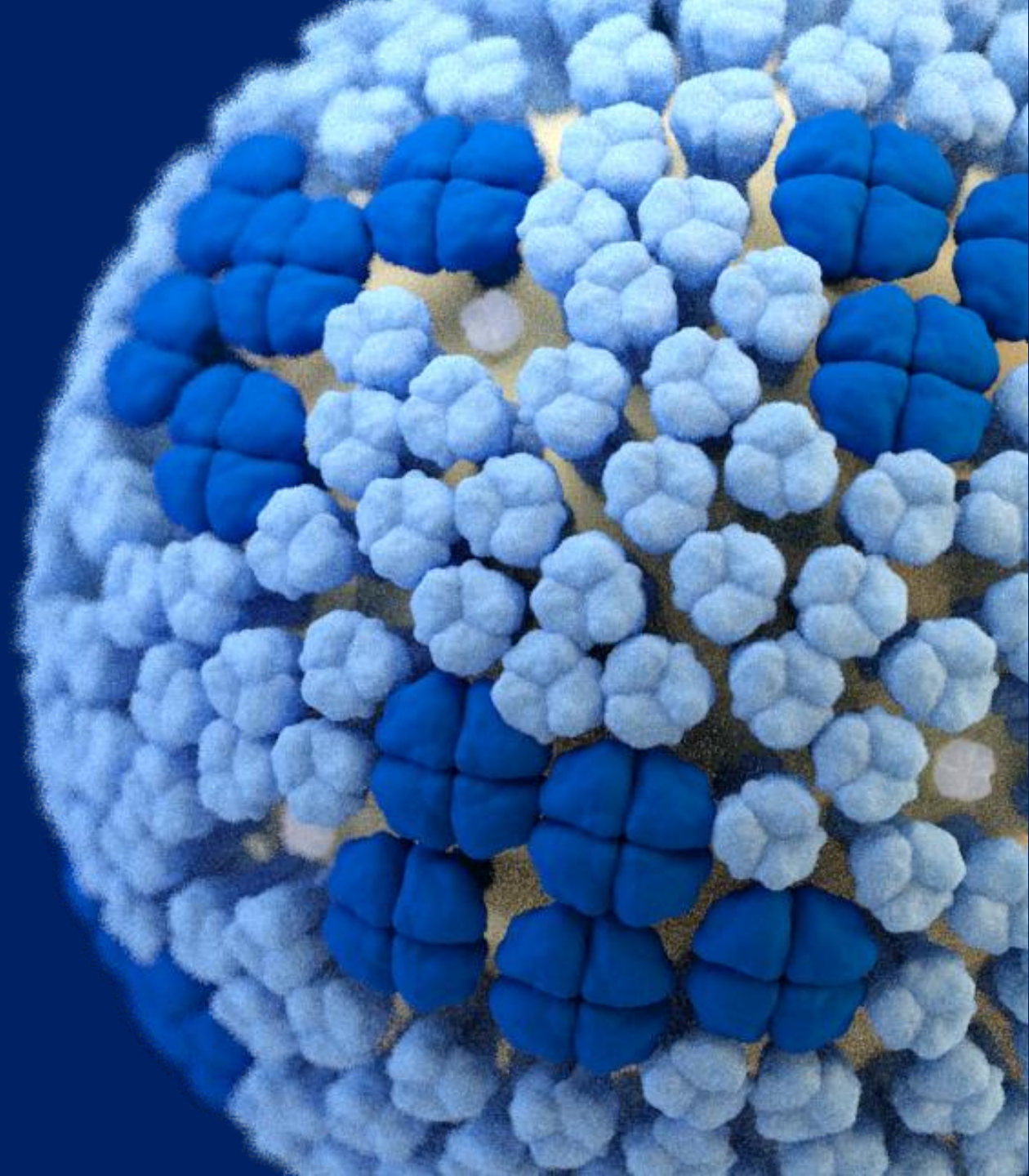


CDC Priorities to Detect, Prevent and Respond to Influenza

Dan Jernigan, MD MPH

October 7, 2020

DJernigan@cdc.gov



Influenza Division Strategic Priorities



Improve influenza detection and control



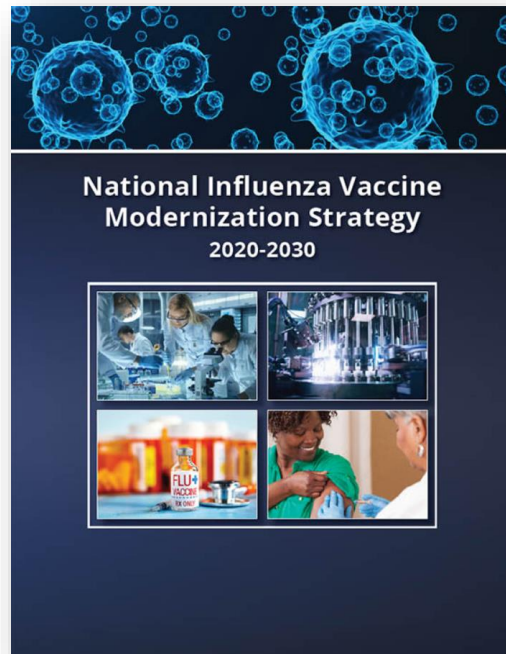
Improve epidemic and pandemic risk assessment and readiness



Improve vaccine impact



National Influenza Vaccine Modernization Strategy



- Objective 1: Strengthen and Diversify Influenza Vaccine Development, Manufacturing, and Supply Chain
- **Objective 2: Promote Innovative Approaches and Use of New Technologies to Detect, Prevent, and Respond to Influenza**
- Objective 3: Increase Influenza Vaccine Access and Coverage Across All Populations

From Infection to Protection: CDC Activities Across the Influenza Spectrum

DETECT

- Global and Domestic Surveillance and Epidemiology
- Virus Characterization
- Risk Assessment
- Diagnostic Guidance
- Testing Capabilities
- Forecasting and Predictive Analytics

CONTROL

- Antiviral Supply Monitoring
- Resistance Monitoring
- Clinical Management and Antiviral Guidance
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- Outbreak Intervention
- Community Mitigation
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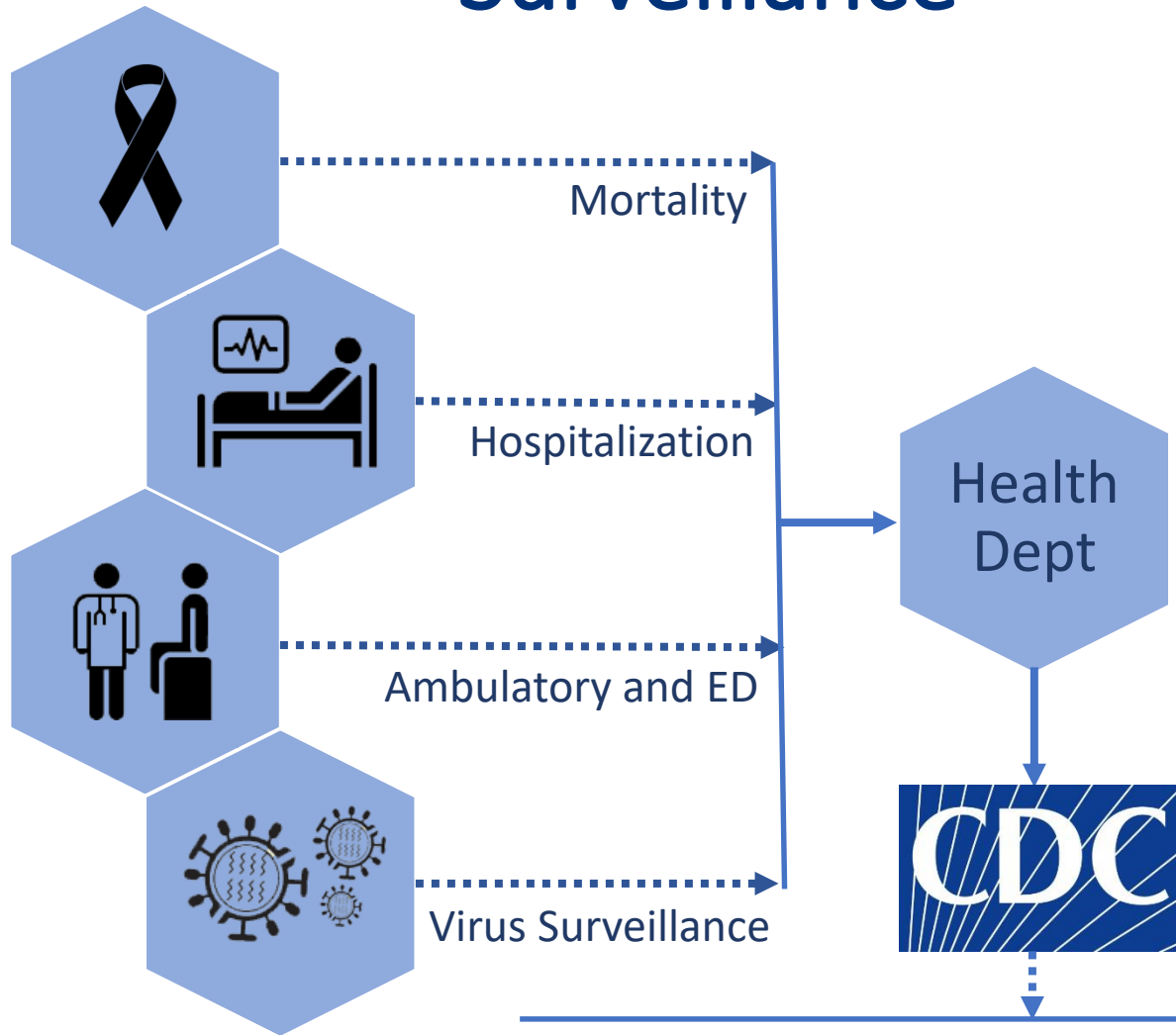
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DETECT: Innovation in Flu Surveillance



