COVID-19 Vaccine Safety Monitoring in Children

Advisory Committee on Immunization Practices (ACIP)
November 2, 2021

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CDC COVID-19 Vaccine Task Force

cdc.gov/coronavirus
Topics

- CDC surveillance systems and processes for monitoring vaccine safety in children*
- FDA, Indian Health Service (IHS), and Department of Defense (DoD) vaccine safety monitoring systems
- COVID-19 Vaccine Safety Technical (VaST) Work Group

* CDC continuously monitors authorized and licensed vaccines administered to children in the United States
CDC vaccine safety monitoring

- COVID-19 vaccines are being administered under the most intensive vaccine safety monitoring effort in U.S. history
- Strong, complementary systems are in place—both new and established

Full list of U.S. COVID-19 vaccine safety monitoring systems

Smartphone-based active safety monitoring

Now available!
- Enrolling children
- 3rd dose reporting

http://cdc.gov/vsafe
Adding a dependent in v-safe

- Participants can register themselves or dependents after dose 1, 2, or 3
- Dependents can be added, even if the primary smartphone account is not a v-safe participant
  - Parent/guardian must create a profile then add dependent
  - Text messaging directed to parent/guardian
- V-safe check in schedule:
  - Once a day (days 0–7)
  - Once a week (weeks 2–6)
  - Once a month (months 3, 6, and 12)
  - Schedule restarts after each dose received
V-safe analytic plan for children aged 5–11 years

- V-safe will aggregate data from health surveys completed on days 0–7 after vaccination for children aged 5–11 years
  - Describe sex, median age, race/ethnicity of vaccinated children
  - Describe local reactions, systemic reactions, and health impacts by dose received

- Compare reactogenicity profile for children aged 5–11 years to adolescents aged 12–17 years

- Reports to VAERS solicited by active telephone follow-up of v-safe participants are included in VAERS analyses
VAERS is the nation’s early warning system for vaccine safety

http://vaers.hhs.gov
VAERS accepts reports from everyone

Regardless of the plausibility of the vaccine causing the event or the clinical seriousness of the event

Key strengths

- Rapidly detects potential safety problems
- Can detect rare adverse events

Key limitations

- Passive surveillance system
- Inconsistent quality and completeness of information
- Reporting biases
- Generally, cannot determine cause and effect
VAERS prespecified adverse events of special interest*  
(as of Oct 27, 2021)

- Death
- Acute myocardial infarction
- Anaphylaxis
- Coagulopathy
  - Thrombocytopenia
  - Deep venous thrombosis or pulmonary embolism
  - Disseminated intravascular coagulopathy
- Guillain-Barré Syndrome (GBS)
- Kawasaki disease
- Multisystem inflammatory syndrome in children (MIS-C)
- Myocarditis, myopericarditis, and pericarditis
- Narcolepsy/cataplexy
- Seizure
- Stroke
- Thrombosis with thrombocytopenia syndrome (TTS)
- Transverse myelitis

* Assessment includes: clinician review of VAERS report, follow-up to obtain and review medical records, application of case definition (where case definition exists), adjudication to classify the report with respect to case definition
Particular focus on myocarditis/myopericarditis reports

- Potential reports identified by Medical Dictionary for Regulatory Activities (MedDRA)* standardized codes assigned to report that could indicate myocarditis or pericarditis

- Clinical abstraction
  - Review of initial report
  - Outreach to healthcare provider involved in reported patient’s care
  - Request and review of medical records
  - Compare abstracted data elements against CDC case definitions for myocarditis and pericarditis

- CDC will conduct periodic analyses of case counts and reporting rates and comparison of reporting rates to background

* www.medra.org
VSD
Vaccine Safety Datalink

- 9 participating integrated healthcare organizations
- Data on over **12 million** persons per year
Vaccine Safety Datalink (VSD) Rapid Cycle Analysis (RCA)

Aims:

- To monitor the safety of COVID-19 vaccines weekly using prespecified outcomes of interest among VSD members.
- To describe the uptake of COVID-19 vaccines over time among eligible VSD members overall and in strata by age, site, and race/ethnicity.

