# CDC plans for COVID-19 vaccine effectiveness evaluation post-authorization and post-licensure

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# Need for post-authorization or post-licensure vaccine effectiveness (VE) estimates

- Real world protection may differ from efficacy under trial conditions
  - Timing and coverage of 2-dose regimens
  - Cold chain requirements may be difficult to implement

- Build on evidence from phase 3 clinical trials including VE for
  - Key subpopulations
  - Severe disease
  - SARS-CoV-2 infection and transmission
  - Duration of protection

# VE policy priorities: Results of internal and external input

| | |
|---|---|
| **Immediate**<br>**First 2-4 months** | • Does vaccine protect against symptomatic disease as expected? |
| Subsequent | • VE against key outcomes<br>  • Severe disease<br>  • Non-severe disease<br>  • SARS-CoV-2 infection and transmission<br>• VE in key subpopulations<br>  • Adults aged ≥65 years, including those in long-term care facilities (LTCF)<br>  • People with key underlying conditions (e.g., immunocompromised, obesity, diabetes)<br>  • Disproportionately affected racial/ethnic populations (Black, Latinx, Native American/ Alaska Native)<br>• VE for regimen-related questions<br>  • Single dose and prolonged dosing intervals; Mixed dose schedules (>1 product) |
| Later stage | • Viral evolution: Do genome changes threaten VE?<br>• Duration of protection<br>• Comparative VE: Is one product better than another? |

# Challenges for observational COVID-19 VE studies

- Decision to be vaccinated may correlate with risk of disease
- Prior infection may bias estimate
- Imperfect laboratory testing poses a risk of misclassification
- COVID-19 epidemiology is highly dynamic
- Multiple products are in use simultaneously

# Currently planned COVID-19 VE assessments

| VE priority | Prospective data collection | Electronic health record (EHR) and claims analyses (coordination across US government) |
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| **Immediate priority** | | |
| Does vaccine work as expected to prevent symptomatic disease? | Test-negative design case-control among healthcare personnel | |
| **Subsequent priorities** | | |
| Older adults, including residents of long-term care facilities (LTCF) | Case-control among adults ≥65 years (COVID-NET linked to CMS); National Healthcare Safety Network | CMS cohort (FDA, CMS)<br>EHR datasets (CDC, VA, FDA) |
| Infection and transmission | Prospective longitudinal cohorts, including among healthcare personnel & frontline workers; case-ascertained household cohorts for transmission | |
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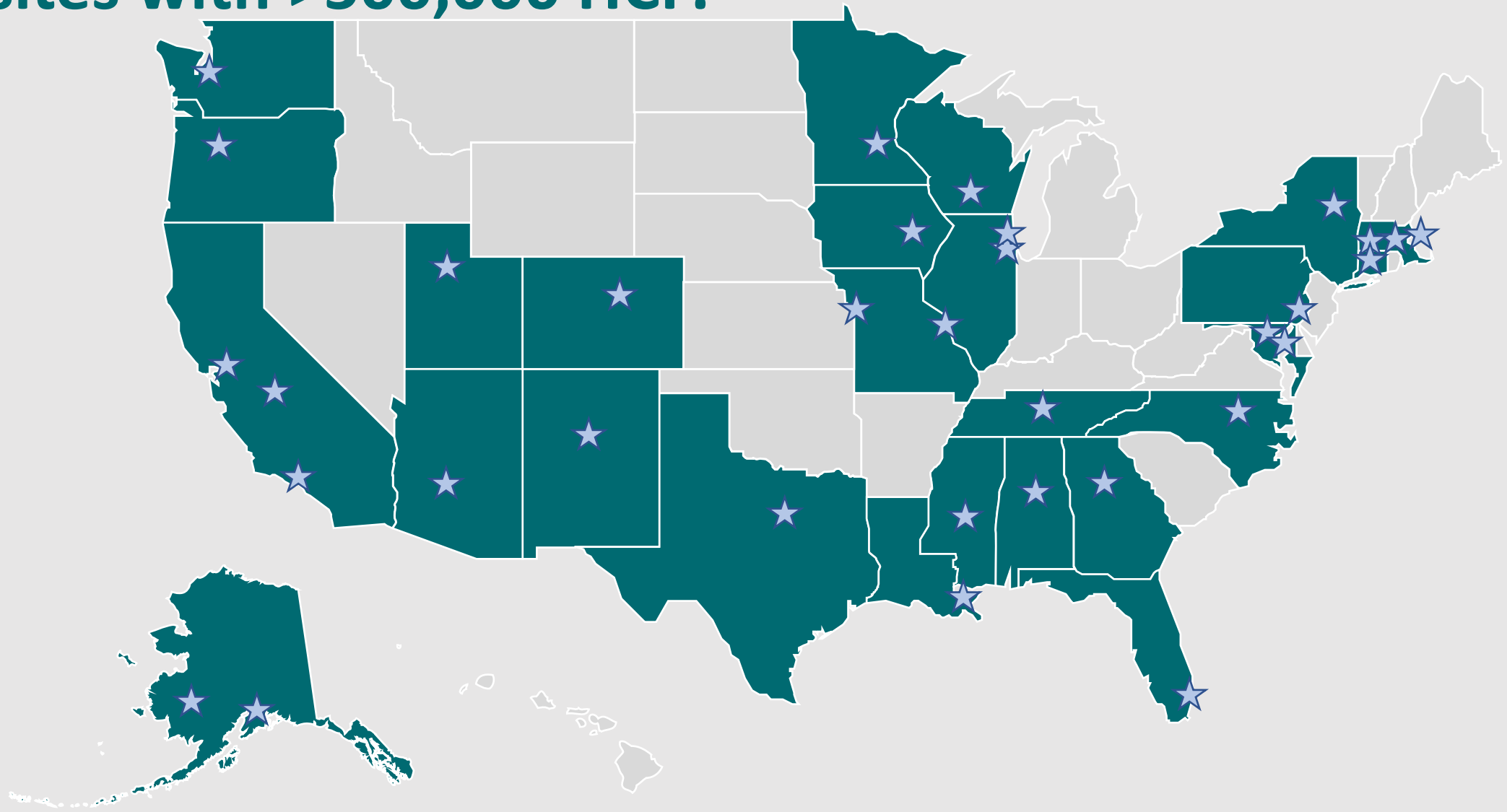
# Assessing VE among healthcare personnel (HCP)

