COVID-19 vaccine post-authorization safety and effectiveness monitoring

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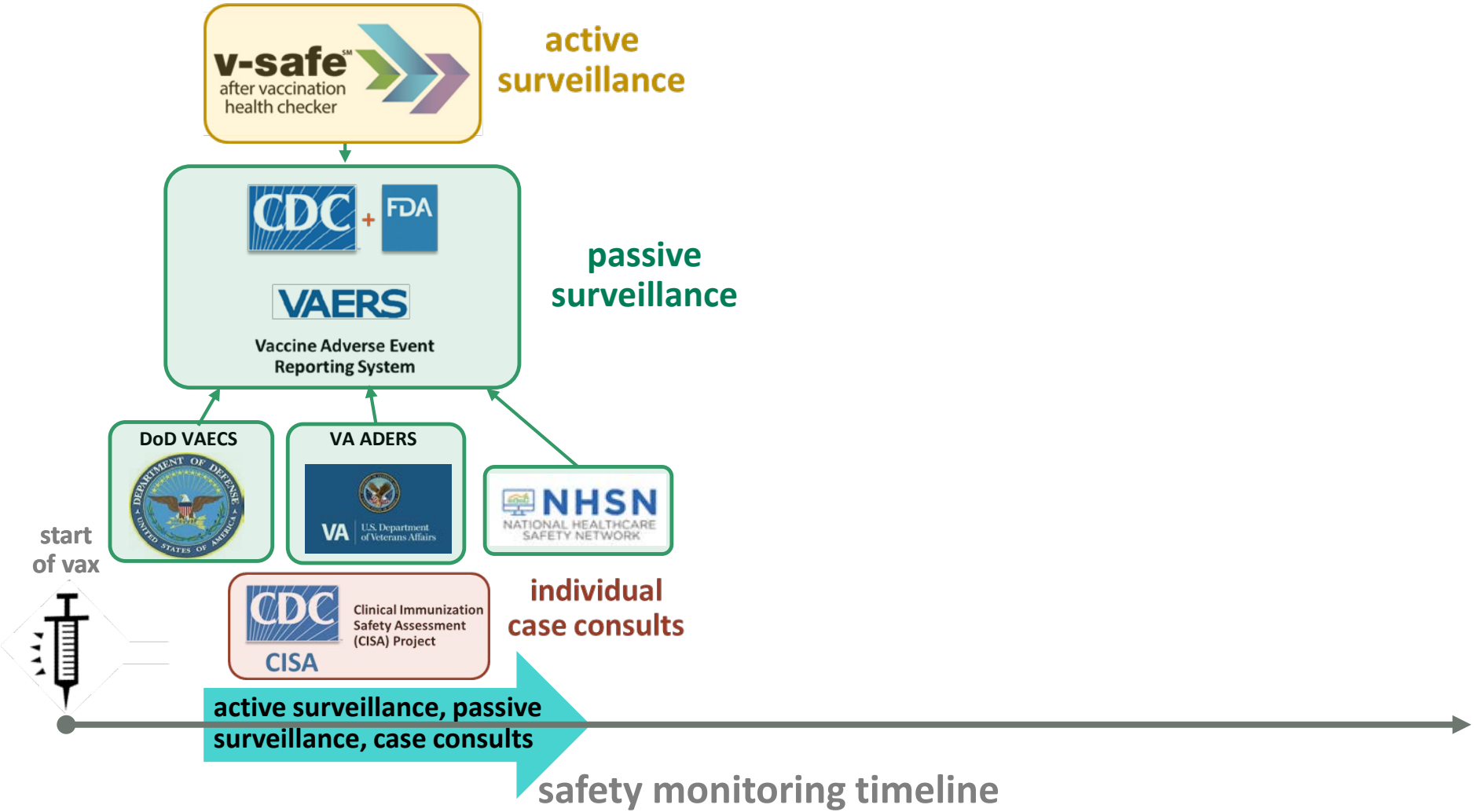
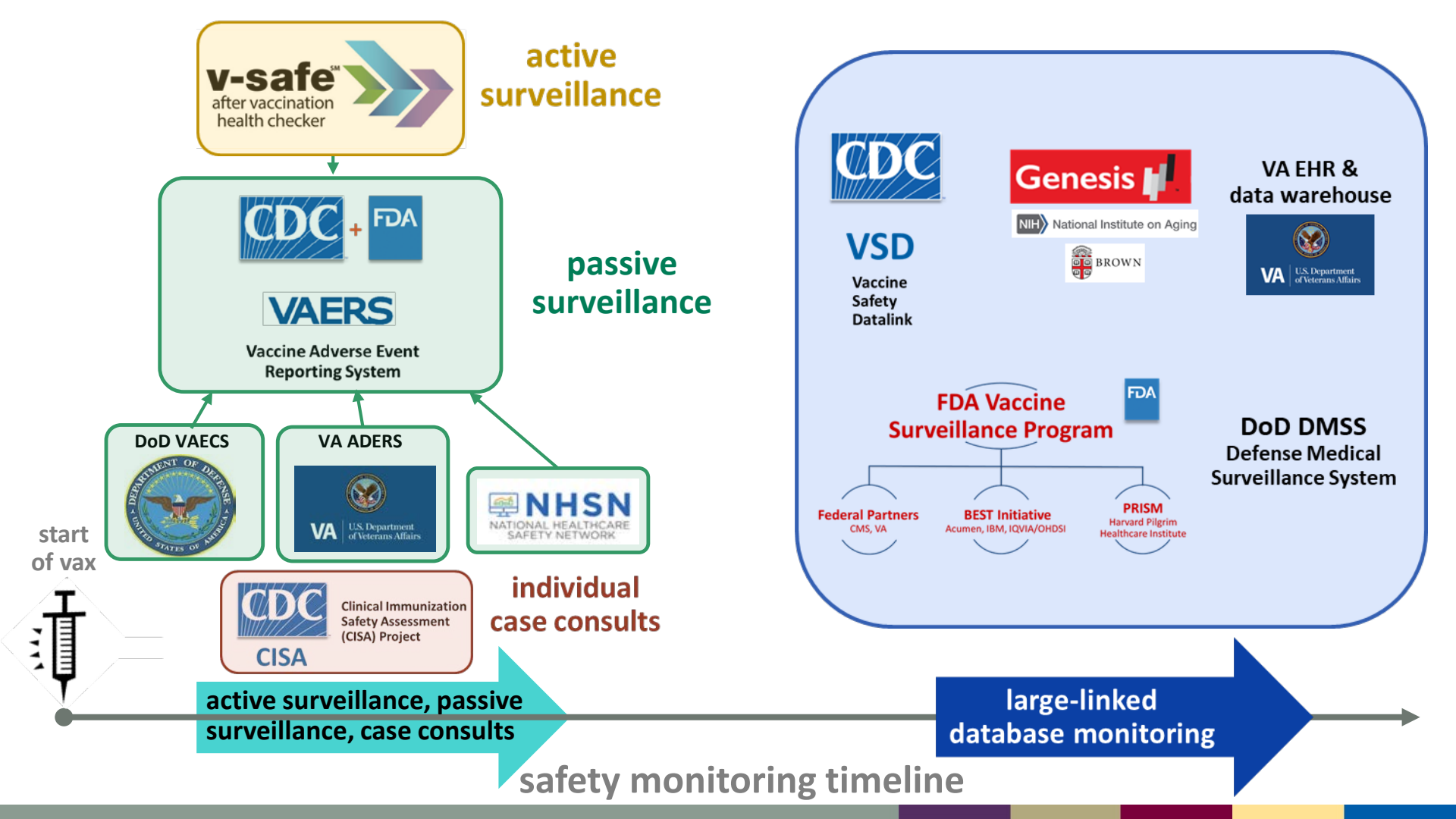
U.S. government vaccine safety monitoring systems, timeline, and covered populations

