Enhanced safety monitoring for COVID-19 vaccines in early phase vaccination

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COVID-19 vaccine safety monitoring in early recipients

- Challenge
  - During the early phase of a national COVID-19 vaccination program, initial doses may be distributed to specific groups such as healthcare personnel and other essential workers
  - In this scenario, activities to enhance traditional vaccine safety monitoring systems (e.g., VAERS) will be necessary
- Response
  - Prepare traditional monitoring systems
  - Conduct active surveillance in early recipients through smartphone- and email-based web surveys
  - Obtain vaccination and safety monitoring data from healthcare facility and long-term care facility surveillance

Vaccine Adverse Event Reporting System (VAERS)
The U.S. early warning safety monitoring system

CDC + FDA

VAERS

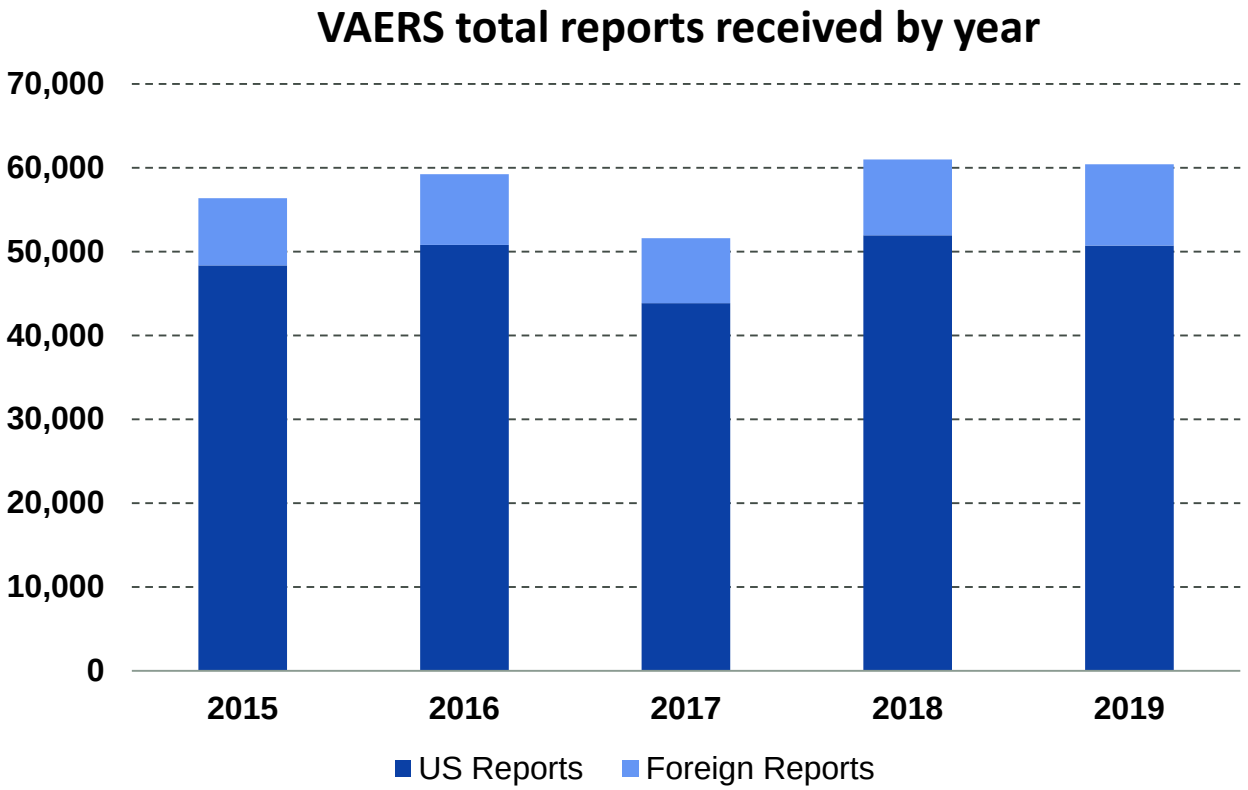
Vaccine Adverse Event Reporting System

Co-managed by CDC and FDA

http://vaers.hhs.gov

Covered populations for COVID-19: Entire U.S. population

- VAERS has all 320 million U.S. residents as a covered population for safety monitoring
- i.e., all ages, races, states, healthy people, those with co-morbidities, etc.



