Public Meeting

NATIONAL VACCINE ADVISORY COMMITTEE

June 13-14, 2024

NVAC

June 14, 2024

CHAIR'S WELCOME

Robert H. Hopkins, Jr., MD, MACP, FAAP
Chair, National Vaccine Advisory Committee

NVAC

Housekeeping and Meeting Minutes

- The meeting is recorded and streamed, so statements made are on the record and may be included in the meeting minutes.
  - **Webcast:** www.hhs.gov/live

- Before speaking, please ensure you are not muted and identify yourself.
- Please speak clearly and mute yourself when not speaking.
- For the members and speakers attending remotely, you are encouraged to be on camera when speaking. Please stop sharing video when not speaking.

Meeting Highlights: June 13

- Being Ready for a Rapid Response: A Proactive Discussion of Production Capabilities
- Pride, Equity, and Community: Mpox Vaccination in 2024
- Fall and Winter Respiratory Diseases: The Vaccination Season Ahead
- Outbreak Update: Measles Cases in Chicago and Cook County
- Breast Cancer Vaccine Innovations in the Works
- Public Comment
- Adjourn

Meeting Highlights: June 14

- Immunization Data: Innovations, Improvements, and Updates
- Saluting Global Immunization Efforts: 154+ Million Lives Saved
- Research Review: An Eye-Opening Study on Switching Arms Between COVID-19 Vaccine Doses
- Federal Agency and Liaison Member Updates
- Towards an Updated National Strategy: Progress and Priorities
- Public Comments
- **Adjourn 2:30 PM Eastern**

Public Comments

- Verbal comments are scheduled for 2:15 p.m., Eastern Time today
  - Please limit all verbal comments to 3 minutes in length.

- Submit written comments to nvac@hhs.gov
  - You may submit written comments. Written comments should not exceed 3 pages in length.
  - Requests for public comment should be sent to NVAC@hhs.gov at least 5 days in advance of a scheduled public meeting.

Upcoming Meetings

- September 12-13, 2024

Learn more: www.hhs.gov/vaccines/nvac

Immunization Data: Innovations, Improvements, and Updates

Dr. Jason Asher
Dr. Shannon Stokley
Rebecca Coyle
Dr. Pamela Belperio
Dr. Patricia Lloyd

NVAC

Center for Forecasting & Outbreak Analytics

Better Data, Better Analytics, Better Response

Center for Forecasting and Outbreak Analytics (CFA)

VISION

To empower people to save lives and protect communities from health threats.

MISSION

To harness cutting-edge analytics to improve response to public health emergencies.

GOALS

Predict

Deliver actionable analysis and response-ready modeling tools

Inform

Generate practical decision support communications products

Innovate

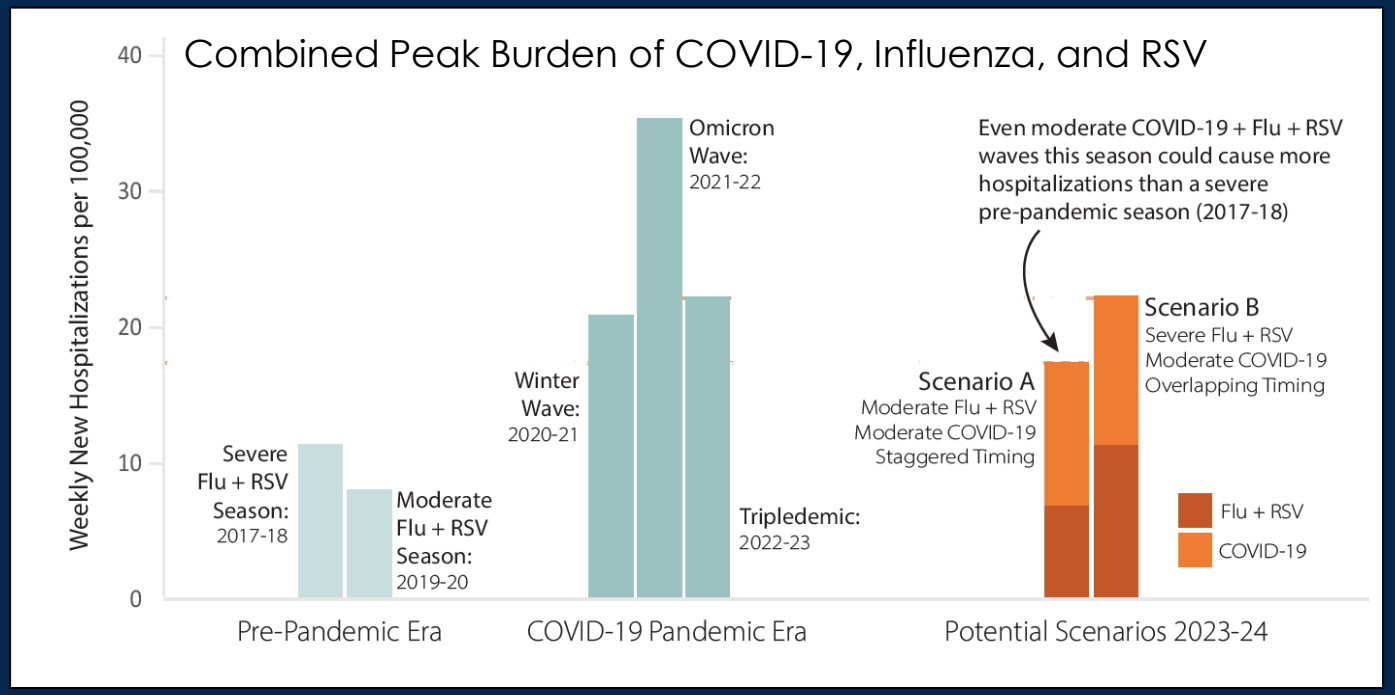
Drive technological and analytic innovation

Advance

Build a world-class forecasting and outbreak analytics organization

Communicating with Public Health Decision Makers: Disease Season Outlook

CDC's first national respiratory season outlook **integrates multiple insights** on COVID-19/RSV/flu



- Based on influenza, COVID-19 and RSV **hospitalization data**
- Integrated data to generate **multiple scenarios** and likelihoods
- **Outlook:** there will be similar total hospitalizations in 2023 to 2022, higher than pre-COVID-19 years

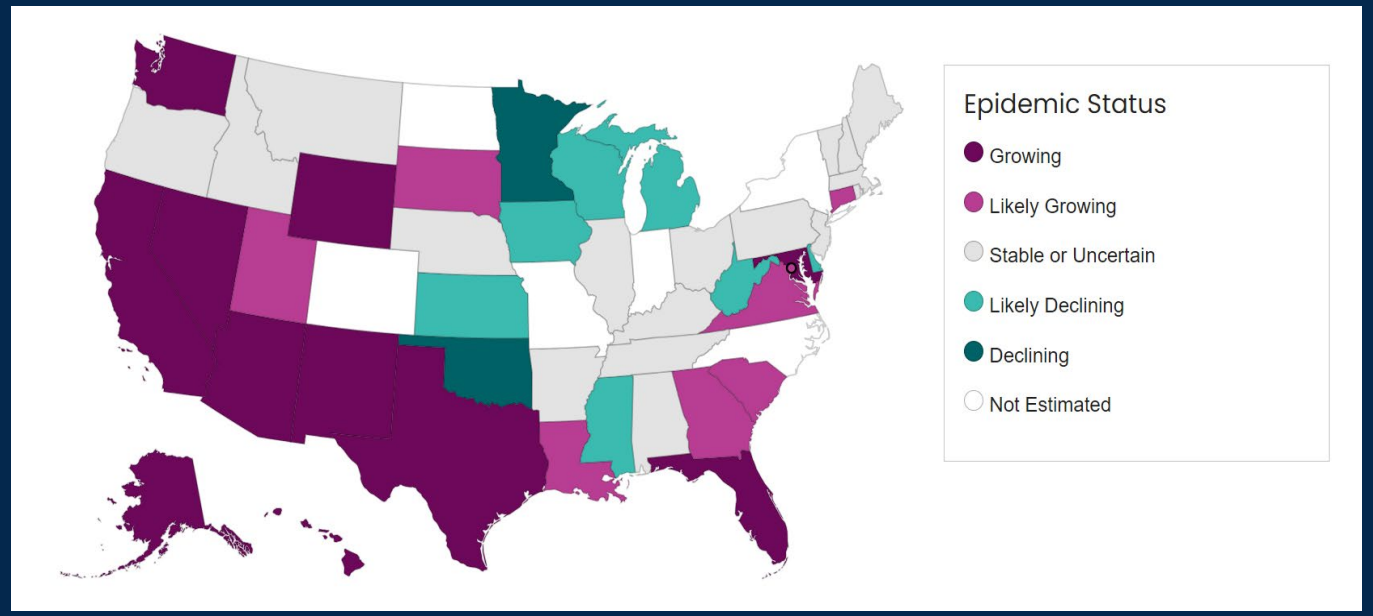
Impact: Public health decision-makers **knew to expect another year of hospitalizations higher than pre-pandemic levels**, so they could plan, allocate resources, and provide guidance to the public.

New Models: Disease Growth Estimates

CDC's first state-level growth estimates of COVID-19 & flu - **see the future disease spread**

- Tells us if a disease is growing, declining or staying the same
- We currently publish COVID-19 and influenza estimates for each state, updated weekly
- CFA & NCIRD collaboration, using reported hospitalization data

Current Epidemic Growth Status (Based on R_t) for States and Territories, Influenza, as of May 28, 2024



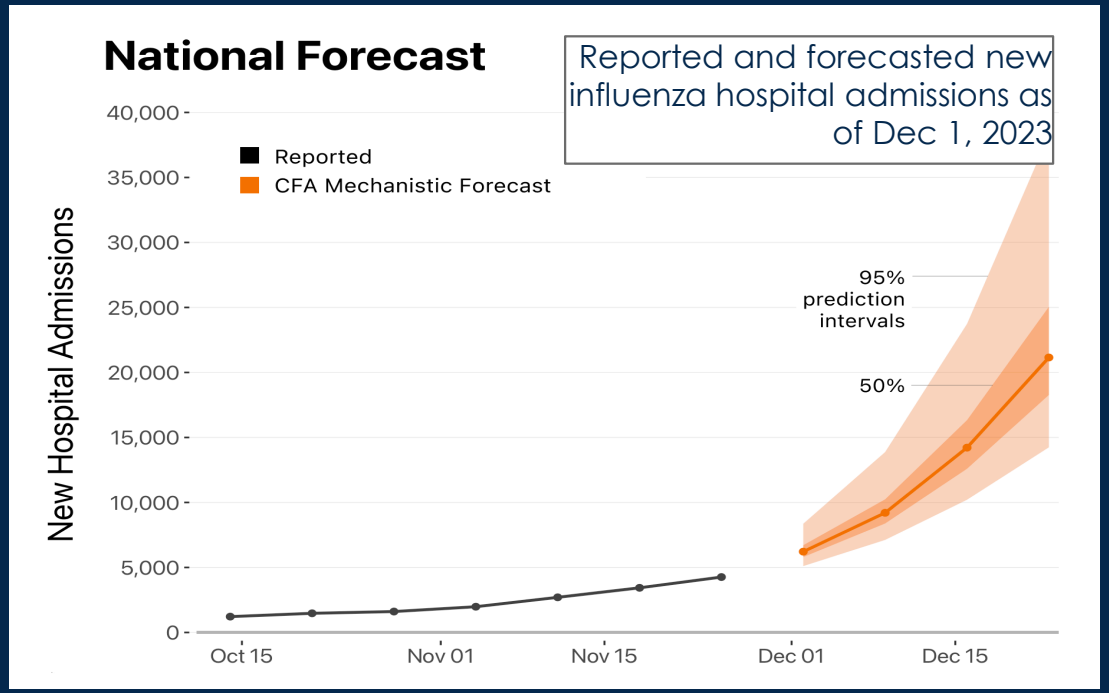
https://www.cdc.gov/forecast-outbreak-analytics/about/rt-estimates.html

Impact: Knowing if COVID-19 or flu infections are currently increasing or decreasing helps jurisdictions and health care systems better prepare, plan for, and respond to these seasonal diseases

Forecast Development: Influenza Forecasting

Supporting the first CDC-developed public forecasts to **see future influenza impact**

- CFA flu forecasts represented the **first time** CDC has authored forecasts with in-house models
- CDC uses CFA work to provide weekly national and state-level forecasts of **influenza hospitalizations**
- CFA can support CDC in future emergencies with best-in-class models using **entirely internal capabilities**



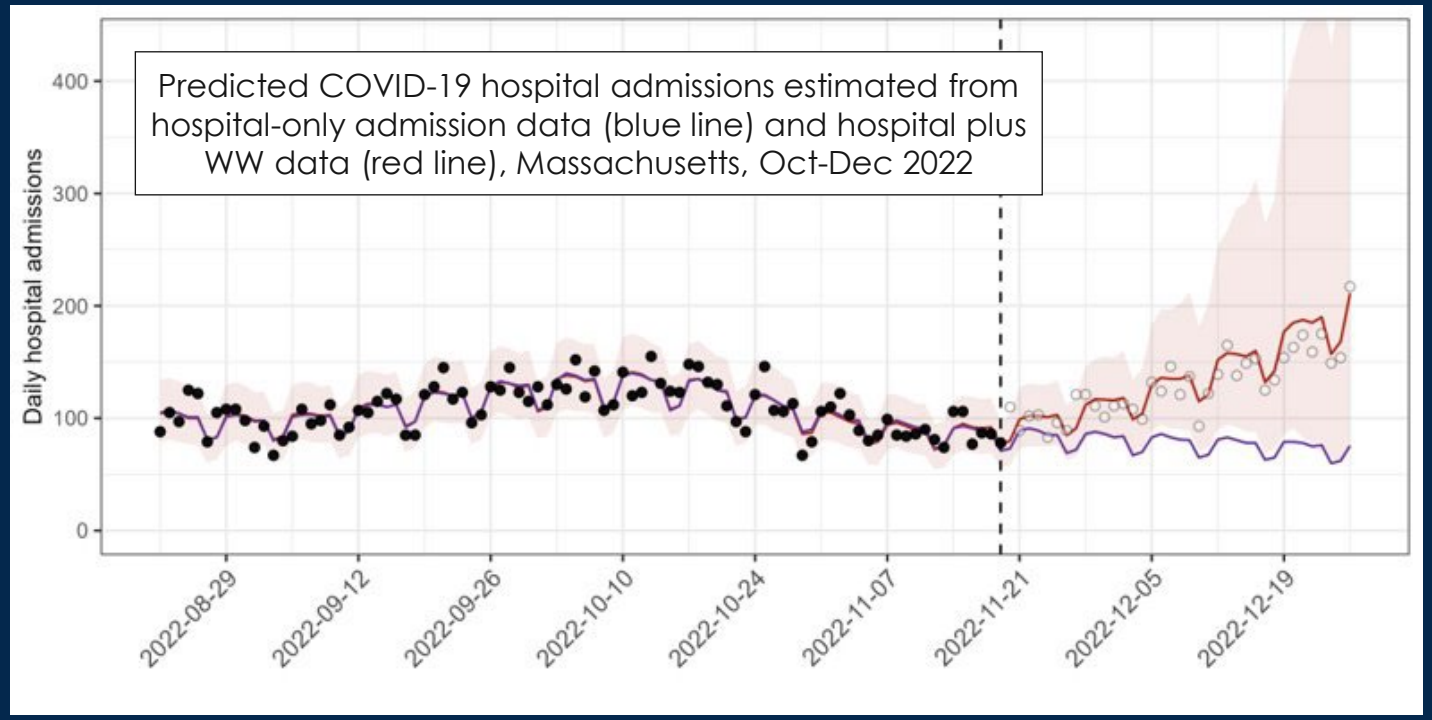
https://www.cdc.gov/flu/weekly/flusight/flu-forecasts.htm

Impact: This information allows STLT and public health decision-makers to monitor the current and near-term future influenza burden, so they can take action as part of their outbreak response.

Driving Innovation: Wastewater Monitoring Data

CFA tested **integrating new data** and showed that it improves forecasts at critical times.

- Adding wastewater data gives a **more accurate forecast** that can detect disease surges
- It has been integrated into CFA's new COVID-19 forecasts and will be extended to others in the future



Impact: CFA will continue to develop new ways to **use wastewater data to make our disease forecasts better**, so public health decision makers can be prepared for changes and surges.

Modeling Support for Measles Outbreak

Rapid public health response **reduced severity** of a measles outbreak in Chicago

- CFA and NCIRD analyzed measles data and created models to **explore potential scenarios** and **better understand measles outbreak risk in the U.S.**

- Models underscored impact of early intervention – without rapid implementation of mass vaccination and screening, there would have been a **69% chance that more than 100 people would have become infected with measles.**

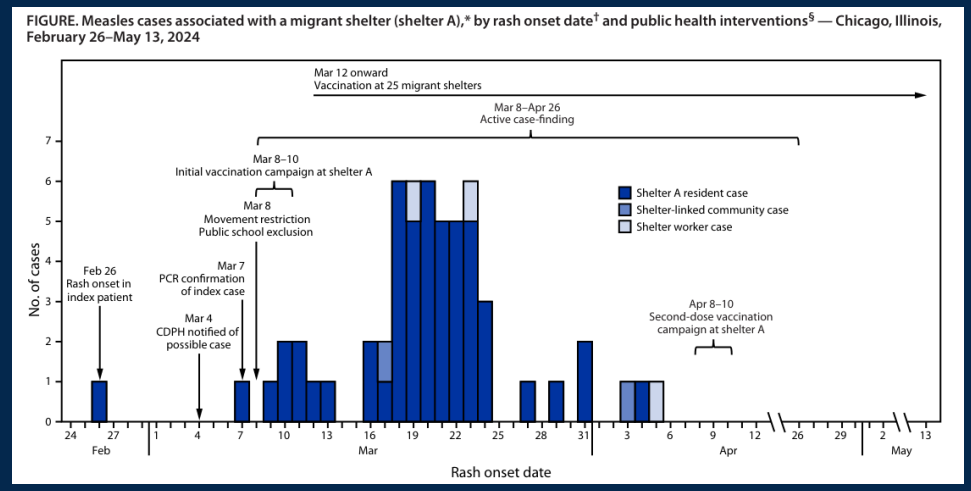

U.S. Centers for Disease Control and Prevention

MMWR

Morbidity and Mortality Weekly Report

Weekly / Vol. 73 / No. 19 May 16, 2024

Measles Outbreak Associated with a Migrant Shelter — Chicago, Illinois, February–May 2024

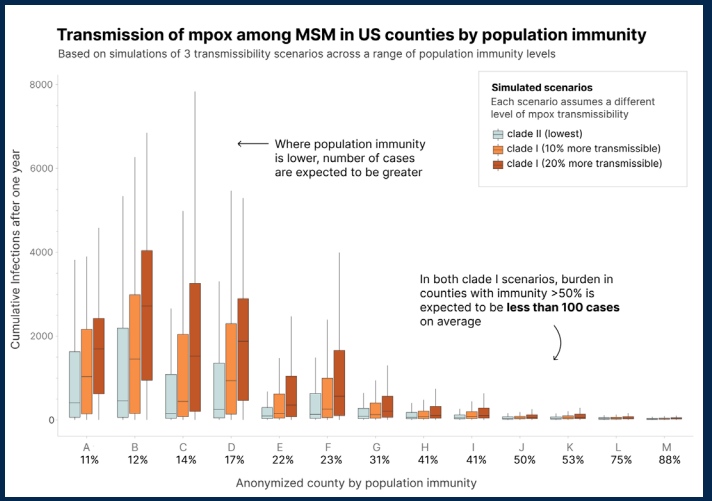


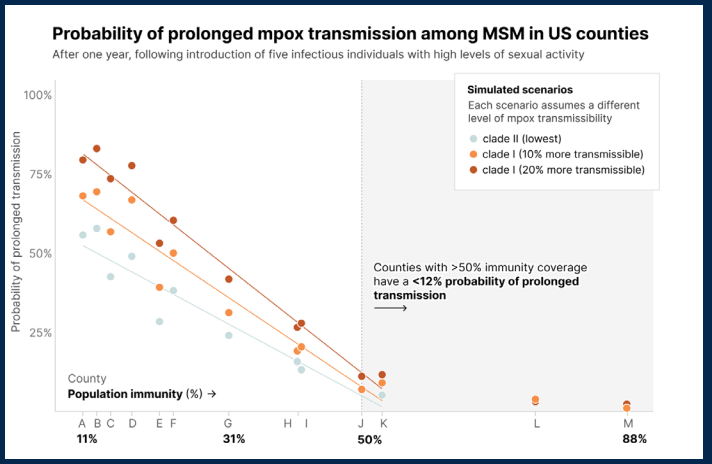
Impact: Models can help decision makers prepare, identify communities at highest risk, and manage healthcare resources during a public health response.

Modeling Simulation: Spread of clade I mpox in U.S.

CFA modeling study explores the potential spread of clade I mpox in the U.S.

- Agent-based transmission model used to explore risk for MSM in U.S. if clade I mpox were to be introduced to this population
- Modeled **varying levels of transmissibility** and **county-specific population-level immunity** among MSM in the U.S.





Impact: Models underscore importance of **population-level immunity** through vaccination.

Center for Forecasting & Outbreak Analytics

Harnessing cutting-edge analytics to improve response to public health emergencies

Empowering people to save lives and protect communities from health threats.

Supporting Immunization Data and Immunization Information Systems

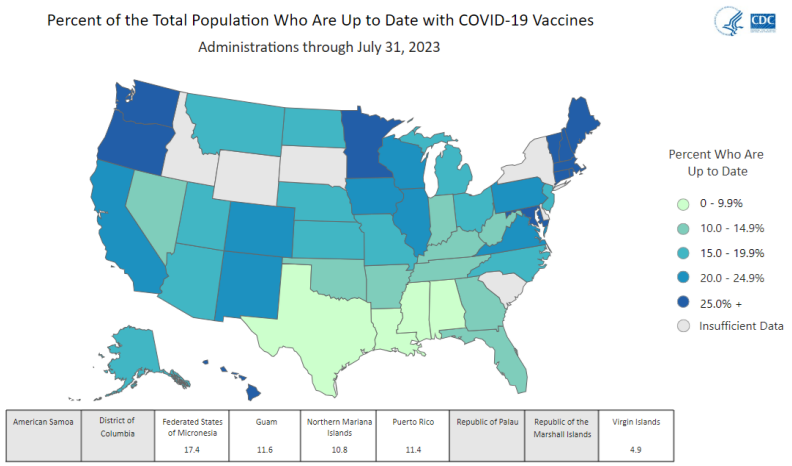
Shannon Stokley, DrPH
Deputy Director for Science Implementation
Immunization Services Division
National Center for Immunization and Respiratory Diseases

June 2024

Understanding vaccination coverage is key to understanding where to focus efforts.

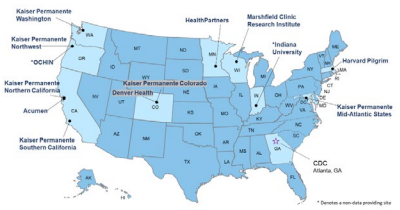
Snapshot of vaccine data sources

Administration data from reporting states



Other surveillance systems

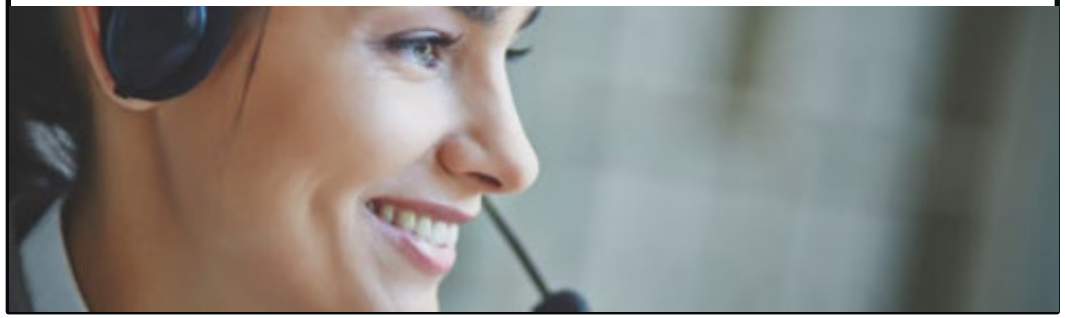
Vaccine Safety Datalink



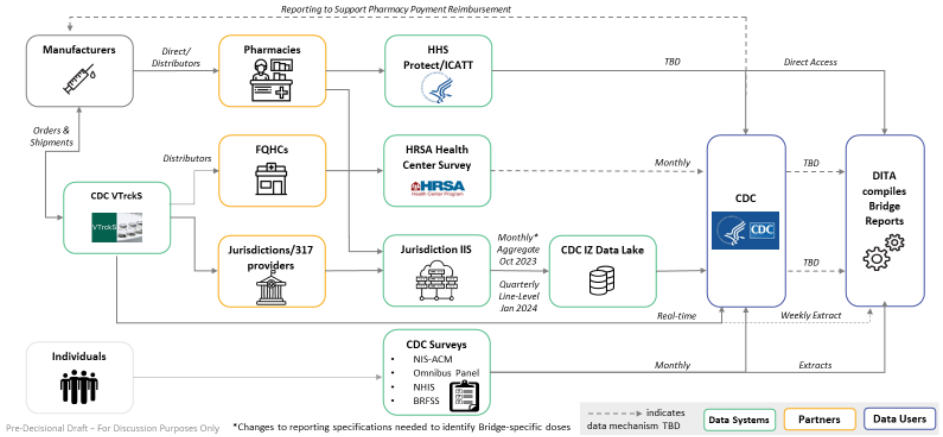
NHSN

National Healthcare Safety Network

National Immunization Surveys

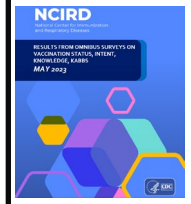


Bridge Access Program for COVID-19 Vaccines



Other data sources

Omnibus surveys



Distribution data

MARKET SCAN®

IQVIA

CMS.gov Centers for Medicare & Medicaid Services

Internet panel survey of pregnant people

Respiratory Virus Data Channel Weekly Snapshot

The amount of respiratory illness (fever plus cough or sore throat) causing people to seek healthcare is **low** nationally. This week, no jurisdictions experienced moderate, high, or very high activity.

Reported on Friday May 31st, 2024.

Summary

Seasonal influenza, COVID-19, and RSV activity is low nationally.

COVID-19

Most key indicators are showing low levels of activity nationally. However, wastewater viral activity is showing increases in some states. We also estimate that COVID-19 infections are growing or likely growing in 19 states and territories, declining or likely declining in 9 states and territories, and are stable or uncertain in 17 states and territories, based on Rt estimates of epidemic growth. An increasing proportion of the variants that cause COVID-19 are projected to be KP.2 and KP.3 (CDC COVID Data Tracker: Variant Proportions).

Influenza

Nationally, seasonal influenza activity remains low. Additional information about current influenza activity can be found at: Weekly U.S. Influenza Surveillance Report | CDC.

RSV

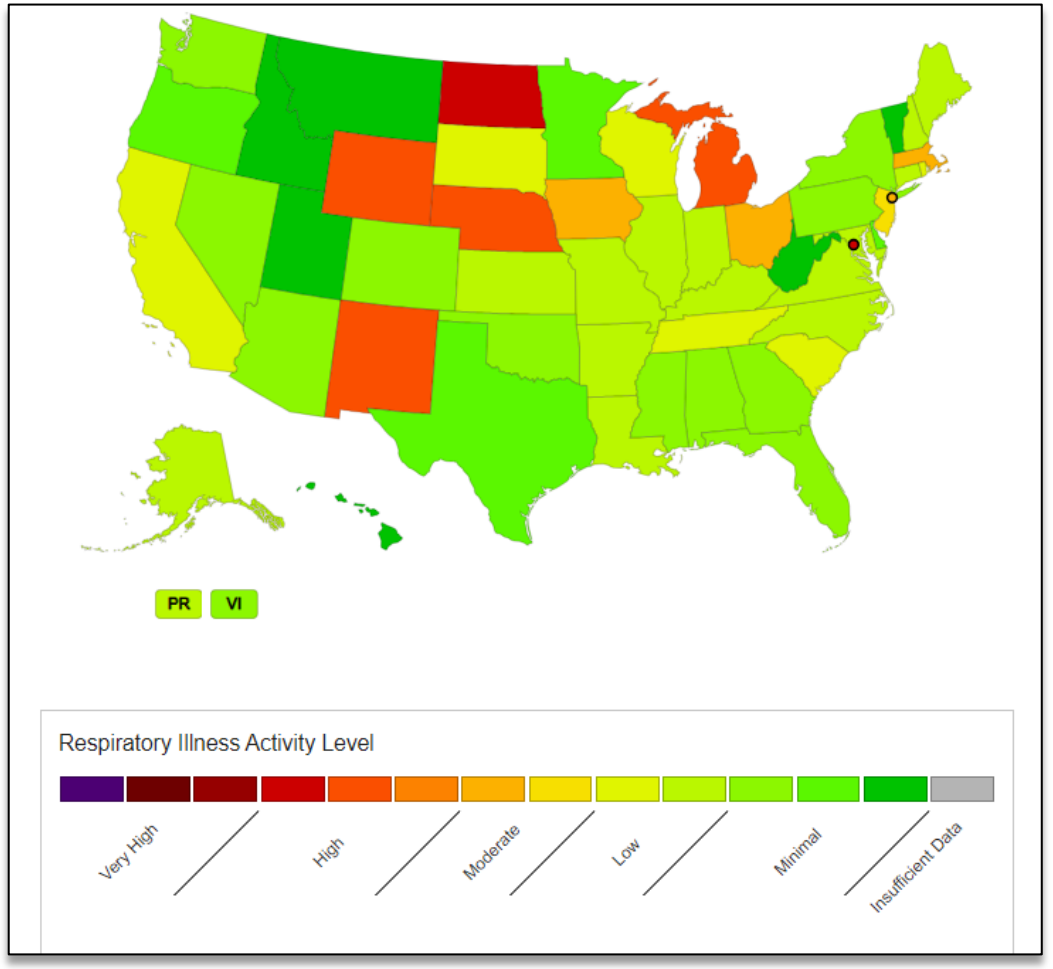
Nationally, RSV test positivity remains low. Hospitalization rates are low in all age groups.

Vaccination

National vaccination coverage for COVID-19, influenza, and RSV vaccines remained low for children and adults for the 2023-24 respiratory illness season. COVID-19 vaccines continue to be recommended and can provide a layer of protection.

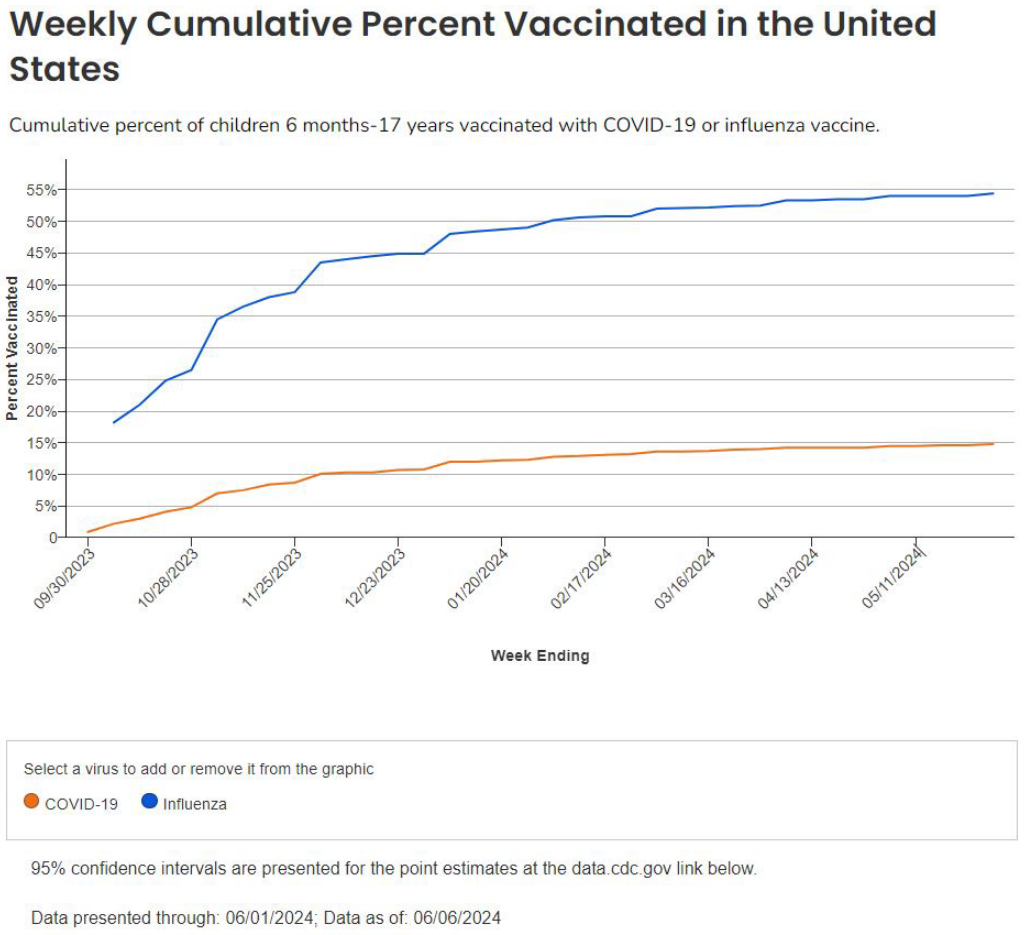
https://www.cdc.gov/respiratory-viruses/data-research/dashboard/snapshot.html

Level of Respiratory Illness Activity (as of April 4, 2024)



Vaccination Trends – Children

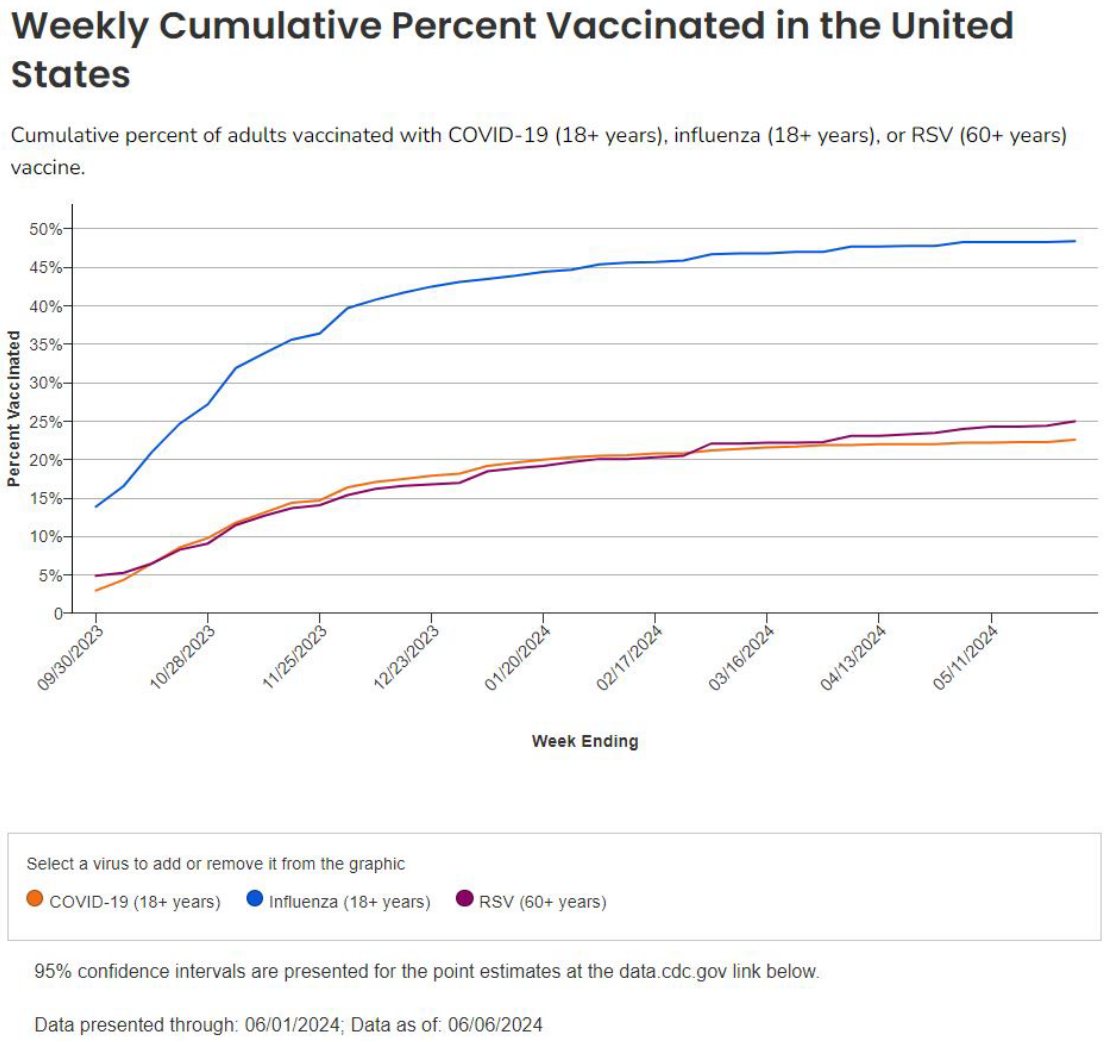
- This page provides an update on receipt of vaccination and intent for vaccination among children for COVID-19 and influenza based on weekly updated National Immunization Survey (NIS) findings.



https://www.cdc.gov/respiratory-viruses/data-research/dashboard/vaccination-trends-children.html

Vaccination Trends – Adults

- This page provides an update on receipt of vaccination and intent for vaccination among adults for COVID-19, RSV, and influenza based on weekly updated Immunization Survey (NIS) findings.



https://www.cdc.gov/respiratory-viruses/data-research/dashboard/vaccination-trends-adults.html

Respiratory VaxView

This page provides access to the weekly COVID-19, flu, and RSV vaccination dashboards. These dashboards provide in-depth vaccination data from a variety of data sources including surveys, healthcare claims, electronic medical records, and immunization information systems data. Select from the options below for the vaccine of interest. Please visit VaxView Vaccination Coverage | CDC for data on routine vaccinations.