USG Approach to Vaccine Safety Monitoring

- Rapid implementation under EUA requires whole of USG approach with initial focus on early populations for vaccination
  - Voluntary active surveillance of adverse events focused on healthcare worker vaccination
  - Rapid follow-up of reported serious adverse events
- As the program continues and more vaccine is given, active surveillance systems will provide increasing useful information on safety in different populations
- Close collaboration of safety experts across USG will facilitate data sharing and rapid recognition and response to safety signals


v-safe
after vaccination health checker
active surveillance
CDC + FDA
VAERS
Vaccine Adverse Event Reporting System
passive surveillance
DoD VAECS
VA ADERS
VA U.S. Department of Veterans Affairs
NHSN
NATIONAL HEALTHCARE SAFETY NETWORK
start of vax
CDC
Clinical Immunization Safety Assessment (CISA) Project
CISA
individual case consults
active surveillance, passive surveillance, case consults
safety monitoring timeline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CDC
VSD
Vaccine Safety Datalink
Genesis
NIH National Institute on Aging
BROWN
VA EHR & data warehouse
VA U.S. Department of Veterans Affairs
FDA Vaccine Surveillance Program
FDA
Federal Partners
CMS, VA
BEST Initiative
Acumen, IBM, IQVIA/OHDSI
PRISM
Harvard Pilgrim Healthcare Institute
DoD DMSS
Defense Medical Surveillance System
active surveillance, passive surveillance, case consults
large-linked database monitoring
safety monitoring timeline

Monitoring systems and populations

	Monitoring systems	Population	Healthcare workers	LTCF residents
early	**VAERS** (CDC & FDA) VA ADERS DoD VAECS CDC NHSN	General U.S. population, VA and DoD patient populations, NHSN acute care and long-term care facilities	Yes	Yes
early	**V-safe** (CDC)	All COVID-19 vaccine recipients eligible	Yes	Limited
later	**VSD** (CDC)	Insured patients in VSD sites	Yes	Limited
later	**FDA-CMS**	Medicare recipients (90+% of 65 y/o in the U.S., including 650K LTCF residents)	Limited	Yes
later	**BEST & PRISM** (FDA)	Insured patients in BEST & PRISM sites	Yes	Limited
later	**VA EHR & data warehouse**	Enrolled VA patients	Limited	Yes
later	**DoD DMSS**	Active duty military (limited info on beneficiaries [i.e., family members, retirees])	Yes	Limited
later	**Genesis HealthCare** (Brown U. & NIH-NIA)	Long-term care facility residents (~35,000 long stay residents)	No	Yes