VAERS timeliness

- VAERS serves as the nation's early warning system to detect possible safety issues with U.S. vaccines
- VAERS traditionally has provided initial data on the safety profile of new vaccines when they are introduced for use in the population
- COVID-19 vaccine report processing times
  - Death reports: 1 day
  - Reports classified as serious: 3 days
  - Reports classified as non-serious: 5 days
- CDC and FDA receive updated datasets daily

VAERS analysis for COVID-19 reports

- FDA scientists review all VAERS reports classified as serious
- Attempts are made to follow-up on all serious* reports to get medical records and other medical documentation
- CDC scientists will review VAERS reports for adverse events of special interest (AESI)
- CDC and FDA coordinate on analysis of VAERS data and both agencies conduct data mining

*Based on the Code of Federal Regulations if one of the following is reported: death, life-threatening illness, hospitalization or prolongation of hospitalization, permanent disability, congenital anomaly or birth defect (FDA routinely reviews all serious reports)

Preliminary list of VAERS AESIs

- COVID-19 disease
- Death
- Vaccination during pregnancy
- Guillain-Barré syndrome (GBS)
- Other clinically serious neurologic AEs (group AE)
  - Acute disseminated encephalomyelitis (ADEM)
  - Transverse myelitis (TM)
  - Multiple sclerosis (MS)
  - Optic neuritis (ON)
  - Chronic inflammatory demyelinating polyneuropathy (CIDP)
  - Encephalitis
  - Myelitis
  - Encephalomyelitis
  - Meningoencephalitis
  - Meningitis
  - Encepholapathy
  - Ataxia
- Seizures / convulsions
- Stroke
- Narcolepsy / cataplexy
- Autoimmune disease
- Anaphylaxis
- Non-anaphylactic allergic reactions
- Acute myocardial infarction
- Myocarditis / pericarditis
- Thrombocytopenia
- Disseminated intravascular coagulation (DIC)
- Venous thromboembolism (VTE)
- Arthritis and arthralgia (not osteoarthritis or traumatic arthritis)
- Kawasaki disease
- Multisystem Inflammatory Syndrome in Children (MIS-C)

Experience from H1N1

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MMWR

Early Release

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Safety of Influenza A (H1N1) 2009 Monovalent Vaccines --- United States, October 1--November 24, 2009

The Food and Drug Administration (FDA) licensed the first 2009 influenza A (H1N1) monovalent vaccines ("H1N1 vaccines") on September 15, 2009 (*1*). The H1N1 vaccines are available as a live, attenuated monovalent vaccine (LAMV) for intranasal administration and as monovalent, inactivated, split-virus or subunit vaccines for injection (MIV). The licensure and manufacturing processes for the monovalent H1N1 vaccines were the same as those used for seasonal trivalent inactivated (TIV) or trivalent live, attenuated influenza vaccine (LAIV); none of these vaccines contains an adjuvant (*1*). Vaccine safety monitoring is an important component of all vaccination programs. To assess the safety profile of H1N1 vaccines in the United States, CDC reviewed vaccine safety results for the H1N1 vaccines from 3,783 reports received through the U.S. Vaccine Adverse Event Reporting System (VAERS) and electronic data from 438,376 persons vaccinated in managed-care organizations in the Vaccine Safety Datalink (VSD), a large, population-based database with administrative and diagnostic data, in the first 2 months of reporting (as of November 24). VAERS data indicated 82 adverse event reports per 1 million H1N1 vaccine doses distributed, compared with 47 reports per 1 million seasonal influenza vaccine doses distributed. However, no substantial differences between H1N1 and seasonal influenza vaccines were noted in the proportion or types of serious adverse events reported. No increase in any adverse events under surveillance has been seen in VSD data. Many agencies are using multiple systems to monitor H1N1 vaccine safety (*2*). Health-care providers and the public are encouraged to report adverse health events that occur after vaccination.