Surveillance began in December 2020.
## Prespecified RCA surveillance outcomes

<table>
<thead>
<tr>
<th>Condition</th>
<th>Settings</th>
<th>Risk window (days)</th>
<th>Chart review</th>
<th>Monitoring only</th>
<th>Exclude if COVID-19 in prior X days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute disseminated encephalomyelitis</td>
<td>E, I</td>
<td>1-21, 1-42</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute myocardial infarction – <em>First Ever</em></td>
<td>E, I</td>
<td>1-21, 1-42</td>
<td>Yes</td>
<td>30 days</td>
<td></td>
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<tr>
<td>Acute respiratory distress syndrome</td>
<td>E, I</td>
<td>0-84</td>
<td>Yes</td>
<td></td>
<td>42 days</td>
</tr>
<tr>
<td>Anaphylaxis – <em>First in 7 days</em></td>
<td>E, I</td>
<td>0-1</td>
<td>Yes</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Appendicitis</td>
<td>E, I</td>
<td>1-21, 1-42</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bell’s palsy – <em>First Ever</em></td>
<td>E, I, O</td>
<td>1-21, 1-42</td>
<td>Yes</td>
<td>30 days</td>
<td></td>
</tr>
<tr>
<td>Cerebral venous sinus thrombosis</td>
<td>E, I</td>
<td>1-21, 1-42</td>
<td>Yes</td>
<td>30 days</td>
<td></td>
</tr>
<tr>
<td>Disseminated intravascular coagulation</td>
<td>E, I</td>
<td>1-21, 1-42</td>
<td>Yes</td>
<td></td>
<td>42 days</td>
</tr>
<tr>
<td>Encephalitis / myelitis / encephalomyelitis</td>
<td>E, I</td>
<td>1-21, 1-42</td>
<td>Yes</td>
<td></td>
<td>30 days</td>
</tr>
<tr>
<td>Guillain-Barré syndrome</td>
<td>E, I</td>
<td>1-21, 1-42</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immune thrombocytopenia</td>
<td>E, I, O</td>
<td>1-21, 1-42</td>
<td>Yes</td>
<td>30 days</td>
<td></td>
</tr>
<tr>
<td>Kawasaki disease</td>
<td>E, I</td>
<td>1-21, 1-42</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multisystem inflammatory syndrome in children/adults (MIS-C/MIS-A)</td>
<td>E, I</td>
<td>0-84</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myocarditis / pericarditis – <em>First in 60 Days</em></td>
<td>E, I</td>
<td>1-21, 1-42</td>
<td>Yes (subgroup)</td>
<td>30 days</td>
<td></td>
</tr>
<tr>
<td>Narcolepsy / cataplexy</td>
<td>E, I, O</td>
<td>0-84</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary embolism – <em>First Ever</em></td>
<td>E, I</td>
<td>1-21, 1-42</td>
<td>Yes</td>
<td>30 days</td>
<td></td>
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<tr>
<td>Seizures</td>
<td>E, I</td>
<td>1-21, 1-42</td>
<td>Yes</td>
<td>30 days</td>
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<tr>
<td>Stroke, hemorrhagic</td>
<td>E, I</td>
<td>1-21, 1-42</td>
<td>Yes</td>
<td>30 days</td>
<td></td>
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<tr>
<td>Stroke, ischemic</td>
<td>E, I</td>
<td>1-21, 1-42</td>
<td>Yes</td>
<td></td>
<td>30 days</td>
</tr>
<tr>
<td>Thrombosis with thrombocytopenia syndrome – <em>First Ever</em></td>
<td>E, I</td>
<td>1-21, 1-42</td>
<td>Yes</td>
<td></td>
<td>30 days</td>
</tr>
<tr>
<td>Thrombotic thrombocytopenic purpura</td>
<td>E, I</td>
<td>1-21, 1-42</td>
<td>Yes</td>
<td></td>
<td>30 days</td>
</tr>
<tr>
<td>Transverse myelitis</td>
<td>E, I</td>
<td>1-21, 1-42</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Venous thromboembolism – <em>First Ever</em></td>
<td>E, I, O</td>
<td>1-21, 1-42</td>
<td>Yes</td>
<td>30 days</td>
<td></td>
</tr>
</tbody>
</table>

**Abbreviations:** E = emergency department; I = inpatient; O = outpatient
VSD analytic strategy for the 5–11-year-old age group

- Statistical analysis will be similar to what is being done for other age groups but will include stratified analyses on 5–11-year-olds
  - For the primary analysis, the number of outcomes observed in a risk interval after COVID-19 vaccination will be compared to the number expected
    - Risk interval **0–7 days** for myocarditis/pericarditis and seizures
    - Risk interval **1–21 days** for other outcomes
- The expected will be derived from “vaccinated concurrent comparators” who are in a comparison interval (days 22-42) after COVID-19 vaccination
- On each day that an outcome occurs, vaccinees who were in their risk interval are compared with similar vaccinees who were concurrently in their comparison interval
  - Comparisons will be adjusted for by single year of age, sex, race/ethnicity, VSD site, as well as calendar date
VSD analytic strategy for the 5–11-year-old age group

- VSD will continue to review medical records and adjudicate any potential cases of myocarditis/pericarditis identified within 1–98 days following any COVID-19 vaccination.