ACIP COVID-19 Vaccine Safety Technical Sub-Group (VaST)

- Built off lessons learned from H1N1 vaccine safety monitoring
- Terms of reference and composition are finalized and VaST is ready to begin reviewing data once implementation commences
  - Co-Chaired by ACIP member and a National Vaccine Advisory Committee (NVAC) member
  - 10 independent expert consultants
  - ACIP federal agency ex officio members (NIH, FDA, OIDP, CMS, HRSA, IHS)
  - Veterans Affairs (VA) and Department of Defense (DoD) liaisons

U.S. government vaccine effectiveness (VE) assessments

Need for post-authorization or licensure VE estimates

- Address evidence gaps from phase 3 clinical trails
  - Limited efficacy information for secondary endpoints (*e.g.*, VE against infection/transmission, VE in key sub-populations)
  - Limited insight into duration of protection
- Real world performance of vaccines
  - Protection may differ from efficacy under trial conditions
    - Most COVID-19 vaccine products require 2 dose regimens and varying cold chain conditions: challenging to implement

VE policy priorities

Immediate First 2-4 months	• **Does a vaccine protect against symptomatic disease as expected?**

Subsequent	• VE against key outcomes
	  • Severe disease
	  • Non-severe disease
	  • SARS-CoV-2 infection (and potentially transmission)
	• VE in key sub-populations
	  • Elderly (including those in LTCF)
	  • People with key underlying conditions (obesity, diabetes)
	  • Disproportionately affected populations (Black, LatinX, Native American)
	• Regimen-related questions
	  • VE of a single dose; VE of mixed dose (more than 1 product) schedules

Later stage	• Duration of protection • Comparative VE: Is one product better than another? • Viral evolution: Do genome changes threaten VE?

Strategies for assessments of VE

- Facilitate rapid launch
  - Leverage existing platforms
  - For early phase vaccination (limited doses), focus on a population likely to be eligible
- Harmonize and coordinate across platforms and US government
  - Align as feasible case definitions, data elements, methods
  - Improve comparability of results
- Combine similar platforms
  - Improve geographic representation/capture of COVID-19 hotspots
  - Increase statistical power
  - Generate more timely and robust VE estimates
- Diversity of methods
  - All observational methods have limitations

Currently planned COVID-19 VE studies: Adults > 18 years

VE priority	Prospective data collection	Electronic health record (EHR) and claims database analyses (coordination across USG)
Immediate priority: Does vaccine work as expected?	Test negative design (TND) case-control among healthcare workers	
Subsequent priorities Severe/hospitalized disease	TND; conventional case-control using facility controls; screening method	EHR datasets (CDC, VA, FDA): Retrospective cohort or TND
Non-severe disease	TND plus conventional (facility controls)	EHR datasets (CDC, VA, FDA)
Infection (transmission)	• Prospective longitudinal cohort/s --Health care & frontline workers • Transmission (index case households)	
Elderly (including a subset analysis of those in LTCF)	TND or conventional case-control among 65+ years (COVID-NET linked to CMS)	CMS cohort (FDA, CMS) EHR datasets (CDC, VA, FDA)
Those with key underlying conditions	*Captured in above studies	CMS (FDA,CMS); EHR datasets (CDC, VA, FDA)
Disproportionately affected racial/ethnic groups	TND in Navajo population; * Also captured in above studies	CMS (FDA, CMS); EHR datasets (CDC, VA, FDA); Exploring IHS EHR (IHS)
Monitor viral drift over time	Leverage SPHERES project and national viral surveillance; explore sample collection from vaccine failures	

Summary – Vaccine Effectiveness

- Planned VE studies will provide a robust assessment of COVID-19 vaccine performance in real-world settings
  - Early VE estimates in groups prioritized for vaccination
  - VE against key outcomes and in important sub-populations
- Data from COVID-19 VE studies will address critical gaps and help guide future use of vaccines

Early Vaccine Evaluation

Early Vaccine Evaluation

- Systems are in place to monitor the safety of COVID-19 vaccination in HCWs and LTCF residents
  - V-safe/VAERS/NHSN will detect adverse event signals for further follow-up and evaluation
  - CMS, Genesis and other claims-based and EHR systems will be used for both signal detection and evaluation
- Vaccine effectiveness in HCWs is the immediate priority and will address the question – Does the vaccine work as expected?
  - TND case-control study in HCWs to start immediately
- Vaccine effectiveness evaluations in older adults, including those in LTCFs, are planned and include both TND and cohort evaluations

Vaccine Safety and Effectiveness Monitoring is a top USG Priority

- Vaccine signal detection is sensitive but not specific
  - Signals are expected to occur, demonstrate robust system
  - Signal assessment may take time to resolve
- Understanding vaccine impact and effectiveness critical to controlling the pandemic
- Vaccine safety and effectiveness data will inform clinical guidance and recommendations for COVID-19 vaccines

Questions