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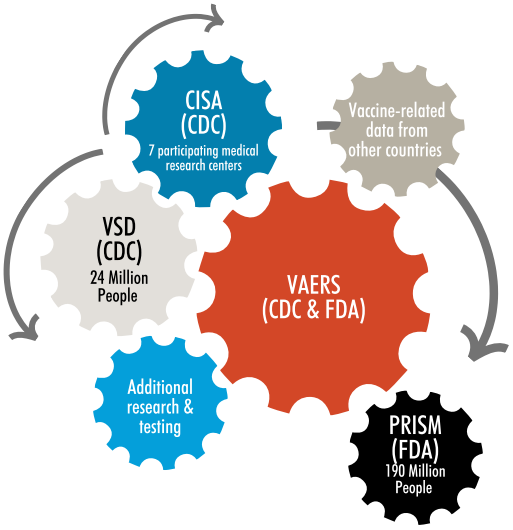
How is Vaccine Safety Monitored in the U.S.?

Vaccine safety monitoring systems in the U.S.

The success of vaccination programs depends not only on vaccines' effectiveness, but also on their safety. Because vaccines are given to millions of healthy people each year, they are held to a very high standard and are continuously monitored for safety.

The U.S. has one of the most advanced systems in the world for assessing vaccine safety. This includes a coordinated and overlapping approach using state-of-the-art technologies and systems working together. Each of the "gears", or systems, supplies a different type of data for researchers to analyze. Together, they work as a well-oiled machine to help provide a comprehensive picture of vaccine safety in the U.S. Each of these systems is detailed below.



Why is it important to monitor vaccines post-licensure?

Monitoring a vaccine after it is licensed or authorized helps ensure that vaccines continue to be safe and effective and the benefits continue to outweigh the risks.

Clinical trials typically involve thousands of participants. However, even large clinical trials may lack adequate sample sizes to identify rare adverse events - an event that may occur after one in 100,000 or one in 1,000,000 doses administered. Post-licensure safety studies help validate safety data from clinical trials and may detect adverse events that were not picked up in clinical trials.

Clinical trials may exclude specific vulnerable sub-populations, such as pregnant women or immunocompromised adults, for whom a vaccine may be indicated. Studies done post-licensure monitor the safety, effectiveness and benefits of vaccination in these populations.

Vaccine Adverse Event Reporting System (VAERS)

VAERS is used by the FDA and the CDC to collect reports of adverse events (possible side effects) that happen after vaccination. The system relies on individuals to send in reports of adverse health events following vaccination – meaning anyone can and should report adverse events to VAERS.

Scientists monitor VAERS reports, looking for adverse events that are unexpected, appear to happen more often than expected, or have unusual patterns. If a safety signal is identified, it is analyzed further using other safety monitoring systems (like VSD) to determine whether a vaccine is associated with a certain outcome and the rate at which it occurs.

What are the strengths of VAERS?

- Anyone can submit reports to VAERS (passive surveillance system)
- Serves as an early warning/hypothesis-generating system for vaccine safety issues. For example, in early 2021, reports to VAERS indicated a possible increased risk of severe allergic reactions following mRNA COVID-19 vaccination. Additional investigation concluded that these reactions are quite rare, happening in less than one in 200,000 doses administered.

What are the limitations of VAERS?

- Cannot determine if a vaccine caused the reported adverse event
- There is no control group to compare rates of adverse events in those who did and did not receive a vaccine (VAERS cannot determine if an adverse event is occurring more often following vaccination than what would be expected in the general population)
- Reports may lack details or contain errors

Vaccine Safety Datalink (VSD)

The VSD is a network of thirteen managed care sites across the U.S. with a combined patient population of more than 24 million people. The VSD can be used to determine if safety signals identified using VAERS are related to vaccination. It can also identify safety signals through real-time monitoring; for example, VSD evaluates particular health-related outcomes that may be associated with vaccination and compares it to the expected number of outcomes in a comparison group.

What are the benefits of VSD?

- Conduct timely vaccine safety studies, including assessments of rare adverse events and longitudinal studies involving prolonged follow-up of individual patients
- Use of a control group – allowing for the comparison of adverse events in those who did and did not receive a vaccine (can compare vaccinated to unvaccinated)

What are the limitations of VSD?