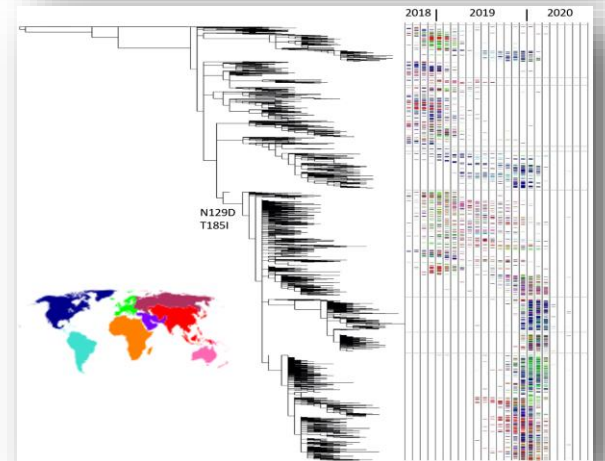
- Comprehensive, layered surveillance that captures viral surveillance, ambulatory care, hospitalization, and mortality data
 - Same systems are being used for COVID-19
 - Surveillance in all U.S. States and through 143 laboratories globally
- Expansion for the 2020-2021 season
 - Adding **471 emergency departments** to outpatient syndromic surveillance system ILINet
 - **Expanding hospitalization surveillance** with new mandated flu reporting from ALL hospitals daily
 - **Increased Flu Surveillance at LTCFs** – Testing COVID-19 specimens collected at LTCFs for flu
 - Adding **Commercial Lab** Flu Reports for County-level views
 - Adding **Real-Time Flu Diagnosis Codes** from >4700 EDs for facility-level views

DETECT: Innovation in Flu Diagnostics

PRIORITY: Expand global and domestic capacity for whole genome characterization of influenza viruses

PRIORITY: Improve CDC's influenza virus characterization and surveillance monitoring systems to inform influenza vaccine composition

- Expanding global and domestic **next-generation sequencing**
 - Implemented cloud-based computing, storage and analysis
 - Piloting enhanced surveillance in key strategic locations globally
- Real-time sequencing and analysis in the field
 - **Developed a portable flu laboratory “Mia” (Mobile Influenza Analysis)**
 - **Sequences the influenza genome and analyze influenza A viruses in real-time in the field during an outbreak**
- Use of **new multiplex CDC test** at PHLs will add flu detection to specimens tested for SARS-CoV-2
 - Additional monitoring from direct diagnostic reporting
- Providing **testing guidance** for use of diagnostics for flu and SARS-CoV-2

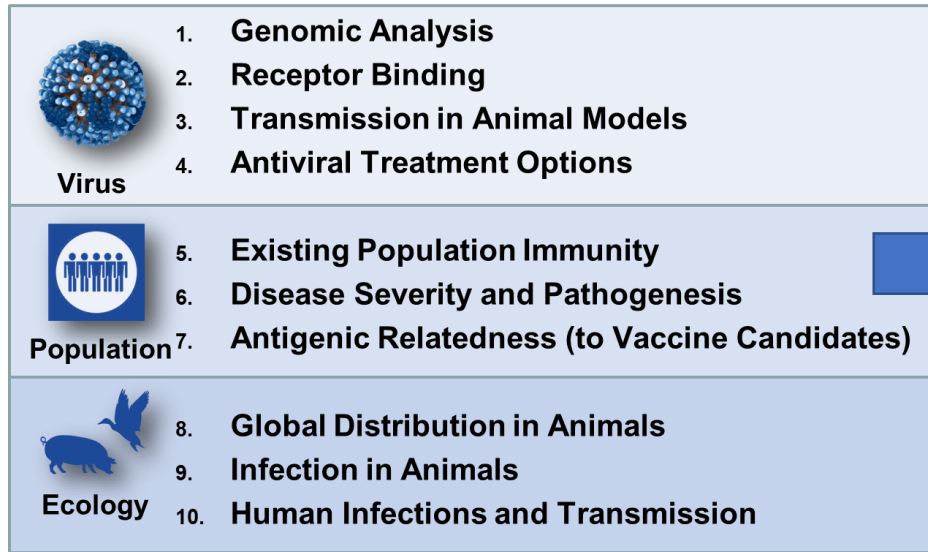


DETECT: Innovation in Influenza Forecasting and Modeling

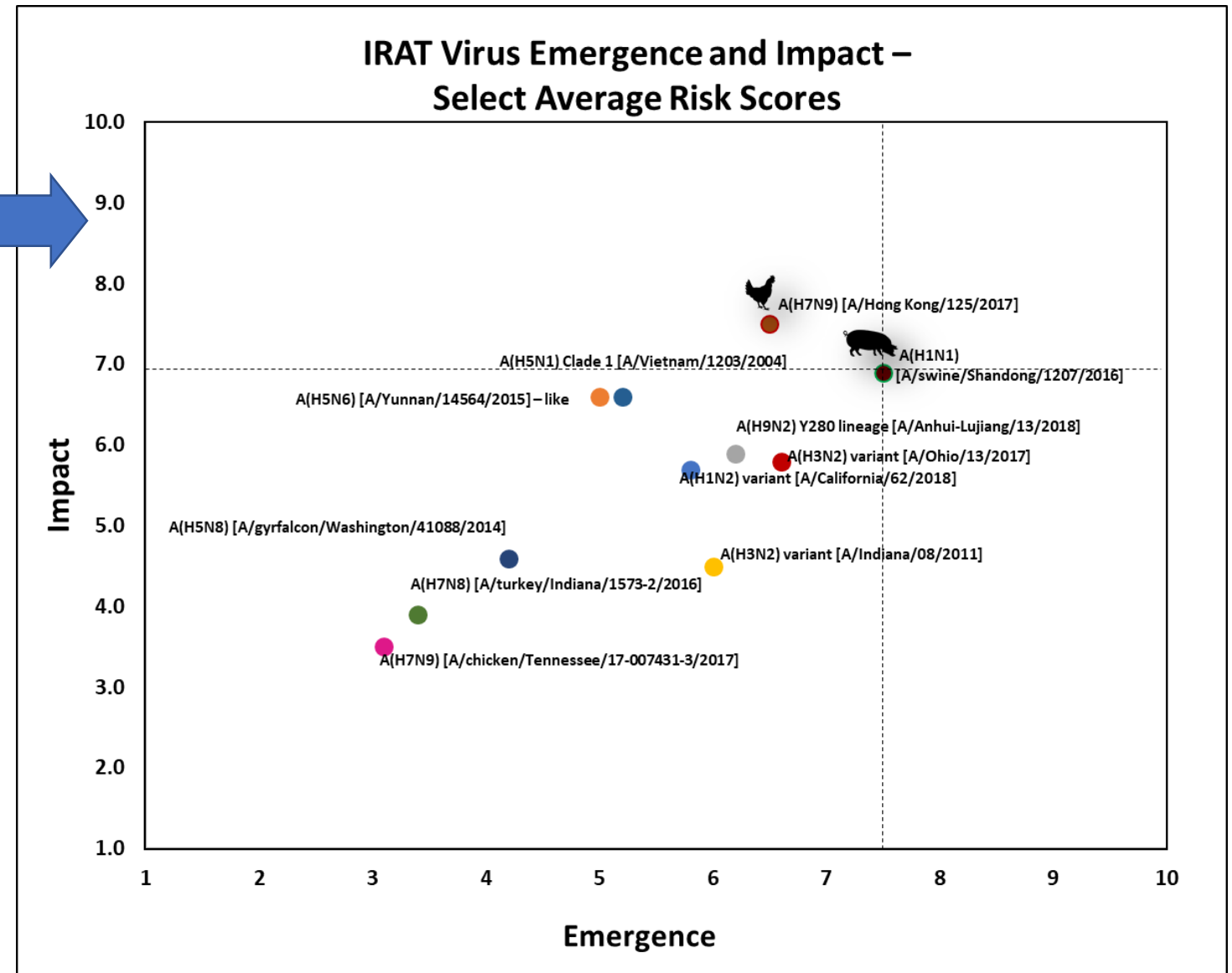
- ILI forecasting to support flu control has been in place for several years.
- This fall, CDC will be forecasting influenza hospitalizations for the public and for healthcare providers for planning.
- This forecast will be publicly available on the CDC website when flu has begun circulating
- CDC maintains several influenza economic and transmission models to help inform prevention and control efforts