- Prospective test-negative design among HCP
  - Enroll HCP who are tested for COVID-19
  - Cases are test positive & controls are test negative

- Objectives:
  - Primary: evaluate VE of a complete schedule of COVID-19 vaccine against laboratory-confirmed symptomatic COVID-19 (by product if feasible)
  - Secondary will include VE by number of doses received, if feasible

- Timeline: January launch and enroll until sites have reached vaccine coverage >80% (2 doses)

# VE assessment is being conducted across 26 states in 34 sites with >500,000 HCP.



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# Assessing VE among adults aged ≥65 years

- CDC-led case-control assessment linking hospitalized cases from COVID-NET with CMS data
- FDA-led cohort analysis of CMS claims data
- Both will conduct separate analyses for adults ≥65 years who reside in
  - Community
  - Long-term care facilities (LTCF)

# Assessing VE among residents of LTCF

- Data from the National Healthcare Safety Network (NHSN) LTCF surveillance and vaccine coverage modules
  - Weekly aggregate counts at the facility level of
    - New laboratory-confirmed COVID-19 cases
    - Vaccination status among all residents and among cases
  - Plan to calculate weekly attack rates among vaccinated and unvaccinated

- Data will be available starting early February
  - Initial analysis will require at least 8 weekly transmissions from LCTF with at least 50% vaccine coverage
  - Plans for ongoing analyses

# Assessing vaccine impact in LTCF

- Ecologic analyses of vaccine coverage and COVID-19 disease rates among residents of LTCF

- Outbreak descriptive analyses before and after vaccine use

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# Assessing VE against infection and transmission

- Leverage ongoing cohort of >5000 HCP and first-responders
  - Weekly testing for SARS-CoV-2 infection
  - Assessment of secondary transmission among household members
  - Cohort began in July 2020 and will continue through March 2022

- Working to expand case-ascertained household transmission studies to general population during widespread adult vaccination

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# Assessing VE for disease severity and key populations

- Test-negative design and conventional case-control with hospitalized controls
  - Designed to assess severe disease/hospitalization and non-severe disease
  - Sites selected to include populations with underlying health conditions, racial/ethnic groups disproportionately affected by COVID-19, and American Indian/Alaska Native populations
- Screening method analyses
- EHR and claims-based assessments

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# Assessing vaccine impact

- Ecologic analyses of the association of disease incidence and/or seroprevalence with vaccine coverage

- Comparisons of expected vaccine impact from models with actual observed impact

# Assessing VE for regimen-related questions

- Single dose
- Prolonged dosing intervals (>3-4 weeks)
- Mixed dose schedules (>1 product)

- All platforms except NHSN will collect individual-level information on dose dates and type
- Best opportunity may come from large prospective, EHR, and claims assessments among the general adult population

