health system for ~1.4 active duty personnel
 - Weak signal for TP/ITP detected
 - Additional review and analysis underway
- **Real Time Immunization Monitoring System (RTIMS):** telephonic/internet surveillance collaboration with JHU focusing on children, pregnant women, HCWs
 - No signals



H1N1 vaccine safety monitoring

- **Post-licensure Rapid Immunization Safety Monitoring (PRISM): linking state immunization registry to managed care organizations' claims data**
 - No signals
- **GBS surveillance: EIP project areas**
 - Potential weak signal for GBS detected
 - Additional review and analysis underway
- **Full Vaccine Safety Risk Assessment Working Group report available at:**
 - http://www.hhs.gov/nvpo/nvac/reports/vsrawg_report_apr2010.html



The challenge of background events in evaluating safety of 2009 H1N1 vaccine

- For every 10 million persons vaccinated
 - Over 20 cases of GBS within 6 weeks of vaccination as coincidence
- For every 1 million pregnant women vaccinated
 - 397 spontaneous abortions within 1 day of vaccination

Black S, et al. Lancet 2009



H1N1 vaccine effectiveness

- **U.S. Flu Vaccine Effectiveness Network: four sites prospectively enrolling patients**
 - VE for prevention influenza-associated health care visits
 - Cases: patients seeking medical care for acute respiratory illness, enrolled, and are rRT-PCR +
 - Controls: those who seek care, but test negative for influenza
- **Sites**
 - Marshfield Clinic (WI)
 - University of Michigan
 - University of Rochester (NY)
 - Vanderbilt University