DETECT: Influenza Risk Assessment for Emerging Novel Influenza Viruses



- Ten risk elements evaluated to develop a risk score:
 - properties of the **virus**
 - **population** immunity
 - animal and human **ecology**
- Scores determined for
 - Risk to **emerge** to cause human pandemic
 - Risk to cause significant human illness **impact** if emerges



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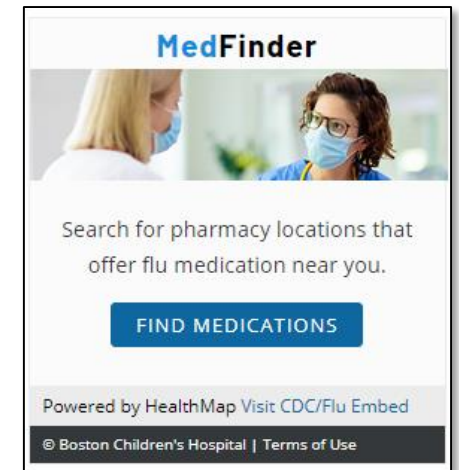
CONTROL: Antiviral Treatment and Monitoring

- **Treatment and Management Guidance:**

- Updated recommendations for clinicians for treating influenza during SARS-CoV-2 co-circulation
- Outbreak management guidance on CDC website for state/local health department response
 - ✓ Cohorting and infection control
 - ✓ Antiviral prophylaxis
 - ✓ Vaccination as appropriate

- **Antiviral Medicine Tool:** *MedFinder* is a free, online service for consumers to search for pharmacy locations that offer anti-influenza drugs

- **Antiviral Monitoring:** Using manufacturer and pharmacy supply and dispensing data, trends in drug availability and use are monitored.
 - Expected 10 M doses available by season start
 - Looking to expand antiviral stocks in LTCFs

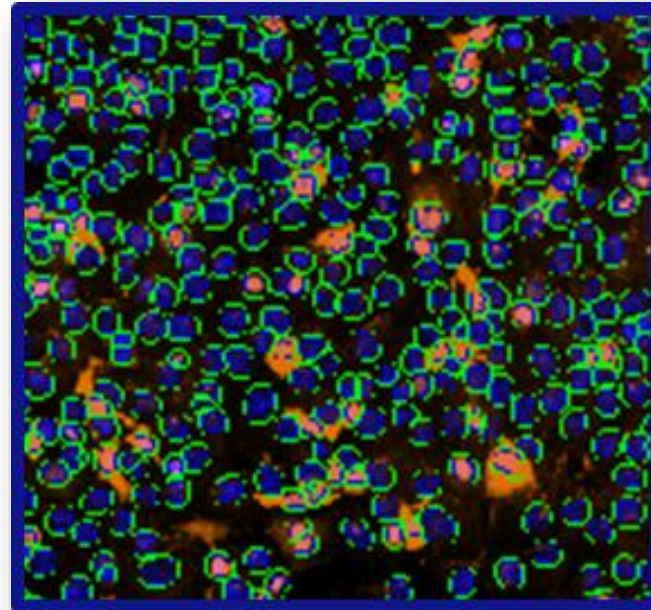


CONTROL: An advanced test to find virus drift and drug resistance

High-content Imaging Neutralization Test utilizes automatic digital microscopy

Improvements over traditional microneutralization:

- High-content imaging for accurate counting of virus-infected cells
- Can directly test clinical specimens for antigenic drift and drug susceptibility
- Simplified protocol (a single cycle infection eliminates the need for cell overlay)
- Expedites antigenic analysis by up to 10 days
- Improves sensitivity of antigenic analysis
- High throughput, automated format



Single Cell Detection of Virus Growth



BioTek Liquid Handler



Celigo (Nexcelom) image cytometer with stacker

CONTROL: Impact of Mitigations in Southern Hemisphere

- Experience from Australia, South Africa, Chile, and other countries in the Southern Hemisphere are seeing very little flu
- Declines attributed to:
 - Changes in the data, as fewer people left their homes to seek medical care for respiratory symptoms
 - Implementation of practices for preventing the spread of SARS-CoV-2, such as school closures, mask wearing, and social distancing
- In the US, there was a 61% decline in the number of respiratory specimens tested for flu, but a 98% decrease in the number testing positive for flu from late February to March
- Given these trends, CDC researchers believe that if there is continued widespread use of COVID-19 prevention strategies, along with seasonal flu vaccination, the impact of flu in the Northern Hemisphere during the upcoming flu season may be reduced
- It is not possible to predict exactly what will happen this fall and winter in the Northern Hemisphere, making it imperative to prepare for circulation of both flu and SARS-CoV-2 viruses

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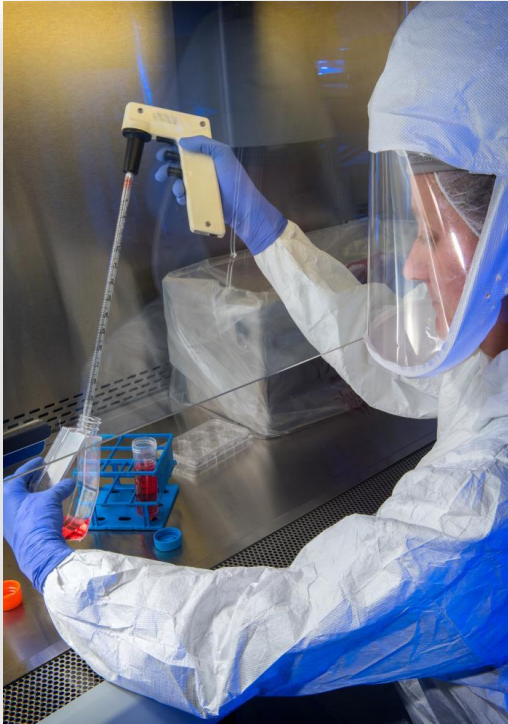
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PREVENT: Improving Vaccine Impact