Reports to VAERS

Health-care providers and manufacturers are required to report to VAERS certain adverse events in vaccinees brought to their attention after vaccination with licensed U.S. vaccines;* however, health-care providers and members of the public also may report other adverse events voluntarily. VAERS enables early detection of potential new, rare, or unusual patterns of adverse events, which then can be investigated using other methods and systems to determine whether an actual association with vaccination exists (*3*). With the initiation of the federal H1N1 vaccination program, VAERS was enhanced by providing VAERS contact information on influenza vaccination record cards, advertising in medical journals, utilizing state vaccine safety coordinators, and increasing the number of staff members who code reports and obtain and review medical records; these changes were made to encourage VAERS reporting and to increase the capacity to analyze additional reports to rapidly identify any safety signals.

CDC and FDA staff members searched the VAERS database to identify all U.S. reports of adverse events after vaccination with H1N1 vaccines and 2009--10 seasonal influenza vaccines during July 1--November 24. The first doses of H1N1 LAMV became available to the public in the United States on October 5, and H1N1 MIV became available the following week. VAERS reports were coded as fatal or nonfatal serious adverse events (defined by federal regulation as those resulting in death, life-threatening illness, hospitalization, prolongation of hospitalization, persistent or significant disability, or congenital anomaly) or as nonserious,† and reporting rates per 1 million doses distributed as of November 20 were calculated.§

VAERS reports coded as serious adverse events are reviewed by medical officers and assigned to predetermined broad diagnostic categories. To verify the reported event, medical records are requested and reviewed for all serious adverse event reports and for any reports (both serious and nonserious) that describe patients with possible Guillain-Barré syndrome or anaphylaxis. Cause of death is determined as stated in medical or autopsy records. Reports to VAERS indicate only that health events occurred after vaccination; causality generally cannot be determined solely by reports to VAERS. Excluded were 62 reports with insufficient information.

Enhanced monitoring programs to meet the challenge of COVID-19

Vaccine safety assessment for essential workers (V-SAFE)

- V-SAFE is a smartphone-based text, text-to-web survey, and email-to-web survey active surveillance program for early vaccine recipients
  - Uses contact information (phone numbers) from the registration process for COVID-19 vaccination of essential workers – up to 20+ million people during the first few months of a vaccination program
  - Conducts health checks on vaccine recipients via text messages and email
    - Daily for first week post-vaccination
    - Weekly thereafter for 6 weeks post-vaccination
  - Active telephone follow-up will be conducted with a person reporting a clinically important* adverse event during any V-SAFE health check
    - A VAERS report will be taken during telephone follow-up, if appropriate

*Refer to slide 14

Vaccine safety assessment for essential workers (V-SAFE)

1. Text messages or email from CDC with follow-up – daily 1st week post-vaccination and weekly thereafter out to 6 weeks

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Healthcare workers, essential workers, etc.

2. Any clinically important event(s) reported by vaccinated person

VAERS call center

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3. Follow-up on clinically important event, complete a VAERS report if appropriate

Symptom check
"Medical symptoms can be classified as:
Mild = you notice symptoms, but they aren't a problem
Moderate = symptoms cause some limitation of your normal daily activities
Severe = symptoms make normal daily activities difficult or impossible"

"Since your vaccination, have you had any of these symptoms?"