# Do viral genome changes threaten VE?

- Prospective platforms for general adult population will collect specimens from cases, where possible, for whole genome sequencing
  - Will not be performed in real time
  - May not be powered for variant-specific VE assessments

- A separate team in the vaccine evaluation unit is dedicated to assessing vaccine breakthrough cases

- Work is part of broader CDC efforts to monitor the impact of SARS-CoV-2 variants

# Assessing VE among children and pregnant women

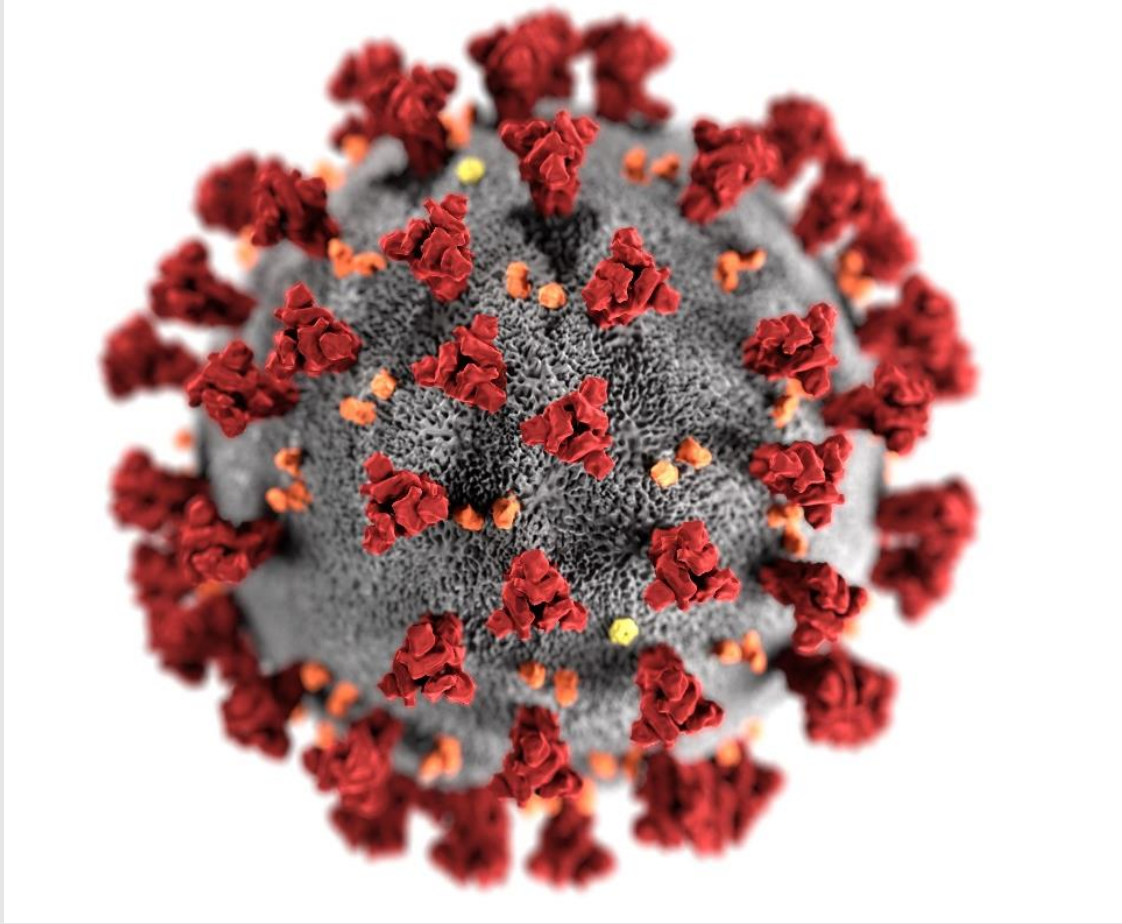
- Children
  - Planning a prospective test-negative design assessment to evaluate VE against COVID-19 hospitalizations
    - Leveraging an existing surveillance network of approximately 20-40 sites for pediatric COVID-19 hospitalizations and multisystem inflammatory syndrome in children (MIS-C)
  - EHR and claims database analyses will be used to estimate VE in children

- Pregnant women
  - Exploring EHR cohort and prospective case-control VE assessments

# Conclusions

- Urgent need for VE data to guide vaccine policy
- VE portfolio leverages multiple platforms, data sources, and methods
- Early VE assessments will focus on healthcare personnel and residents of LTCF
- Portfolio will continue to evolve as more information from Phase 3 trials and real-world evidence become available

# Questions?



For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

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