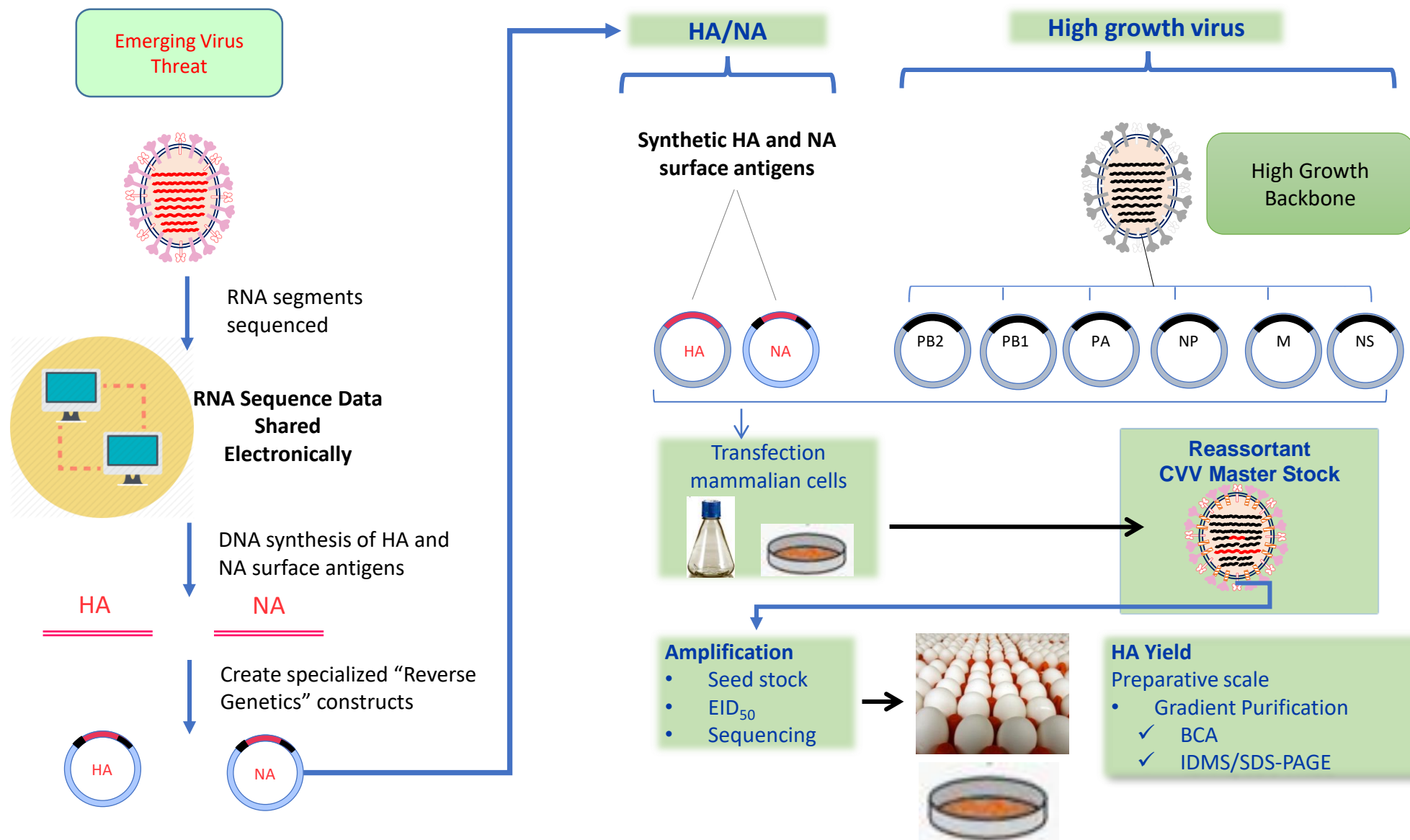


- **PRIORITY:** Expanding virus characterization and increasing capacity of CDC laboratories to support manufacturers of vaccine
 - Begun a genomic approach for the selection of ideal cell-based candidate influenza vaccine viruses (CVVs) for isolation, characterization and down selection
 - Use of reverse genetics for synthetic virology to develop CVVs
- **PRIORITY:** Enhance evaluation of vaccine effectiveness (VE)
 - Expanded enrollment in outpatient clinics in multiple states to enable the U.S. Flu Vaccine Effectiveness (VE) Network to assess the effectiveness of cell based, recombinant and adjuvanted vaccines
- **PRIORITY:** Enhancing communication to increase vaccination
 - 2020-2021 expanded campaign
 - Focus on reducing disparities in vaccination
 - Discussed on Day 3 of Listening Session



This Season a Flu Vaccine is More Important than Ever!