Vaccination coverage is the estimated percentage of people who have received specific vaccines. Vaccination coverage information is used to identify areas and groups with lower vaccination coverage so public health departments, healthcare partners, and schools can take action to help improve vaccination coverage and protect everyone from vaccine-preventable diseases. During the COVID-19 Public Health Emergency (PHE), CDC tracked nearly all COVID-19 vaccines administered. However, the end of the PHE limits the completeness of COVID-19 vaccine administration data CDC receives. As a result, survey data are now the primary source for tracking vaccination coverage for COVID-19, RSV, and flu. Other available data sources will be used to provide additional insight into the vaccination landscape.

Weekly COVID-19 Vaccination Dashboard >

Weekly Flu Vaccination Dashboard >

Weekly RSV Vaccination Dashboard >

https://www.cdc.gov/vaccines/imz-managers/coverage/respvaxview/index.html

CDC's Vision for Immunization Information Systems

CDC | NCIRD | Immunization Services Division

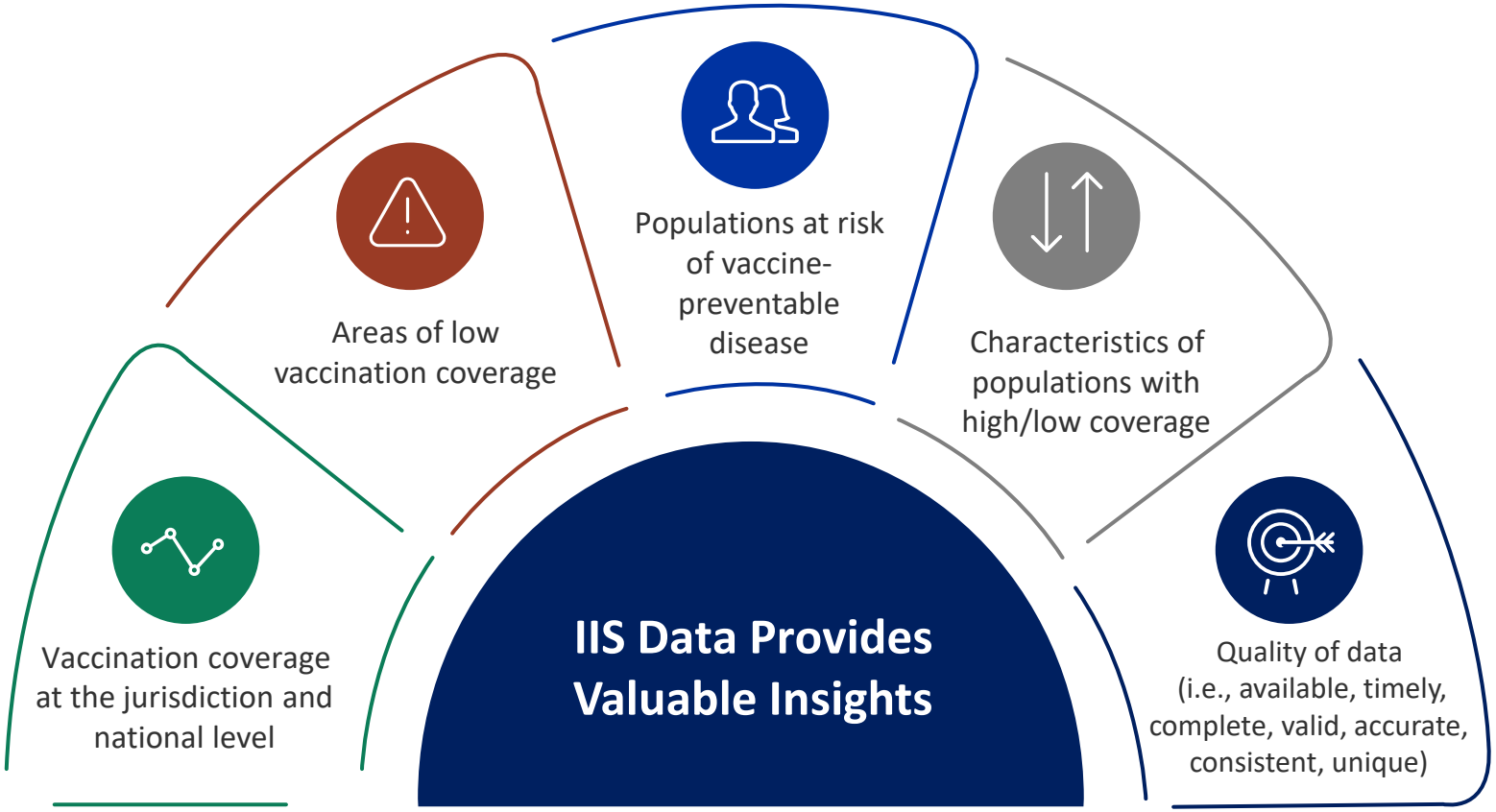
CDC's Vision for Immunization Information Systems

Immunization Information Systems (IISs) support the **standardized capture and exchange of high-quality, individual-level immunization data** for all doses of Advisory Committee on Immunization Practices (ACIP) recommended vaccines.

These data are linked across jurisdictions, providers, partners, and other individual-level data sources to **inform public health actions.**

Understanding Immunization Data for Public Health

Building on advancements made during the COVID-19 pandemic, IIS data give valuable insights at the national level.



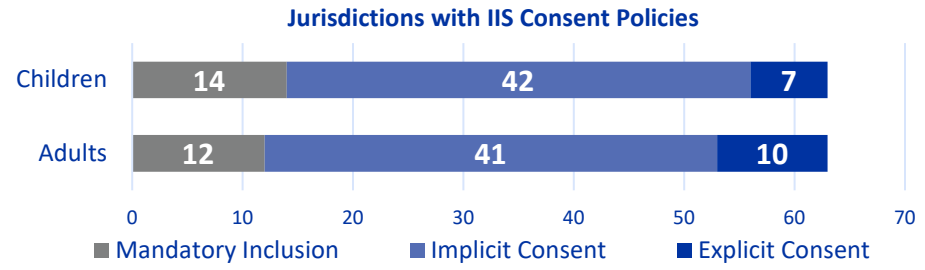
IIS Data Policy Landscape

Consent and provider reporting policies may limit a jurisdictions ability to collect, exchange, and report data. Most jurisdi ctions have a citable law, rule, or regulation that govern IIS data, while a few base policy on the Department of Health or programmatic policy.

Consent

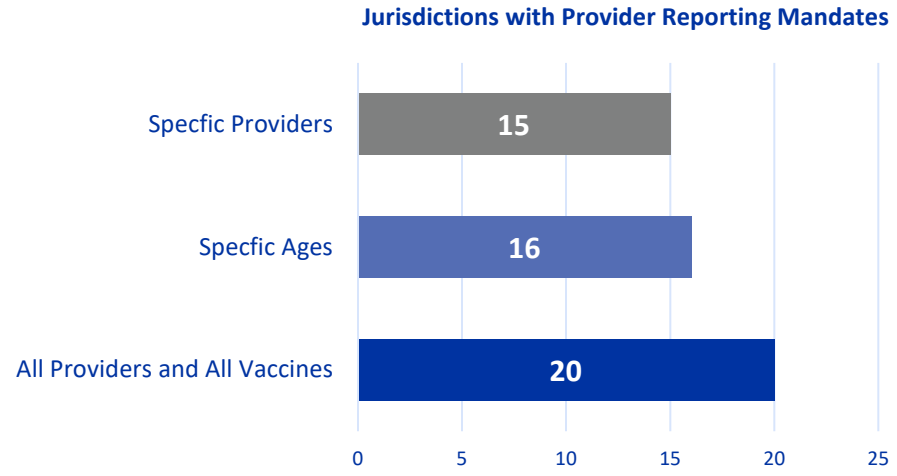
Consent is whether an individual has the right to decide if their demographic and immunization data is included in the IIS. Parents or guardians give implicit or explicit consent for children under the age of 18.

- **Mandatory inclusion:** Includes vaccine recipients in IIS with *no possibility to opt out*
- **Implicit consent:** Includes vaccine recipients in IIS unless they *choose to opt out*
- **Explicit consent:** Includes vaccine recipients in IIS only if explicit *consent is obtained to opt in*



Provider Reporting

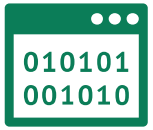
Provider reporting requirements are mostly governed by policy that is a citable law, rule, or regulation. These requirements are unique to each jurisdiction and are based on various factors (e.g., age, vaccines)



Palau did not provide policy information.

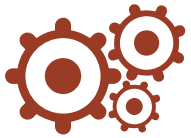
Strategic Priorities for IISs

Based on CDC's data modernization effort to *accelerate data into action* and lessons from the COVID-19 response, IDAB supports these priorities for the IIS.



Technology Infrastructure

- Meet **IIS Functional Standards** to increase standardization of IIS functionality and data elements and support program and provider immunization processes.
- Test functionality to ensure standardization using AIRA's Measurement and Improvement Initiative.



Data Quality

- Improve data quality through use of **IIS Data Quality Blueprint** to prioritize meaningful, quantifiable measures and **IIS Data Quality Reports** to identify actionable improvements.

Data Exchange

- Increase interoperability and data sharing between jurisdictions and providers via **IZ Gateway.**
- Use **PPRL** to allow cross-jurisdiction data matching.

Technology and Standards

Functional Standards and Operational Guidance Statements (OGS)

These describe the underlying operations, data quality, and technology needed by IISs to support immunization programs, vaccination providers, and other immunization stakeholders and their immunization-related goals. They help assure that IISs attain a level of consistency in support of common clinical, programmatic, and public health immunization goals

HL7 v2.5.1 Implementation Guide for Immunization Messaging, Release 1.5

Guidance to help IIS comply with national standards, best practices, and the latest Health Level Seven (HL7) conformance methodology.

Measure Your IISs Adherence to Standards with Measurement and Improvement Initiative

Measurement and Improvement (M&I) Initiative supports system testing to help guide individual IIS in aligning with identified standards

https://www.cdc.gov/vaccines/programs/iis/func-stds.html

Data Quality: Immunization Data Reporting at the National Level

DUAs and Data Reporting

Pre-COVID-19

Jurisdictions use IISs to manage the Vaccines for Children (VFC) program and understand their jurisdiction's vaccine coverage.

- **13** jurisdictions signed Data Use Agreements (DUAs)
- Routine data reported quarterly and flu data reported monthly
- Data use was limited

COVID-19 Response

Federally provided vaccine, provider agreements, and a COVID-19-specific DUA superseded state reporting and data sharing laws to allow reporting to CDC.

- **64** jurisdictions with DUAs
- COVID-19 data reported daily, then weekly

Present

New DUA allows reporting of routine vaccination data across the lifespan.

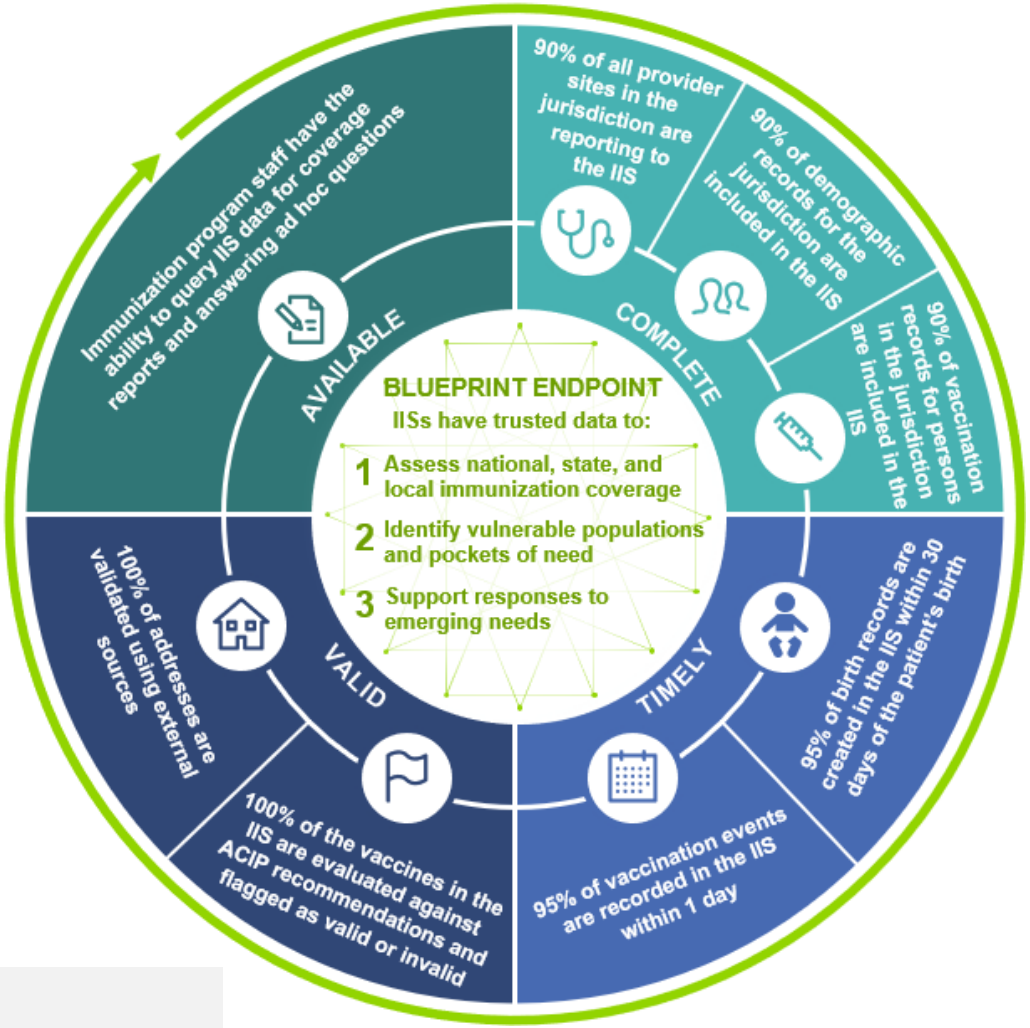
- **54** jurisdictions with DUAs
- Line-level routine data reported quarterly
- Aggregate RSV, flu, COVID-19 data reported monthly

Latest Data Reporting

April Aggregate Jurisdiction Data Submissions *submitted in May 2024*				Q1 2024 Routine Data Submission *submitted in April 2024*
Flu Data	**RSV Data**	**COVID-19 All Data**	**COVID-19 Bridge Data**	**Record Level Routine Data**
51	51	50	50	51 *16 PPRL*

Data Quality:
IIS Data Quality Blueprint

The blueprint guides awardee activities to improve data quality by prioritizing a **small set of meaningful, quantifiable** measures.



IIS Data Quality Endpoint

- IISs will be ***the*** **trusted source** for reliable immunization data
- IISs will produce data to support:
  - Immunization coverage assessments
  - Identification of pockets of need
  - Responses to emerging needs

7 Data Quality Characteristics

Available | Complete | Timely | Valid | Accurate | Consistent | Unique

Data Quality:
Feedback and Reports

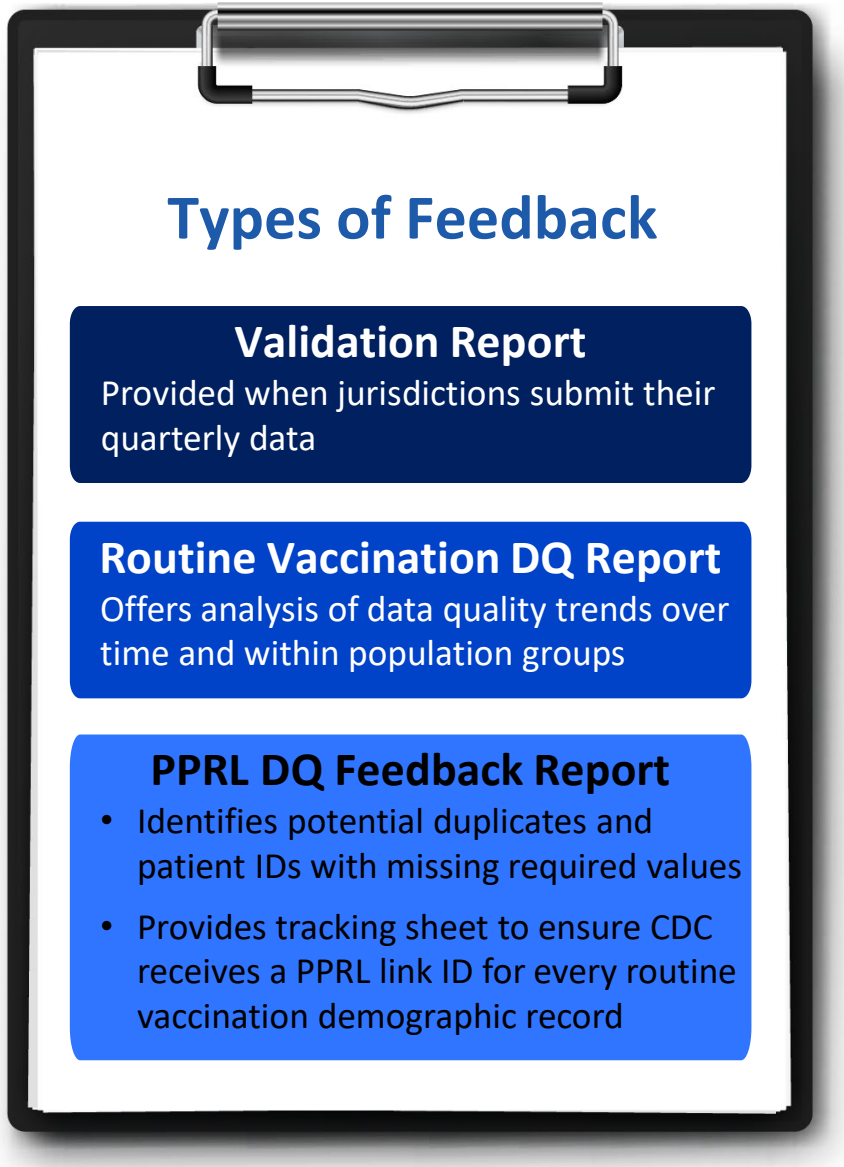
CDC aims to provide jurisdictions with timely feedback and technical assistance to support data quality improvements.

Data quality monitoring and assistance

Provide jurisdictions with an assessment on the completeness and accuracy of IIS data along with targets and strategies to improve quality

Data quality in action

- ✓ **Q4 2023:** 104 million demographic records submitted for PPRL. CDC could assign a PPRL link ID to **94%** of the records.
- ✓ **Goal:** increase this percentage over time by making process improvements and highlighting patient IDs with missing values in the PPRL DQ Feedback Report.

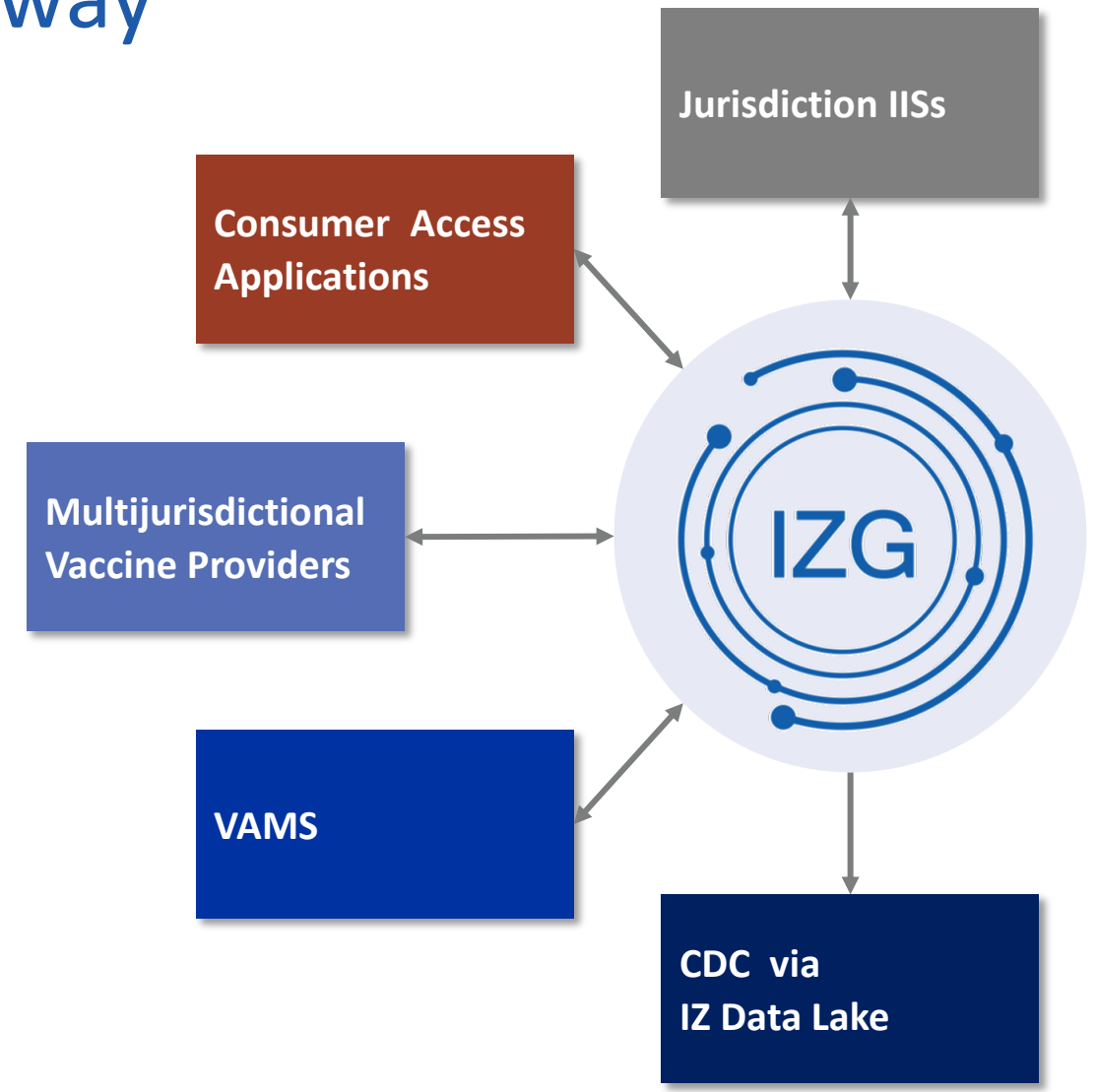


Data Exchange:
The Immunization (IZ) Gateway

The IZ Gateway is a policy framework and cloud-based message routing system that facilitates data exchange among IISs, vaccine providers, direct-to-consumer applications, and data submission to CDC.

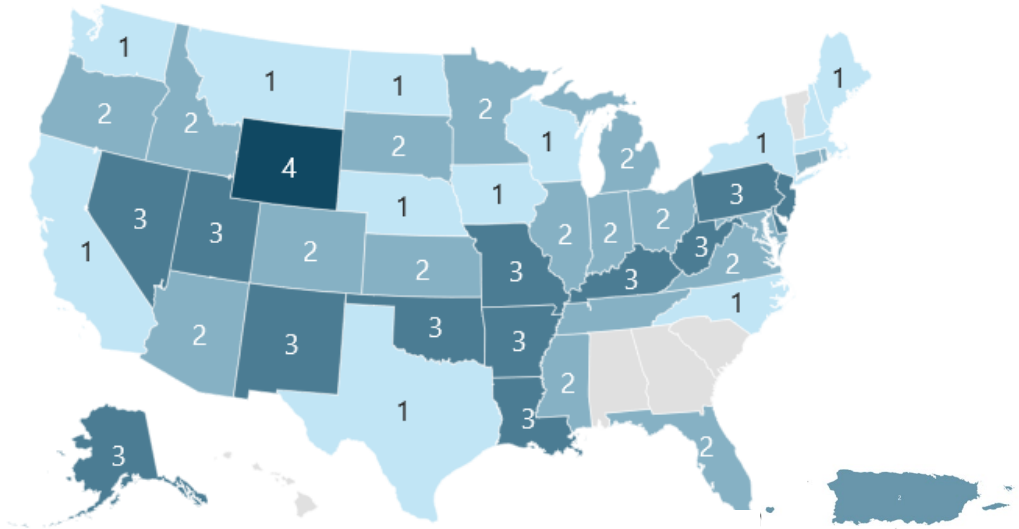
Message routing technology enables uniform application of **data quality assurance, messaging, and security industry standards** and best practices for all participants.

Policy framework ensures compliance with each **jurisdiction's data sharing laws and policies.**



Data Exchange:
IZ Gateway Data Exchange Metrics

Jurisdictions Participating in the IZ Gateway



Onboarded, Not Pictured

- *Washington D.C.*
- *Philadelphia*
- *NYC*
- *Chicago*
- *San Antonio*
- *Houston*

IZ Gateway Exchange Metrics		Impact
Completed Baseline Onboarding	**63 Jurisdictions**	**These jurisdictions are prepared to implement other use cases**
Participating in IIS-to-IIS Data Exchange	**36** jurisdictions with **205** active exchanges	**32** IIS have more complete records for citizens vaccinated outside their jurisdiction
IIS and Multijurisdictional Provider Data Exchange	**7** providers* with **4,220** facilities in **42** jurisdictions	**42** jurisdictions have data on citizens vaccinated at large, multijurisdictional provider organizations
Consumer Access System Exchange with IIS	**1** platform exchanging with **6** jurisdictions	**6** jurisdictions streamlined their citizens' access to their consolidated vaccination records
IIS Data Exchange with CDC (data submission)	**20** jurisdictions submit routine vaccination data to DLP through DEX and NDLP storage container	CDC offers jurisdictions the option to **automatically send their routine vaccination data to CDC** rather than using a manual submission process

*Multijurisdictional Providers: Veterans Administration (VA) VistA, VAMS, DocStation, AZOVA, VA Oracle Health, Fond du Lac, Department of Defense

Updated 06/4/24

Data Exchange: Local Implementation Guide Standardization and Digitization Project

Local implementation guides (IGs) are not standardized, which causes onboarding delays, IZ Gateway challenges, and data sharing issues. This project streamlines the local IG development process, increasing efficiency and effectiveness in healthcare data exchange.

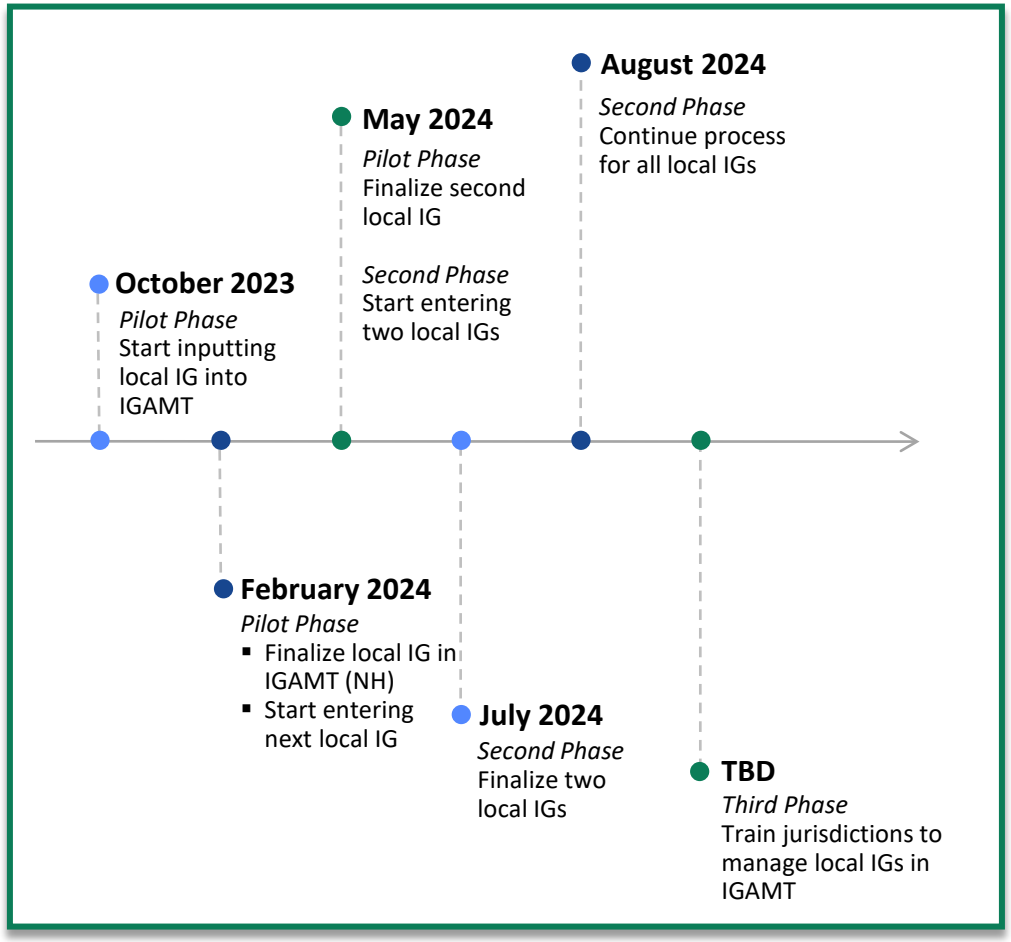
Standardize

Standardizing local IGs ensures each jurisdiction's guide:

- Follows national standards
- Complies with the latest HL7 conformance methodology
- Adheres to best practices

Digitize

The National Institute of Standards and Technology's (NIST) HL7 Implementation Guide Authoring and Management Tool (IGAMT) is used to digitize each jurisdiction's IG, making all IGs more accessible and usable (e.g., creating a jurisdiction-specific validation tool).



