Update on immunization safety monitoring: Tdap administered to pregnant women

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Outline

- **Overview of Immunization Safety Office post-licensure safety monitoring activities**
- **ISO monitoring of safety of Tdap administered during pregnancy**

Immunization Safety Office (ISO) Mission

To assess the safety of vaccines administered to children, adolescents and adults

- **Comprehensive approach to vaccine safety includes:**
  - **Surveillance to detect possible adverse events following vaccination in a timely way**
  - **Investigation of possible adverse events following vaccination to determine causality and risk factors**
  - **Development of strategies for prevention of adverse events following vaccination**
  - **Vaccine safety research**
  - **Timely communication and education to partners and the public**
- **Work with other Federal agencies and other organizations to further vaccine safety mission**

CDC's Immunization Safety Office: Postlicensure Vaccine Safety Monitoring Infrastructures

System	Collaboration	Description
Vaccine Adverse Event Reporting System (VAERS)	CDC and FDA	• US frontline spontaneous reporting system to detect potential vaccine safety problems
Vaccine Safety Datalink (VSD)	CDC and Healthcare Plans	• Large linked database system used for active surveillance and research
Clinical Immunization Safety Assessment (CISA) Project	CDC and Academic Centers	• Expert collaboration which conducts individual clinical vaccine safety assessments and clinical research

Vaccine Adverse Event Reporting System (VAERS) (co-managed CDC and FDA)[1]

- **US spontaneous reporting system for adverse events after vaccination**

Strengths

- National data; accepts reports from anyone
- Rapid signal detection; rare adverse events (AE)
- Collects information about vaccine, characteristics of vaccinee, AE[2]
- Data available to public

Limitations

- Reporting bias
- Inconsistent data quality and completeness
- Generally cannot assess if vaccine caused an AE
- Lack of unvaccinated comparison group
- Pregnancy inconsistently reported

1. VAERS website: http://vaers.hhs.gov
2. Some reports have no adverse event

Vaccine Safety Datalink

- Collaboration between CDC and 9 health plans
- Data on over 9 million persons per year
- Links vaccination data to health outcome (outpt, ED, inpt) and demographic data