PREVENT: Synthetic Virology Used to Generate Vaccine Viruses at CDC

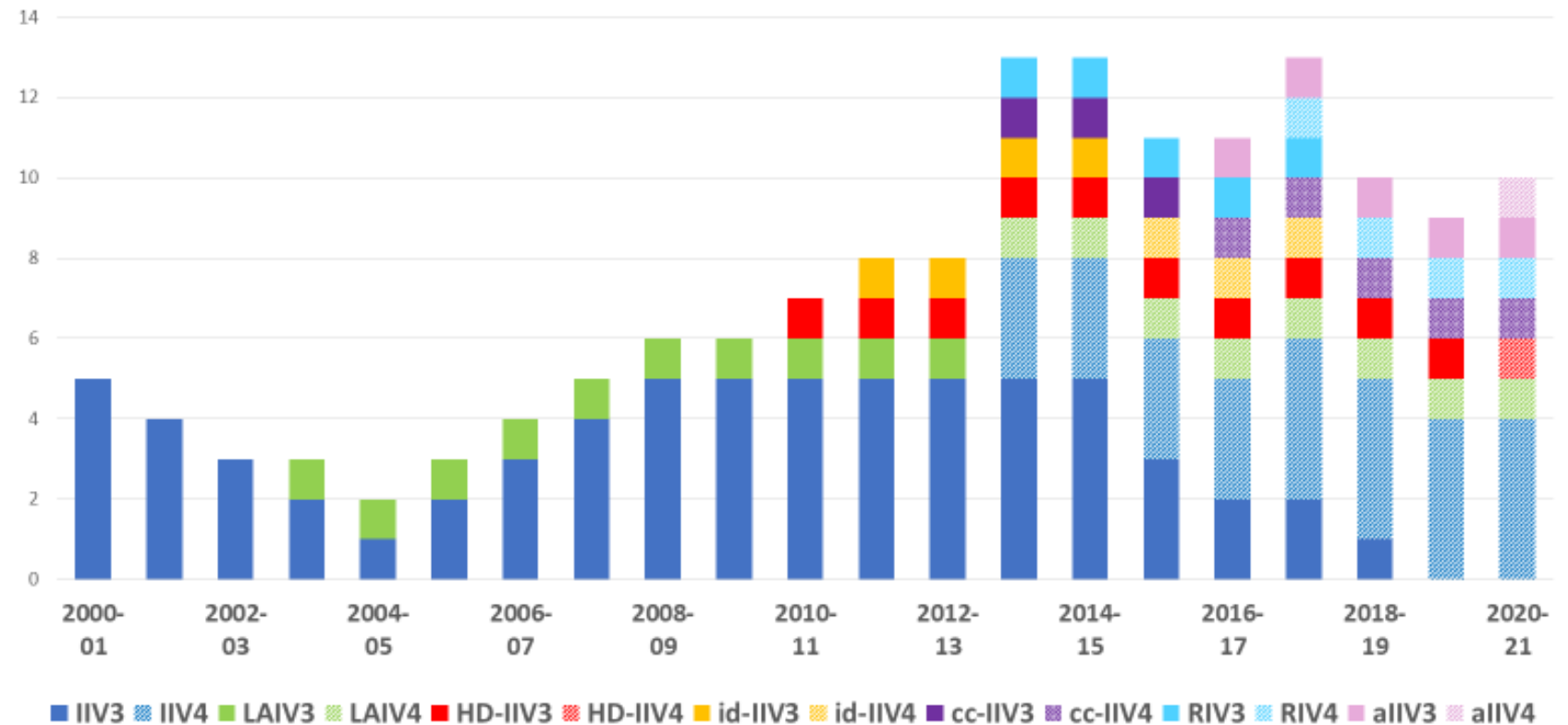


PREVENT: Monitoring Vaccine Effectiveness

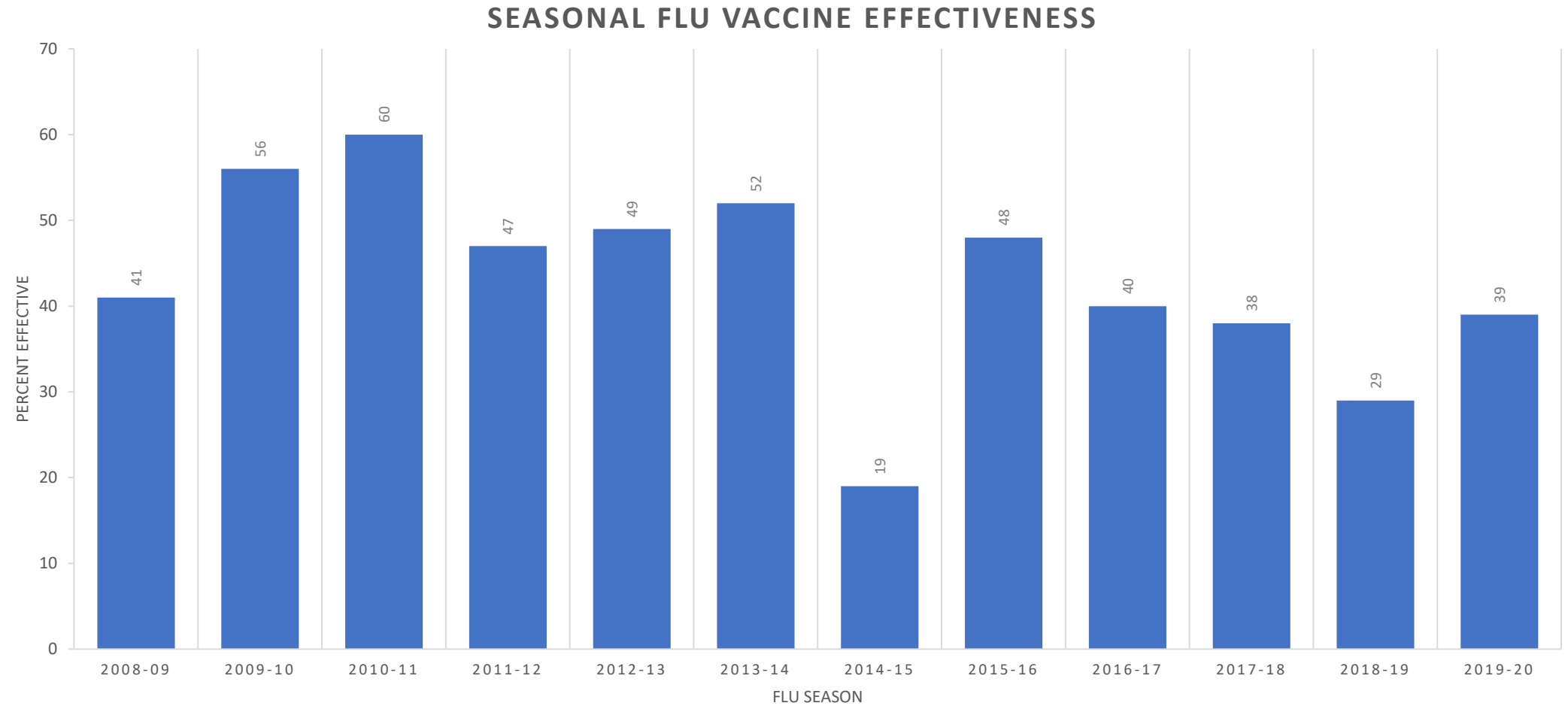
Challenges to Vaccine Effectiveness Monitoring

- Universal recommendation: all ages ≥ 6 months
- Annual vaccination
- 4 vaccine subtypes/lineages
- Frequent vaccine strain updates
- Many vaccine formulations

U.S. Seasonal Influenza Vaccines Since 2000-01
Number of unique products available by season



PREVENT: Annual Estimates of Seasonal Influenza Vaccine Effectiveness, 2008-20



PREVENT: Monitoring Vaccine Effectiveness

- All CDC affiliated networks are currently enrolling and collecting data on COVID-19 cases
- Outpatient Network – US Flu VE Network
 - 55 ambulatory care clinics, ages >6 months
 - Combined with genomic sequence data for clade-specific VE
 - Allows annual determination of influenza illness averted
- Hospital Networks
 - Hospitalized Adults Influenza VE Network (HAIVEN)
 - New Vaccine Surveillance Network (NVSN)
- ICU Networks of Adult and Pediatric Patients
 - Evaluates VE for severe ICU related outcomes
 - Also used to characterize multi-system inflammatory syndrome (MIS-C)
- Electronic Medical Record (EMR) platforms
 - VISION – Virtual network for VE
 - PREVENT – Pregnancy Influenza Vaccine Effectiveness Network

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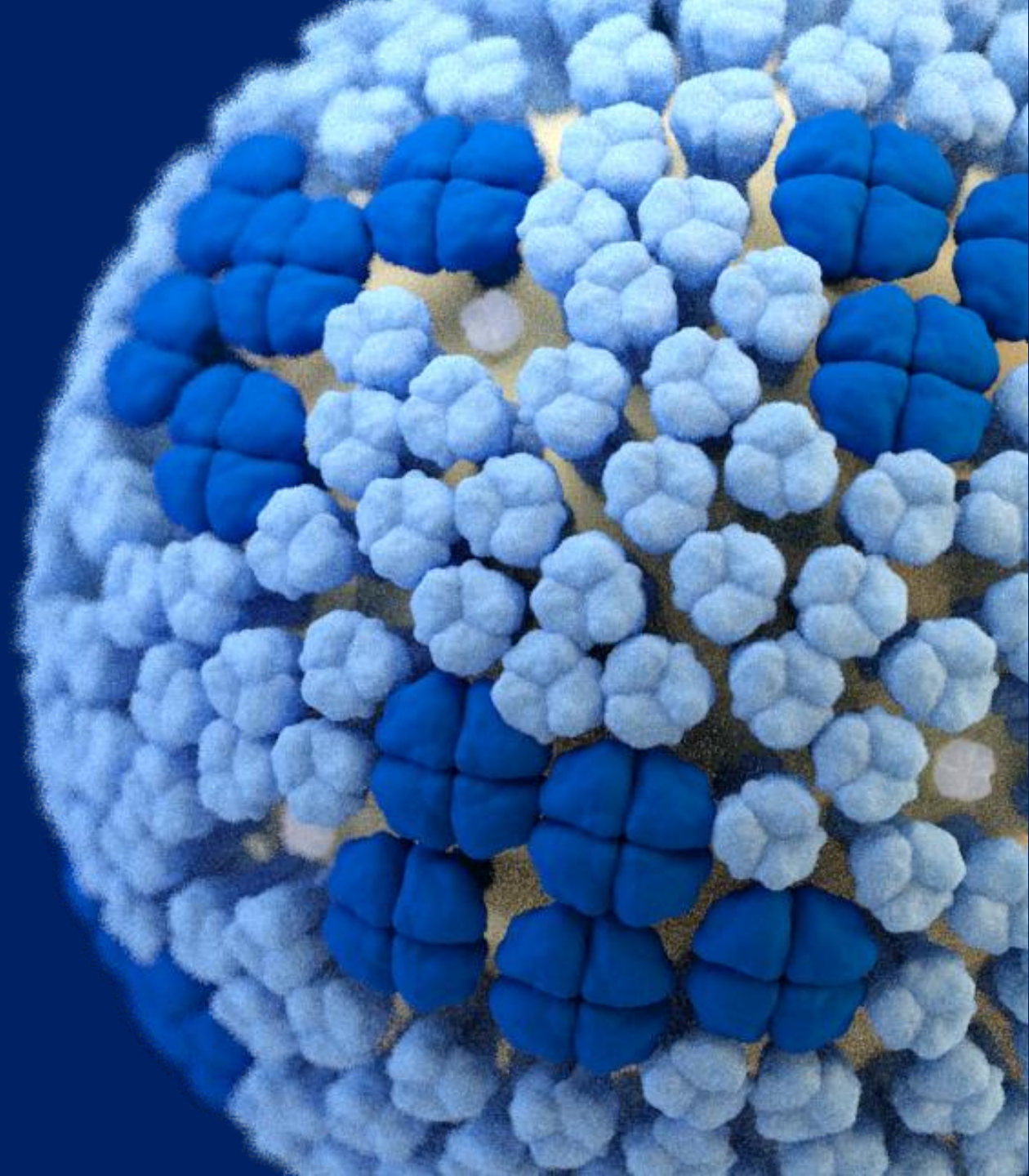
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CDC Priorities to Detect, Prevent and Respond to Influenza

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Implementing the NIAID Strategic Plan for a Universal Influenza Vaccine

Alan Embry, PhD

Chief, Respiratory Diseases Branch

Division of Microbiology & Infectious Diseases

NIAID, NIH, DHHS



Adjusted Influenza Vaccine Effectiveness Estimates in the U.S.