IIS Funding: CDC's FY 2025 President's Budget Request

FY 2025 President's Budget (PB) Request

CDC FY25 PB Request (budget authority, PPHF, Evaluation Funds)..... $9.683 Billion

Accounts/Funding Lines	Proposed Amount	Change from FY2023 budget
Immunization and Respiratory Disease Total	$731,933,000	**+$50,000,000**
Acute Flaccid Myelitis	$6,000,000	No change
Influenza Planning and Response	$231,000,000	No change

Request is $50,000,000 above the FY23 appropriated level, and would support

- Ongoing work on COVID-19 and the highest priority activities of the immunization program
- Dedicated resources to urgent public threats
- Staffing expertise needed for effective national public health monitoring and prevention of respiratory viruses
- **Continued efforts to modernize immunization information systems**
- Implementation of new strategies for vaccine equity, building vaccine confidence, and expanding the scientific evidence base

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

AIRA
AMERICAN IMMUNIZATION REGISTRY ASSOCIATION

The Promise of IIS Modernization

Rebecca Coyle, MSEd
Executive Director

Public Health Modernization Efforts

Coordinated by the Office of the National Coordinator for Health IT (ONC) and the CDC Office of Public Health Data, Surveillance, and Technology (OPHDST)

Initial focus on surveillance systems including case reporting, laboratory, emergency department visits, and vital statistics data

https://www.cdc.gov/ophdst/about/advancing-data-for-public-health-action.html

CDC/OPHDST Vision for Public Health Data

Public Health Data Goals

1. Strengthen the core of public health data
2. Accelerate access to analytics and automated solutions to support public health investigations and advance health equity
3. Visualize and share actionable insights to inform public heath action
4. Advance more and interoperable public health data

https://www.cdc.gov/ophdst/about/advancing-data-for-public-health-action.html

The Pursuit of IIS Modernization

- Cloud hosting – allows for scalability
- Achieving standards
  - All jurisdictions are participating in Measurement & Improvement
- FHIR (Fast Healthcare Interoperability Resources) for certain features
  - Bulk query (requesting lots of records at one time)
- The IZ Gateway is working
- Re-thinking how IIS are structured (modular)

IIS Modernization Efforts

Significant funding during the pandemic was put towards immunization-related work, including IIS

Resources to maintain recent IIS enhancements and additions beyond June 2025 are unknown

June 30, 2025

2020

July 2025

Pandemic-era funding ends June 30, 2025

Opportunities

Vision

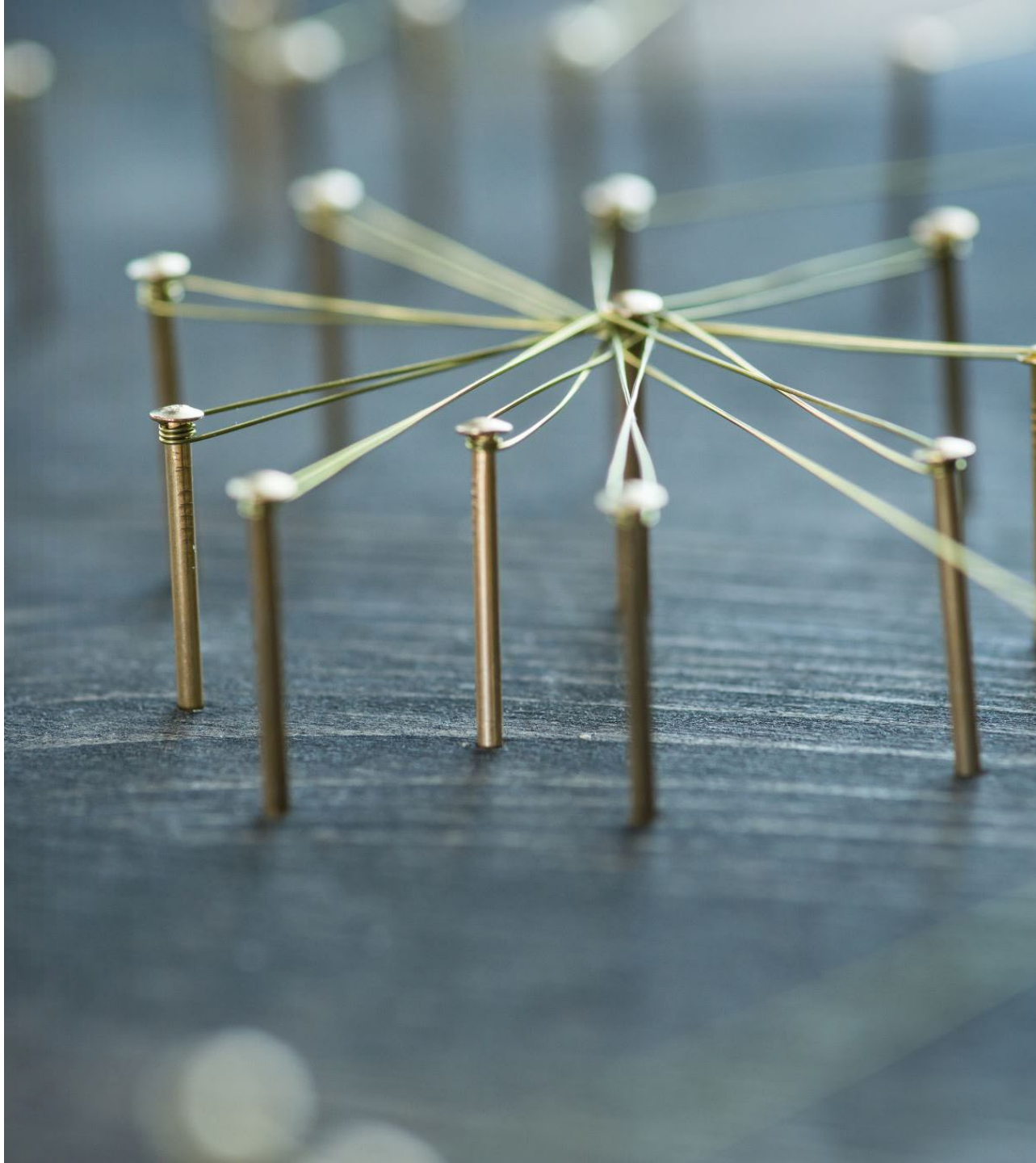
- Key discussions are needed to define the vision
- Need to identify the goals of modernizing IIS
  - What should every IIS be able to do and by when?
  - How will these efforts be funded and by whom?
  - What are the measures of success?

Policies

- Policies must be part of modernization efforts
- Strong policies provide value for all
  - Required and timely provider reporting
  - Ability to look up histories
  - Individuals should have access to their records
  - Ability to use data

Sharing Core Functions

- Matching
- Deduplication
- Dashboards
- Potential onboarding



Funding

- New strategies for funding IIS must be considered
- If we want public health in the next emergency – we must fund it today

Thank You

Immunization Data: Innovations, Improvements, and Updates

VHA IZ Gateway Project Overview

NVAC Meeting
June 14, 2024

Pam Belperio PharmD, BCPS
Deputy Director, Population Health Solutions
Community Data Integration (CDI) Council, Co-Chair
Department of Veterans Affairs

VA | U.S. Department of Veterans Affairs

VHA – Impact on Public Health and Clinical Care

Largest integrated healthcare system in the U.S.

Over 9 million enrolled Veterans

- 6.2 million receive VA care
- ~32% receive care in the community

1,321 health care facilities

- 172 VA Medical Centers (VAMC)
- 1,138 outpatient sites of care
- 18 Veteran Integrated Service Networks (VISN)

2 Electronic Health Record (EHR) systems

- VistA: Veterans Health Information Systems and Technology Architecture
- Oracle Health Millennium (6 locations)

2021_Enrollee_Data_Findings_Report-508_Compliant.pdf (va.gov);Integrated Veteran Care Program Office communication March 2023.
https://www.va.gov/health/aboutVHA.asp#:~:text=The%20Veterans%20Health%20Administration%20%28VHA%29%20is%20the%20largest,Veterans%20enrolled%20in%20the%20VA%20health%20care%20program.

VHA Challenges of Direct Data Exchange with Jurisdictions

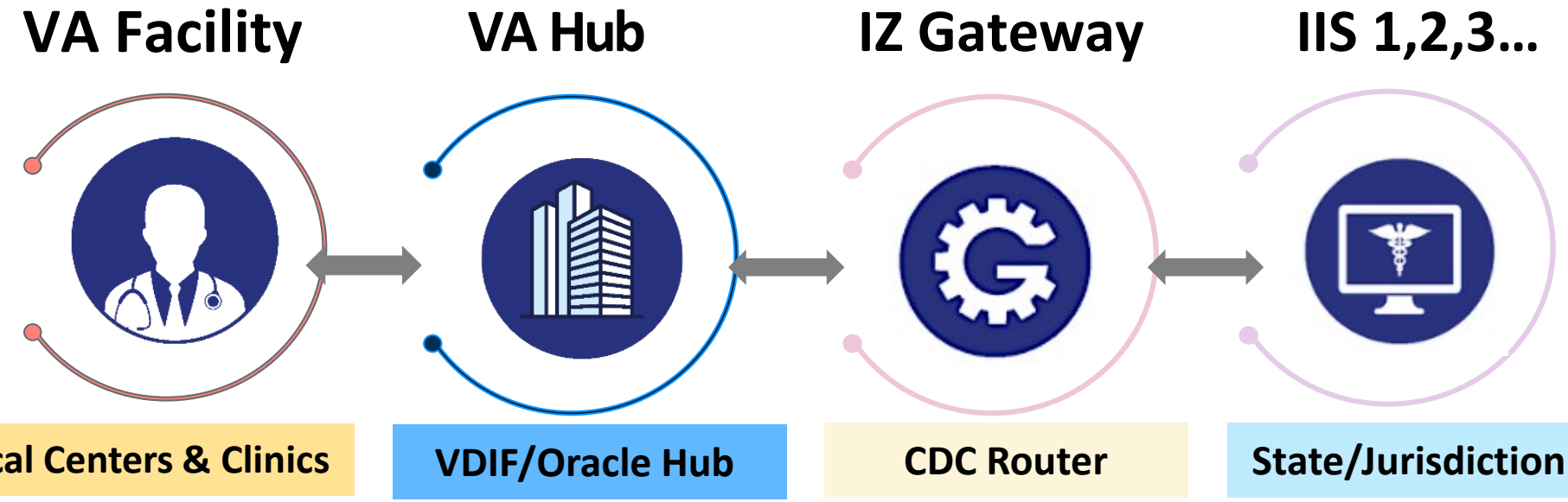
Federal, state, and local law and policy complicate the process:

- Different requirements across states and agreements
- Requirements not fitting within VHA clinical workflows or systems
- State requirements/laws that do not align with Federal legal and privacy requirements
  - Modifications often necessary before signature
  - Federal Supremacy clause (*U.S. Constitution, Article IV, Paragraph 2*): VA is subject to Federal Law which takes precedence over State law

Federal law (38 U.S.C. § 5701) ***prohibits disclosure of health information****, including Veteran name and address,* ***to State/Jurisdictional Public Health Authorities for disease and immunization reporting unless explicitly mandated by State law or*** *the Veteran has provided individual,* ***signed authorization to disclose.***

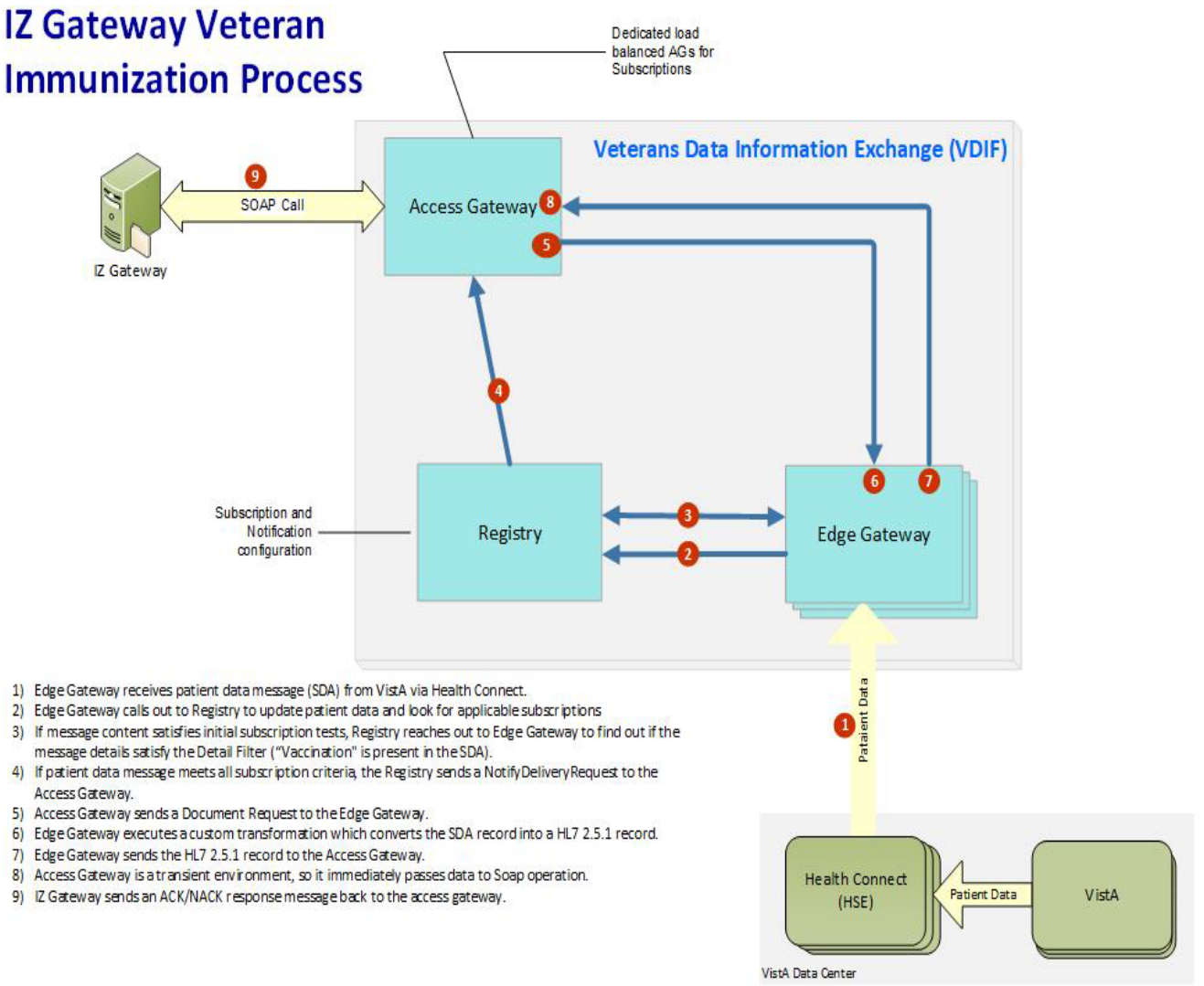
VHA - IZ Gateway Immunization Information Exchange

- **Provides a national automated solution**
  - ✓ *Avoids multiple individual point-to-point connections*
  - ✓ *Standardized policy infrastructure avoids multiple individual agreements*
- **Single multi-jurisdictional provider agreement for all IZ Gateway users, managed by CDC**
  - ✓ *No patient authorization required: Federal law allows VA to disclose immunization data with other federal agencies for public health reporting purposes without Veteran authorization*
- **Single point of connection to exchange immunization data between VA, IZ Gateway and multiple state/jurisdiction IIS**



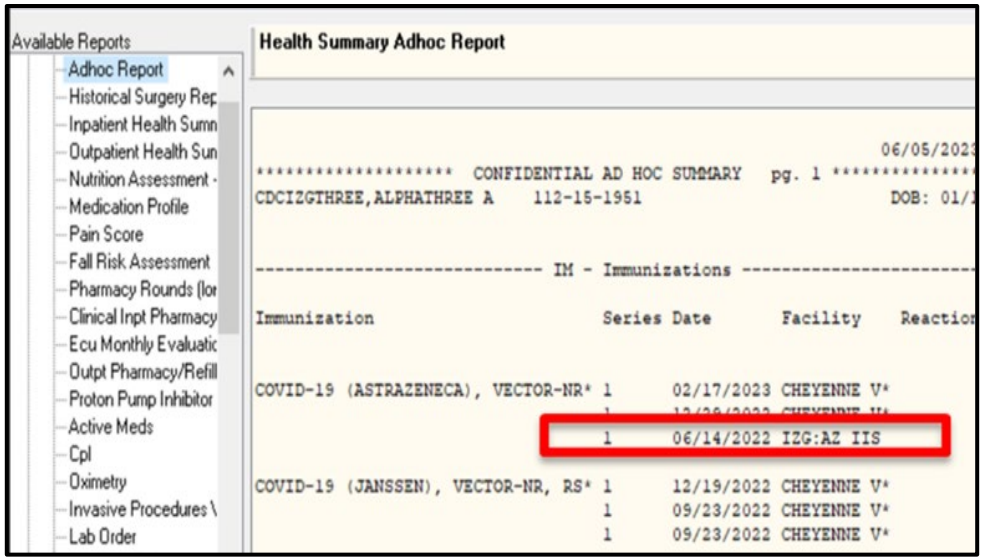
Connecting VistA to IZ Gateway

- **Centralized infrastructure,** fully automated interface
- Veterans Data Integration and Federation Enterprise Platform (**VDIF**): middleware platform that provides access to Veteran data in VistA
  - VDIF executes a **custom transformation** of the immunization information into (or from) an HL7 2.5.1 immunization message
  - **Seamless integration** and data exchange of immunization information to and from VistA through VDIF to the CDC IZ Gateway and the state IIS's



VHA Immunization Exchange Functionality

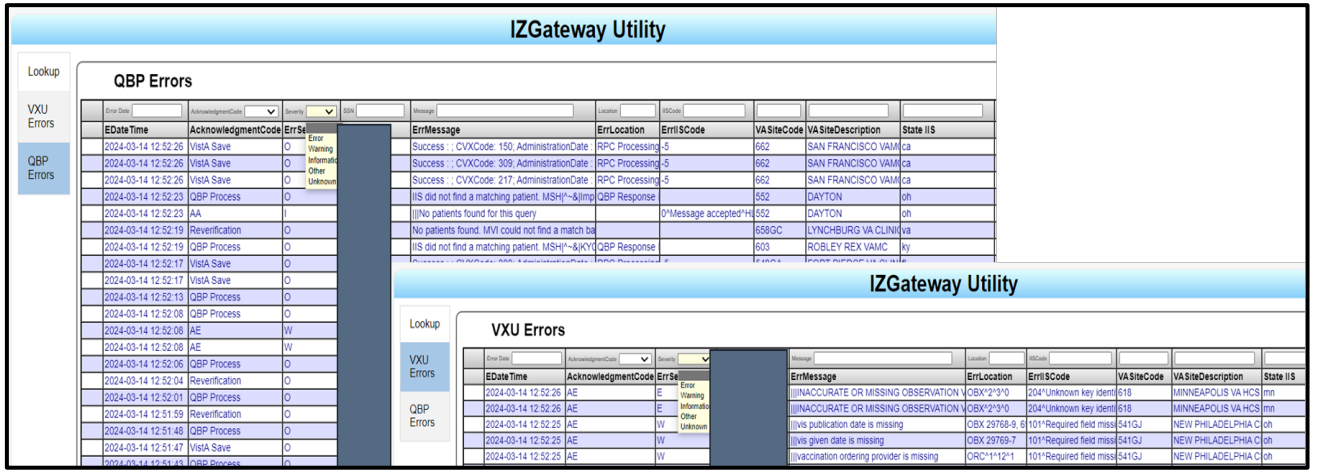
- **Reporting** of all VA administered vaccination data to the state/jurisdictional IIS; triggered when:
  - vaccine encounter is documented in VistA
  - vaccine administration documented in Oracle Health medication administration record



- **Querying** of state/jurisdictional IISs for Veteran vaccination data
  - VistA (pre-fetch): triggered automatically by appointment date, imported back into VistA, viewable in EMR
  - Oracle Health: manual query initiated by provider in immunization component of Mpage

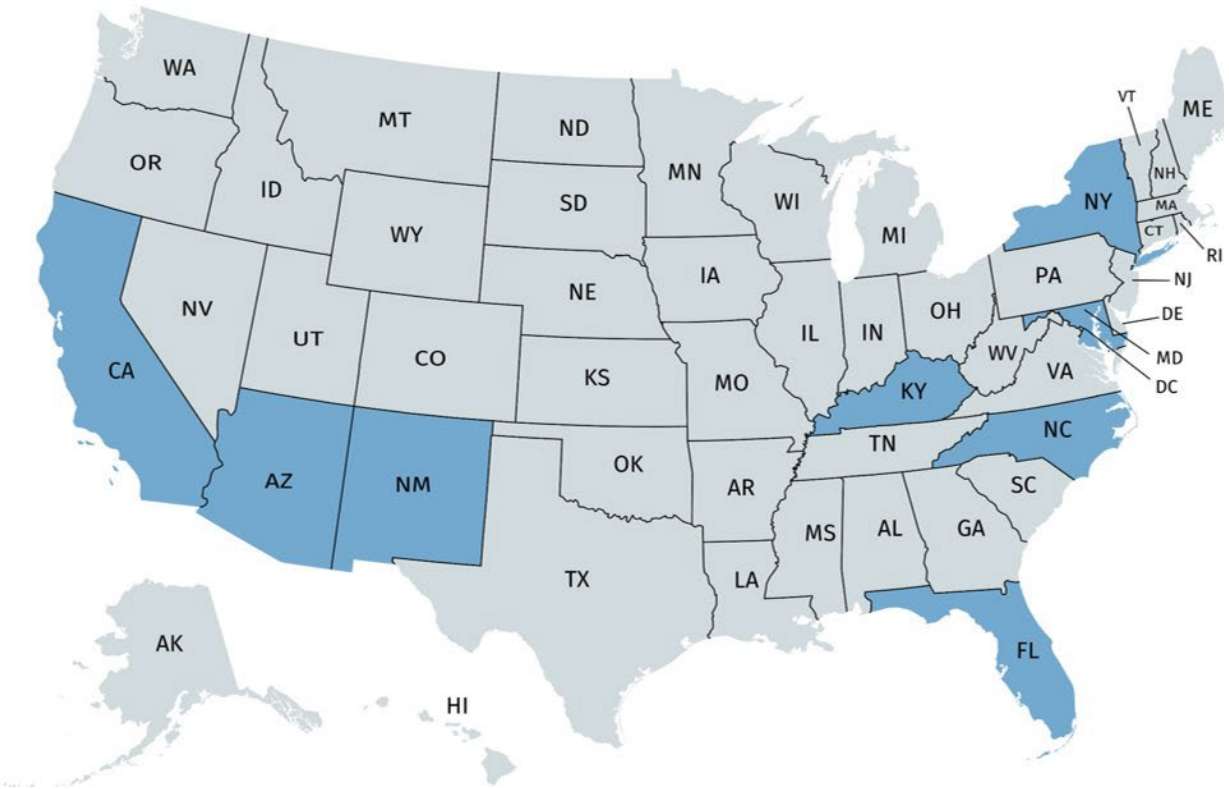
- **Error Handling Dashboard** to identify immunization records rejected by the State and track responses to queries
  - Oracle Cerner: Error Report available in Discern Analytics

- **Accounting of Disclosure dashboard** to capture each VistA immunization reported to IZ Gateway

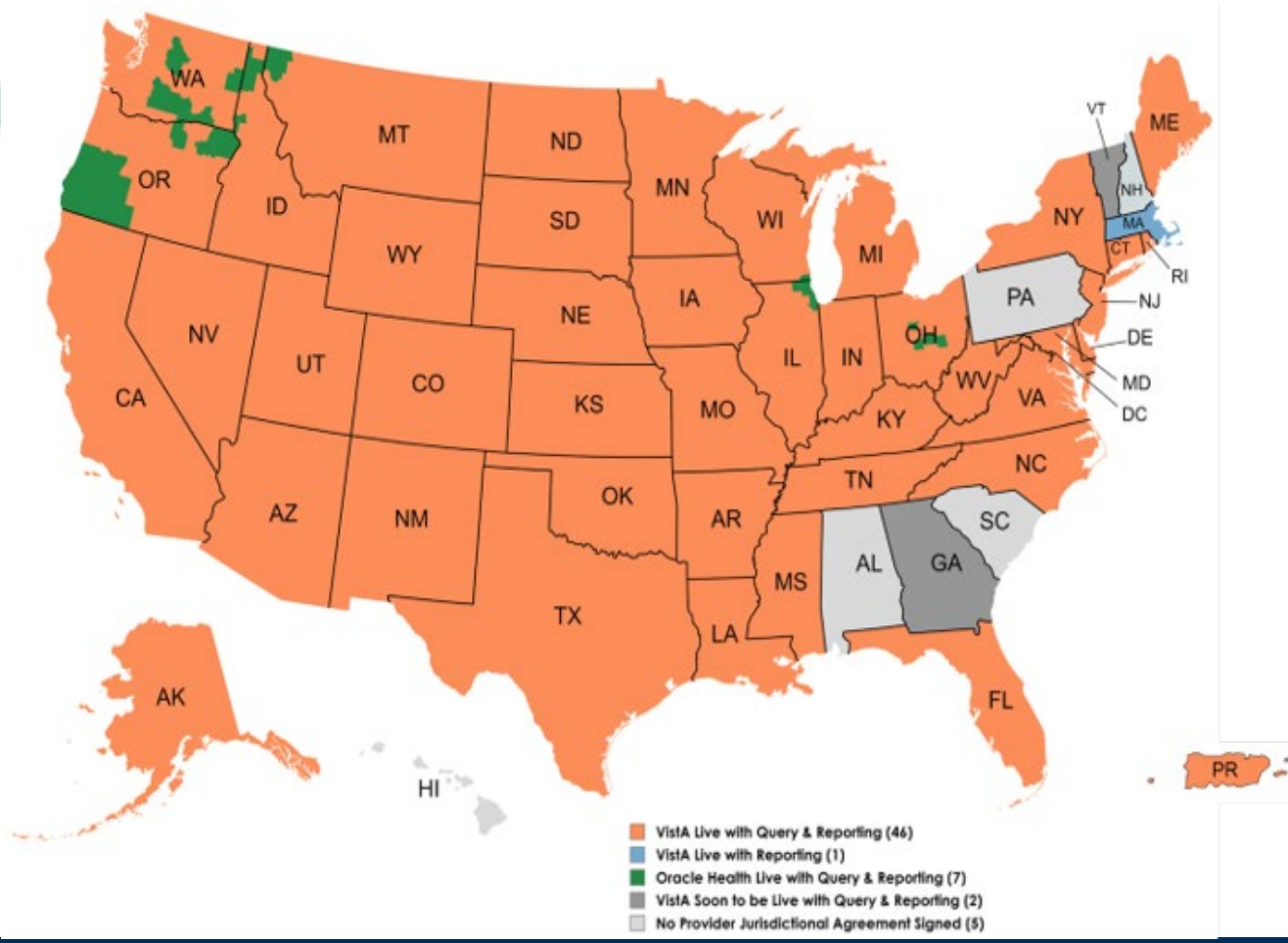


Progress (Because Everyone Loves a good “Before” and “After”)

August 2022



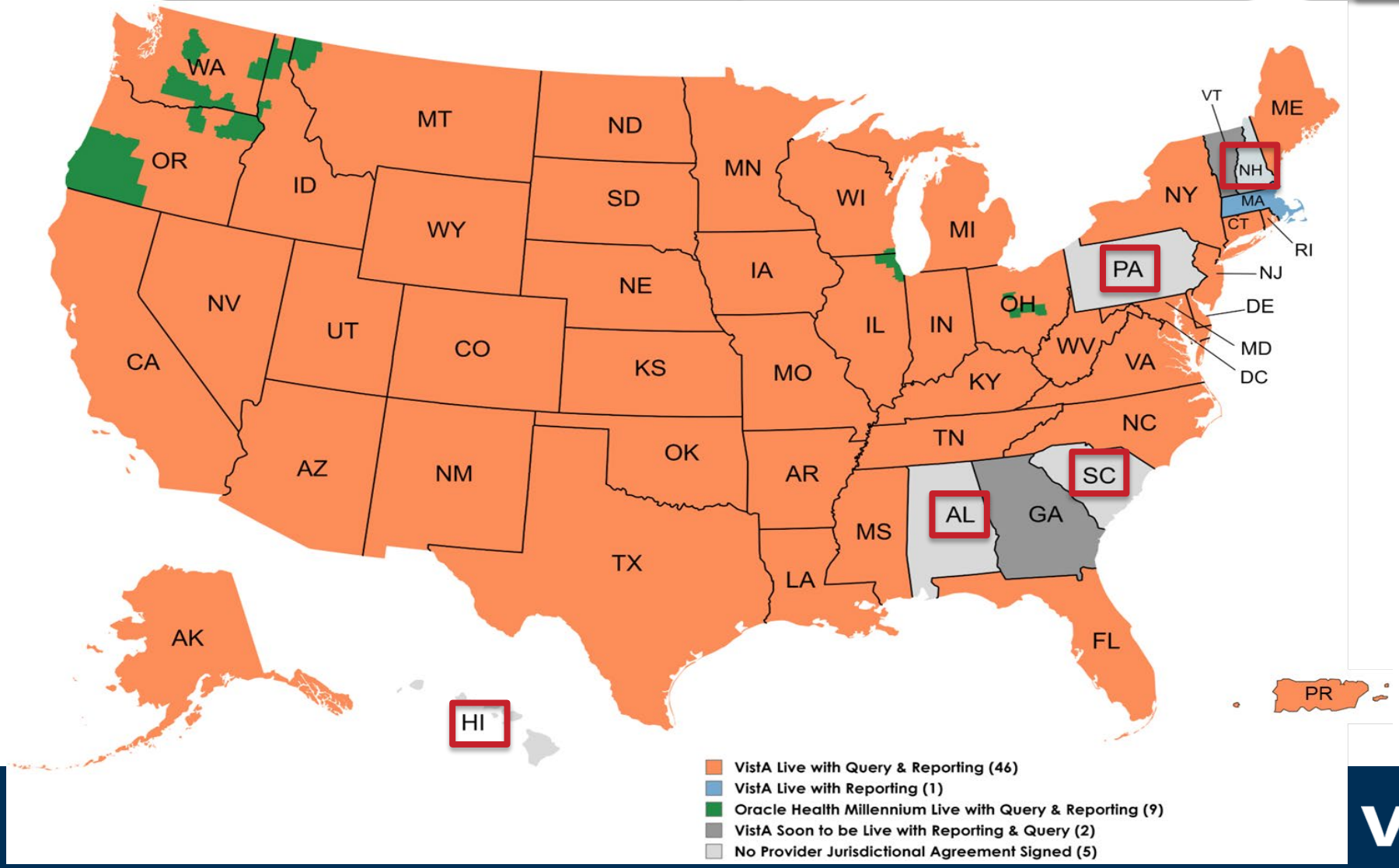
June 2024



VHA Health Solutions
Data as of 5/31/24

VHA IZ Gateway Collaborations serves Veterans and Providers

Live with Automated Query and Reporting	Agreement signed;Testing Planned	Awaiting Agreements
47	2	5



Total Number of Vaccinations SENT to IISs via Automated REPORTING:

➢ **6,257,836**

for >4,167,024 Veterans

Total Number of Vaccinations RECEIVED from IIS QUERY:

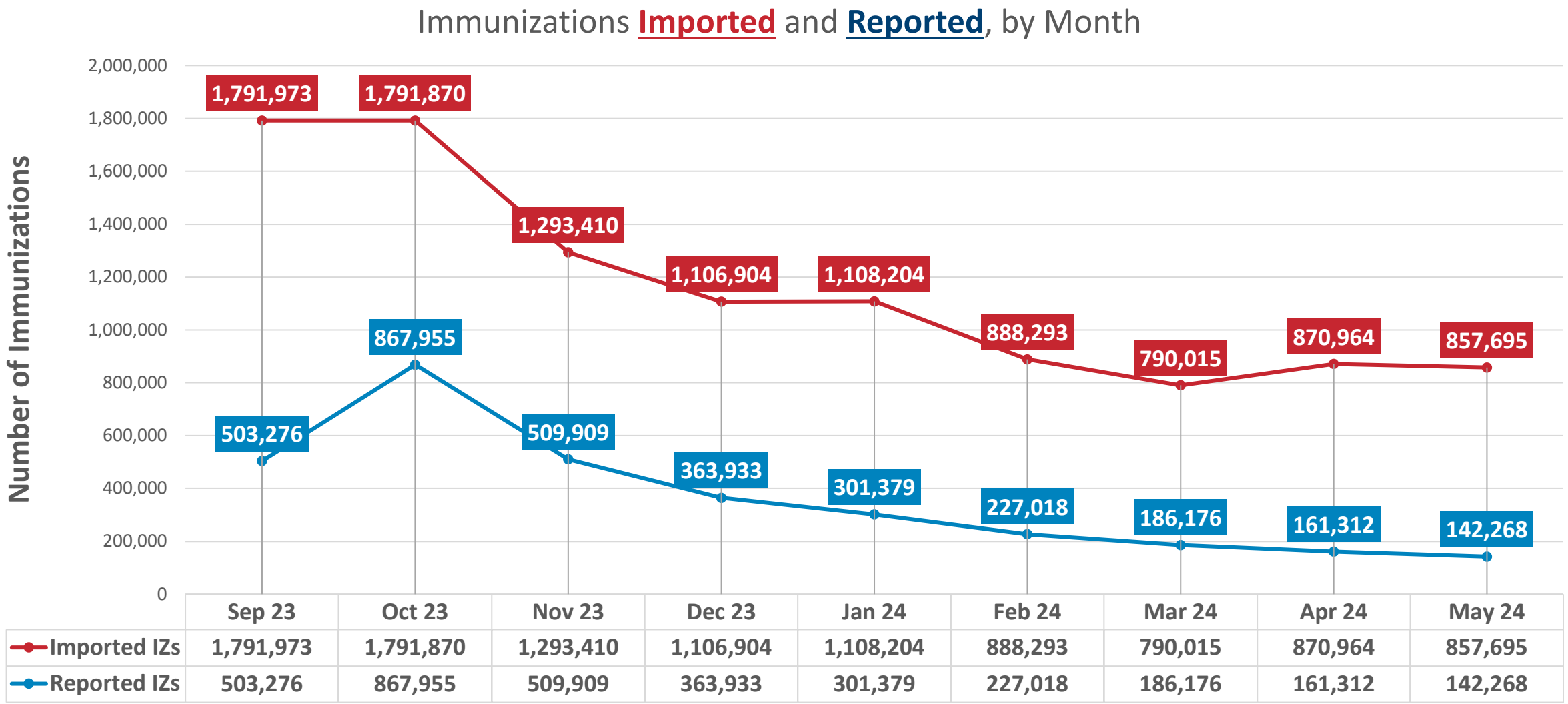
>12,857,970

for >2,230,761 unique Veterans

Source: VHA CDW Data as of 5/31/24

VA | U.S. Department of Veterans Affairs

Monthly VA Immunization Exchange via IZ Gateway



	Sep 23	Oct 23	Nov 23	Dec 23	Jan 24	Feb 24	Mar 24	Apr 24	May 24
Imported IZs	1,791,973	1,791,870	1,293,410	1,106,904	1,108,204	888,293	790,015	870,964	857,695
Reported IZs	503,276	867,955	509,909	363,933	301,379	227,018	186,176	161,312	142,268

Remaining Challenges

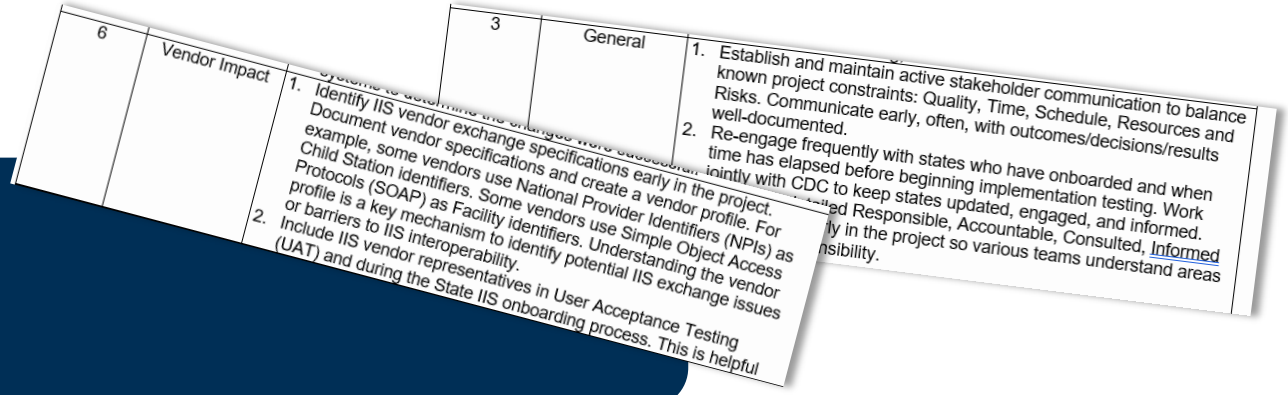
- 5 states have not signed the necessary IZ Gateway Multi-jurisdictional Provider agreement
- **IMPACT**:
  - Incomplete vaccination records for VA and Community providers and state/jurisdiction health departments for ~530,000 Veterans in those states
  - Inconsistent care services available to Veterans
  - Risk of duplicate immunizations
  - Challenges in tracking and targeting outreach interventions

State	Number of Veterans Impacted	Average Number of vaccines given per day	Number of VA facilities in state	Cited Issue
Alabama	114,503	782	19	Other priorities
Hawaii	29,053	190	9	Other priorities
New Hampshire	30,388	160	7	Legal barriers; NH does not plan to pursue
Pennsylvania	214,666	2110	42	Under legal review
South Carolina	140,737	1232	14	Legal barriers; SC does not plan to pursue

NVAC recommendations for engaging remaining states to prioritize IZ Gateway connection with VHA?