- May not have enough patients to detect extremely rare adverse events
- May not capture vaccine administration data outside of the health system
- Cannot determine if an association between an adverse event and vaccination is causal

Clinical Immunization Safety Assessment Project (CISA)

The CISA Project is a national network of vaccine safety experts from the CDC, seven medical research centers, and other partners. The project addresses vaccine safety issues, conducts high quality research, and assesses complex clinical adverse events following vaccination through active surveillance.

What are the benefits of the CISA Project?

- Serves as a vaccine safety resource for U.S. health care providers and assists CDC and its partners in evaluating emerging vaccine safety issues
- Can implement prospective, multi-site clinical studies with hundreds of subjects and has the ability to recruit controls
- Can assess vaccine safety in sub-populations (e.g. pregnant women, infants, and children)
- Receives detailed clinical data on patients and can collect biological samples from patients

What are the limitations of the CISA Project?

- Small sample sizes may limit CISA's ability to study rare adverse events
- Clinical trials can be labor and resource intensive, and it can be challenging to recruit and retain subjects

Post-licensure Rapid Immunization Safety Monitoring System (PRISM)

PRISM is the largest vaccine safety surveillance system in the U.S., with access to information for over 190 million people. PRISM uses a database of health insurance claims to identify and evaluate possible vaccine safety issues.

What are the strengths of PRISM?

- Large patient population allows the system to identify and analyze rare health outcomes that would otherwise be difficult to assess
- Linked to some immunization and birth registries - allowing for more complete vaccine exposure data
- Access to denominator data for vaccine exposure, which allows the FDA to estimate a measure of association between a vaccine and adverse events

What are the limitations of PRISM?

- There is a lag in time for accessing the PRISM data
- Medicare population is not as well represented in PRISM
- May not be representative of those without insurance coverage

V-safe

V-safe, a new active surveillance program in the U.S., is a smartphone-based tool that used text messaging and web surveys to provide personalized health check-ins after an individual received a COVID-19 or mpox (Monkeypox) vaccine. In March 2023, enrollment in v-safe for mpox vaccine closed. As of May 2023, CDC closed enrollment in v-safe for COVID-19 vaccines. Since its launch in December 2020, over 10 million v-safe participants completed over 151 million health surveys about their experience following COVID vaccination. Data from this system have been included in more than 20 scientific publications. A new version of v-safe will be launched later in 2023 and will allow users to share their post-vaccination experience with new vaccines.

What are the strengths of v-safe?

- Anyone can enroll in v-safe
- Another way to quickly validate safety data from clinical trials or identify potential safety issues
- Regular reminders to complete a survey help to capture more safety data
- CDC can follow-up with participants and submit VAERS reports, as needed

What are the limitations of v-safe?

- V-safe data may not properly represent the post-vaccination experiences of the entire population. For example, early registrants were predominantly younger. Populations who might not have access to electronic devices to complete web-based survey (ex. older populations and socioeconomically disadvantaged populations) were less likely to be enrolled.

The Biologics Effectiveness and Safety (BEST) Initiative

The BEST initiative is an active surveillance system managed by the FDA. This system is comprised of large-scale claims data, electronic health records (EHR), and linked claims-EHR. Similar to VSD or PRISM, the BEST initiative can be used for in-depth analyses if safety concerns are identified from other sources, such as VAERS.

What are the strengths of the BEST initiative?

- Near real-time analysis with available data
- Use of a control group, allowing for the comparison of adverse events in those who did and did not receive a vaccine (can compare vaccinated to unvaccinated)
- Ability to assess safety of vaccine in sub-populations (ex. those with pre-existing conditions, pregnant women)

What are the limitations of the BEST initiative?

- May not be representative of those without insurance coverage
- Cannot determine if an association between an adverse event and vaccination is causal

Additional research and testing

There are many other departments and agencies involved in assessing the safety of vaccines. The Department of Defense (DoD), the U.S. Department of Veterans Affairs (VA), and the Indian Health Service (IHS) have systems to monitor vaccine safety and do vaccine safety research. The National Institutes of Health (NIH) and the Office of Infectious Disease and HIV/AIDS Policy (OIDP) also support ongoing research on vaccines and vaccine safety.

Vaccine-related data from other countries

The U.S. also monitors and assesses high-quality data on vaccine safety and effectiveness from other countries. For example, the United Kingdom and Qatar have large, national healthcare systems. Data from these countries allow scientists and researchers to evaluate vaccine safety at a population level. It also allows for comparison of people who have and have not been vaccinated, while controlling for various factors and health outcomes. These data can validate U.S. safety monitoring results and inform what signals the U.S. vaccine safety monitoring systems should be assessing and monitoring.

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