Site Reaction:
"Pain, redness, swelling or itching at or near the injection site" ☐ No ☐ Yes
(If YES) Check all that apply: ☐ Pain ☐ Redness ☐ Swelling ☐ Itching

(If checked Pain) ☐ Mild ☐ Moderate ☐ Severe
(If checked Redness) ☐ Mild ☐ Moderate ☐ Severe
(If checked Swelling) ☐ Mild ☐ Moderate ☐ Severe
(If checked Itching) ☐ Mild ☐ Moderate ☐ Severe

Systemic (Body System) Reaction:
"Chills" ☐ No ☐ Yes
(If YES) ☐ Mild ☐ Moderate ☐ Severe

"Headache", "Joint pains" or "Muscle or body aches" ☐ No ☐ Yes
(If YES) Check all that apply: ☐ Headache ☐ Joint pain ☐ Muscle or body aches

(If checked Headache) ☐ Mild ☐ Moderate ☐ Severe
(If checked Joint pains) ☐ Mild ☐ Moderate ☐ Severe
(If checked Muscle or body aches) ☐ Mild ☐ Moderate ☐ Severe

"Fatigue or tiredness" ☐ No ☐ Yes
(If YES) ☐ Mild ☐ Moderate ☐ Severe

"Nausea", "Vomiting", "Diarrhea", or "Abdominal pain" ☐ No ☐ Yes
(If YES) Check all that apply: ☐ Nausea ☐ Vomiting ☐ Diarrhea ☐ Abdominal pain

(If checked) "Nausea" ☐ Mild ☐ Moderate ☐ Severe
(If checked) "Vomiting" ☐ Mild ☐ Moderate ☐ Severe
(If checked) "Diarrhea" ☐ Mild ☐ Moderate ☐ Severe
(If checked) "Abdominal pain" ☐ Mild ☐ Moderate ☐ Severe

"Rash, not including the immediate area around the injection site" ☐ No ☐ Yes
(If YES) ☐ Mild ☐ Moderate ☐ Severe

"Any other symptoms or health conditions you want to report"
☐ No ☐ Yes, describe: _____

Health impact
"Did any of the symptoms or health conditions you reported TODAY cause you to (check all that apply):"

Defines clinically important

☐ "Miss work?"
☐ "Be unable to do your normal daily activities?"
☐ "Get care from a doctor or other healthcare professional?"
(If "Get care…" checked) "What type of healthcare visit did you have? (check all that apply)"
☐ Telehealth, virtual health, or email health consultation
☐ Outpatient clinic or urgent care clinic visit
☐ Emergency room or emergency department visit
☐ Hospitalization
☐ Other, describe: _____

Onscreen completion thank you message:

Thanks for completing today's check in. Depending on your answers, we may give you a call to follow up.

If your symptoms bothered you, we encourage you to report your experience to the Vaccine Adverse Event Reporting System (VAERS). End