Lessons Learned

Need for standardization



- Message handling differences across jurisdictions
- IIS variation in HL7 elements requiring customization for multi-jurisdictional providers
  - Differences in MSH-4, MSH-22
- Custom ACK codes received from IIS/vendors
  - No standard ACK among IIS indicating if a vaccination message was rejected, successful, or data did not populate in the IIS record
- Inconsistent error messages returned
- Abbreviated street/city names (i.e, Colorado SPGS) → Patient address standardization using Project US@ would be beneficial

Creation of a baseline/normalized VXU HL7 message

Creation of Error Handling Dashboard to parse ACK error messages

Outcomes and Advancements

Before IZ Gateway

- Fragmented data systems
- Limited interoperability
- Reliance on manual processes
- Challenges in immunization tracking, compliance and reporting issues
- Incomplete Veteran records

After IZ Gateway

- Nationwide integration
- **Expanded interoperability** and enhanced functionality; **public health collaboration**
- Elimination of manual processes
- Standardized reverification and deduplication, seamless integration into health record
- Improved healthcare delivery, comprehensive Veteran records
- Expanded immunization information for end-users, within VHA and externally

Immunization Information Systems (IIS) in claims-based vaccine safety and effectiveness studies

Dr. Patricia Lloyd, ScM PhD
Health Statistician
Office of Biostatistics and Pharmacovigilance
Center for Biologics Evaluation and Research
U. S. Food & Drug Administration

National Vaccine Advisory Committee
June 14, 2024

Outline

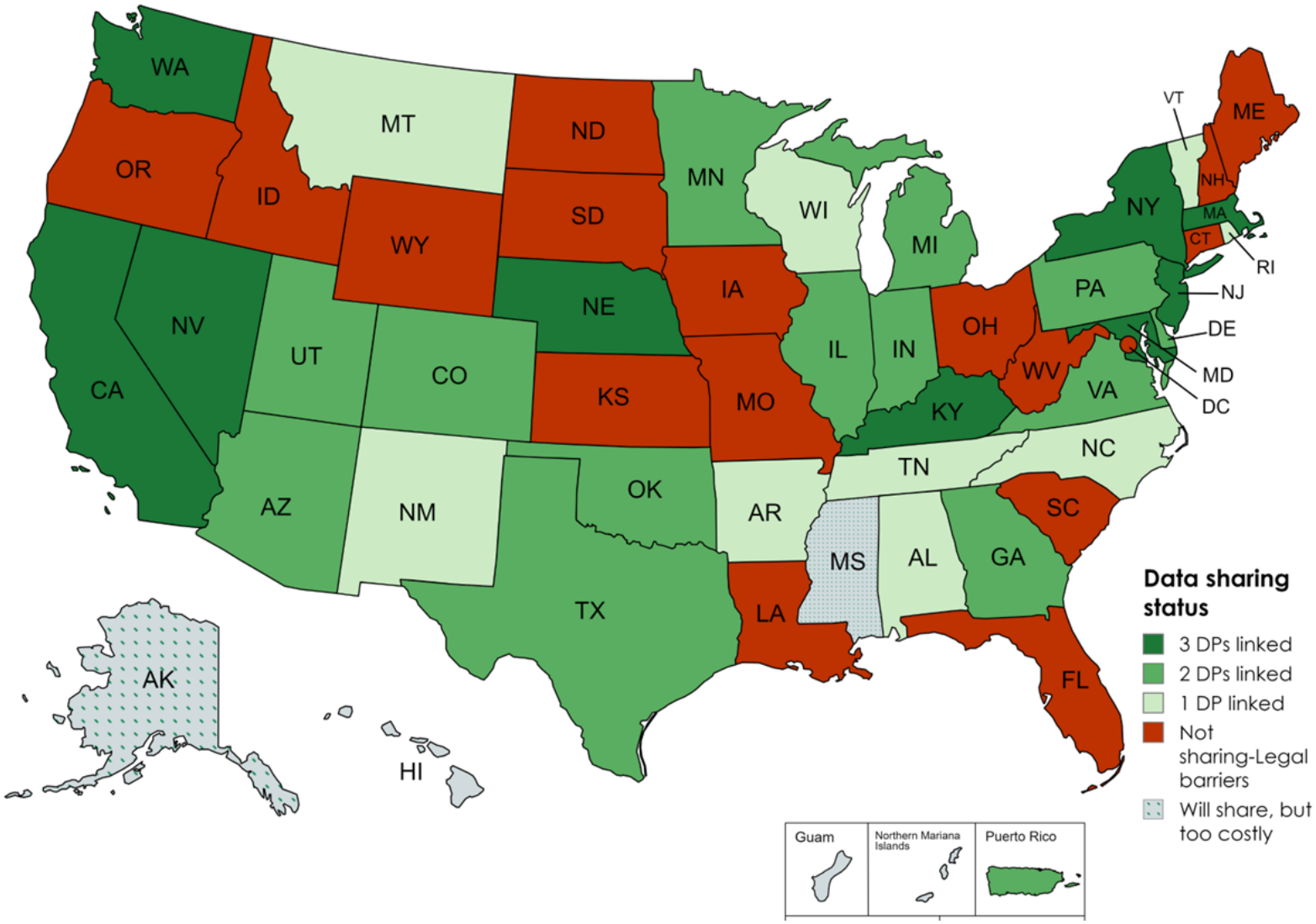
- CBER Active Surveillance Program
- IIS-Claims Data Linkage
- Regulatory and Public Health Impact
- Conclusions

CBER Active Surveillance Program Collaborative

Through multiple contracts and partnerships, CBER works with a diverse group of epidemiologists, data scientists and clinical experts to conduct active surveillance studies.

BEST: Biologics Effectiveness and Safety
CERSI: Centers of Excellence in Regulatory Science and Innovation

Status of CBER-BEST and Data Partners IIS Jurisdiction Outreach



Last updated April 2024

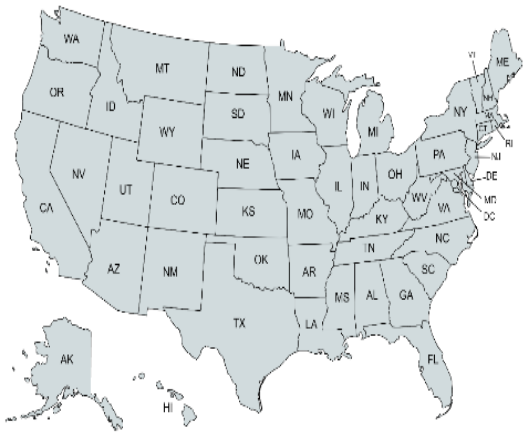
Note: Sharing data means made at least 1 data linkage/exchange with an FDA DP.

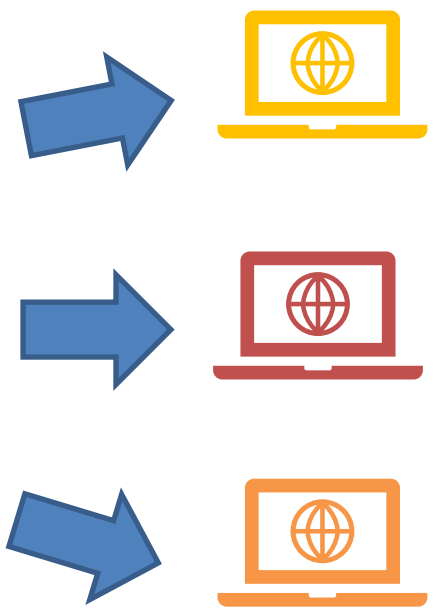
IIS Partnership with FDA: Flow of Data

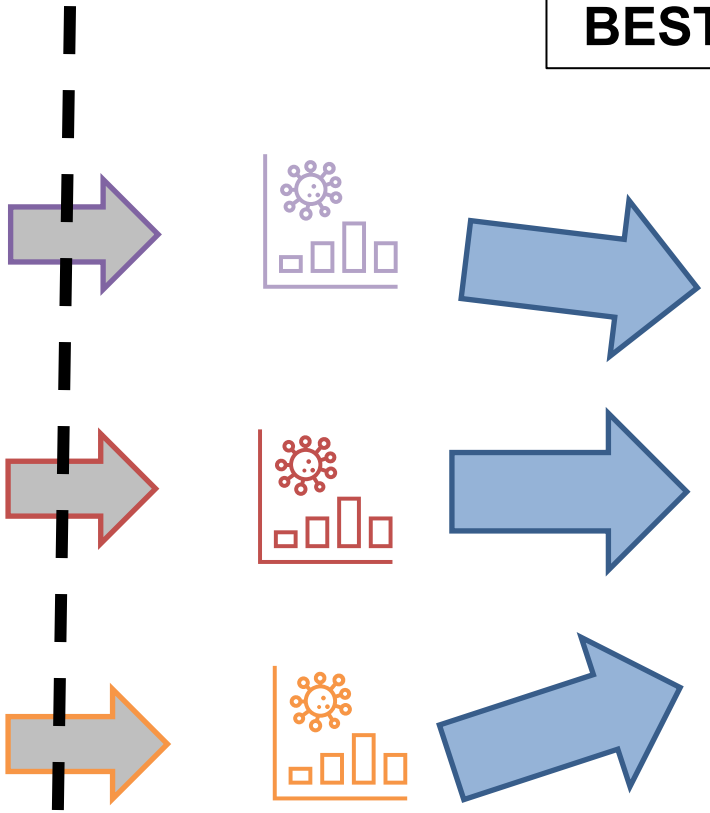
IIS

Data Partners

FDA/CBER BEST System







IIS share vaccination data on health plan members with **BEST health plan data partners**

Data partners clean, validate, aggregate and analyze linked vaccination and claims data per FDA protocols

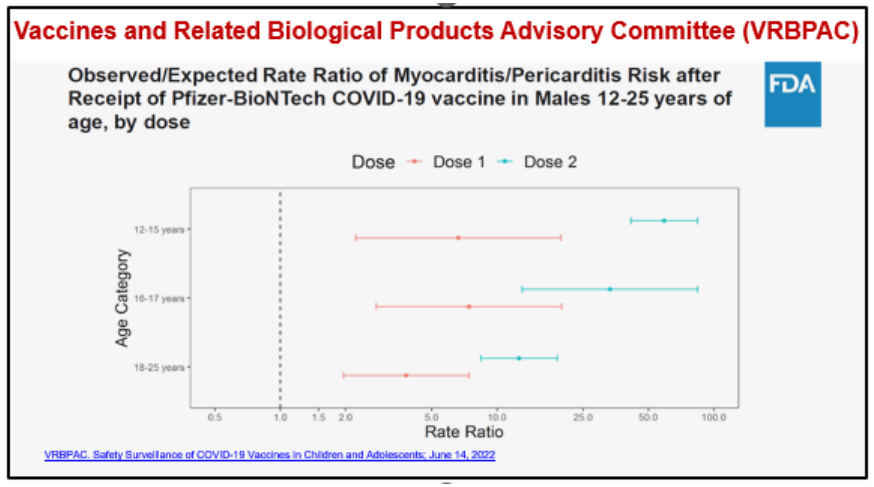
Data Partners provide aggregated summary data to **FDA/CBER**, to monitor vaccine safety and effectiveness.

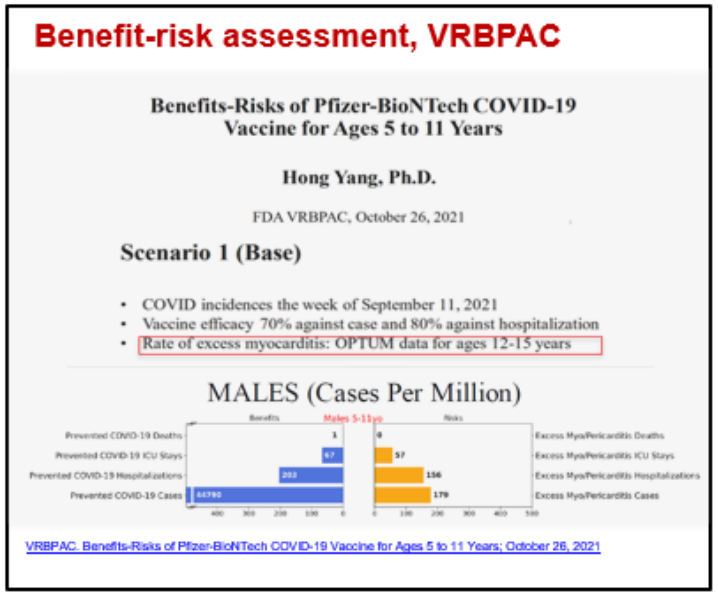
IIS COVID-19 Data Linkage Feasibility Study (Single DP)

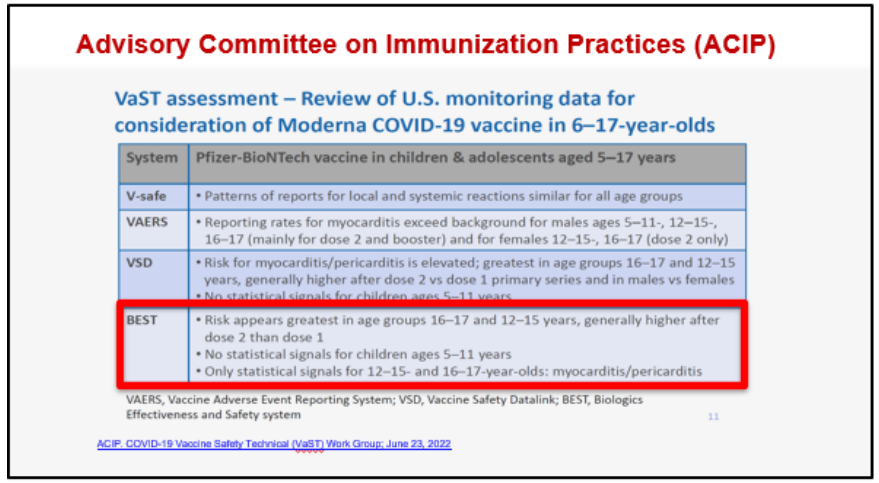
	Total study population (Age <64)	At least one dose		Completed series	
		Claims[a]	Combined IIS/Claims[b]	Claims[a]	Combined IIS/Claims[b]
		No. (%)	No. (%)	No. (%)	No. (%)
Total (12/2020-12/2021)	5,112,722	1,676,235 (32.8%)	2,458,231 (48.1%)	1,248,637 (24.4%)	2,143,556 (41.9%)
Deidentified States					
State 1	643,602	201,474 (31.3%)	316,177 (49.1%)	145,137 (22.6%)	287,198 (44.6%)
State 2	158,385	47,831 (30.2%)	76,820 (48.5%)	38,294 (24.2%)	68,478 (43.2%)
State 3	1,143,375	422,934 (37.0%)	520,249 (45.5%)	310,479 (27.2%)	404,913 (35.4%)
State 4	696,305	184,312 (26.5%)	265,936 (38.2%)	135,725 (19.5%)	228,643 (32.8%)
State 5	786,234	255,544 (32.5%)	401,634 (51.1%)	193,105 (24.6%)	366,046 (46.6%)
State 6	318,060	136,090 (42.8%)	167,745 (52.7%)	102,514 (32.2%)	144,224 (45.3%)
State 7	330,165	124,739 (37.8%)	191,327 (58.0%)	101,157 (30.6%)	180,397 (54.6%)
State 8	360,267	110,016 (30.5%)	179,787 (49.9%)	83,987 (23.3%)	159,617 (44.3%)
State 9	87,663	18,927 (21.6%)	40,901 (46.7%)	12,709 (14.5%)	36,876 (42.1%)
State 10	219,939	54,303 (24.7%)	105,376 (47.9%)	39,386 (17.9%)	95,468 (43.4%)
State 11	254,098	76,424 (30.1%)	133,781 (52.7%)	54,735 (21.5%)	122,816 (48.3%)
Multiple states[c]	114,629	43,641 (38.1%)	58,498 (51.0%)	31,409 (27.4%)	48,880 (42.6%)

Schneider KL, Bell EJ, Zhou CK, Yang G, Lloyd P, Clarke TC, Wilkinson M, Myers EE, Amend KL, Seeger JD, Chillarige Y, Forshee RA, Shoaibi A, Anderson SA, Wong HL. Use of Immunization Information Systems in Ascertainment of COVID-19 Vaccinations for Claims-Based Vaccine Safety and Effectiveness Studies. JAMA Netw Open. 2023 May 1;6(5):e2313512. doi: 10.1001/jamanetworkopen.2023.13512. Erratum in: JAMA Netw Open. 2023 Jun 1;6(6):e2321247.

Regulatory and Public Health Impact





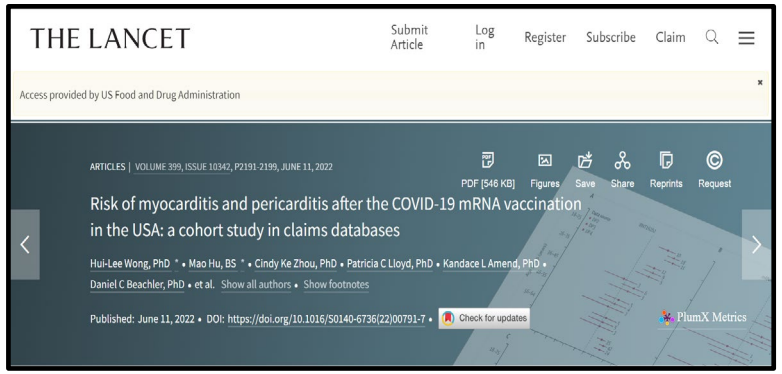


BEST studies have contributed to EUA and approvals during numerous FDA advisory panels.

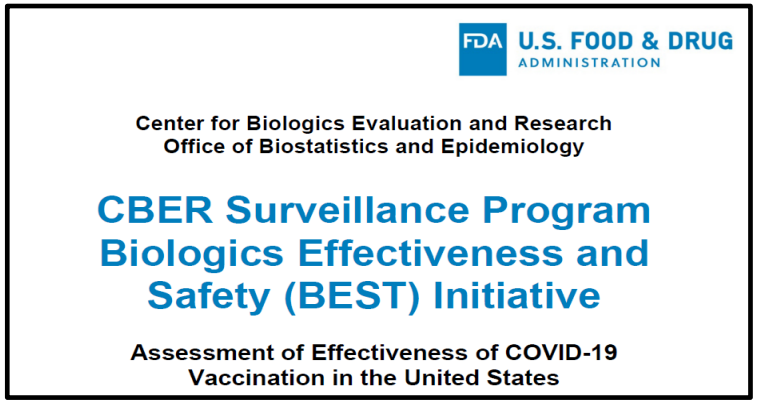
BEST studies provided risk estimates for input in benefit–risk assessment for regulatory decision making.

As part of the both passive and active US surveillance system, BEST studies contribute to the advisory committee that determines the public health policies regarding vaccines in the US.

Regulatory and Public Health Impact

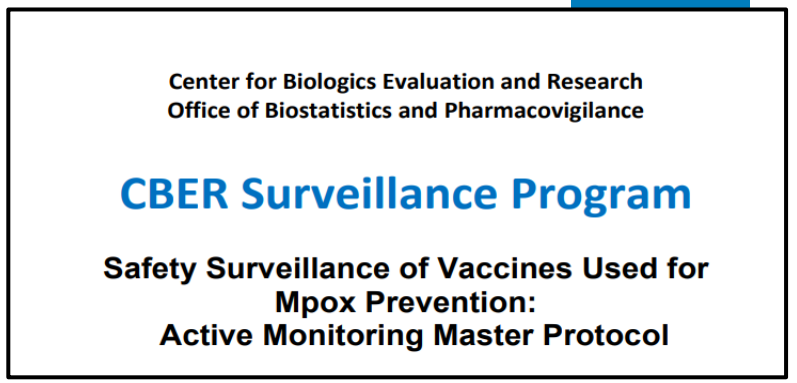


IIS data are crucial to FDA safety assessment/surveillance, e.g. defining the risk of Myocarditis/pericarditis after mRNA vaccines in young males.



IIS data provide more power to detect any potential rare safety outcomes after vaccine receipt.

IIS data are crucial for absolute vaccine effectiveness (VE) studies.



IIS data were essential to measure exposure for JYNNEOS and ACAM2000.

Vaccinated in Claims Only ~10% Vaccinated in IIS ~90%

IIS data were critical to give us the ability to do monitoring.

Conclusions

- BEST Initiative contributes to FDA CBER's mission to ensure biologic products safety and effectiveness through active surveillance.
- IIS data complements COVID-19 claims data adding up to 50% more immunization information for timely, evidence-based regulatory decision making.
- IIS mpox data captured nine times as many vaccine administrations as claims data.
- Continued and expanded IIS data linkage is needed for BEST to continue generating rapid and comprehensive response to the COVID-19 pandemic, mpox, seasonal influenza, and future outbreaks that require vaccine administration.

Acknowledgments

- Steven Anderson
- Richard Forshee
- Joann Gruber
- Carla Zelaya
- Tainya Clarke

- FDA BEST Partners:
  - Acumen, CMS, Optum, Carelon Research

www.bestinitiative.org

Questions?

Immunization Data: Innovations, Improvements, and Updates

Discussion

NVAC

Public Meeting

NATIONAL VACCINE ADVISORY COMMITTEE

June 13-14, 2024

Break

NVAC

Saluting Global Immunization Efforts: 154+ Million Lives Saved!

So Yoon Sim

NVAC

EPI 50-year impact analysis

National Vaccine Advisory Committee (NVAC) meeting
14 June 2024

So Yoon Sim sims@who.int
WHO Department of Immunization, Vaccines and Biologicals (IVB)

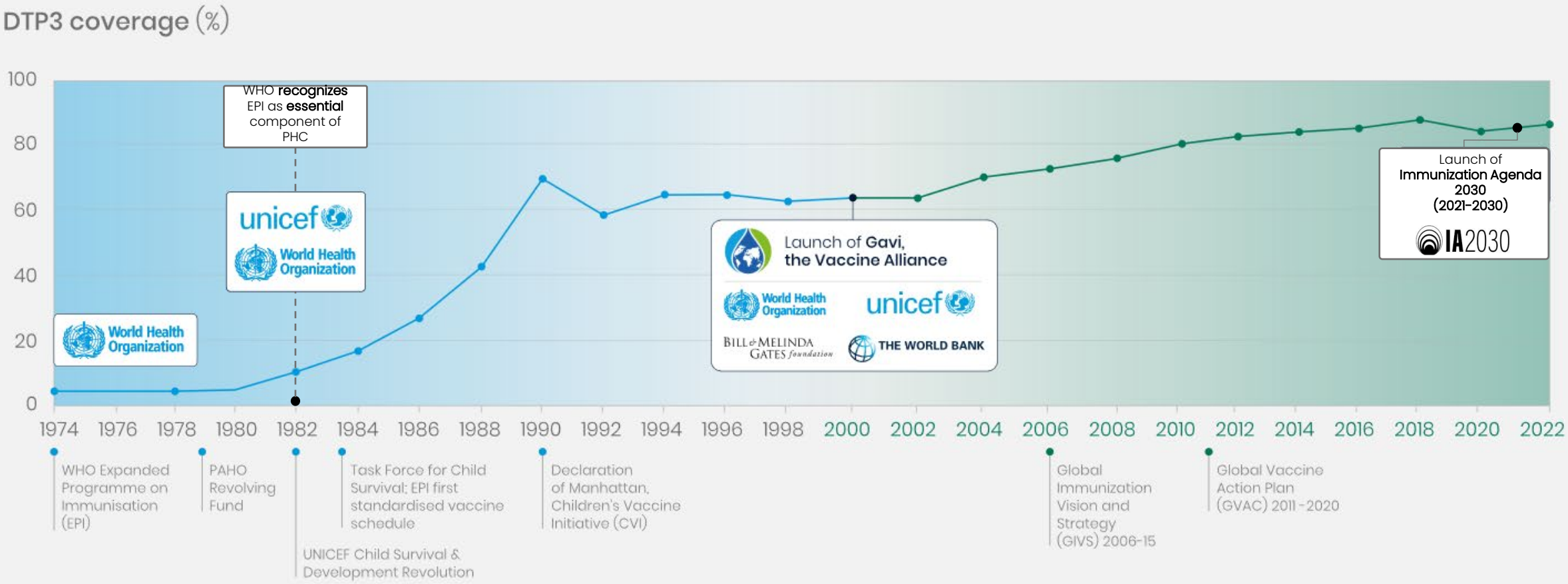
World Health Organization | IVB

Agenda

1. The 50th EPI anniversary & “Humanly Possible” campaign
2. Analysis scope
3. Methods
4. Results
5. Q&A and discussion with NVAC

The 50th EPI anniversary & “Humanly Possible” campaign

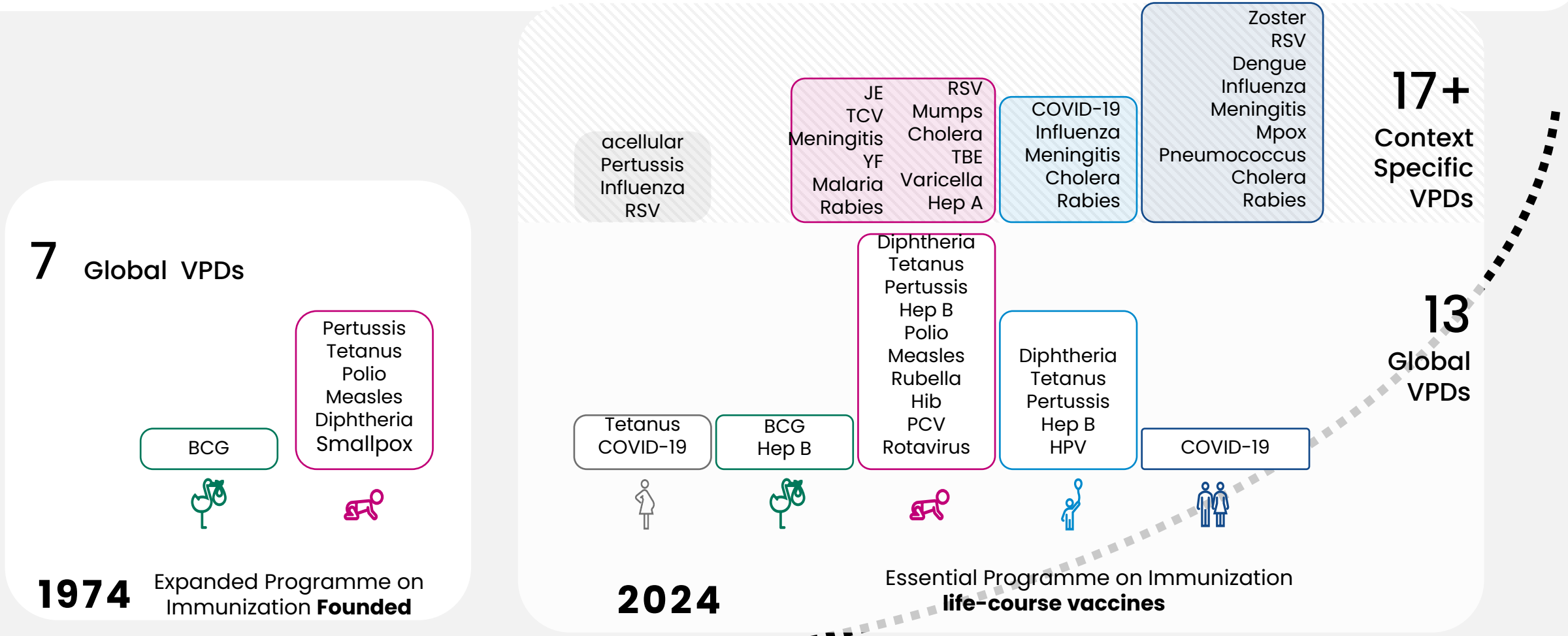
Over these 50 years, immunization programmes around the world have driven toward equity and access as a foundation of PHC



Note: DTP3 coverage in 1974 based on estimates from Keja K, Chan C, Hayden G, Henderson RH. Expanded programme on immunisation. World Health Stat Q. 1988;41(2):59-63. PMID: 3176515. DTP3 coverage from 1980 onwards based on WUENIC estimates, July 2023.

The #vaccine preventable diseases has massively expanded

F*rom 7 VPDs in 1974…… to >13 in 2024*



Note: *BCG: bacillus Calmette–Guérin; Hib: Haemophilus influenzae type b; HPV: human papillomavirus; JE: Japanese Encephalitis; PCV: pneumococcal conjugate vaccine; RSV: respiratory syncytial virus; TBE: Tick-Borne Encephalitis; TCV: typhoid conjugate vaccine; YF: yellow fever.

EPI@50 & 2024 World Immunization Week

Global immunization efforts have saved at least 154 million lives over the past 50 years

World Health Organization unicef Gavi BILL & MELINDA GATES foundation

WHO, UNICEF, Gavi, and Bill & Melinda Gates Foundation launch "Humanly Possible" campaign to scale up vaccination programmes around the world during World Immunization Week 2024

MEDIA CONTACTS

WHO Media Team
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Launch of "Humanly Possible" campaign

- Theme of non-branded/White Label campaign
- Coordinated through IA2030, across partners (WHO, UNICEF, Gavi, BMGF)
- The worldwide communication campaign calls on world leaders to advocate, support and fund vaccines and the immunization programmes
- Reaffirming their commitment to public health, while celebrating one of humanity's greatest achievements.

For more information:
https://www.worldimmunizationweek.org/

EPI@50 analysis published in the Lancet on 2 May 2024

Contribution of vaccination to improved survival and health: modelling 50 years of the Expanded Programme on Immunization

Andrew J Shattock, Helen C Johnson, So Yoon Sim, Austin Carter, Philipp Lambach, Raymond C W Hutubessy, Kimberly M Thompson, Kamran Badizadegan, Brian Lambert, Matthew J Ferrari, Mark Jit, Han Fu, Sheetal P Silal, Rachel A Hounsell, Richard G White, Jonathan F Mosser, Katy A M Gaythorpe, Caroline L Trotter, Ann Lindstrand, Katherine L O'Brien, Naor Bar-Zeev

Summary

Background WHO, as requested by its member states, launched the Expanded Programme on Immunization (EPI) in 1974 to make life-saving vaccines available to all globally. To mark the 50-year anniversary of EPI, we sought to quantify the public health impact of vaccination globally since the programme's inception.

Methods In this modelling study, we used a suite of mathematical and statistical models to estimate the global and regional public health impact of 50 years of vaccination against 14 pathogens in EPI. For the modelled pathogens, we considered coverage of all routine and supplementary vaccines delivered since 1974 and estimated the mortality and morbidity averted for each age cohort relative to a hypothetical scenario of no historical vaccination. We then used these modelled outcomes to estimate the contribution of vaccination to globally declining infant and child mortality rates over this period.

Findings Since 1974, vaccination has averted 154 million deaths, including 146 million among children younger than 5 years of whom 101 million were infants younger than 1 year. For every death averted, 66 years of full health were gained on average, translating to 10·2 billion years of full health gained. We estimate that vaccination has accounted for 40% of the observed decline in global infant mortality, 52% in the African region. In 2024, a child younger than 10 years is 40% more likely to survive to their next birthday relative to a hypothetical scenario of no historical vaccination. Increased survival probability is observed even well into late adulthood.

Interpretation Since 1974 substantial gains in childhood survival have occurred in every global region. We estimate that EPI has provided the single greatest contribution to improved infant survival over the past 50 years. In the context of strengthening primary health care, our results show that equitable universal access to immunisation remains crucial to sustain health gains and continue to save future lives from preventable infectious mortality.

Analysis scope

EPI 50-year impact analysis

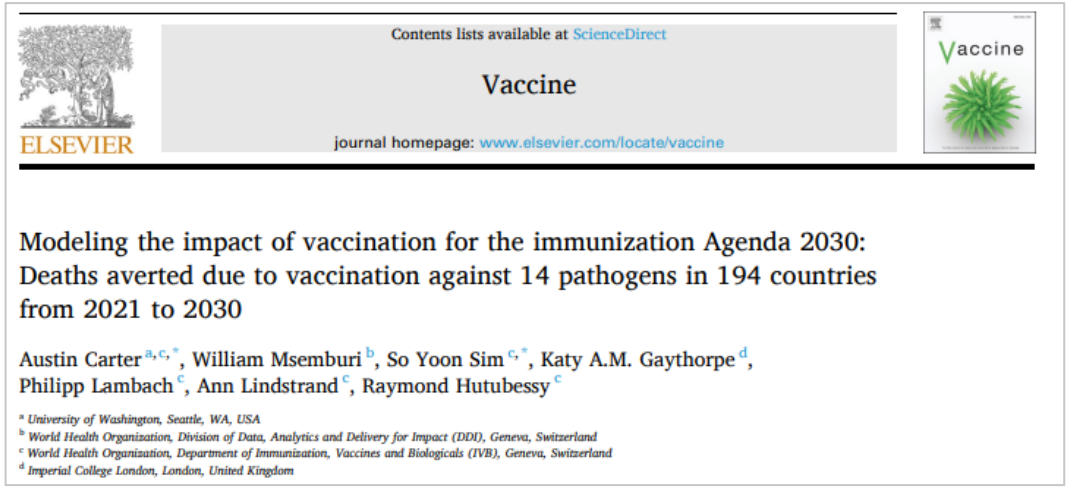
- Historical public health impact of vaccination for pathogens within EPI
  - **Time-frame:** 50 years (June 1974- May 2024)
  - **Country scope:** global (194 countries)
  - **Pathogens scope:** 14 vaccine preventable diseases
    - 11 from 13 global VPDs (diphtheria, Haemophilus influenzae type B, hepatitis B, measles, pertussis, poliomyelitis, rotavirus, rubella, Streptococcus pneumoniae, tetanus, and tuberculosis)
    - 3 from 17 context-specific VPDs (Japanese encephalitis, Neisseria meningitidis A, and yellow fever)

- Uses a framework developed by WHO, first used for IA2030 analysis
  - **Counterfactual:** no vaccination since 1974
  - **Metric:** Calendar year of impact
  - **Models:** VIMC, external, WHO-developed, Geographic and temporal extrapolation
  - **Outcomes:** deaths averted, years of life gained, years of full health gained (DALYs averted), proportion of infant mortality reduction attributable to vaccination

- Goal of the analysis
  - Quantify the impact of vaccination in the last 50 years based on a solid scientific analysis
  - Conservative approach, robust minimum

Previous analysis: Immunization Agenda 2030 (IA2030) Impact Goal indicator 1.1

1. Scientific analysis



Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

ELSEVIER

Modeling the impact of vaccination for the immunization Agenda 2030: Deaths averted due to vaccination against 14 pathogens in 194 countries from 2021 to 2030

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[d] Imperial College London, London, United Kingdom

2. Advocacy

New UN-led global immunization push aims to save more than 50 million lives

© UNICEF/Jannatul Mawa | A young boy is vaccinated against measles and rubella during a national vaccination campaign in Bangladesh.