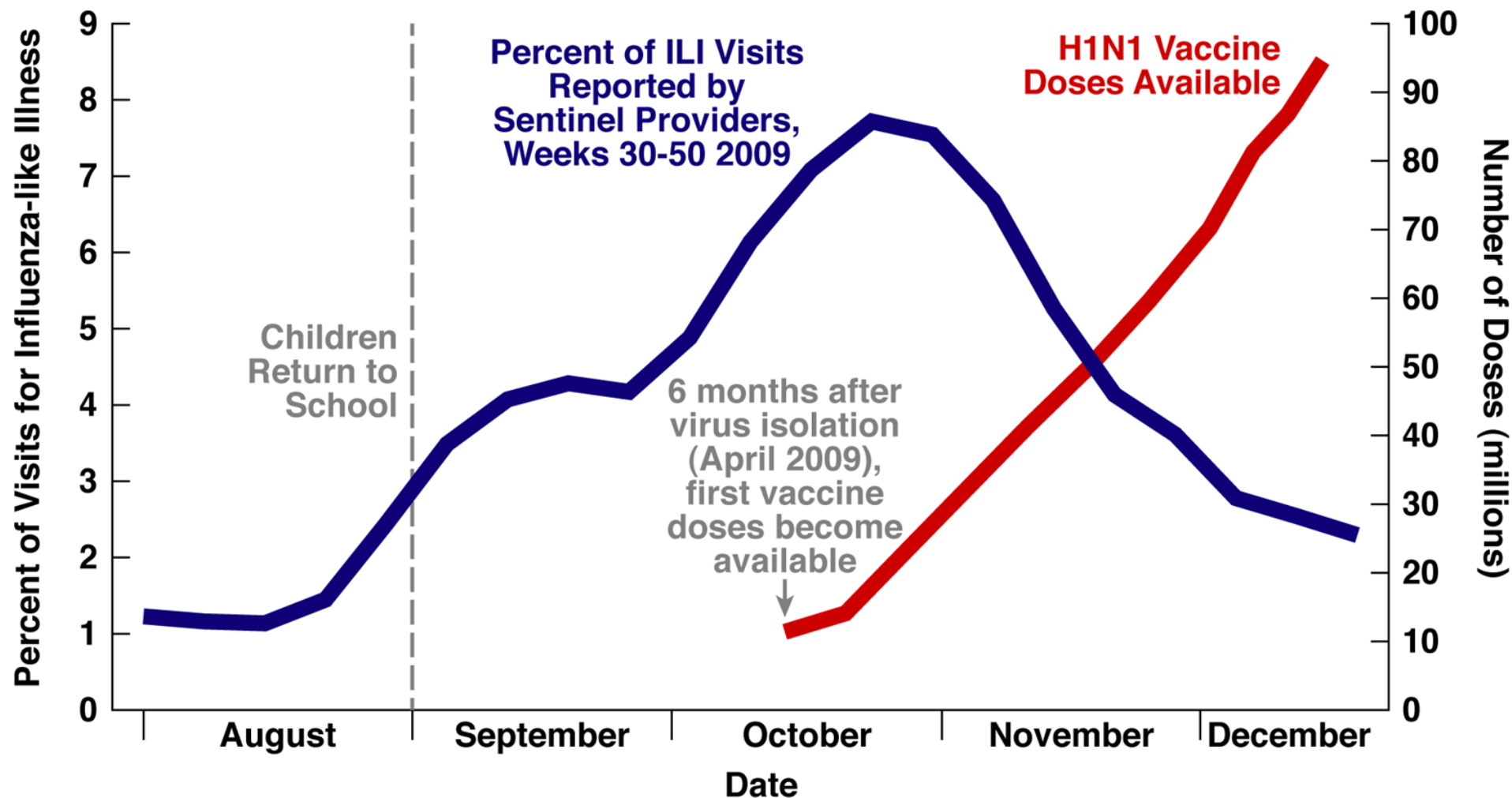
Source: CDC

AS Fauci/NIAID

Influenza Pandemics Occur

Year	Subtype	Deaths
1918	H1N1	>50 million
1957	H2N2	>1 million
1968	H3N2	>1 million
2009	H1N1	~151K-575K

Vaccine Lags Behind 2009 H1N1 Influenza Pandemic



August 1, 2018
Volume 218
Issue 3



The Journal of Infectious Diseases

A Universal Influenza Vaccine: The Strategic Plan for the National Institute of Allergy and Infectious Diseases

EJ Erbeling, D Post, E Stemmy, PC Roberts, A Deckhut Augustine,
S Ferguson, CI Paules, BS Graham, AS Fauci

NIAID Universal Influenza Vaccine Targets

A universal flu vaccine should



Be at least 75% effective



Protect against group I and II influenza A viruses

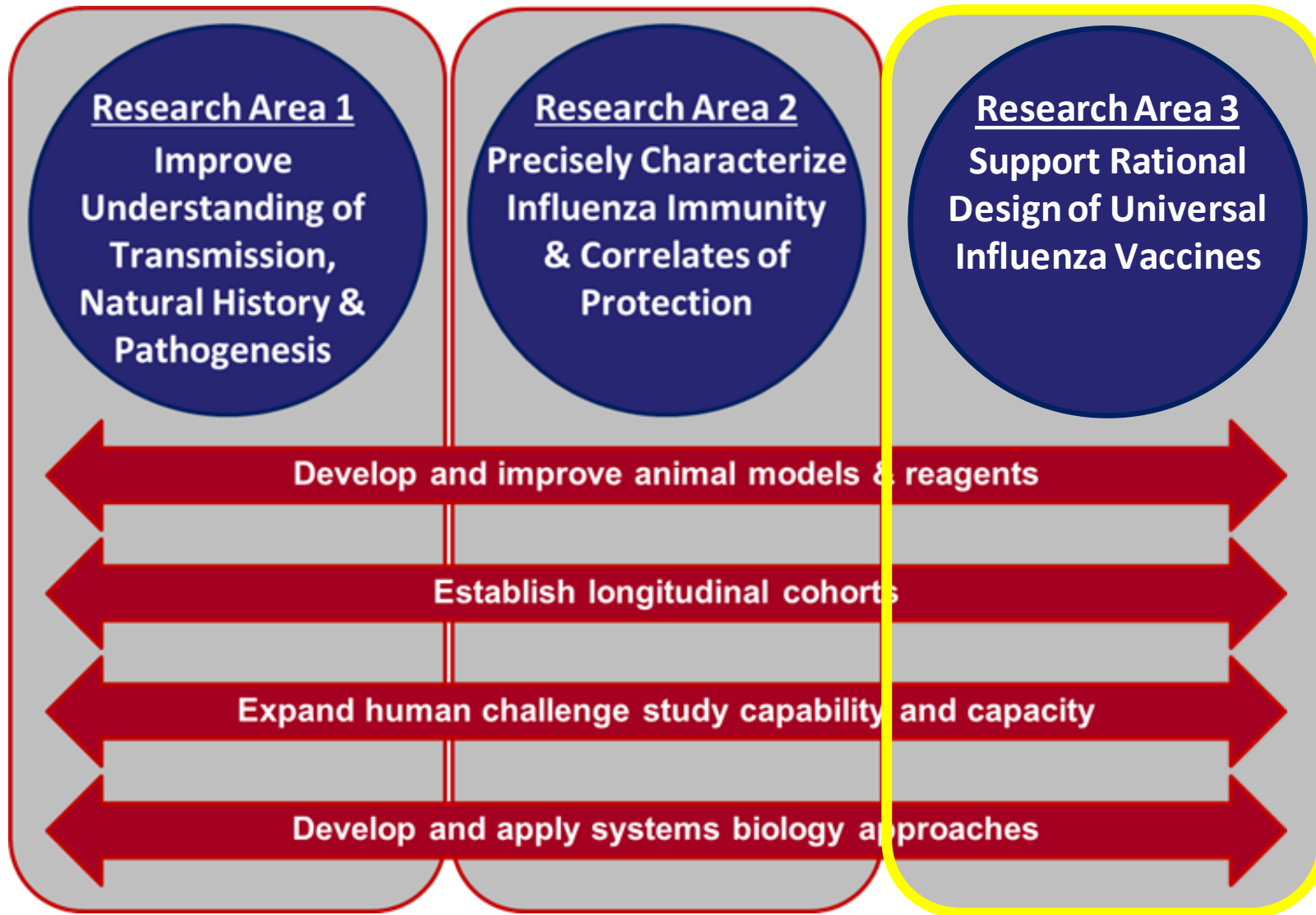


Have durable protection that lasts at least 1 year



Be suitable for all age groups

NIAID Universal Influenza Vaccine Strategic Plan



CIVICs: A Comprehensive Program for Universal Influenza Vaccine Development

External Advisory Board

Vaccine Centers

- Iterative vaccine design, preclinical testing and in-depth immunologic analyses
- Assay & reagent development