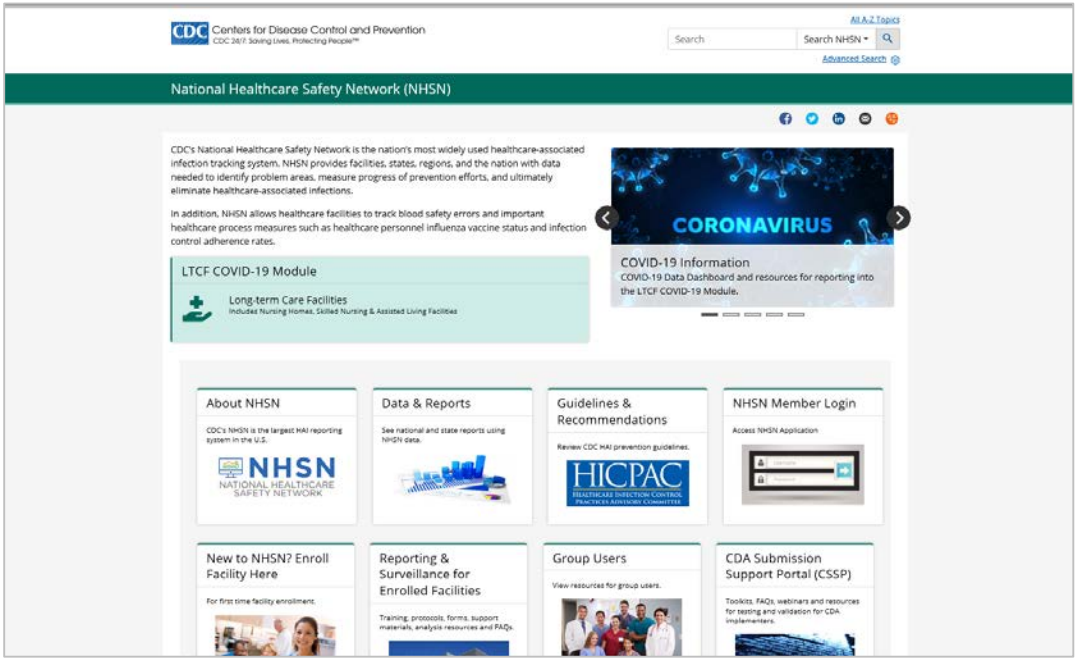
Smartphone-based monitoring

- CDC has validated the basic text messaging collection methods for vaccine safety monitoring*
- Smartphone-based safety monitoring of early COVID-19 vaccine recipients will allow estimation of:
  - Rates of local and systemic reactogenicity
  - Rates of clinically important adverse events following immunization
- Smartphone-based safety monitoring of early COVID-19 vaccine recipients will allow comparison of observed rates of adverse events:
  - With background rates in the population
  - With known rates following other types vaccinations (e.g., flu)

*Stockwell et al. A multi-site feasibility study to assess fever and wheezing in children after influenza vaccines using text messaging. Vaccine. 2017; 35(50):6941-6948.
Stockwell et al. Feasibility of Text Message Influenza Vaccine Safety Monitoring During Pregnancy. Am J Prev Med. 2017; 53(3):282-289.

Enhanced VAERS reporting using National Healthcare Safety Network (NHSN) sites

- COVID-19 vaccine safety surveillance and facilitated VAERS reporting for healthcare workers and LTCF residents



NHSN modules for COVID-19 vaccination

- NHSN sites will track weekly vaccine doses administered by dose number (i.e., denominator) in healthcare workers and LTCF residents
- NHSN sites are well positioned to identify adverse events among COVID 19 vaccine recipients at their sites (i.e., numerator)
  - VAERS staff will match reports in VAERS to NHSN sites using facility address information (i.e., identify reports originating from NHSN facilities)
  - Allows for calculation of crude overall reporting rates and adverse event-specific reporting rates

Established monitoring systems in a general vaccination program

Established monitoring systems and timeliness

- VAERS
  - Reports received and processed within days of program implementation
- Clinical Immunization Safety Assessment (CISA) Project: case reviews
- Vaccine Safety Datalink (VSD) and VA electronic health record monitoring
  - Data available within a couple weeks of encounter with medical system
- FDA CMS data monitoring, includes 650K nursing home residents
  - Data may be available within several weeks of an encounter with medical system
- FDA BEST and Sentinel and large insurer/payer databases*
  - Data availability variable depending on source (couple weeks to several months)

*Biologics Effectiveness and Safety (BEST) System.

Summary

Summary

- VAERS will play an important role in characterizing the safety profile of COVID-19 vaccine(s) in the early stages of a vaccination program
  - Signal detection is of paramount importance

    but
  - VAERS data can also provide reassurance if no concerning safety signals are detected
- Additional systems such as V-SAFE and NHSN will enhance traditional vaccine safety monitoring systems, such as VAERS
- Traditional large-linked database systems (VSD, CMS, VA EHR etc.) will quickly accumulate safety data when vaccines become widely available

Questions?