3. Monitoring & Evaluation

IG1: Prevent Disease

1.1 50 million future deaths averted globally from vaccination delivered by 2030

Cumulative number of deaths averted

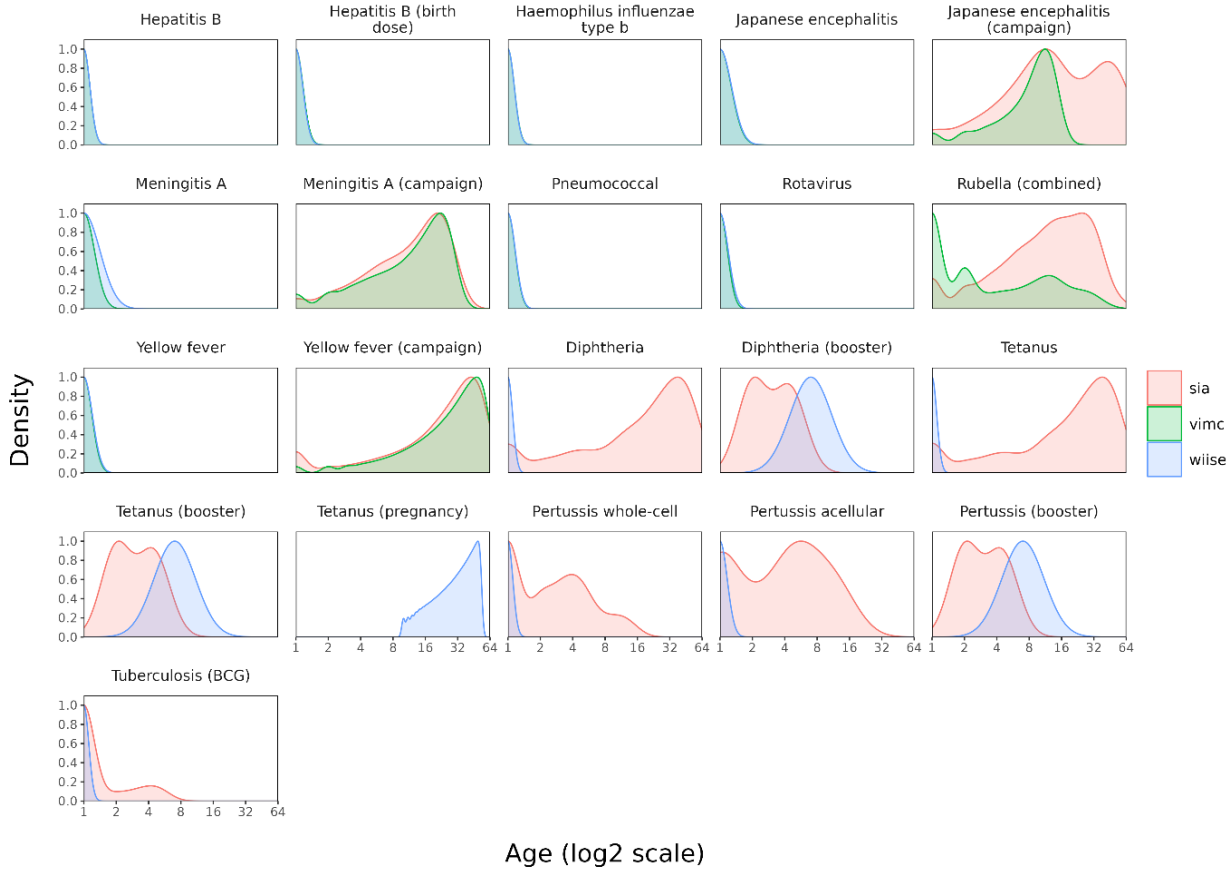
8M — 50M

EXPLORE DATA

Cumulative future deaths averted globally as of 2022 to be on track towards 2030 target

Methods

Coverage estimates



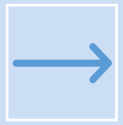
Age distribution at vaccination, by antigen, data source

Data sources

- WHO Immunization Dashboard (for routine immunization)
- WHO Supplementary Immunization Activities database (for SIA)
- WHO Polio Information System (for SIA)
- Vaccine Impact Modelling Consortium (VIMC) coverage estimates (for RI and SIA)

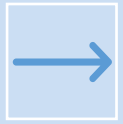
Models

Three model forms



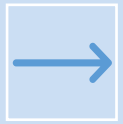
Dynamic transmission models

2 diseases: measles (ensemble of n=2) and polio



A suite of VIMC transmission models

8 diseases: Hib, hepB, JE, IPD, rotavirus, rubella, mening A and YF



Upgraded static disease burden models

4 diseases: diphtheria, tetanus, pertussis, and TB

Models

Three model forms

- Dynamic transmission models
  2 diseases: measles (ensemble of n=2) and polio
- A suite of VIMC transmission models
  8 diseases: Hib, hepB, JE, IPD, rotavirus, rubella, mening A and YF
- Upgraded static disease burden models
  4 diseases: diphtheria, tetanus, pertussis, and TB

Extended by geographical imputation and temporal extrapolation

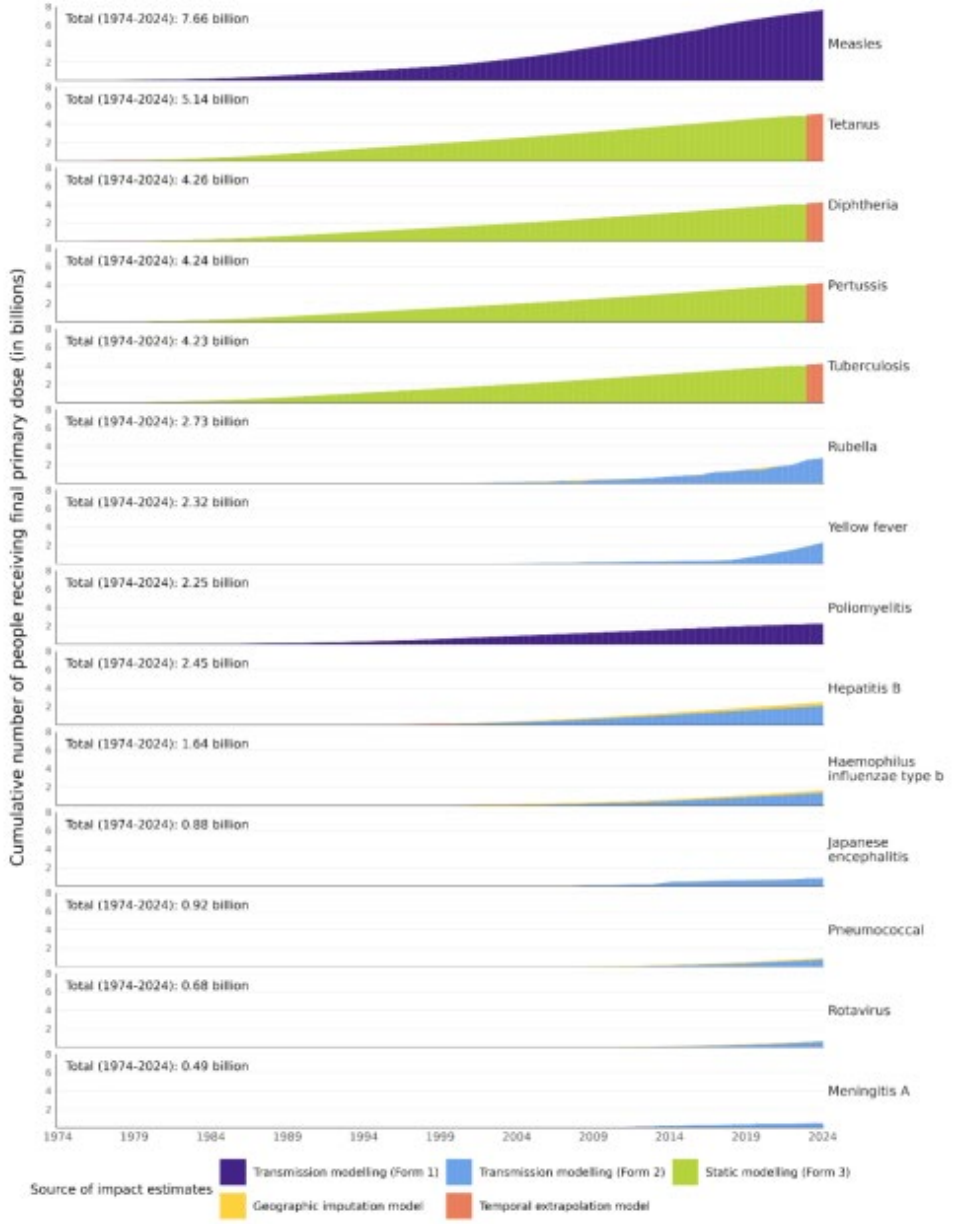


Figure S6 The relative contribution of vaccine impact estimation methods.

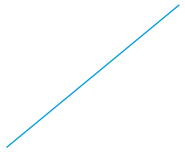
Temporal extrapolation: Not every dose is equal

Reflecting the reality:

- Vaccines have indirect benefits
- When vaccines prevent transmission → protect unvaccinated too
- The total benefit increases but the direct individual marginal benefit decreases

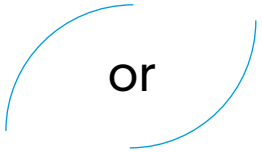
Our models:

- Fitted four different models to observed data on cumulative impact vs. cumulative coverage

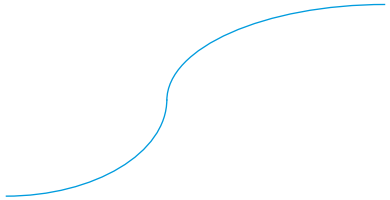


Linear: Each dose is equal, coverage has no effect

or



Logarithmic or Exponential: Each additional dose has lesser OR greater effect



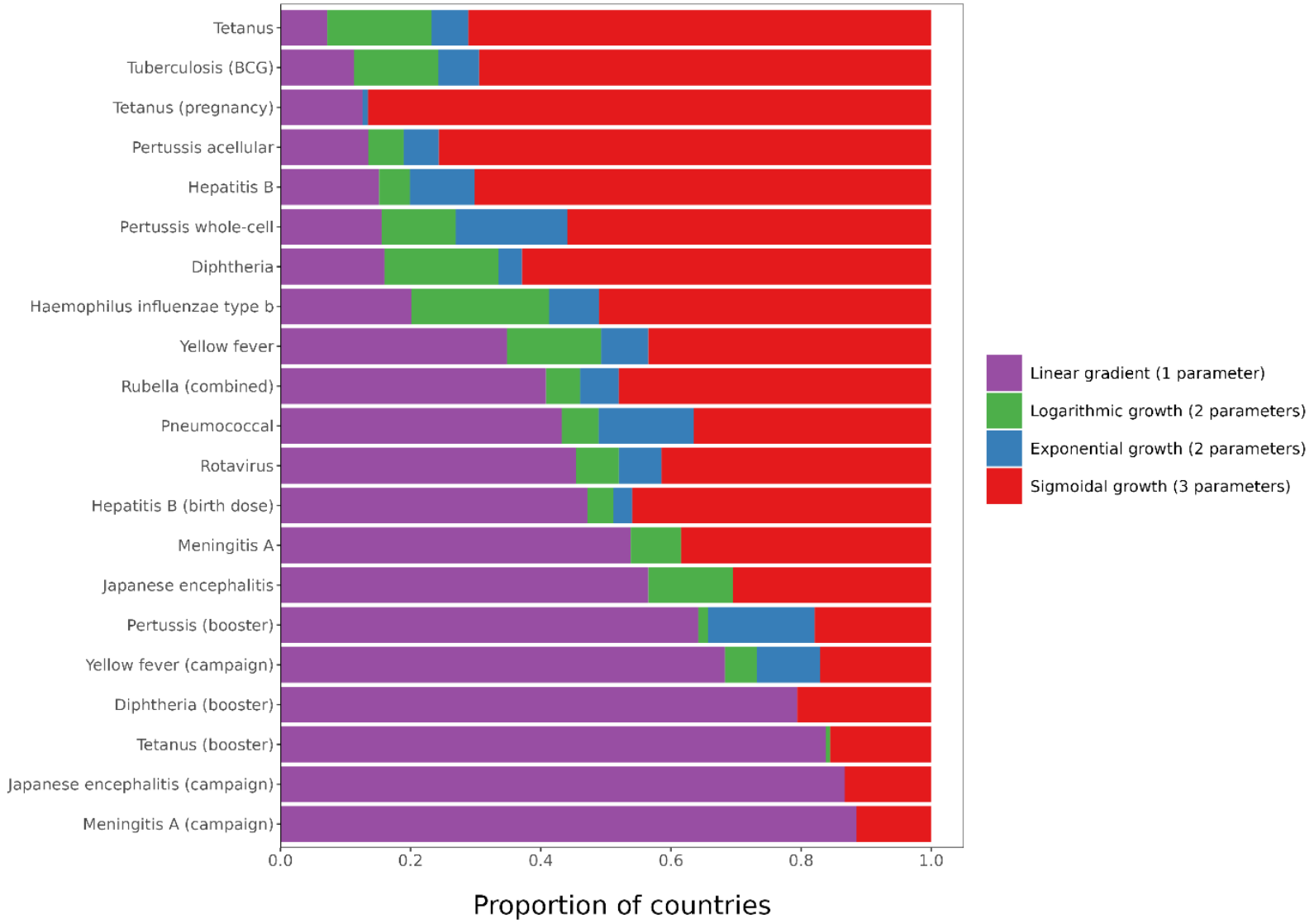
Sigmoidal: The programme takes time to become established but eventually each dose becomes less impactful

Model variation:
Each place and time look different and are tricky to predict but at the cumulative space, the relationship stabilizes

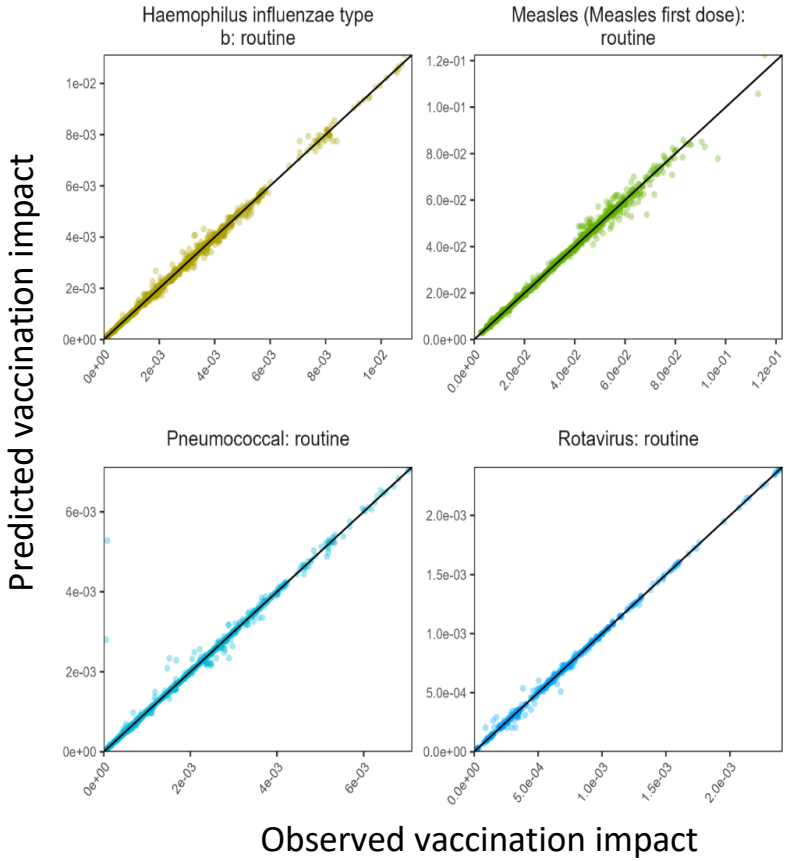
- Best fitting models were selected using the corrected Akaike Information Criterion (AICc) → ensures we are parsimonious

Temporal extrapolation: Not every dose is equal

Proportion of countries with each functional form by disease-vaccine-activity



Imputation for gaps in place and time



Model validation: predicted vs observed impact

- To impute impact in countries for which we had no results, we estimated the impact of predictors that give rise to differences between countries
- Fitted regression models to each country, for each vaccine activity, using an AICc model selection approach
- Predictor variables included:
  - Vaccination coverage, up to 4 years lag
  - Gini coefficient (inequality)
  - Health spending
  - Malnutrition
  - Maternal mortality
  - Access to clean water and sanitation, etc.
- The fitted time series regression models were used to impute vaccination impact in countries for which we did not have estimates
- Coefficients of correlation were sampled for selected predictors from the fitted distributions of neighboring countries
- *We plan to extend these methods to help strengthen vaccine program impact*

Results

Results

- Vaccination has averted 154 million deaths since EPI launch in 1974.
- Measles accounted for 60% of the total benefits (94 million of 154 million deaths averted).
- The majority of deaths averted are in children under 5. More than 9 billion years of life have been saved.
- Vaccination also prevents the long-term consequences associated with severe disease, especially polio. 10.2 billion years of full health have been gained (DALYs averted).

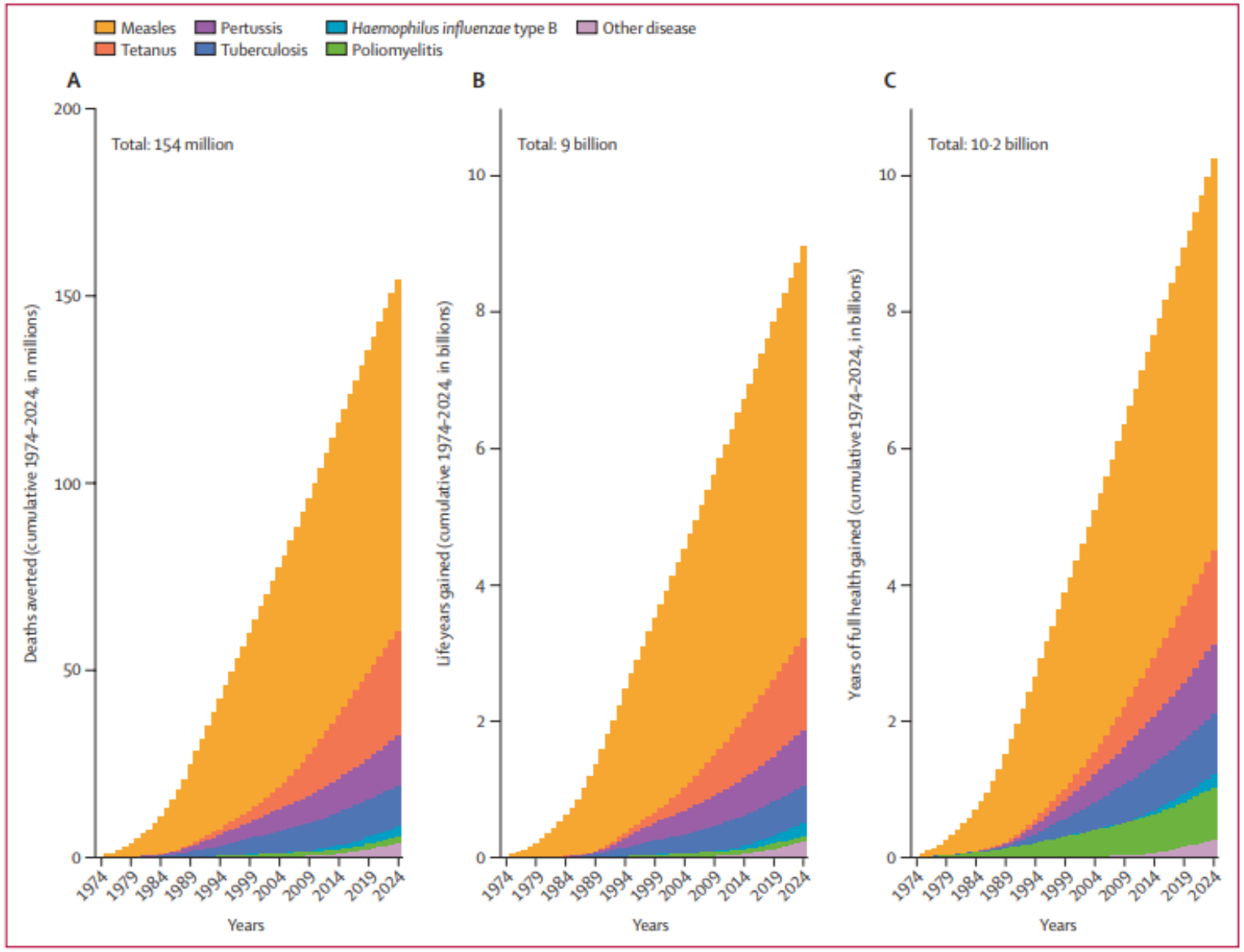


Figure: Deaths averted, years of life saved, and years of full health gained due to vaccination

Results

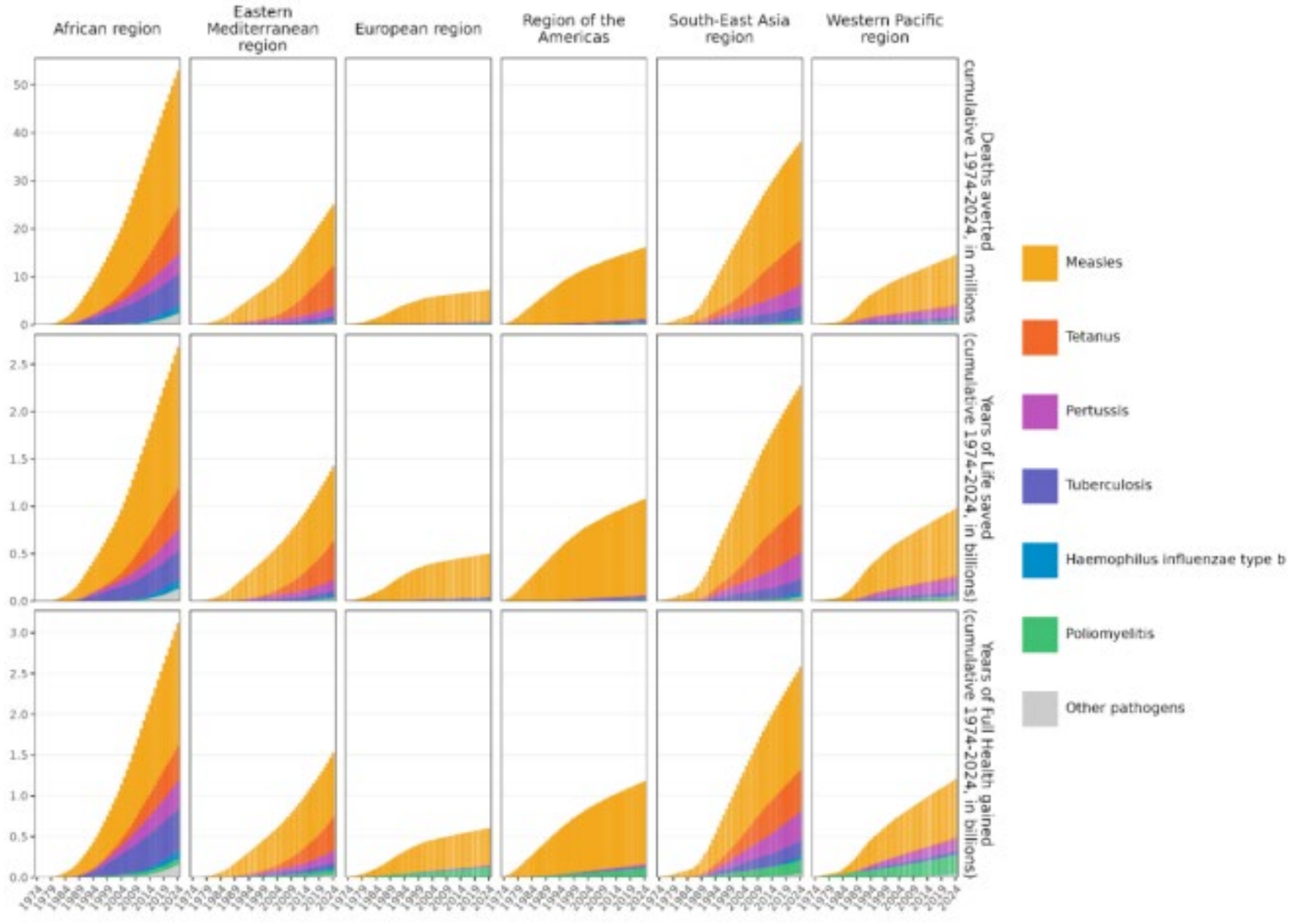


Figure: Deaths averted, years of life saved, years of full health gained due to vaccination by WHO region

Results

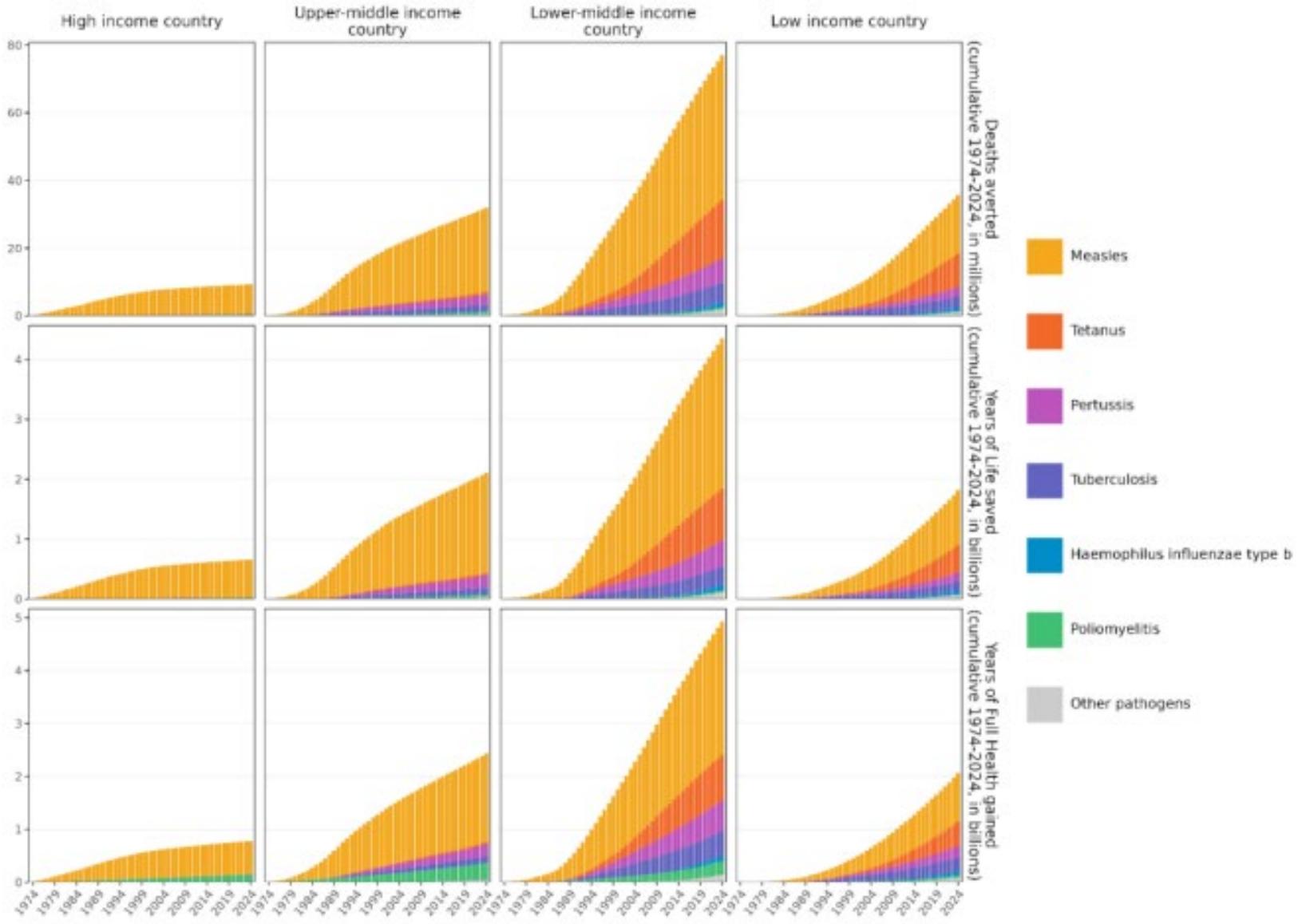


Figure: Deaths averted, years of life saved, years of full health gained due to vaccination by World Bank income status (as classified in 2024)

Results

- Infant mortality was falling before the 1974 launch of EPI and continues to fall due to multiple causes
- Between 1974 and 2024, 40% of the reduction in infant mortality is attributable to vaccination
- Consider this plot decade by decade, in context of large-scale interventions
- Contribution of non-vaccine factors has increased over time and is becoming more important.

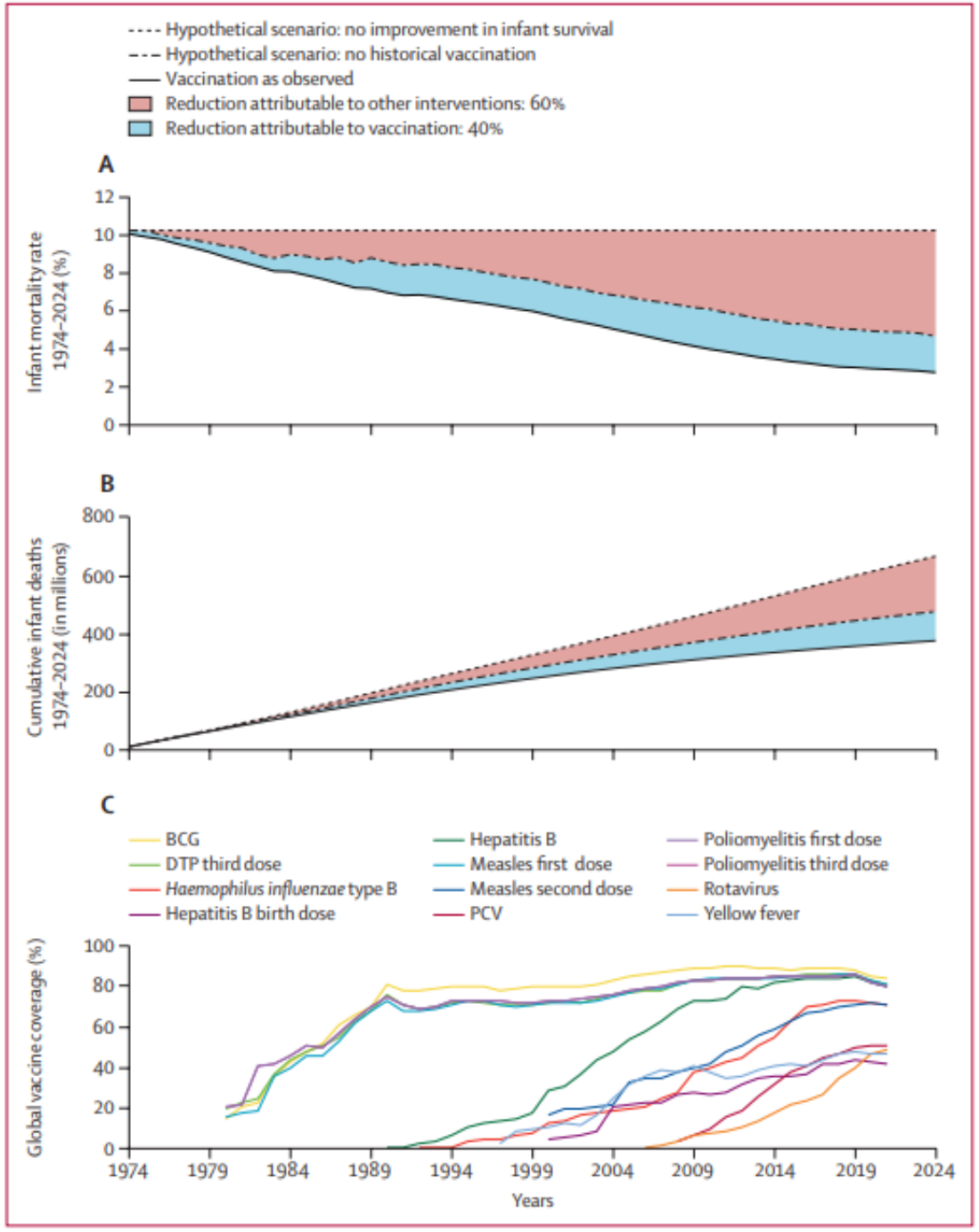


Figure: Infant mortality 1974–2024, the proportional effect of vaccination on overall decreasing trends, and global vaccine coverage

Results

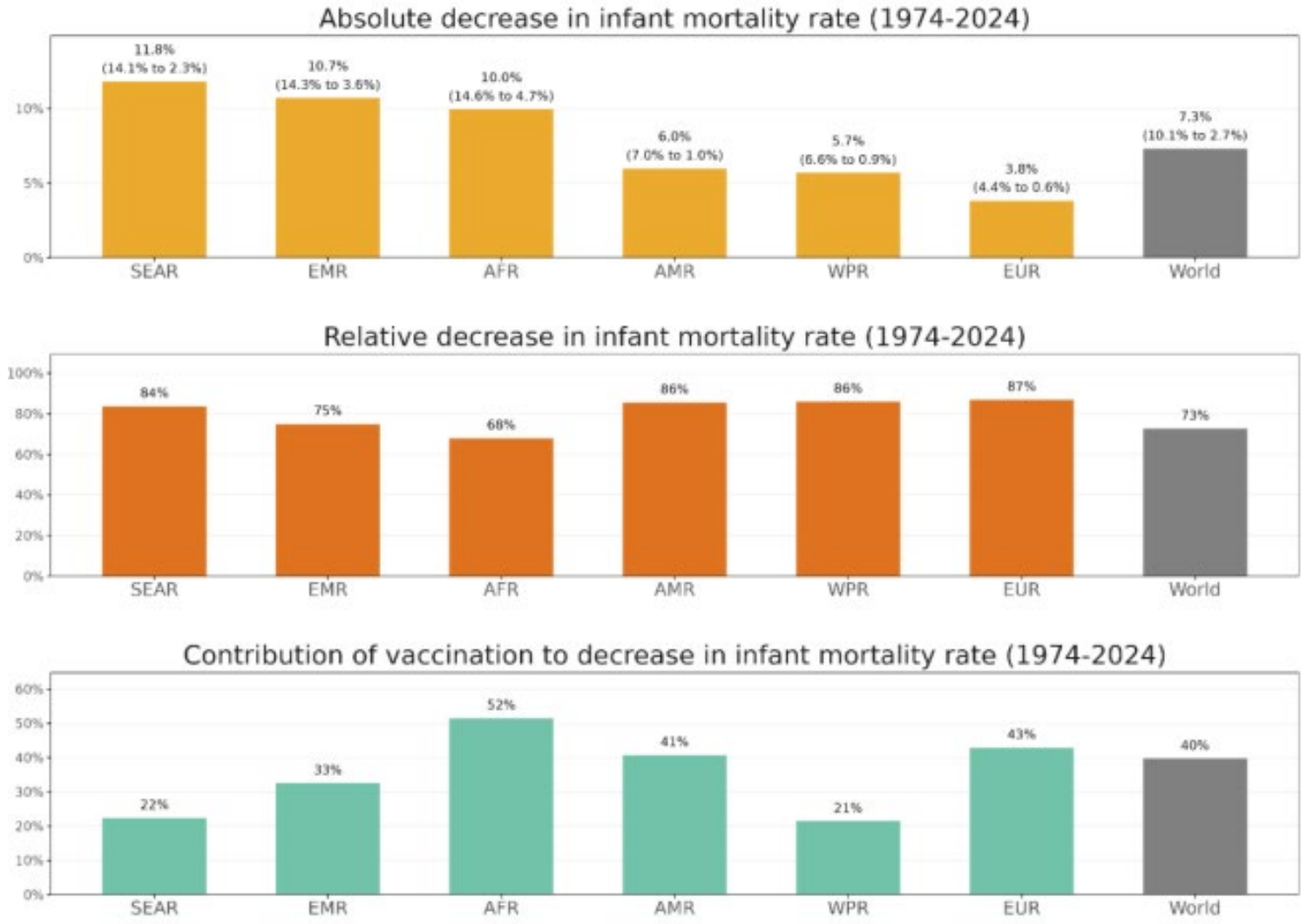


Figure S3 Absolute and relative decrease in infant mortality and contribution of vaccination to the decrease in infant mortality, by region, 1974 – 2024. Regional acronyms: AFR = African region, AMR = Region of the Americas, EMR = Eastern Mediterranean region, EUR = European region, SEAR = South-East Asia region, WPR = Western Pacific regio