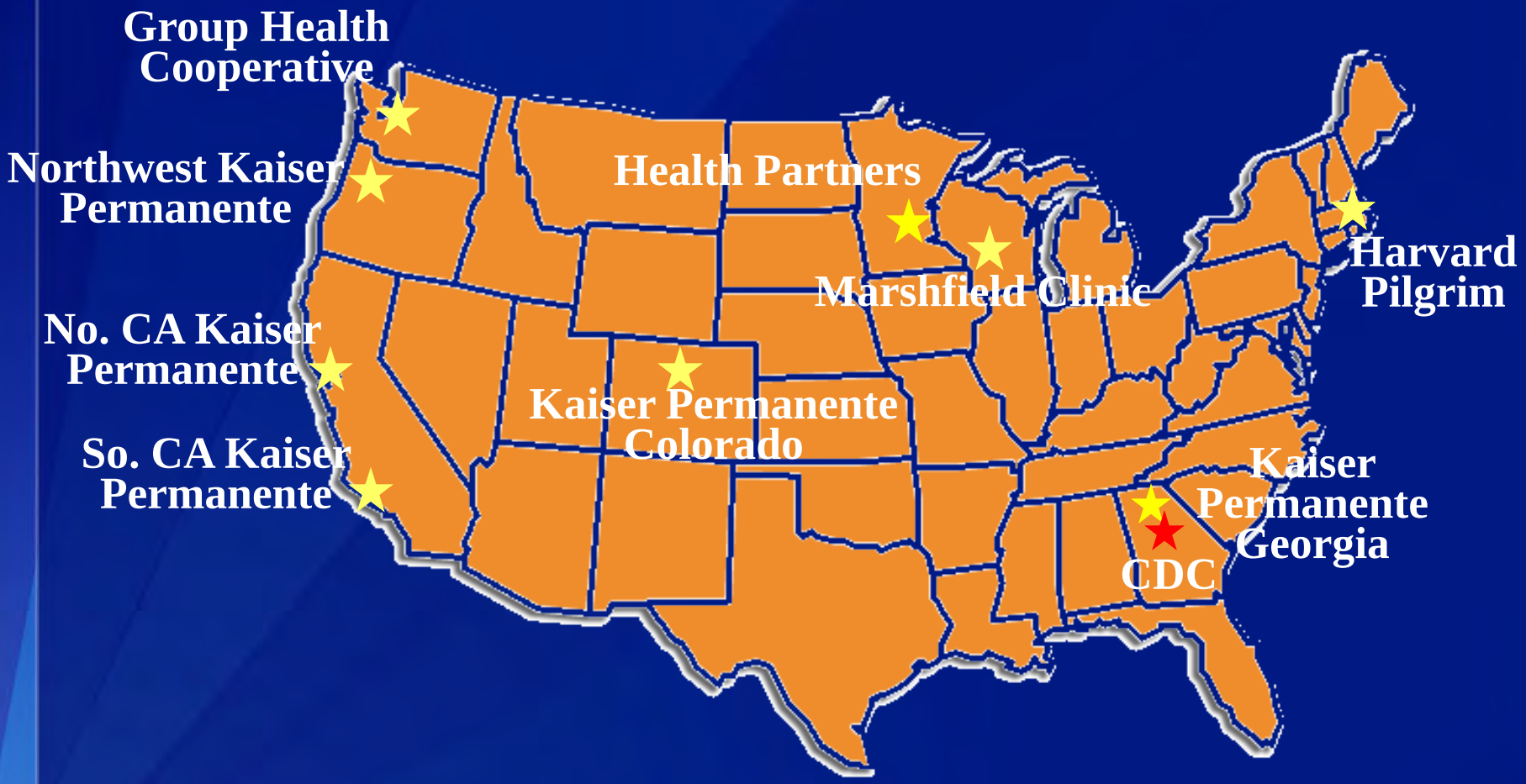
Strengths

- All medical encounters are available
- Vaccine registry data
- Can calculate rates
- Can review medical records
- Tested algorithm to identify pregnancies
- Annual birth cohort = 100k

Limitations

- Sample size may be inadequate for very rare events
- Vaccines administered outside of medical home may not be captured
- Potential for lack of socioeconomic diversity

Vaccine Safety Datalink Sites: 2013



Clinical Immunization Safety Assessment (CISA) Project

- Collaboration between CDC and 7 academic centers
- Conducts clinical evaluation and research

Strengths

- Can implement prospective, multi-site clinical studies (hundreds of subjects)
- Expertise in vaccine safety and many clinical areas, including ob/gyn
- Access to pregnant women receiving vaccines
- Detailed clinical/data on mom and baby
- Can collect biological specimens
- Ability to recruit controls

Limitations

- Sample size limited to study rare adverse events
- Potential challenges to recruit and retain pregnant women
- May not have access to vaccine records for vaccines given outside site
- Potential for lack of geographic or race/ethnicity diversity
- Clinical studies may be labor and resource-intensive

CISA Project Sites and Principal Investigators (PI)

- Boston Medical Center, MA
  - PI: Colin D. Marchant, MD
- Cincinnati Children's Hospital Medical Center, OH
  - PI: Steven Black, MD
- Columbia University, NY
  - PI: Dr. Anne Gershon, MD and Philip LaRussa, MD
- Duke Clinical Research Institute, Duke University, NC
  - PI: Emmanuel "Chip" Walter, MD, MPH
- Johns Hopkins University, MD
  - PI: Neal Halsey MD
- Kaiser Permanente Northern California (KPNC), CA
  - PI: Roger Baxter, MD and Nicola Klein, MD, PhD
- Vanderbilt Medical Center, TN
  - PI: Kathryn M. Edwards, MD

ISO monitoring of safety of Tdap administered during pregnancy

Tdap in Pregnancy: Data from VAERS

- 132 reports to VAERS in women who received Tdap[a] during pregnancy or infants exposed in utero (2005-2010)[b]
  - 77% of reports had Tdap during first trimester
  - 42% described no adverse event
- No unusual or unexpected pattern of maternal, fetal, or infant outcomes

Outcome	Number of reports
Spontaneous abortion (SAB)	22
Fetal death	2
Preterm birth	2
Major birth defect	1 (gastroschisis)

- Monitoring is continuing

a. Zheteyeva et al. Safety of Tdap in pregnancy. *Am. J. Obstet Gyn*ecol. 2012;207:59.e1-7.
b. Before routine recommendation for Tdap in pregnant women; Adacel or Boostrix was administered

Tdap in Pregnancy: VSD Studies

- **Implemented in VSD**
  - Resource support from the National Vaccine Program Office (NVPO)
- **Phase 1** (anticipated completion: August 2013)
  - Assess Tdap vaccine coverage among pregnant women, 2007-2011
- **Phase 2** (anticipated completion: no later than July 2015)
  - Cohort safety study (matched vaccinated /unvaccinated pregnant women)
  - Outcomes: acute events (0-42 days post-vaccination), maternal health and selected birth outcomes (data from 2007-11)
- **Phase 3** (anticipated completion: July 2015)
  - Include 2012-13 data for phase 2 outcomes and if sufficient power, stillbirths and select congenital anomalies
  - Reassess coverage data

Summary: Monitoring for maternal Tdap safety

- ACIP recommendations for Tdap administration during pregnancy relatively recent
  - Expected low Tdap vaccination coverage among pregnant women currently*
- Monitoring in VAERS is ongoing
- Available exposure data currently is limited, but safety studies in VSD have been initiated
- Potential for targeted prospective clinical studies in CISA

*2.6%, unpublished internet panel survey Aug 2011-Apr 2012 (J. Liang, October 2012 ACIP presentation)

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