**Manufacturing &
Toxicology Core**

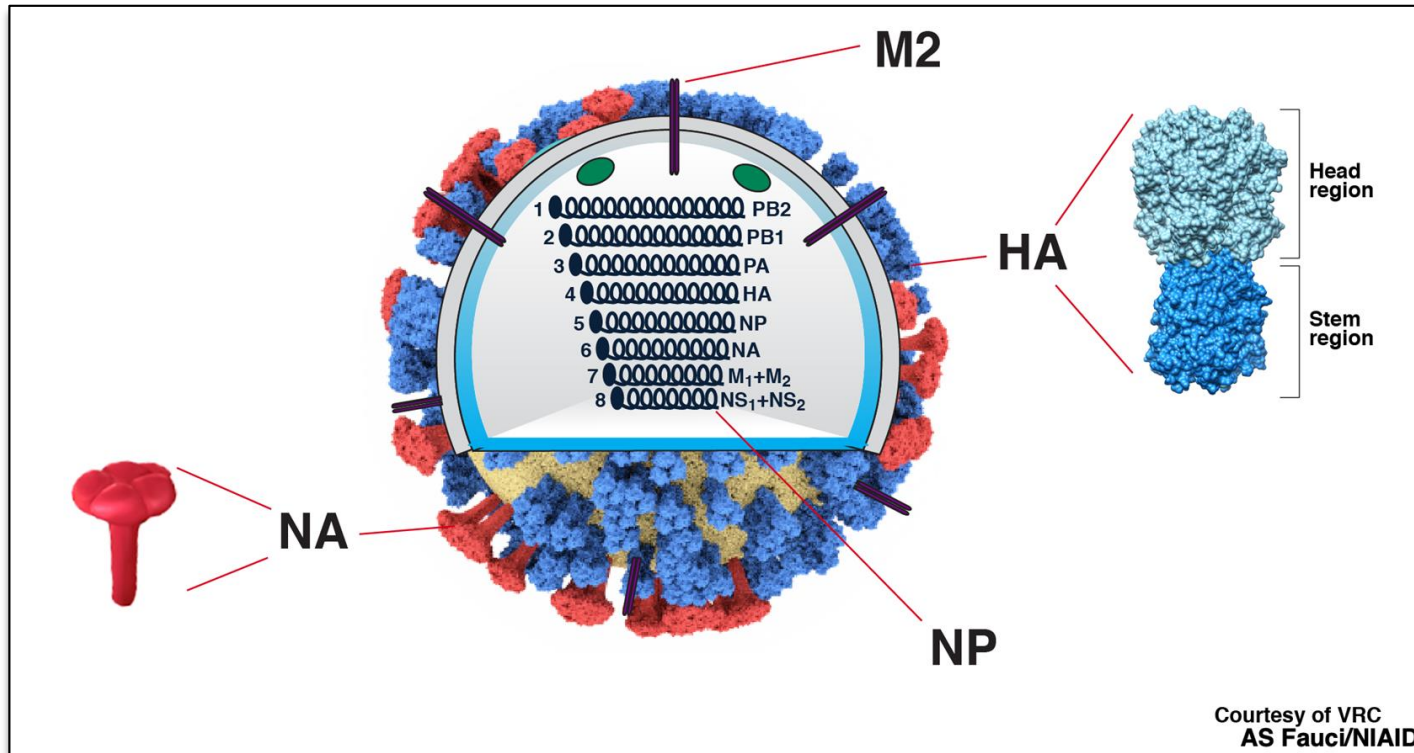
**Clinical
Cores**

**Statistical, Data
Management &
Coordination Center
(SDMCC)**

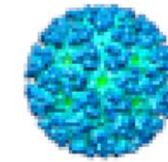
Multidisciplinary Network to Accelerate Development of Universal Influenza Vaccines



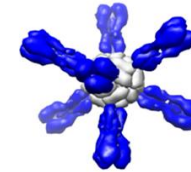
A Broad Spectrum of Approaches



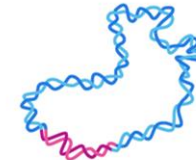
Recombinant protein



LAIVs, VLPs



Nanoparticle

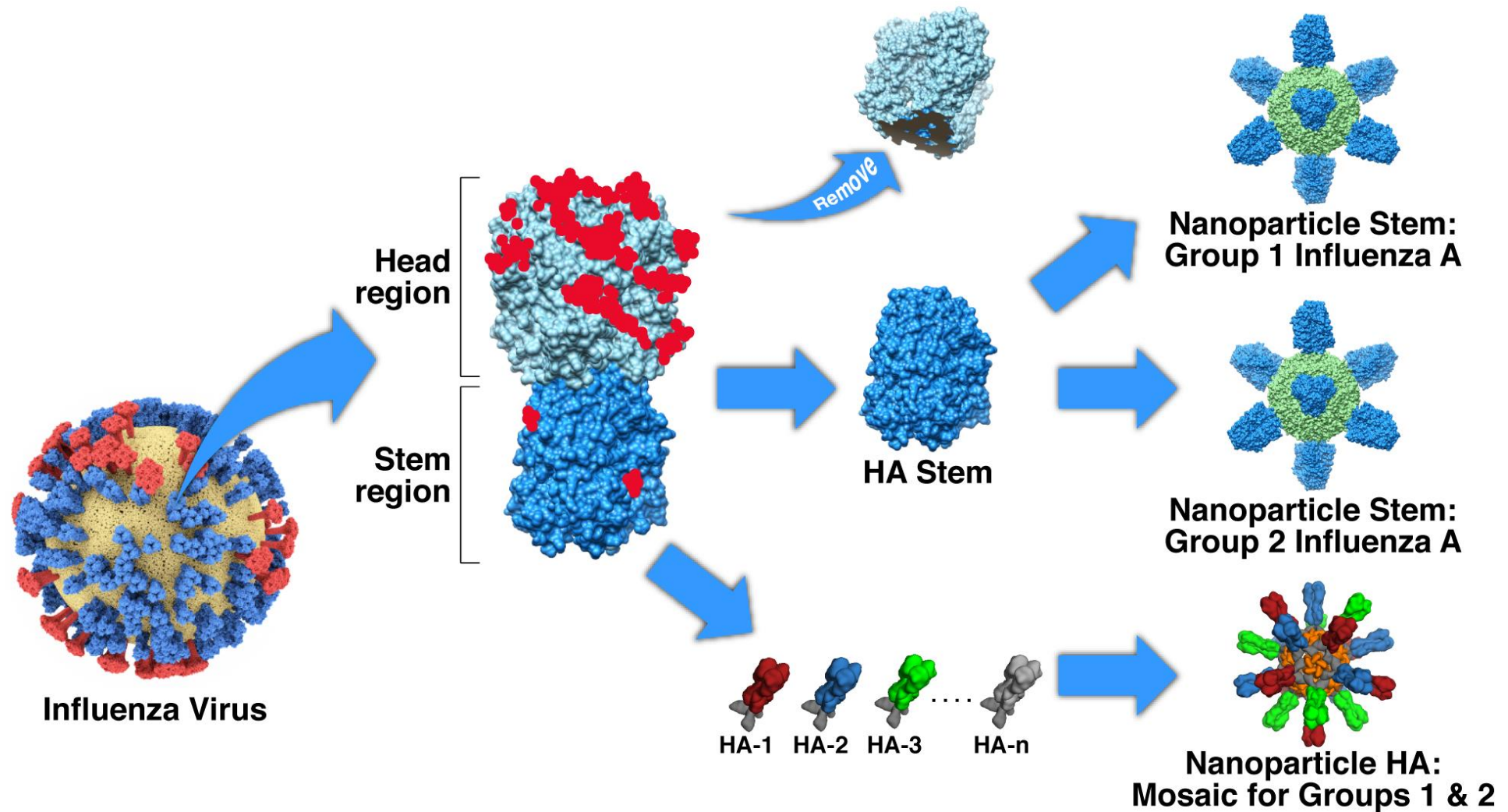


DNA, RNA



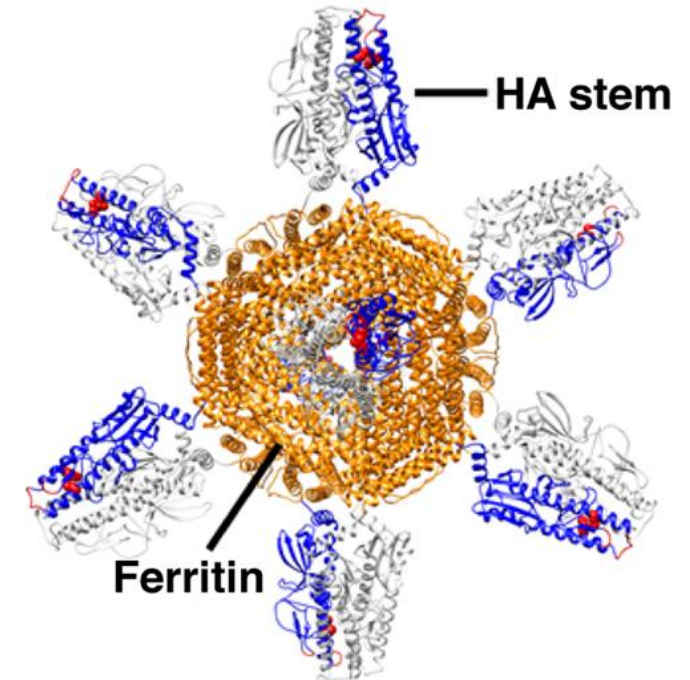
Microneedle patch

Nanoparticle Platform for Universal Influenza Vaccines



HA Stem Nanoparticle Phase 1 Underway (VRC 321)