Results

Increase in survival probability:

- In 2024, a child at any age under 10 years is at least 40 percent more likely to survive to their next birthday compared to a hypothetical scenario of no vaccination in the past 50 years, globally
- Protective benefits continue past the age of 50, globally

Greatest absolute benefits in Eastern Mediterranean and African Regions (approaching 2.5 percentage point reduction in infant mortality)

Greatest relative benefits in the Western Pacific, Americas and Eastern Mediterranean Regions, up until early adulthood

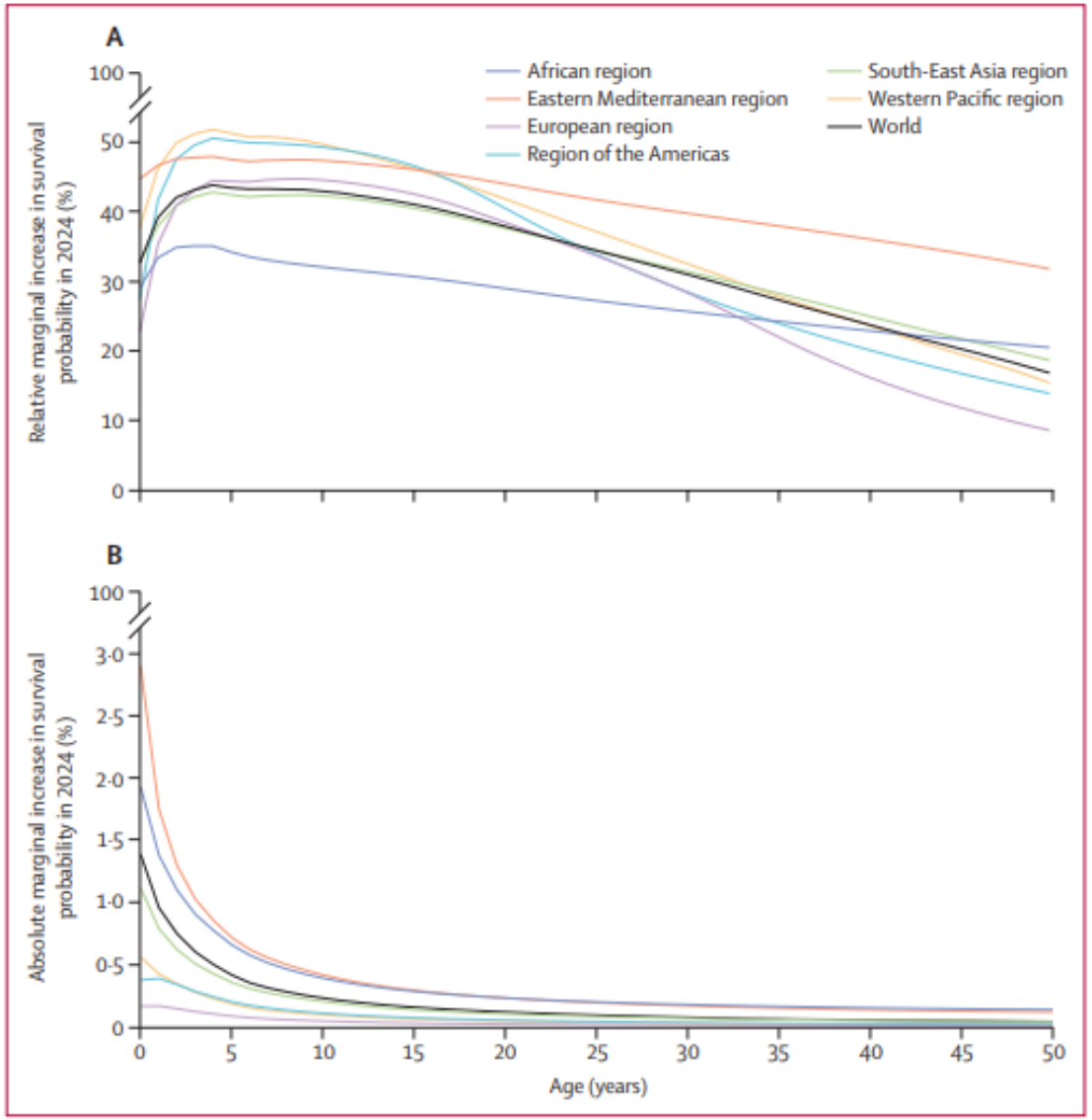


Figure: Marginal increase in survival probability in 2024 by year of life and WHO Region, compared with the hypothetical scenario of no historical vaccination
Relative represents proportional percent change in this baseline risk.

Conclusions

- Since 1974, EPI has saved over 154 million lives (of whom 146M children, 101M infants)

- Measles vaccination accounted for 60% of this benefit and is the single greatest contributor in all settings, preventing ~94 million deaths and saved over 5.7 billion years of life

- For every life saved, 66 years of full health were gained (disability-adjusted life years averted) on average, translating to 10.2 billion years of full health gained.

- Prevention of poliomyelitis was especially prominent in disability averted

- Vaccination has accounted for 40% (52% in AFR) of the reduction in infant mortality since 1974.

- In 2024, a child at any age under-10 is 40% more likely to survive to their next birthday relative to a hypothetical scenario of no historical vaccination.

- This increased survival probability is observed even well into late adulthood.

Messages from “Humanly Possible” campaign

We can make it possible for everyone to benefit from the life-saving power of vaccines by:

- Ensuring vaccines are high on the priority list for governments in all countries;
- Advocating for vaccines to be an integral part of the planning and investment of health care across the life course;
- Making sure immunization programmes are adequately financed and resourced in all countries;
- Accelerating research and innovation that advances access to, and support for, vaccines;
- Speaking out on the impact of vaccinations locally, nationally and globally

More information: https://www.who.int/campaigns/world-immunization-week/2024

Resources

- **Article published on the Lancet:**
  https://doi.org/10.1016/S0140-6736(24)00850-X

- **Open-source code library (WHO GibHub repository):**
  https://github.com/WorldHealthOrganization/epi50-vaccine-impact

- **DOI for WHO GitHub repository:**
  https://zenodo.org/doi/10.5281/zenodo.10974443

- **FAQ for study findings:**
  https://github.com/WorldHealthOrganization/epi50-vaccine-impact/blob/master/Frequently%20Asked%20Questions.pdf

- **Our World in Data:**
  https://ourworldindata.org/vaccines-children-saved

Thank you

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Saluting Global Immunization Efforts: 154+ Million Lives Saved!

Discussion

NVAC

Research Review: An Eye-Opening Study on Switching Arms Between COVID-19 Vaccine Doses

Dr. Marcel Curlin

NVAC

Effect of contralateral boosting on humoral responses to mRNA COVID-19 vaccination

Marcel Curlin, MD
Department of Medicine, Division of Infectious Diseases
Oregon Health and Sciences University
June 14th, 2024

Effect of contralateral boosting on humoral responses to mRNA COVID-19 vaccination

Experimental work

- Disclosures and Funding
- Terminology and abbreviations
- Experimental design
- Research Data
- Acknowledgments

Commentary

- Strengths and Limitations
- Interpretation
- Speculation on mechanism
- Recommendations

DISCLOSURES AND FUNDING

Disclosures - none

Funding

- MJ Murdock Charitable Trust
- OHSU Foundation
- NIH R01A1145835, P51OD011092, UL1TR002369

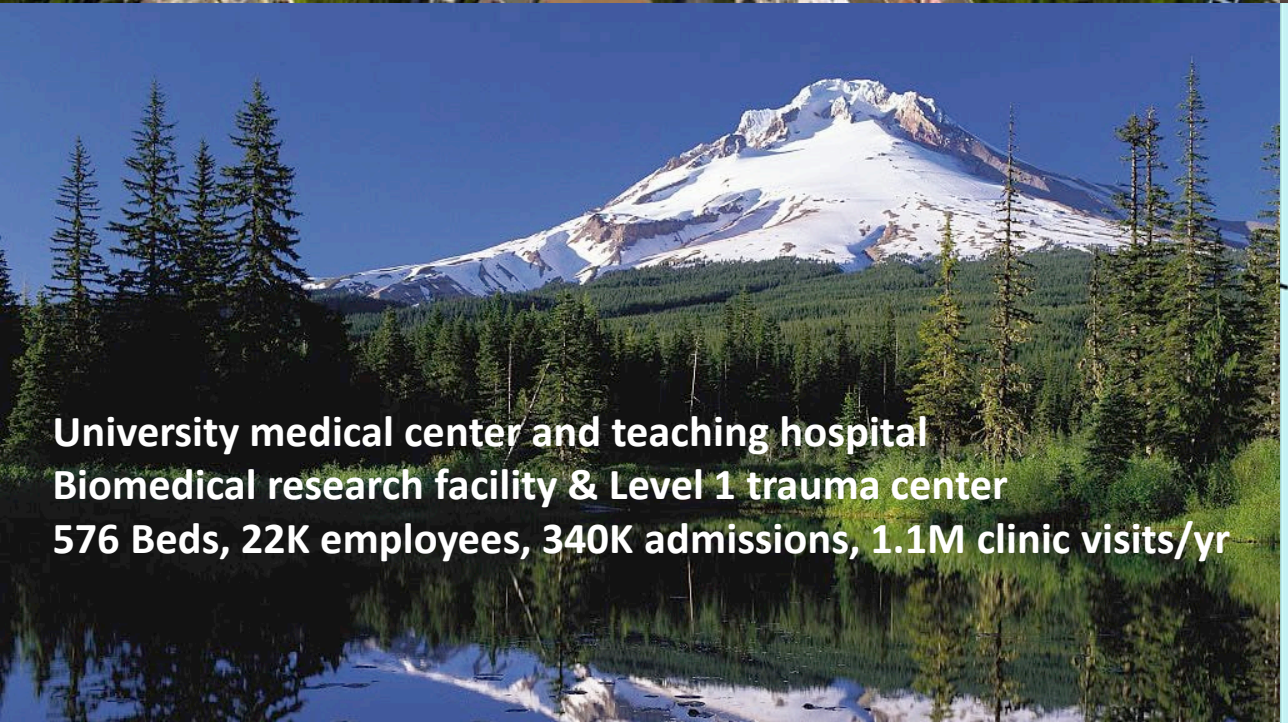
The funders had no role in the design, conduct or interpretation of this study

Research conducted with OHSU IRB approval and written informed consent by study participants

TERMINOLOGY AND ABBREVIATIONS

BAb	Binding antibodies
BNT162b2	Pfizer-BioNTech 1st generation COVID-19 vaccine
C19 study	OHSU COVID-19 serology study
HCW	Healthcare workers
NAb	Neutralizing antibodies
OHSU	Oregon Health & Sciences University
Ppt	Study participant
V1	Vaccine dose 1
W1	Wave 1 (sampling visit 1)

BACKGROUND - Oregon Health and Sciences University



University medical center and teaching hospital
Biomedical research facility & Level 1 trauma center
576 Beds, 22K employees, 340K admissions, 1.1M clinic visits/yr

Serves the region between Seattle & San Francisco

BACKGROUND - context

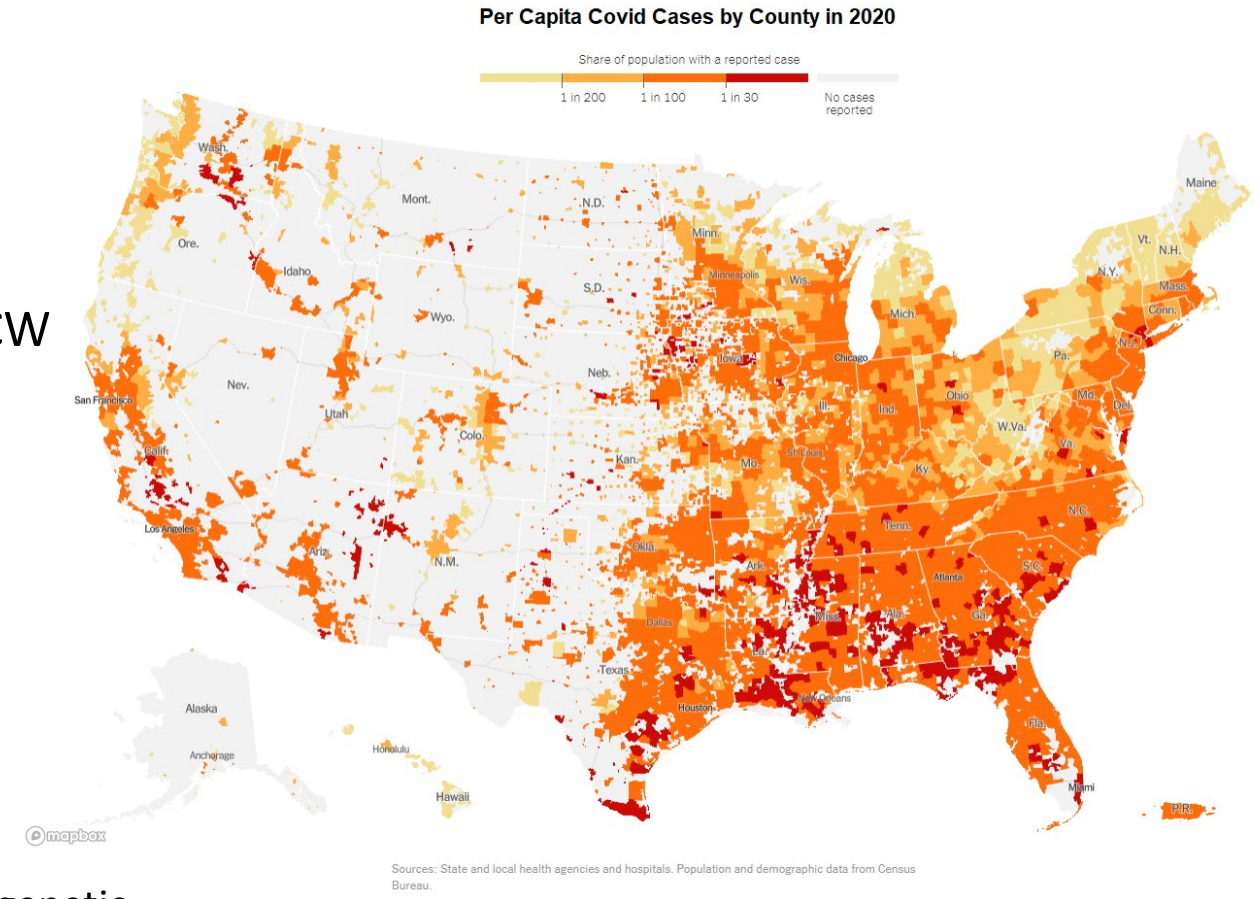
In 2020 new respiratory pandemic was sweeping through the country

New mRNA COVID-19 vaccines first available to HCW late 2020

- Pfizer, Moderna
- OHSU vaccinating ~1000 HCW per day

However, many fundamental knowledge gaps

- Seroprevalence of unrecognized infection
- Immune responses to vaccination
- Interaction between natural infection, vaccination, viral genetic evolution



BACKGROUND – C19 study

C-19 serology study - prospective cohort study of adult HCW receiving first-time COVID-19 vaccination

Objective: understand immune responses to COVID-19 vaccination and natural infection

Data collection and study procedures

- Demographics
- Vaccination and infection history
- Peripheral blood samples
- Vaccination with BNT162b2

A total of 2016 participants enrolled between Dec 2020 and March 2021

BACKGROUND – C19 study

C19 serology study

Wave 1 ***Wave 2*** ***Wave 3*** ***Wave 4*** ***Wave 5***
Ongoing

baseline *post-vaccine* *pre-boost* *post-boost*

OHSU vaccine rollout

Vaccination 1 & 2

Booster

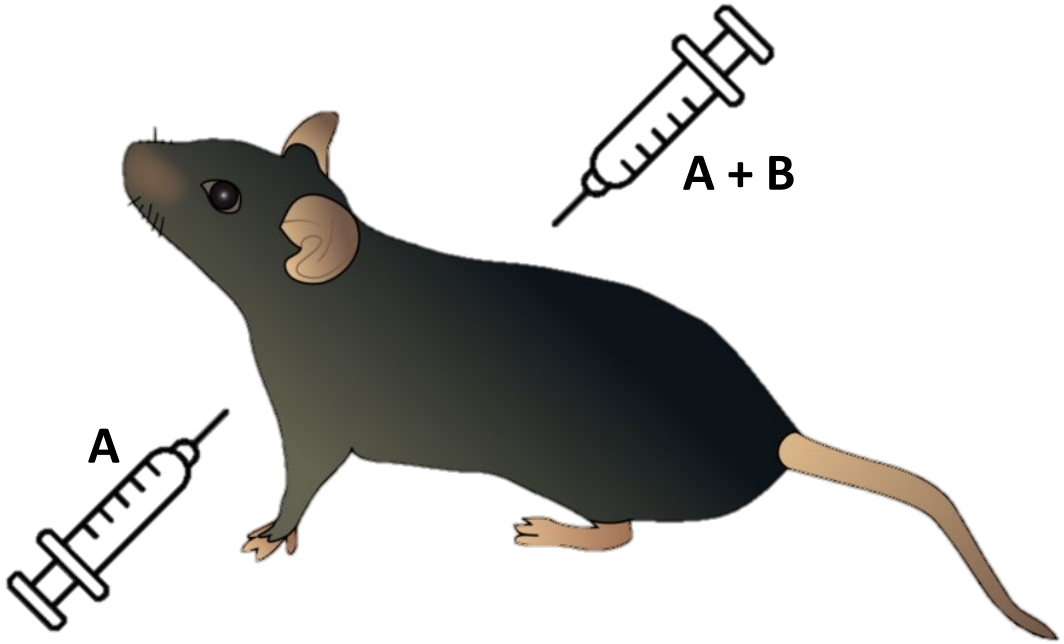
COVID-19 Epidemic, Oregon 2020-2021

ARM RANDOMIZATION - rationale

General assumption in medical practice that vaccine site selection does not matter.

However, antigen presentation in response to local exposure is regional

Animal studies: immunodominance during sequential vaccination can be broken by distributing site of vaccination (immunodominance, original antigenic sin, imprinting).



Sequential vaccination of mouse with antigen A followed later by antigens A + B. Heterotopic vaccination allows responses to both A and B at boosting.

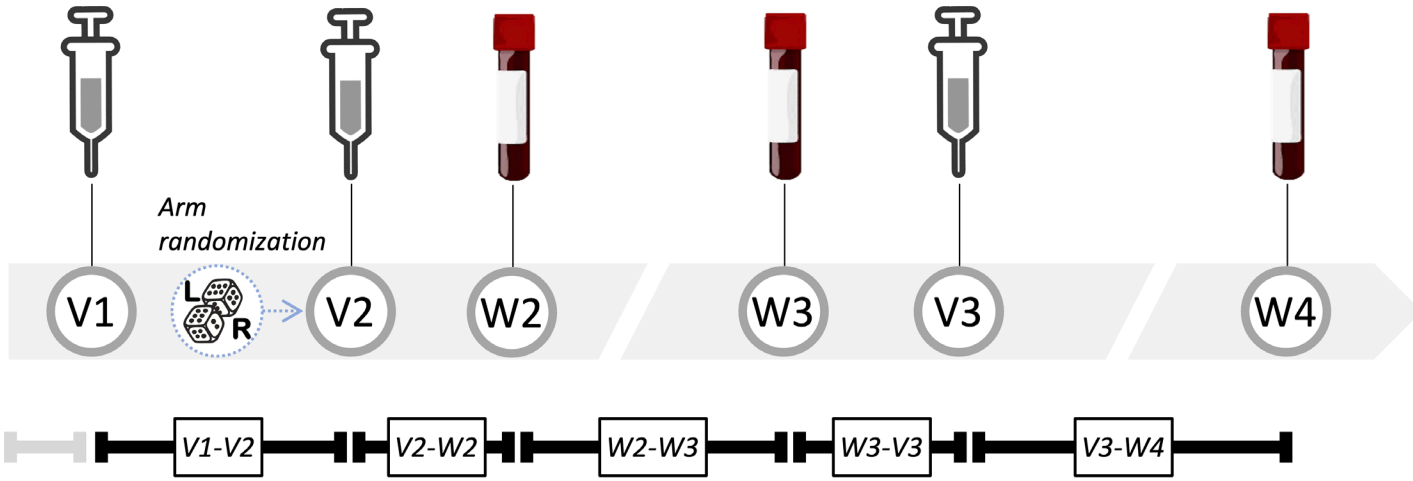
1. Kuraoka M, et al, Sci Immunol. 2022
2. Iro MA, et al. Lancet Infect Dis. 2015
3. Ziegler, EBioMedicine. 2023
4. Peck, FB Jr, Ind Med Surg. 1964

ARM RANDOMIZATION - methods

Pre-randomized each participant to ipsilateral or contralateral group

Offered enrollment into substudy at V2.
Group assignment revealed after enrollment.

Longitudinal measurement of antibody responses

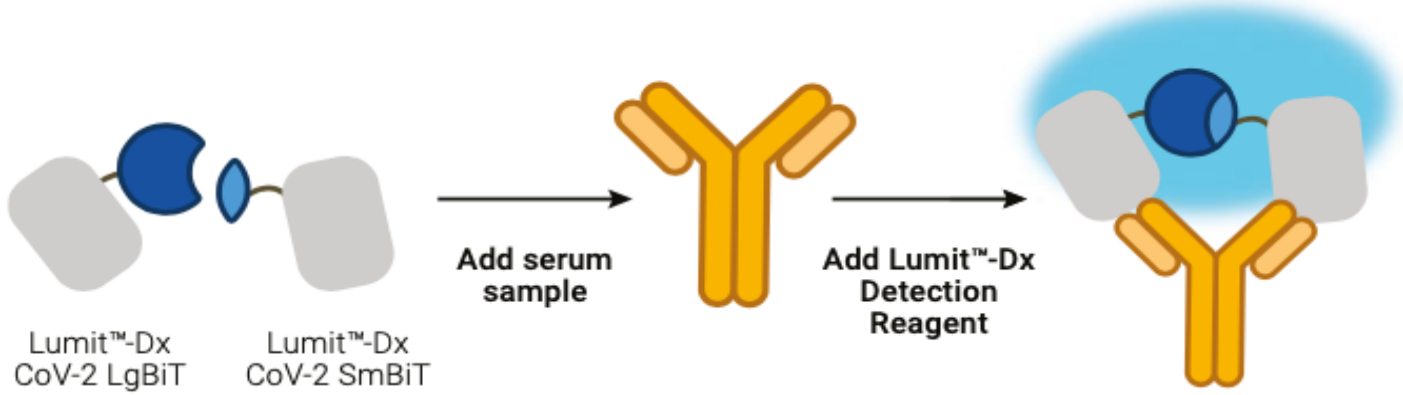


Timeline of vaccinations (V1-V3), arm-randomization, and study visits (W3-W4) for blood collection

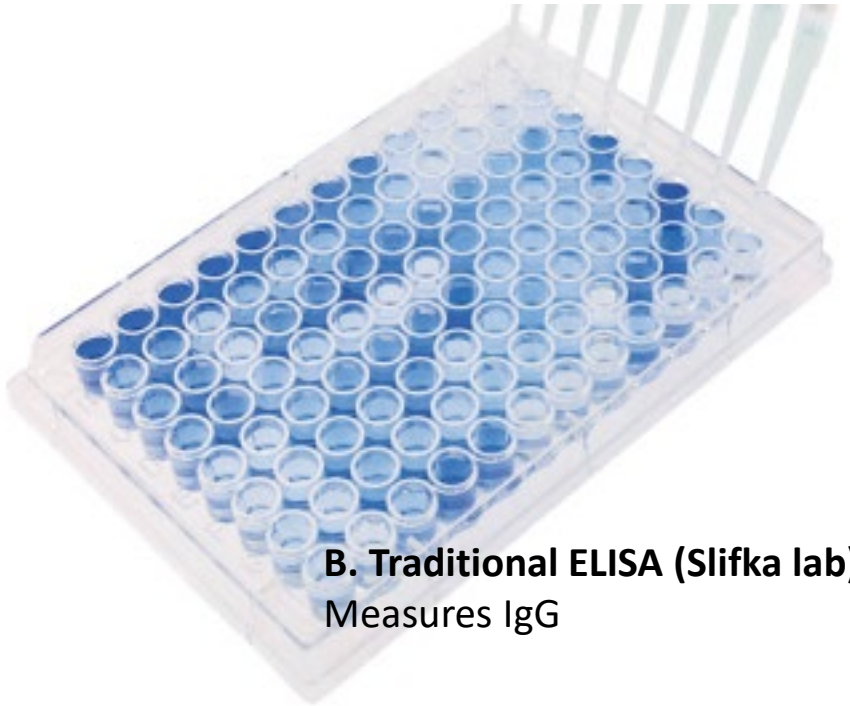
Analysis of three groups

- all ppts with information on arm usage
- all randomized ppts
- subset matched on gender, age, time intervals

ARM RANDOMIZATION - assays

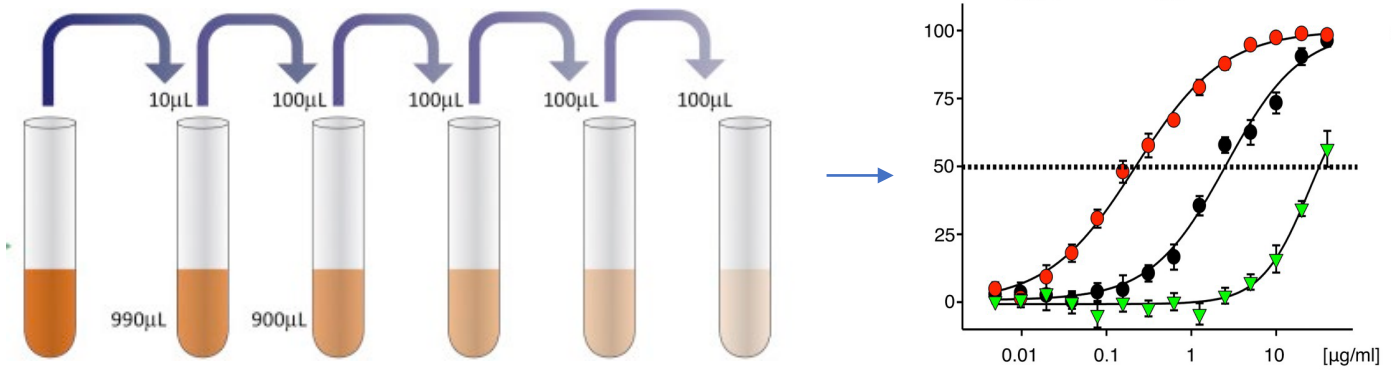


A. Lumit DX™ SARS-CoV-2 immunoassay (Promega – OHSU lab) – antibody binding produces chemiluminescence. Readout is in relative light units (RLU). Measures total Ig.

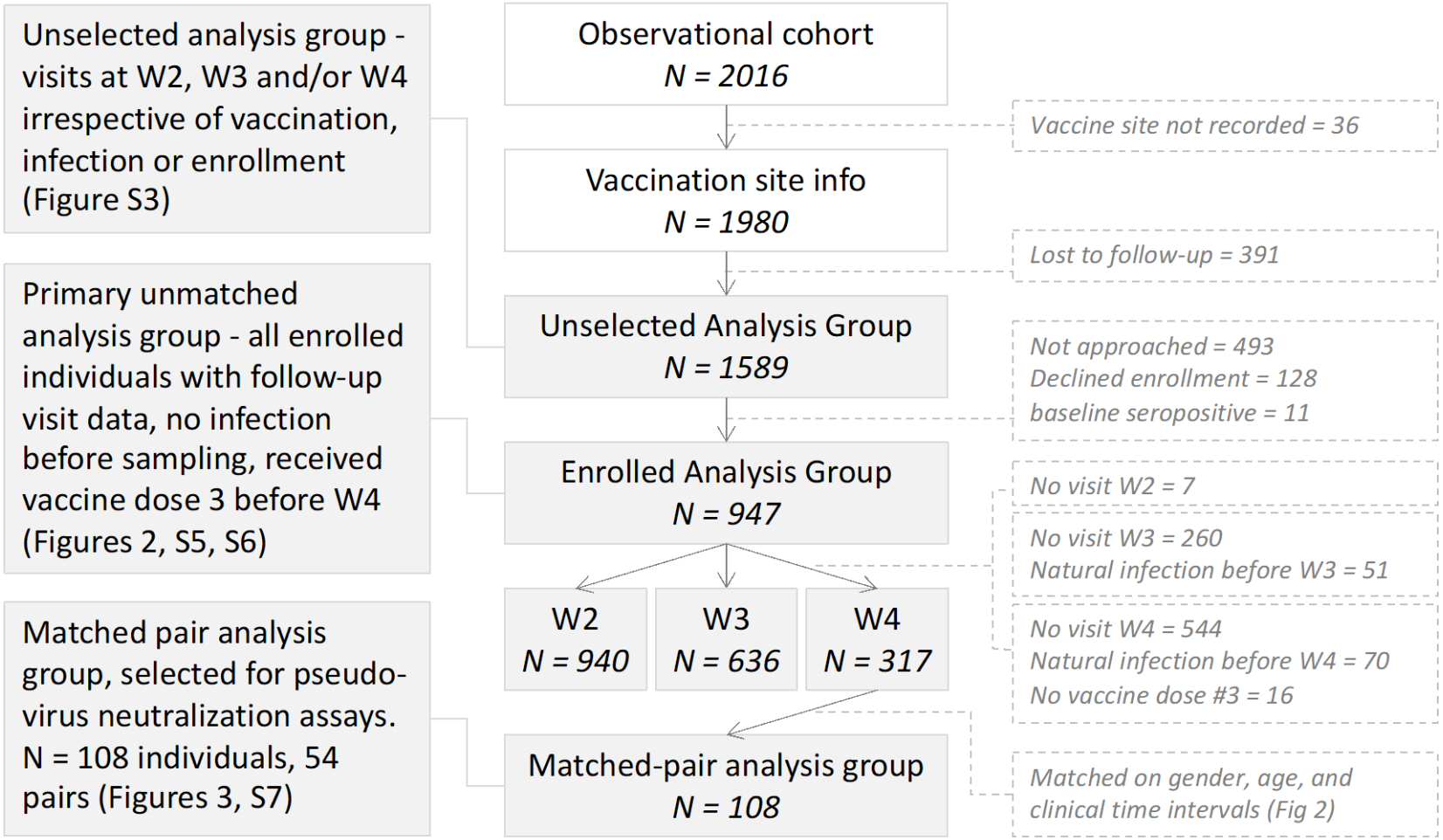


B. Traditional ELISA (Slifka lab)
Measures IgG

C. Pseudovirus neutralization
Montefiori lab



ARM RANDOMIZATION – enrollment and groups

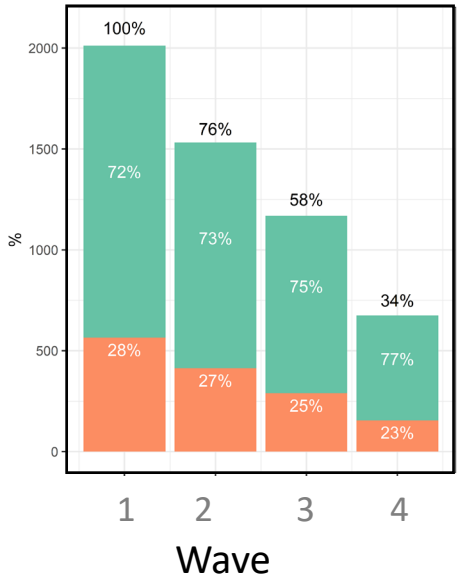


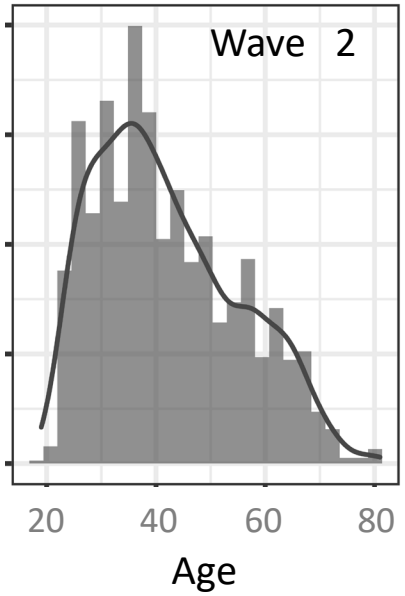
Group accruals

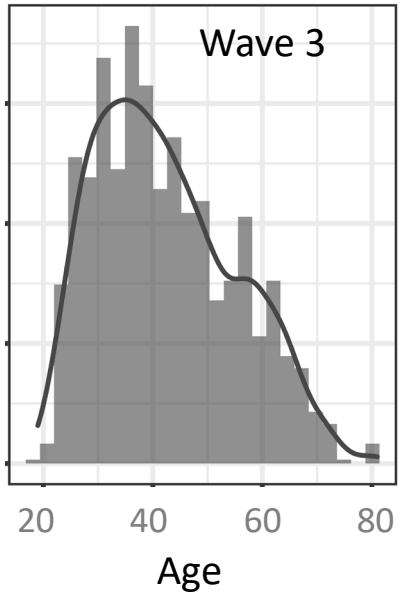
ARM RANDOMIZATION - demographics

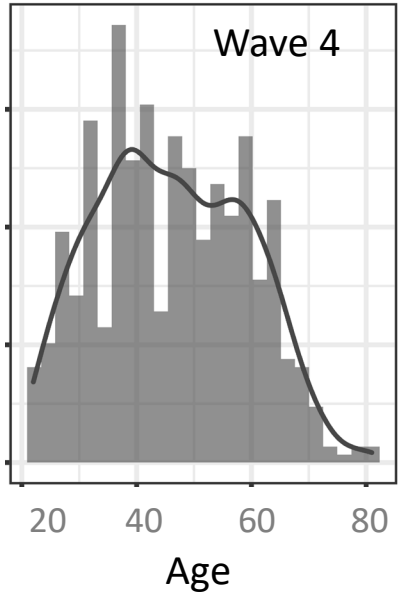
Demographics, enrollment and randomization