- In addition, VSD will conduct chart review of all identified cases of GBS, acute disseminated encephalomyelitis, transverse myelitis, anaphylaxis, and cerebral venous sinus thrombosis within 1–98 days following any COVID-19 vaccination.

- VSD is able to capture information on simultaneous vaccinations.
CISA
Clinical Immunization Safety Assessment (CISA) Project

7 participating medical research centers with vaccine safety experts

- Clinical consult services†
- Clinical research

†More information about clinical consults available at http://www.cdc.gov/vaccinesafety/Activities/CISA.html
Clinical case reviews and clinical consults on complex cases of vaccine adverse events

Technical consultation on clinical guidance and clinical considerations for use of COVID-19 vaccines*

Contributions to enhanced surveillance for adverse events

Clinical research, including in pediatric populations

FDA CBER
Active Surveillance Program

CBER: Center for Biologics Evaluation and Research
BEST: Biologics Effectiveness and Safety

Slide courtesy Hui-Lee Wong, PhD, MSc, U.S. FDA
Indian Health Service (IHS) vaccine safety monitoring systems

- Passive Surveillance
  - Vaccine Adverse Event Reporting System (VAERS)
    - VAERS Functionality ("IHS" in item #26) permits analysis of AEs in IHS system of care
  - IHS Safety Tracking & Response System
    - Federal and participating tribal sites
    - Worker-related AEs and vaccine administration errors

- Active Surveillance
  - IHS Sentinel Survey
    - Biweekly survey of AEs, including vaccine administration errors
    - 58 federal and tribal sites representing IHS Areas
    - Supports reporting to VAERS
• DoD Vaccine Adverse Event Reporting System (VAERS) data - *Spontaneous adverse event reporting for DoD population*

• Vaccine Adverse Event Clinical System (VAECS) *Case tracking and evaluation of adverse events following immunizations in the DoD and DoD-affiliated populations*

• DoD Electronic Health Record and Defense Medical Surveillance System – *Large linked electronic health records (AHLTA/MHS GENESIS) and administrative data systems for near real-time safety monitoring and research*

• Joint Trauma System/COVID 19 Vaccine Breakthrough Metrics- *Case tracking of COVID-19 infection 14 days or greater following receipt of vaccine*
COVID-19 Vaccine Safety Technical (VaST) Work Group

- Serve as the central hub for technical subject matter expertise from federal agencies conducting post-authorization/approval safety monitoring
- Weekly or biweekly review of data on adverse events of special interest (AESI)
- Shared learning including all members, federal partners, and subject matter experts
- Review, evaluate, and interpret post-authorization safety data
- Advise on analyses, interpretation, and data presentation
- Independent discussion of findings by VaST members

VaST plans
- Review safety data on 5–11-year-olds as soon as available
- Continue close review of myocarditis data
- Provide updates to the ACIP COVID-19 Vaccines Working Group and ACIP on COVID-19 vaccine safety
What can you do for vaccine safety?

- Report adverse events following vaccination to VAERS even if you aren’t sure if the vaccination caused the adverse event
- Enroll yourself in v-safe
- Healthcare providers, encourage your patients to enroll in v-safe
- Parents and guardians, you can enroll your children in v-safe

Please get involved, your participation matters
Acknowledgments

- V-safe Team
- V-safe Pregnancy Registry Team
- VAERS Team
- Clinical Immunization Safety Assessment (CISA) Project
- CDC team investigating long-term effects of myocarditis
- VSD Team, VSD participating sites, and investigators from Kaiser Permanente Northern California and the Marshfield Clinic Research Institute
- FDA/Center for Biologics Evaluation and Research
- Indian Health Service
- U.S. Department of Defense, Defense Health Agency
Disclaimer

- The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention (CDC)
- Mention of a product or company name is for identification purposes only and does not constitute endorsement by CDC
Thank you!

For more information, contact CDC
1-800-CDC-INFO (232-4636)

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