- Phase 1 trial to evaluate dose, safety, tolerability and immunogenicity of influenza H1 stabilized stem ferritin vaccine in healthy adults
- Current status: 52/53 enrolled. Safe and well tolerated.
- Headless group 2 HA stem trimer on ferritin (VRC 323) starting fall 2020



Iterative Design and Development

A universal flu vaccine should



Be at least 75% effective



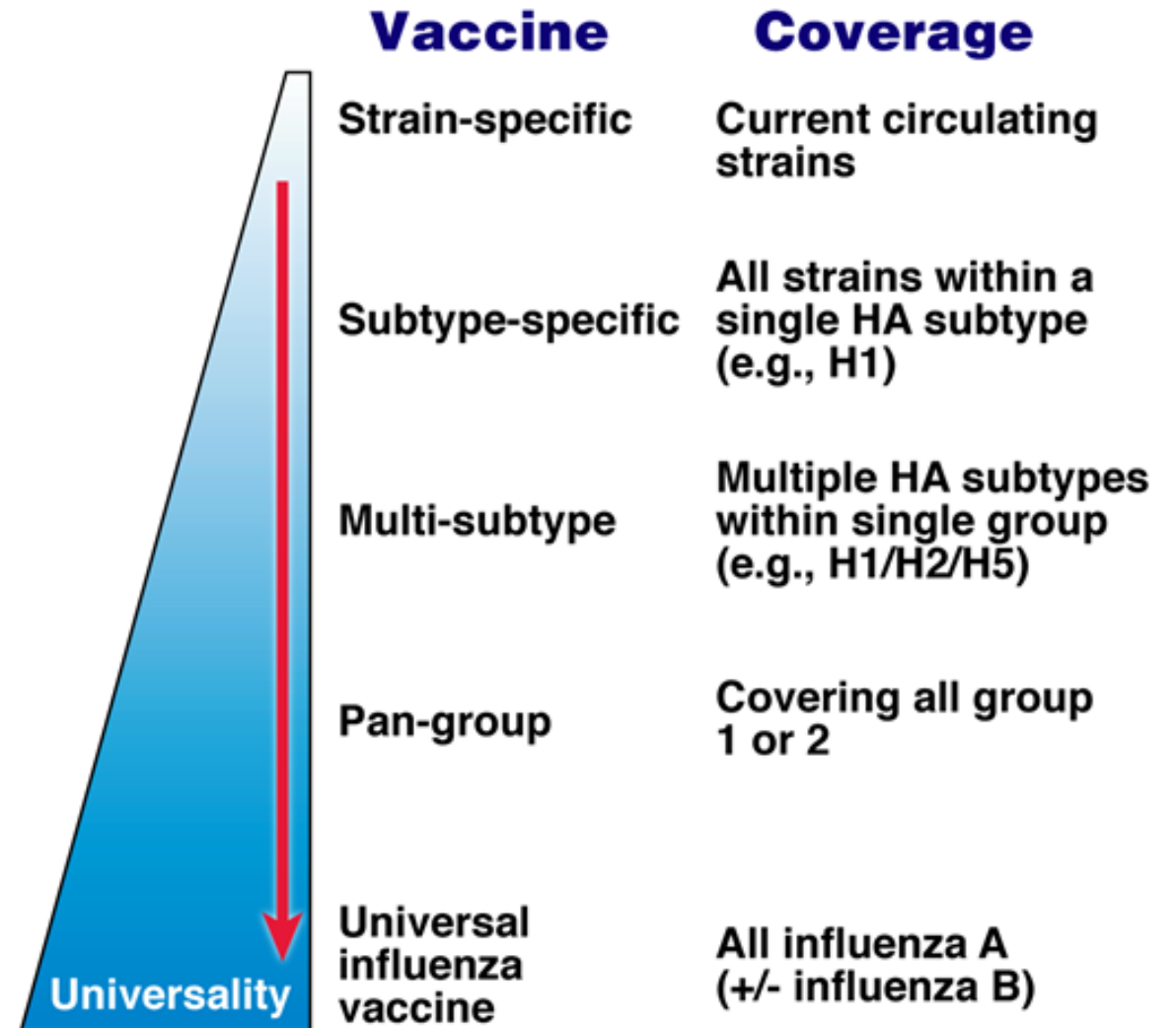
Protect against group I and II influenza A viruses



Have durable protection that lasts at least 1 year



Be suitable for all age groups



NIAID-Supported Clinical Trials Informing Universal Vaccine Strategies



RedeeFlu (M2SR LAIV)

- Phase I H3N2 M2SR prime and IIV4 boost in subjects 9-17 years of age



M-001 Peptide Vaccine

- Phase II M-001 prime and IIV3/IIV4 boost in healthy adults



Adjuvanted Seasonal Vaccines

- Phase 1 study of Fluzone[®] or Flublok[®] with or without either AF03 or Advax-CpG55.2[™] adjuvant in healthy subjects 18-49 years of age

Expanding Influenza Human Challenge Capacity

- Human challenge study successfully conducted at 4 NIAID VTEU sites
 - H1N1pdm09 strain (Dr. Matt Memoli, NIAID)
- GMP manufacture of 2 new influenza challenge strains
 - H3N2 (Clade 3C3a)
 - H1N1 (Clade 6B.1)
- Dose-finding human challenge study planned for 2021



NIH researchers infect volunteers with the flu virus in an ongoing effort to improve vaccines. AP PHOTO/CHARLES DHARAPAK

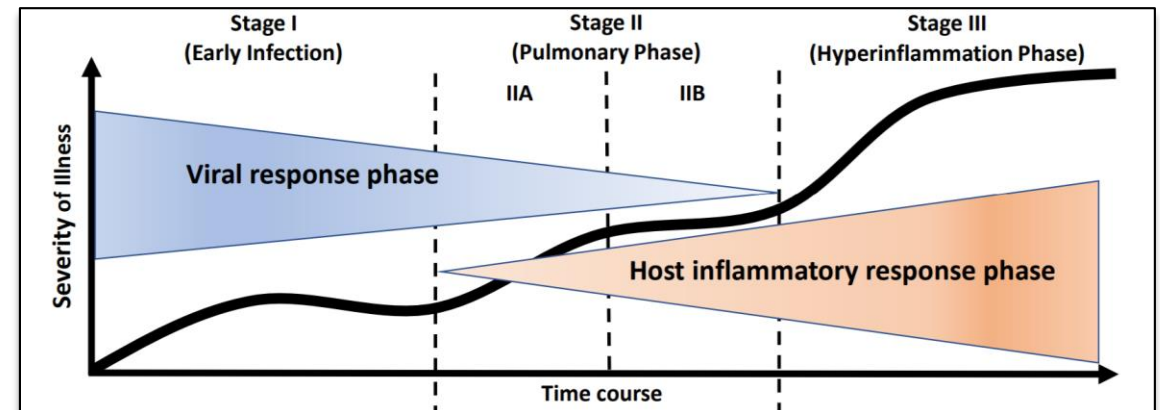
Studies that intentionally infect people with disease-causing bugs are on the rise

By [Jon Cohen](#) | May. 18, 2016, 3:00 AM

Science

Advances In COVID-19 Will Inform Influenza Strategies

- Together with USG partners, advancing novel vaccine platforms
- Innovations in diagnostic technologies
- Natural history studies to compare COVID-19 and influenza disease course and immunopathology
- Therapeutic strategies to treat severe disease



Thank you