- More women than men
- Median age 40, range 19-81
- Proportions remained stable over time



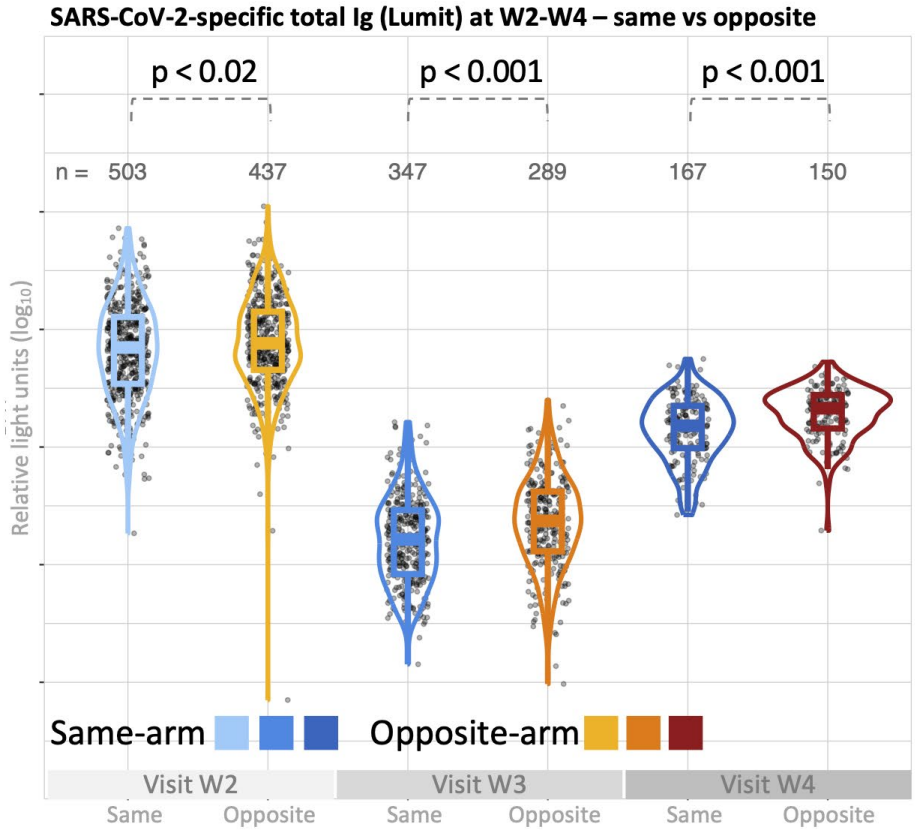


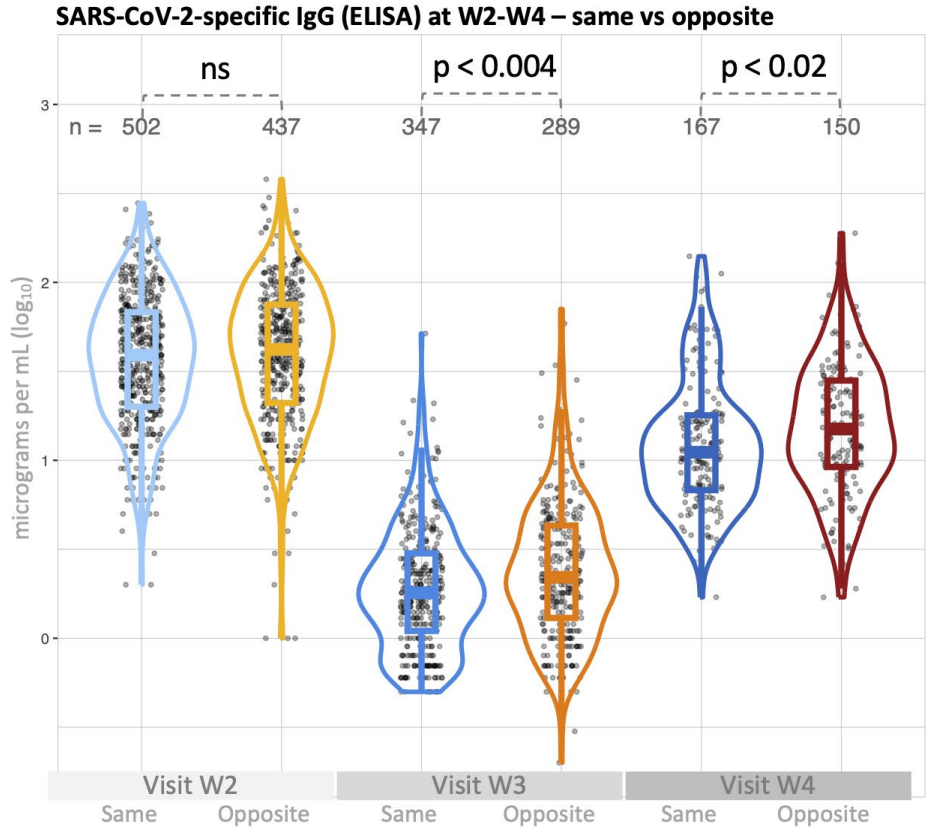




ARM RANDOMIZATION – immune responses

1. SARS-CoV2 BAb titers are higher in contralateral group.
2. Effect greater over time, particularly for IgG

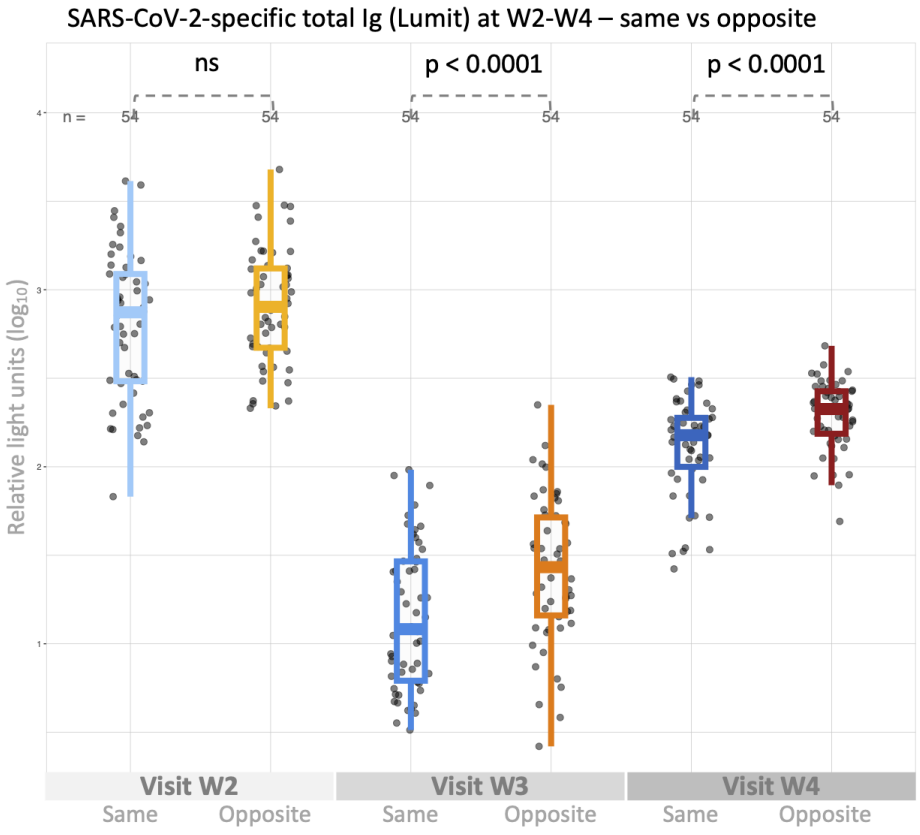


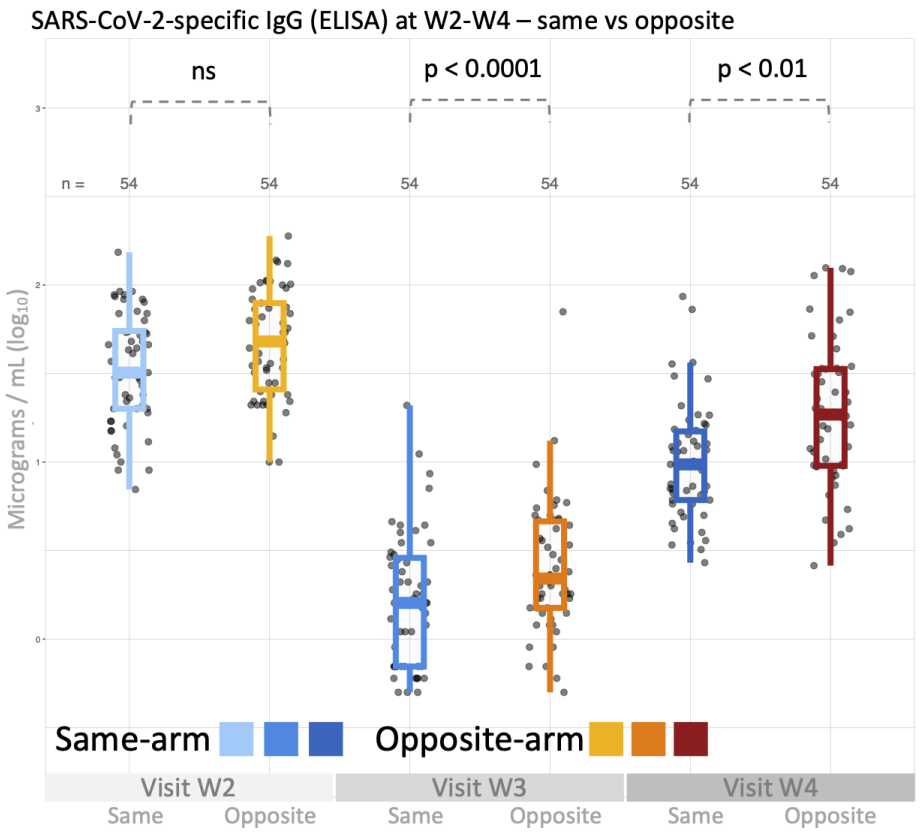


Log 10 COVID-19-specific BAb titers by treatment arm (same vs opposite) in the enrolled analysis group (N = 947)

ARM RANDOMIZATION – immune responses

1. SARS-CoV2 BAb titers are higher in contralateral group.
2. Effect greater over time, particularly for IgG

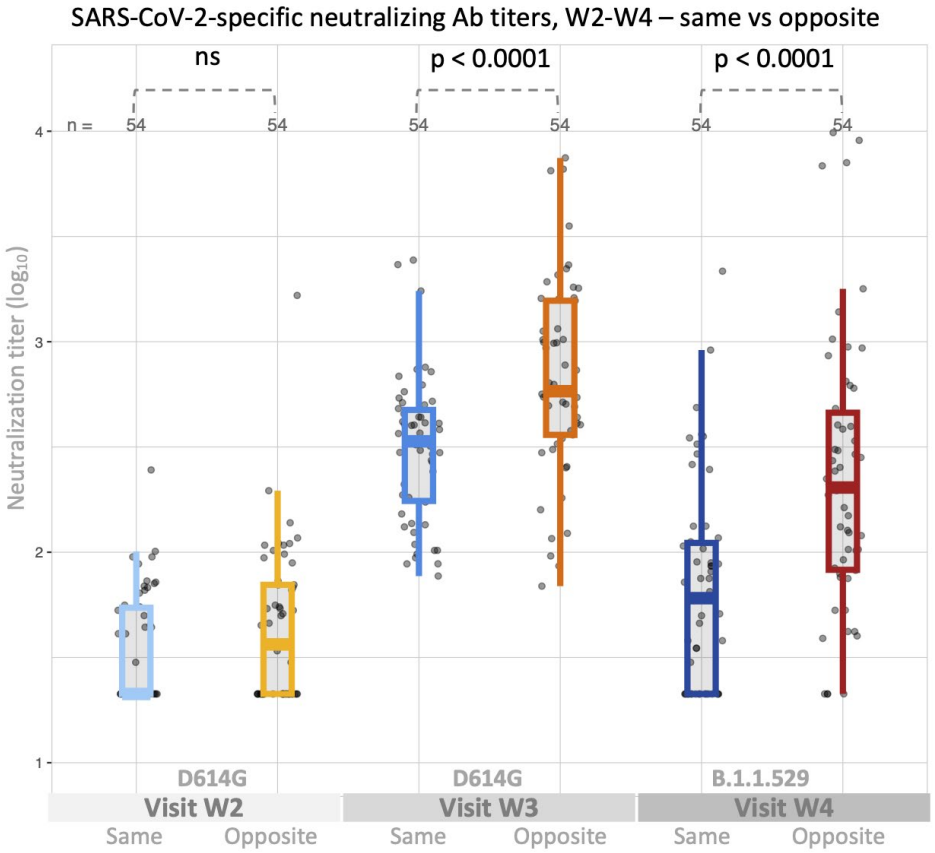




Log 10 COVID-19-specific BAb titers by treatment arm (same vs opposite) in matched pair group (N = 108)

ARM RANDOMIZATION – immune responses

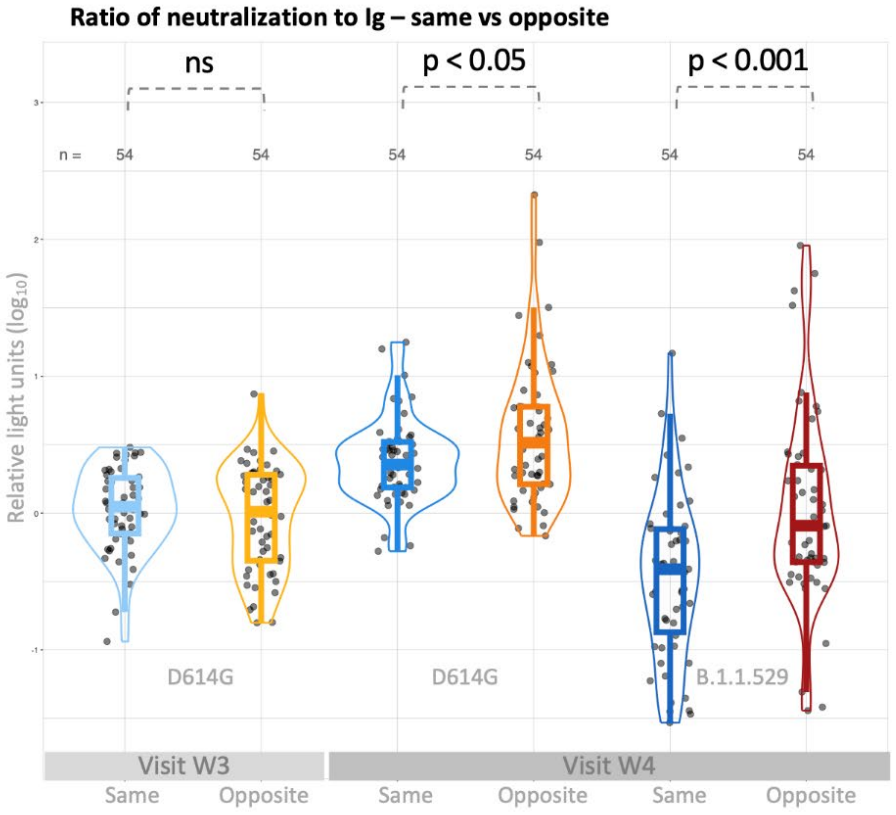
1. SARS-CoV2 BAb titers are higher in contralateral group.
2. Effect greater over time, particularly for IgG
3. Effect also seen in NAb titers
4. Highest with heterologous challenge (i.e. omicron)

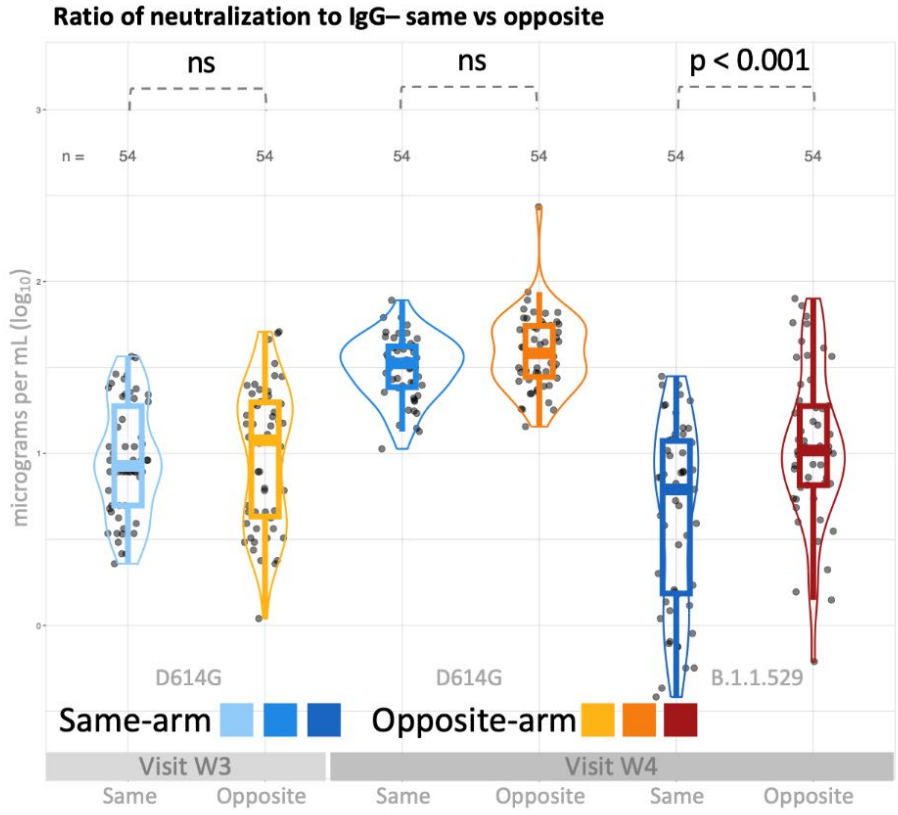


Log 10 COVID-19-specific NAb titers by treatment arm (same vs opposite) in the matched pair group (N = 108)

ARM RANDOMIZATION – immune responses

1. SARS-CoV2 BAb titers are higher in contralateral group.
2. Effect greater over time, particularly for IgG
3. Effect also seen in NAb titers
4. Highest with heterologous challenge (i.e. omicron)
5. Antibody quality is higher in contralateral group





Ratio of NAb titer to BAb treatment arm (same vs opposite) in the matched pair group (N = 108)

ARM RANDOMIZATION – immune responses

1. SARS-CoV2 BAb titers are higher in contralateral group.
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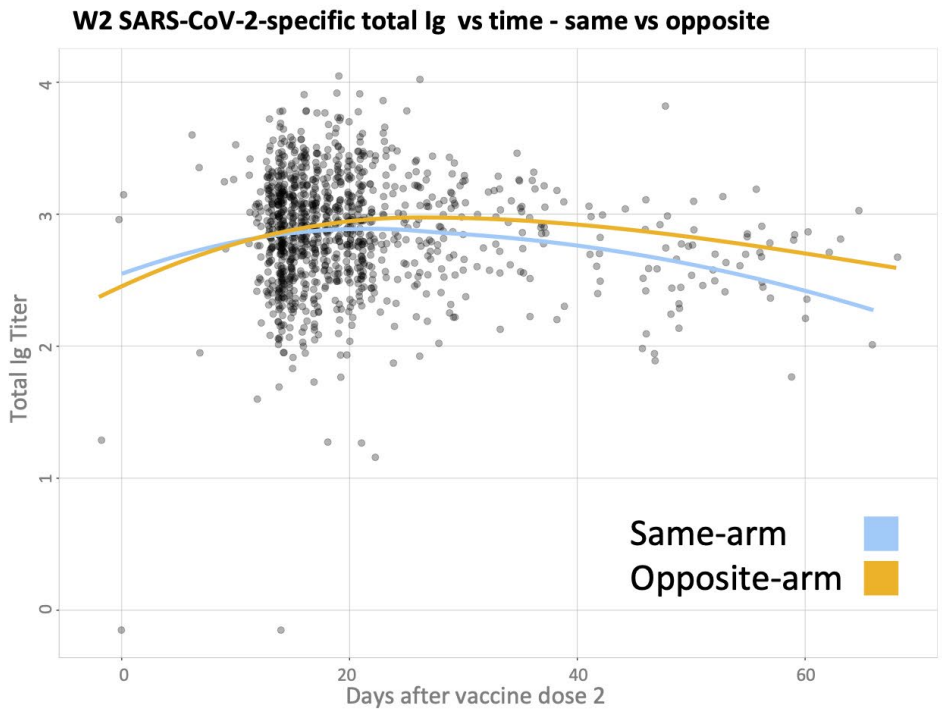
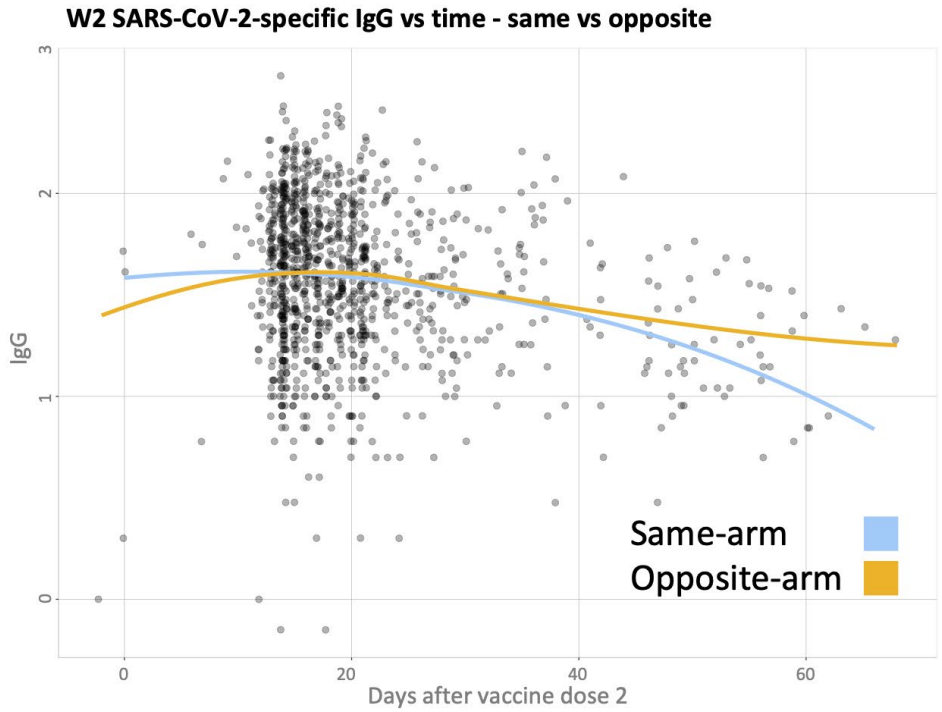
6. Effect is time-dependent, with cross-over around 2-3 weeks after boosting





Log 10 COVID-19-specific NAb titers after dose 3 by arm group (same vs opposite) by time since vaccine dose 2 (V2)

ARM RANDOMIZATION – immune responses

1. SARS-CoV2 BAb titers are higher in contralateral group.
2. Effect greater over time, particularly for IgG
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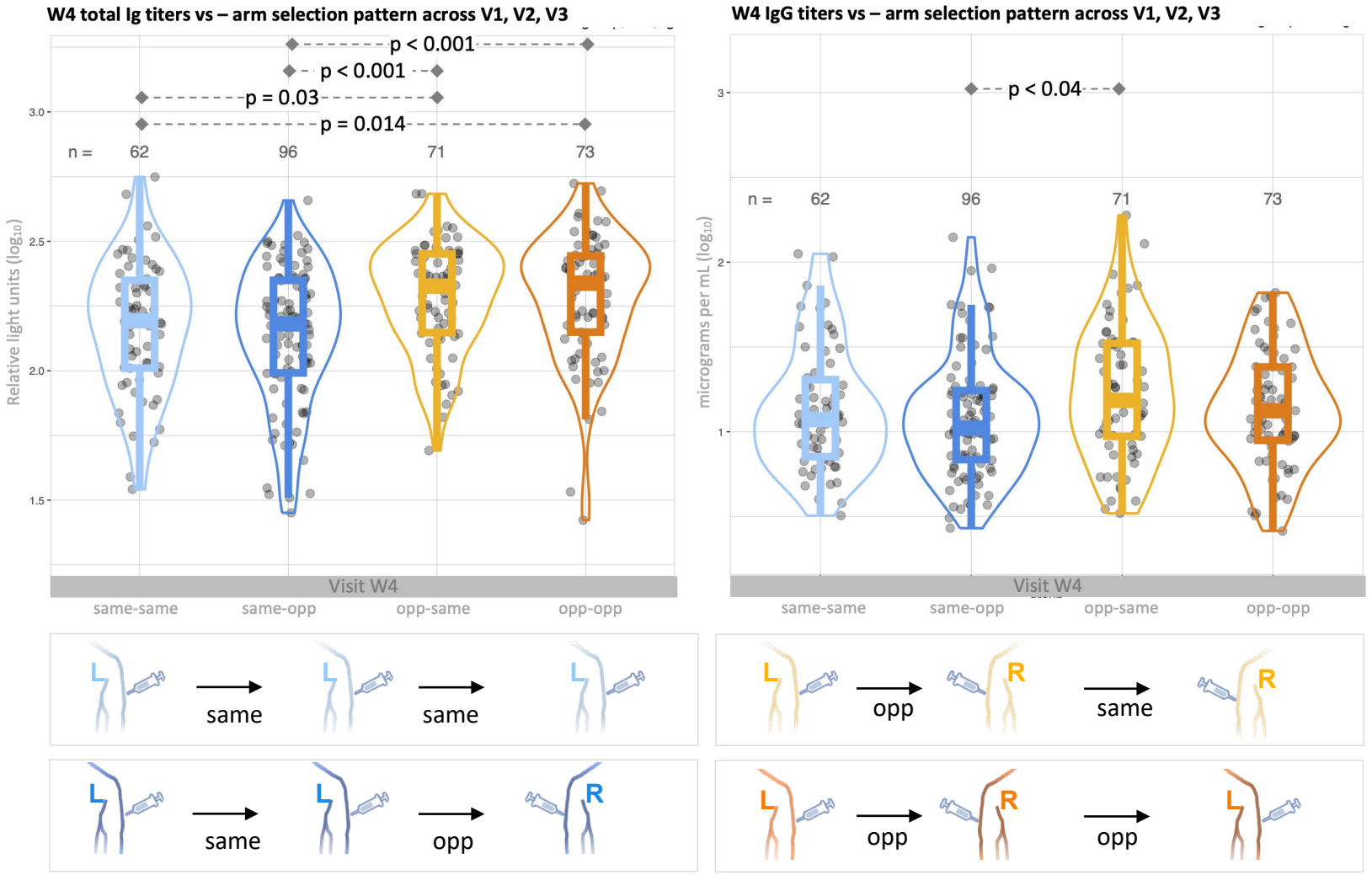
7. First two doses are most important



Log 10 COVID-19-specific NAb titers after dose 3 by all 4 possible treatment arm combinations

ARM RANDOMIZATION – immune responses

Observations

1. SARS-CoV2 BAb titers are higher in contralateral group.
2. Effect greater over time, particularly for IgG
3. Effect also seen in NAb titers
4. Highest with heterologous challenge (i.e. omicron)
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7. First two doses are most important

Relative response by time and assay

Immune responses (log_{10} titer)	Same Mean (SD)	Opposite Mean (SD)	Fold change*	P value
Enrolled Analysis Group (n = 947)§				
W2 total Ig (RLU)	2.82 (0.41)	2.90 (0.41)	1.2	0.020
W2 IgG (µg/mL)	1.56 (0.37)	1.60 (0.39)	1.1	0.302
W3 total Ig (RLU)	1.22 (0.38)	1.38 (0.40)	1.4	<0.001
W3 IgG (µg/mL)	0.31 (0.40)	0.40 (0.41)	1.2	0.004
W4 total Ig (RLU)	2.14 (0.29)	2.30 (0.21)	1.4	<0.001
W4 IgG (µg/mL)	1.16 (0.45)	1.26 (0.40)	1.3	0.021
Matched Pairs (n = 108)				
W2 total Ig (RLU)	2.81 (0.42)	2.89 (0.33)	1.2	0.30
W2 IgG (µg/mL)	1.53 (0.31)	1.65 (0.32)	1.3	0.06
W3 total Ig (RLU)	1.16 (0.41)	1.39 (0.42)	1.7	0.005
W3 IgG (µg/mL)	0.22 (0.38)	0.39 (0.37)	1.5	0.019
W3 pNAb titer (D614G, ID50)	1.19 (0.55)	1.35 (0.62)	1.5	0.151
W3 pNAb titer (D614G, ID80)	0.87 (0.32)	1.00 (0.45)	1.3	0.093
W4 total Ig (RLU)	2.14 (0.25)	2.26 (0.24)	1.3	0.007
W4 IgG (µg/mL)	1.02 (0.32)	1.24 (0.42)	1.7	0.002
W4 pNAb titer (D614G, ID50)	2.52 (0.35)	2.82 (0.53)	2.0	<0.001
W4 pNAb titer (D614G, ID80)	2.10 (0.36)	2.38 (0.48)	1.9	<0.001
W4 pNAb titer (B.1.1.529) ID50)	1.66 (0.72)	2.27 (0.76)	4.0	<0.001
W4 pNAb titer (B.1.1.529) ID80)	1.09 (0.56)	1.63 (0.76)	3.4	<0.001

ARM RANDOMIZATION – immune responses

Observations

1. SARS-CoV2 BAb titers are higher in contralateral group.
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ACKNOWLEDGEMENTS

Dr. Mark Slifka

Dr. William Messer and laboratory

OCTRI Bioinformatics Team

Dr. David Montefiori and laboratory

OHSU C19 research team:
Christopher Malibiran, Devin Schoen, Hiro Ross, Joseph Easly, Laura Craft, Madison Egan, Madison Wahl, Marcus Curlin, Mari Tasche, Matthew Strnad, Maya Herzig, Olivia Glatt, Peter Sullivan, Rick Mathews, Sara McCrimmon, Sarah Siegel, Taylor Anderson, Teresa Xu; Bradie Winders, Kristin Bialobok

Hiro Ross

OHSU clinical Lab
Steve Kazmierczak, Rebecca O'Gara, Juanita Petersen, Amber Halse

OHSU Institutional Review Board

OHSU Occupational Health

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M.J. Murdock Charitable trust
OHSU Foundation

Devin Schoen

Study participants
OHSU faculty, staff and patients who contributed to this study.

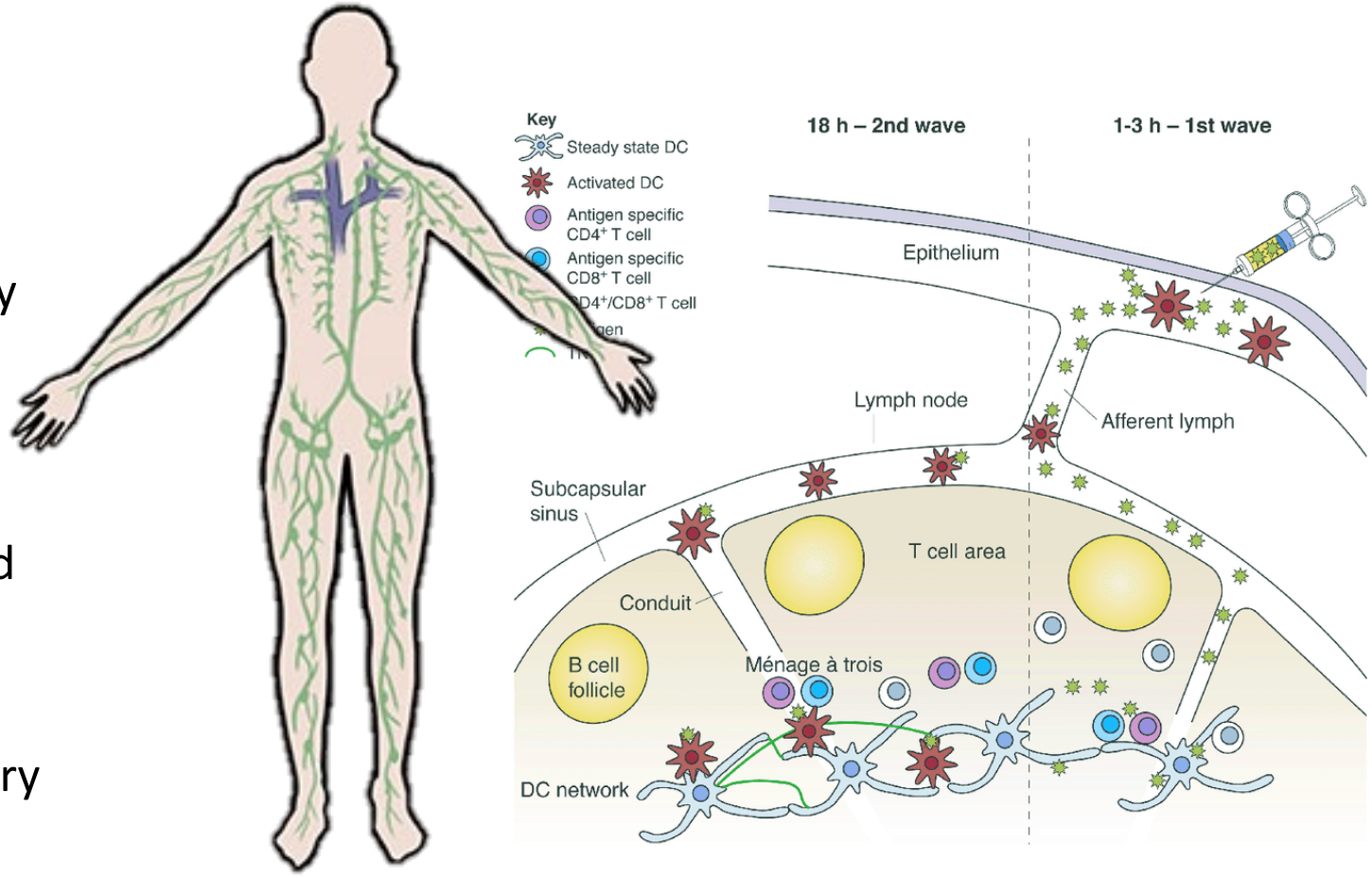
THOUGHTS ON MECHANISM

Antibody presentation is a regional phenomenon

Ipsilateral second dose may preferentially boost primary responses

Contralateral second dosing may allow recruitment of additional newly activated naive B cells

Ultimately promote larger pool of memory B cells



INTERPRETATION

No downside to contralateral vaccination in adults

Too early for broad treatment recommendations

Need additional studies

- Prospective
- Children
- Different vaccine platforms
- Cellular immunity

SIGNIFICANCE

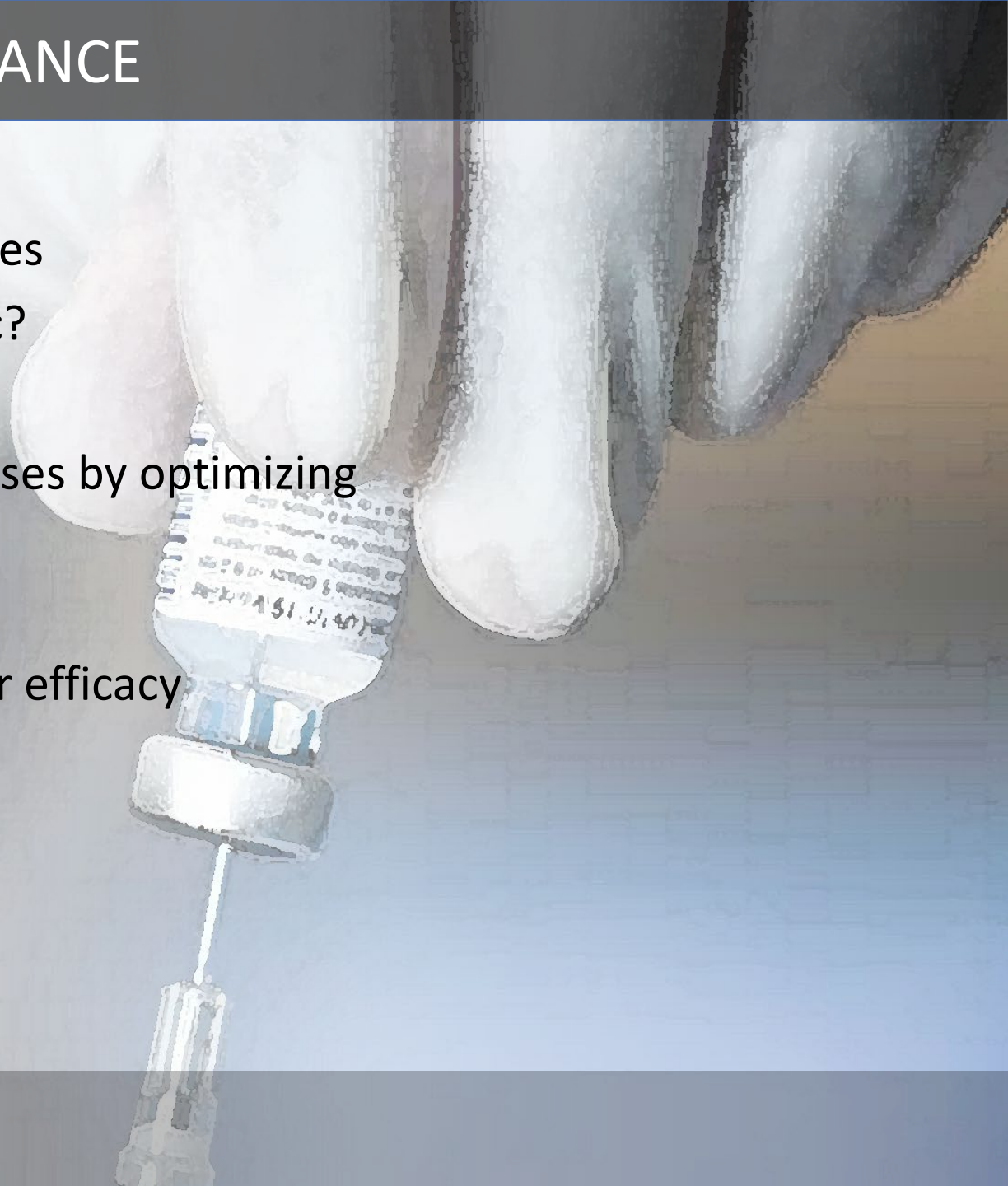
Other factors may also affect immune responses

- Are they additive, competitive or synergistic?