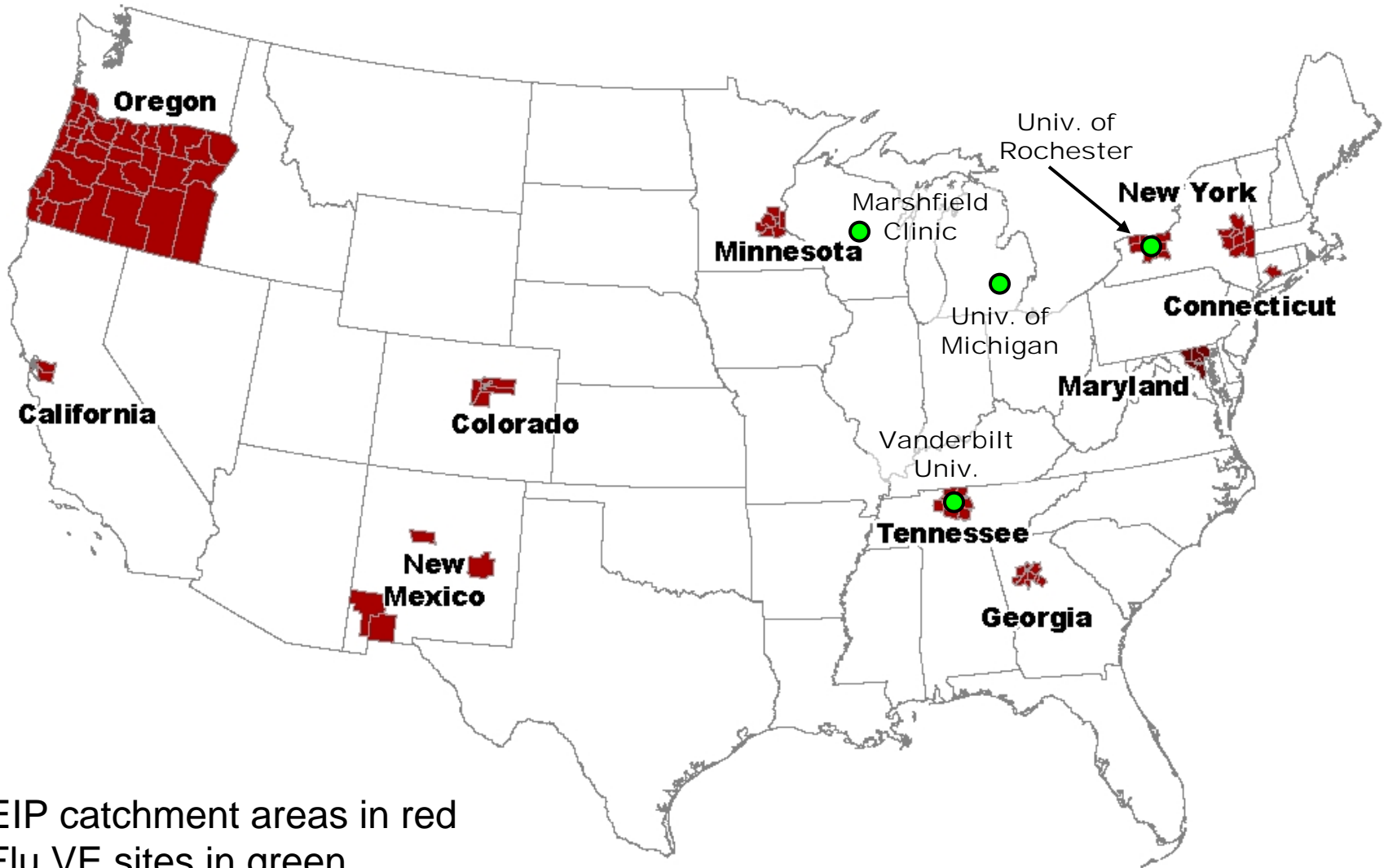


H1N1 vaccine effectiveness

- **Emerging Infections Program (EIP) sites – 10 total**
 - **VE for prevention of influenza hospitalizations diagnosed by provider-ordered tests**
 - **Cases: hospitalized patients in 10 EIP areas**
 - **Controls: age- and community-matched persons who are not hospitalized with an acute respiratory illness up to the date of admission of their corresponding case**



Vaccine Effectiveness Assessment



EIP catchment areas in red
Flu VE sites in green

Next steps

- **Ongoing vaccination with monovalent H1N1 vaccine**
- **Ongoing assessment of response**
 - **Impact of vaccination / antiviral treatment**
 - **Evaluation of school located vaccination and applicability for seasonal influenza vaccination**
- **Centralized, federally managed recovery and disposal of unused H1N1 vaccine**



Next steps

- **Implications for the seasonal influenza program**
 - Surveillance for influenza disease
 - Enhanced vaccination coverage estimates
 - Improving vaccination coverage (HCWs, pregnant women, vulnerable/at risk populations, adults in general)
 - Better vaccine technology
 - Maintaining and building on relationships and gains made with adult vaccine providers
- **Preparing for the next pandemic**



2010-11 seasonal flu vaccine

- **Vaccines and Related Biological Products Advisory Committee (VRBPAC) recommendations for 2010-11 seasonal influenza vaccine**
 - *A/California/7/2009 (H1N1)*-like virus strain
 - *A/Perth/16/2009 (H3N2)*-like virus strain
 - *B/Brisbane/60/2008*-like virus strain
- **ACIP recommendations**
 - Universal recommendation for influenza vaccine
 - Simplifies messaging to both providers and patients



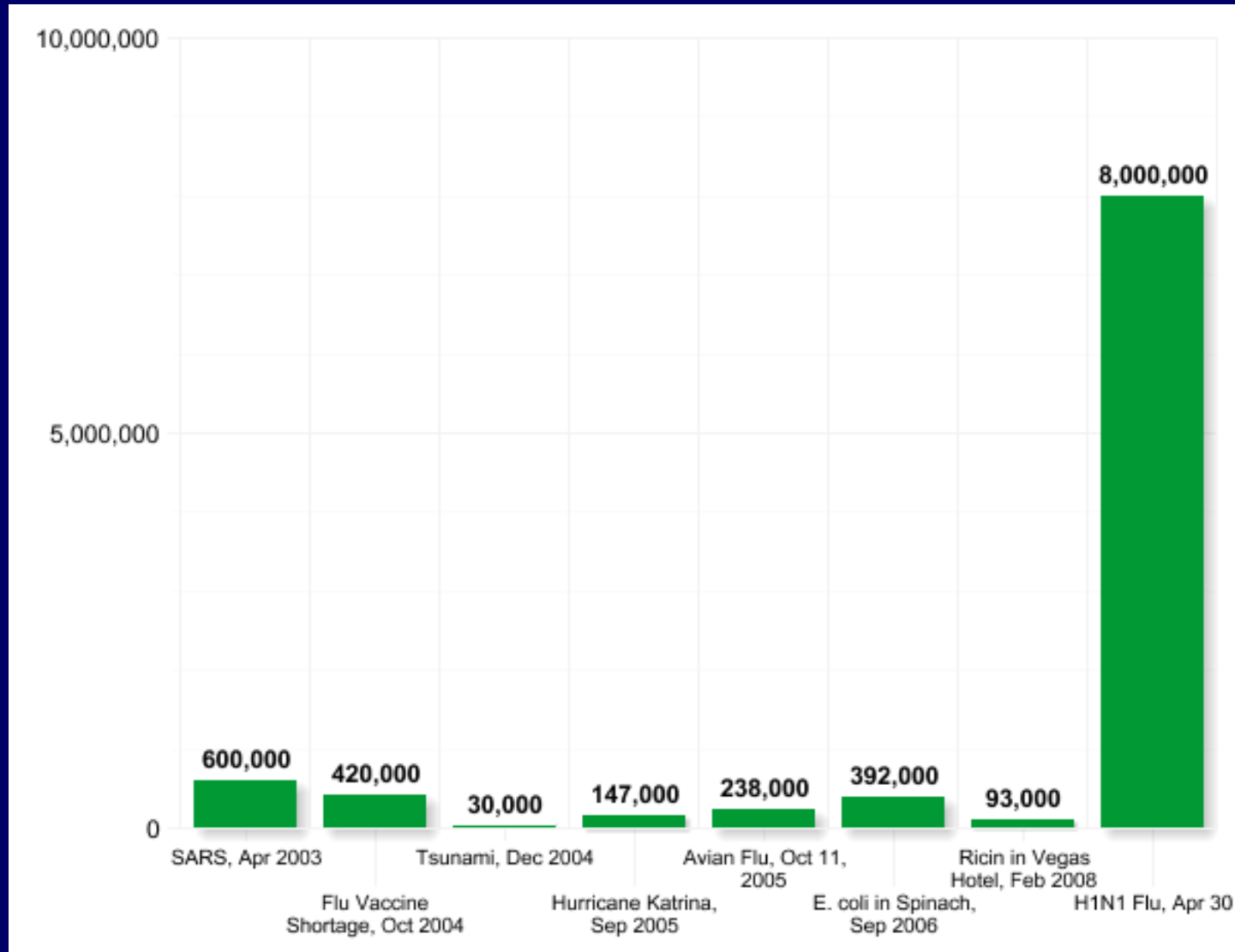
Lessons learned

- Need to fill communication vacuum
- Commitment to share what we knew
- Acknowledge uncertainty
- Openness
- We live in the “Misinformation Age”
 - False rumors spread quickly
 - Misinformation circulates in e-mails for prolonged periods
- Communications must be consistent
- Questions should be encouraged
- Expectation management is crucial



Communicating early and intensively

How did CDC website hits compare with previous responses?



Lessons learned

- **Finding the “sweet spot” is challenging**
 - Encouraging vaccine uptake v. limited supply
 - Focusing on persons at-risk v. avoiding repeat of 2004-05
 - Creating robust safety monitoring systems v. reassuring medical providers and the public
- **Better technology is needed**
 - Faster and more dependable methods of developing and mass producing pandemic influenza vaccines are needed



Lessons learned

- **Automation and tracking and monitoring technology should be further developed and implemented**
 - VTrckS for ordering and tracking distribution being developed and implemented
 - Electronic tracking of vaccine administration with link to an electronic health record for each vaccinee will provide the most robust method of vaccine tracking and safety monitoring
 - Assess feasibility of enhanced bar coding of vaccine products
- **Long-range planning needs to occur even during the intensity and urgency of the immediate response**
 - Ramp down operations and vaccine recovery and disposal



Unified public health response



President Obama and HHS Secretary Kathleen Sebelius receive H1N1 Vaccine

- Planning process / exercises
- Ensuring 2 way communication
 - Outreach and conference calls with commitment to follow up
 - Liaisons at CDC
- Respect / trust



Acknowledgements

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