By how much can we improve immune responses by optimizing non-pharmacologic factors?

Cases near the threshold immune response for efficacy

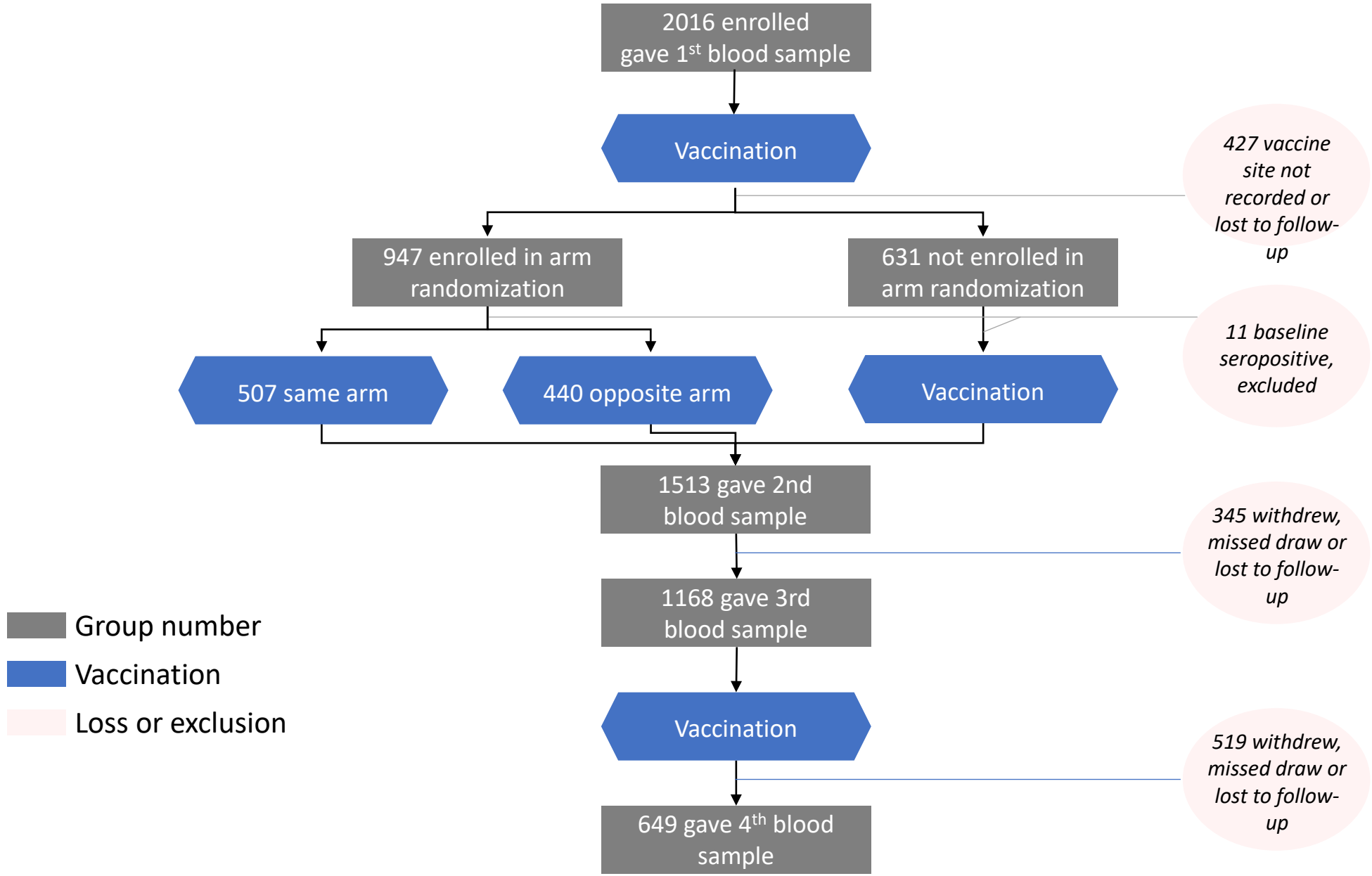
- Patients with heightened susceptibility
- Durability of immunity
- Newly developed vaccines



THANK YOU!

Questions?

ENROLLMENT AND RETENTION



Time intervals and age by arm vaccination site

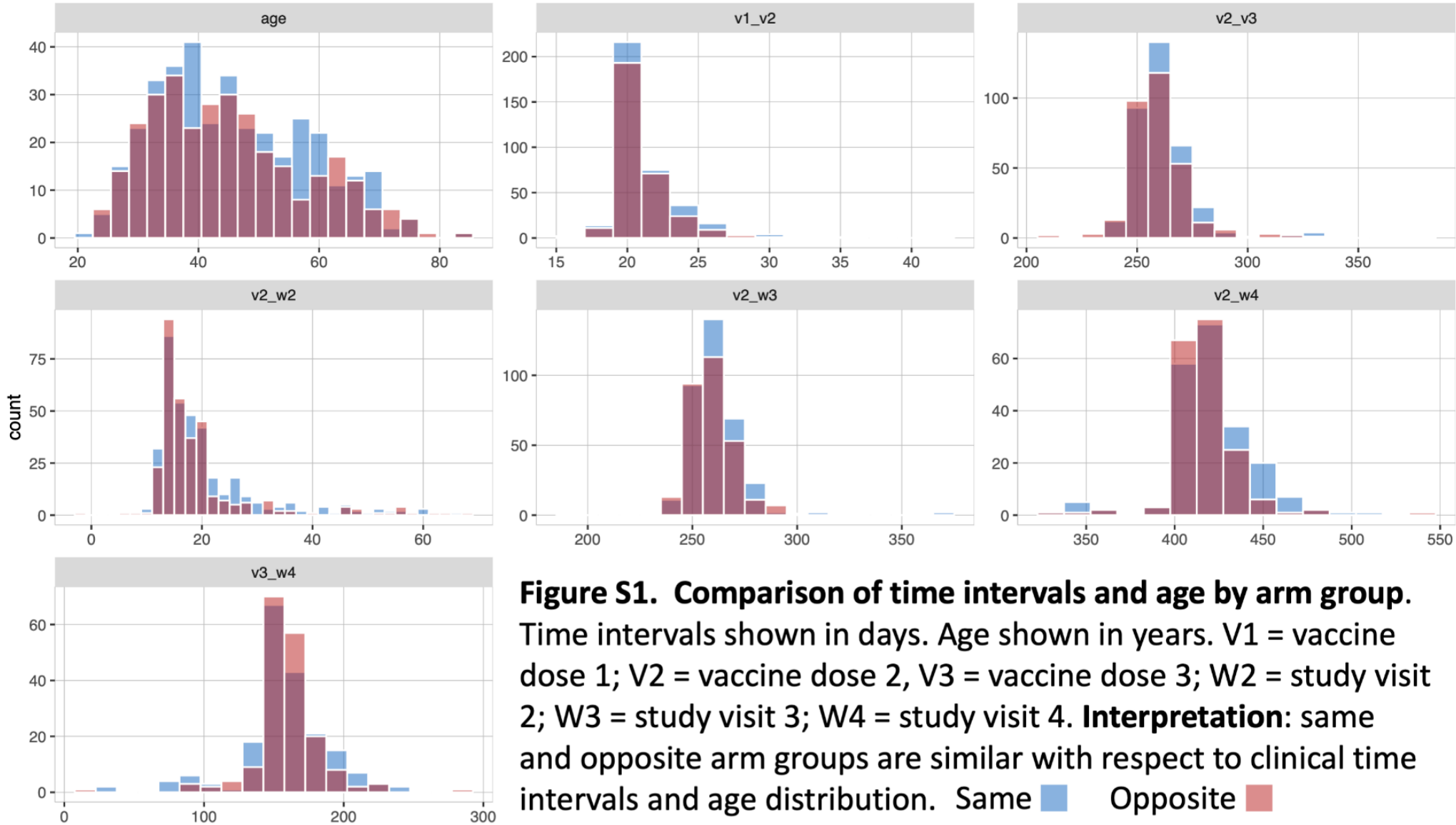
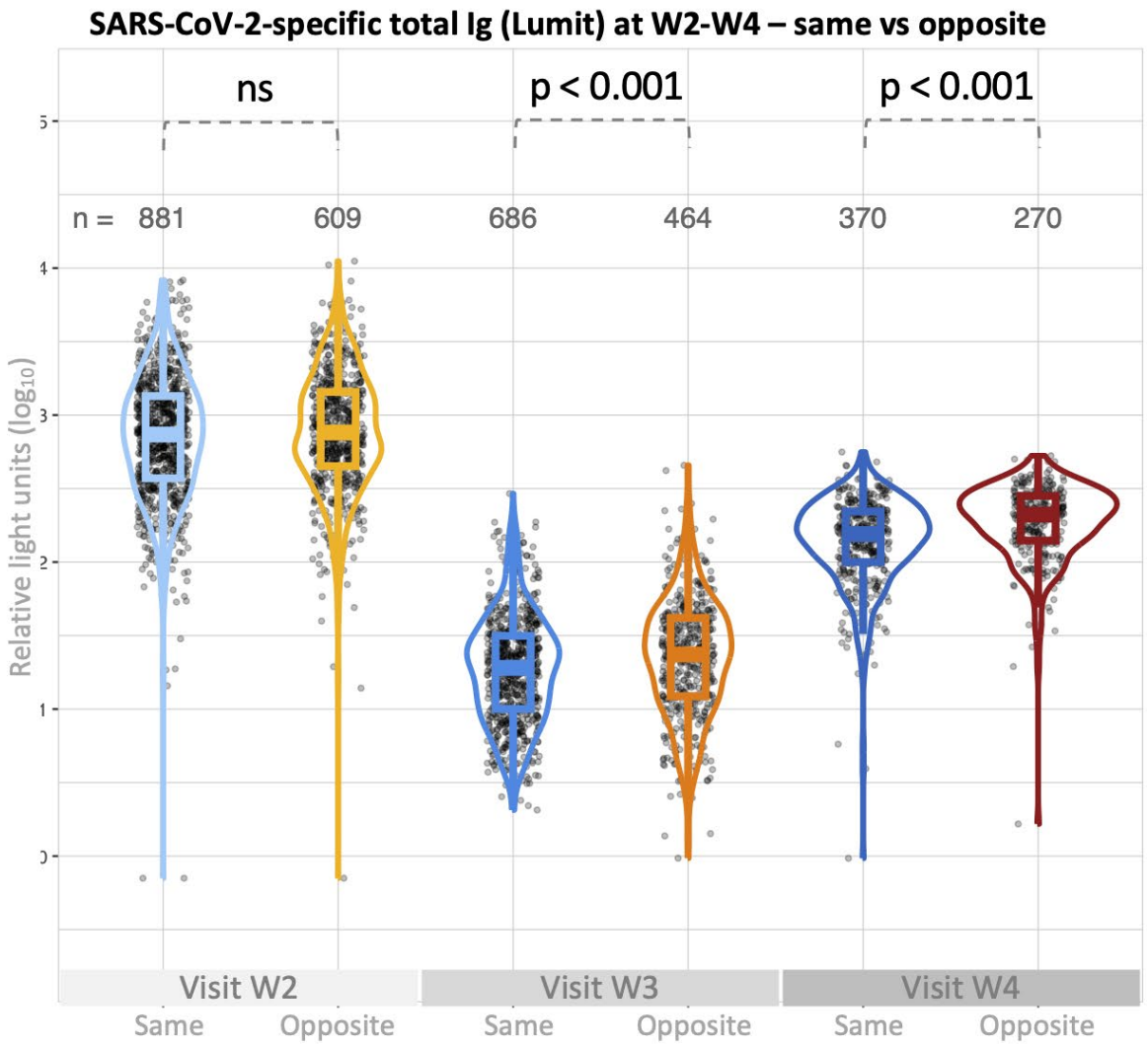
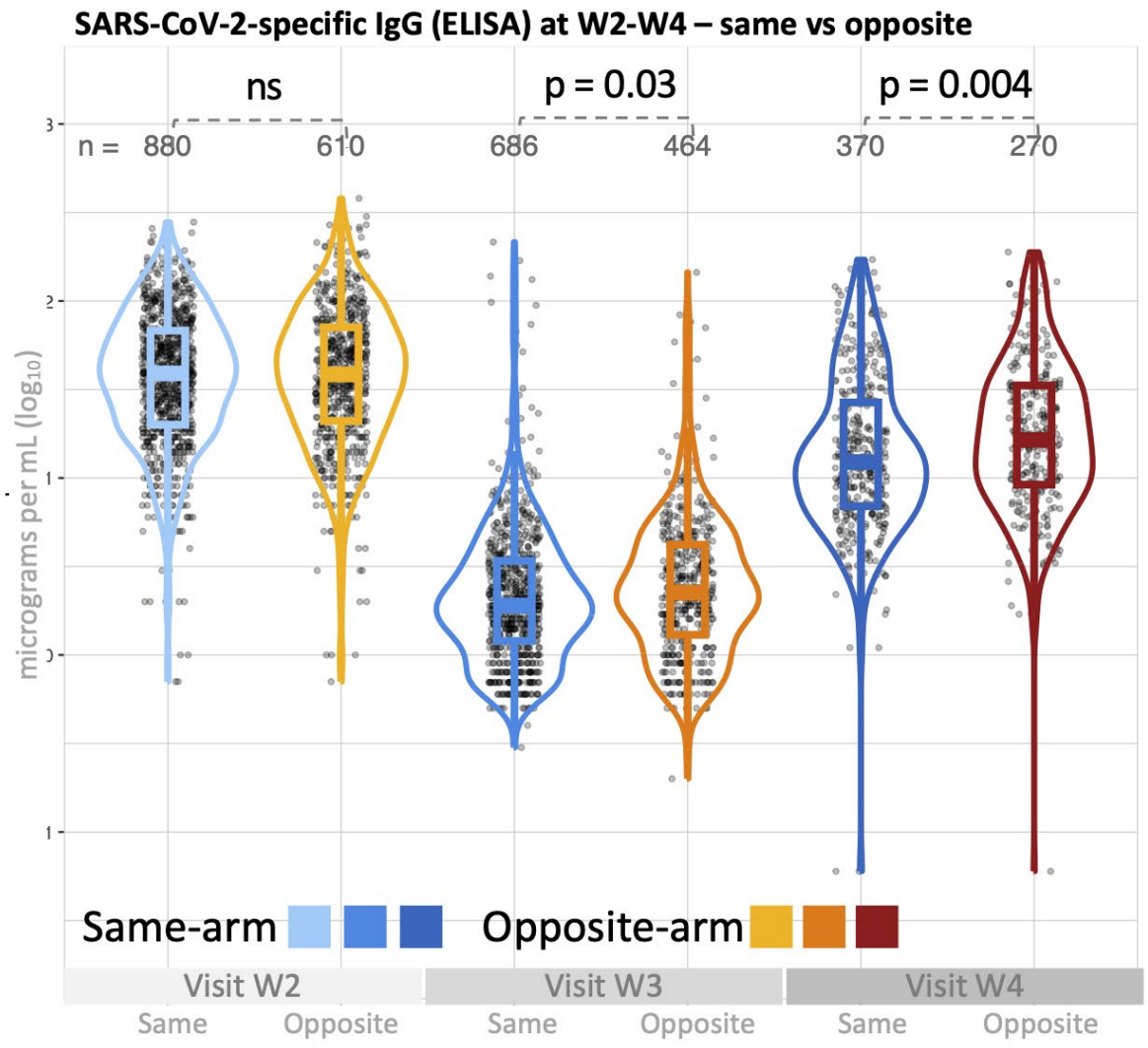
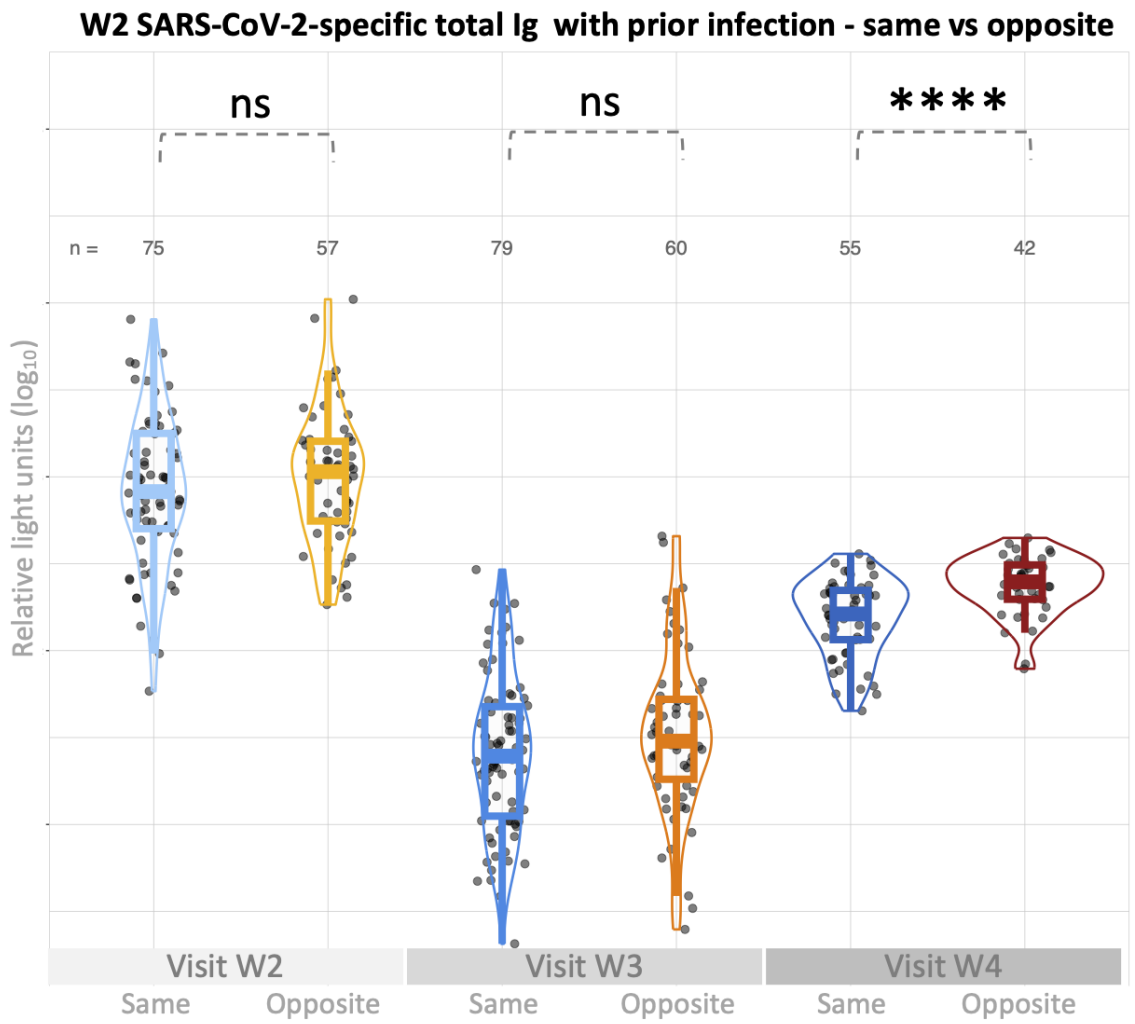


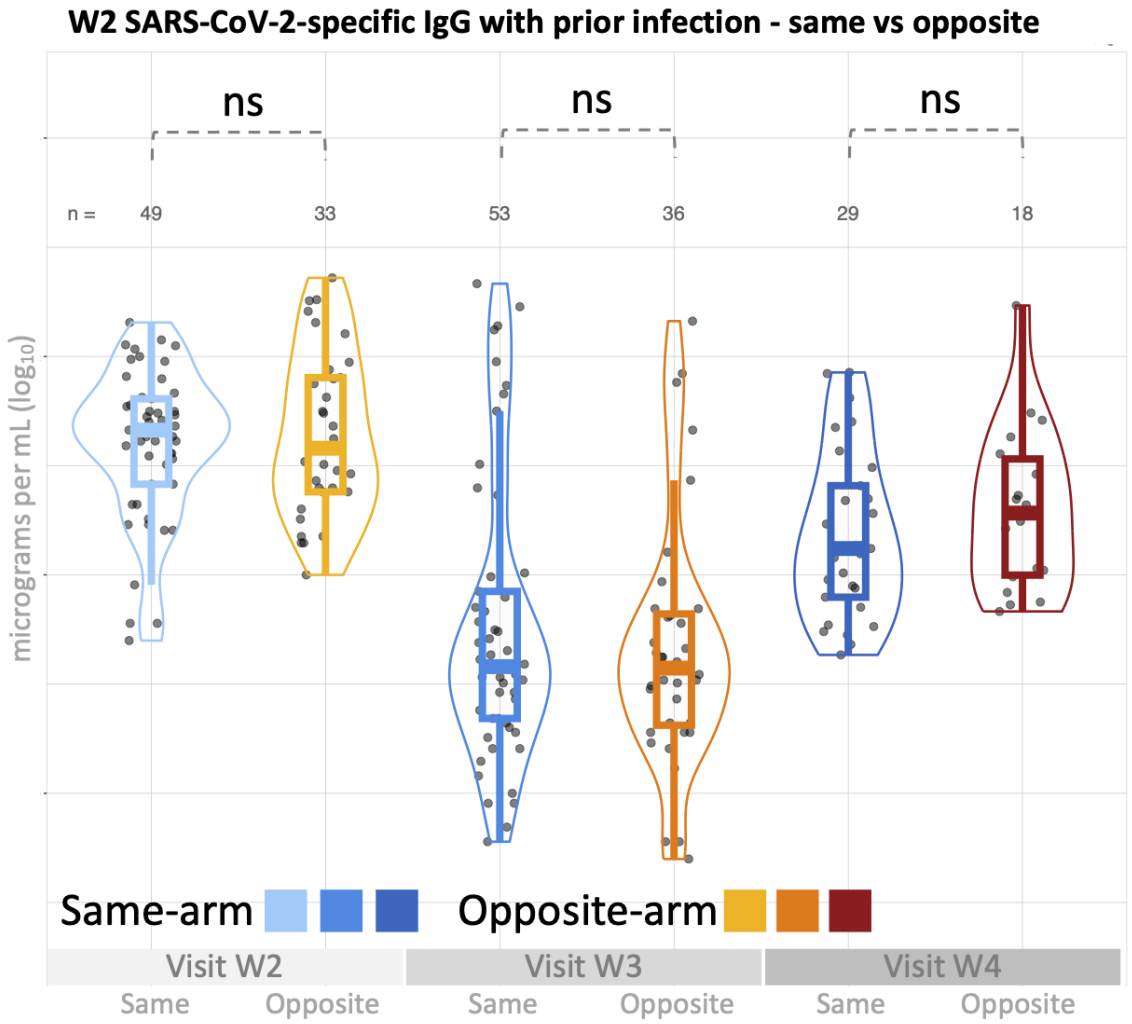
Figure S1. Comparison of time intervals and age by arm group. Time intervals shown in days. Age shown in years. V1 = vaccine dose 1; V2 = vaccine dose 2, V3 = vaccine dose 3; W2 = study visit 2; W3 = study visit 3; W4 = study visit 4. **Interpretation**: same and opposite arm groups are similar with respect to clinical time intervals and age distribution. Same Opposite





Log 10 COVID-19-specific BAb titers in unselected participants by arm group (same vs opposite) by time since vaccine dose 2 (V2)





Log 10 COVID-19-specific BAb titers in participants with prior infection by arm group (same vs opposite) by time since vaccine dose 2 (V2)

Fall and Winter Respiratory Diseases: The Vaccination Season Ahead

Discussion

NVAC

Liaison Member and Federal Agency Updates

NVAC

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Meeting

NATIONAL VACCINE ADVISORY COMMITTEE

June 13-14, 2024

Lunch

Resume at 1:15 PM ET

NVAC

Towards an Updated National Strategy: Progress and Priorities

Dr. Chinedu Okeke
Dr. Maureen Goodenow

NVAC

National Vaccines Strategic Plan 2026-2030: Preliminary Planning and Stakeholder Feedback

Chinedu Okeke MD, MPH-TM, MPA

Maureen Goodenow Ph.D.

Office of Infectious Disease and HIV/AIDS Policy (OIDP)

Office of the Assistant Secretary for Health
U.S. Department of Health and Human Services

Friday, June 14, 2024

OASH | Office of the Assistant Secretary for Health

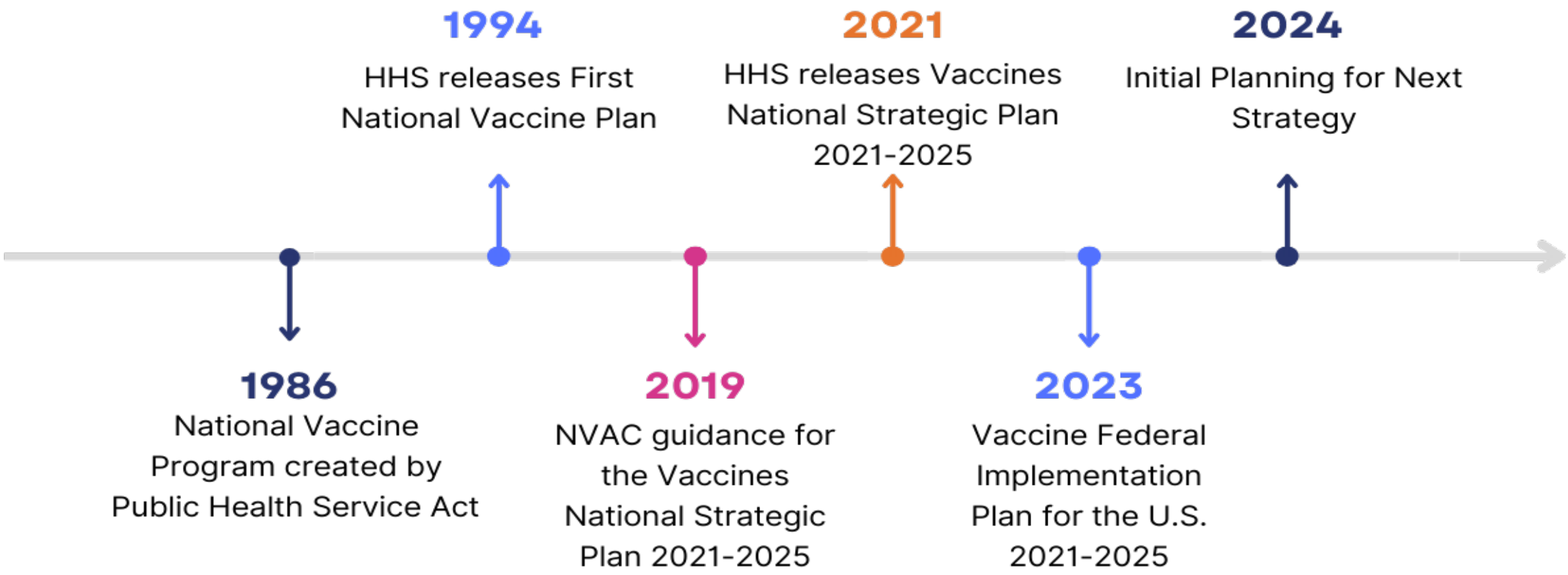
Overview

- Background and context
- Current National Vaccine Strategic Plan 2021-2025
- Updated 5-year NVSP 2026-2030
- ASH NVAC charge
- Timeline for VNSP 2026-2030 development process
- Discussion

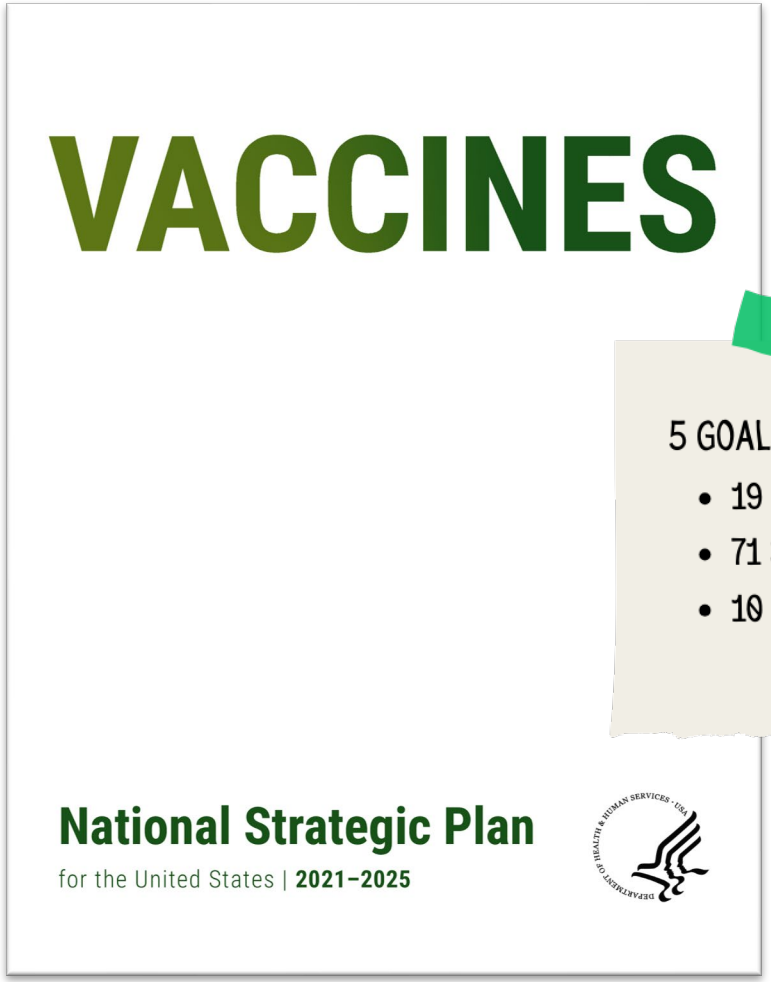
Background: National Vaccine Program

- National Vaccine Program established in 1986. Complies with Section 2105 of the Public Health Service Act.
- Purpose: achieve optimal prevention of adverse reactions and human infectious diseases
- These responsibilities are reflected in Vaccine Plans:
  - ✓2010 National Vaccine Plan
  - ✓Two mid-course reviews of 2010 plan
  - ✓2016 National Adult Immunization Plan
  - ✓Vaccines National Strategic Plan 2021-2025

Timeline: Background and Current Status



National Vaccines Strategic Plan 2021-2025



FEDERAL DEPARTMENTS

- Department of Defense
- Department of Health & Human Services
- Department of Veteran Affairs
- U.S. Agency for International Development

HHS AGENCIES/OFFICES

- Agency for Healthcare Research & Quality
- Biomedical Advanced Research & Development Authority
- Centers for Disease Control and Prevention
- Centers for Medicare & Medicaid Services
- U.S. Food and Drug Administration
- Health Resources and Services Administration
- Indian Health Services
- National Institute of Health
- Office of the Assistant Secretary for Health

National Strategic Plan 2021-2025: Goals

VISION

The United States will be a place where vaccine-preventable diseases are eliminated through safe and effective vaccination over the lifespan.

Goal #1 Foster innovation in vaccine development and related technologies

Goal #2 Maintain the highest levels of vaccine safety

Goal #3 Increase knowledge of and confidence in routinely recommended vaccines

Goal #4 Increase access to and use of all routinely recommended vaccines

Goal #5 Protect the health of the nation by supporting global immunization efforts

Next National Vaccine Plan: NVAC Charge

- Review and assess goals, objectives, and indicators in the current NVSP
- Keep and/or propose new goals if needed
- Prioritize three top objectives within each of the 5 goals
- Propose new indicators that measure if goals and objectives are achieving desired outcome

Next National Vaccine Plan: NVAC Charge, Continued

Seek input from a diverse set of experts in the development of the report

Seek input/feedback from diverse stakeholders to reflect the needs of those communities

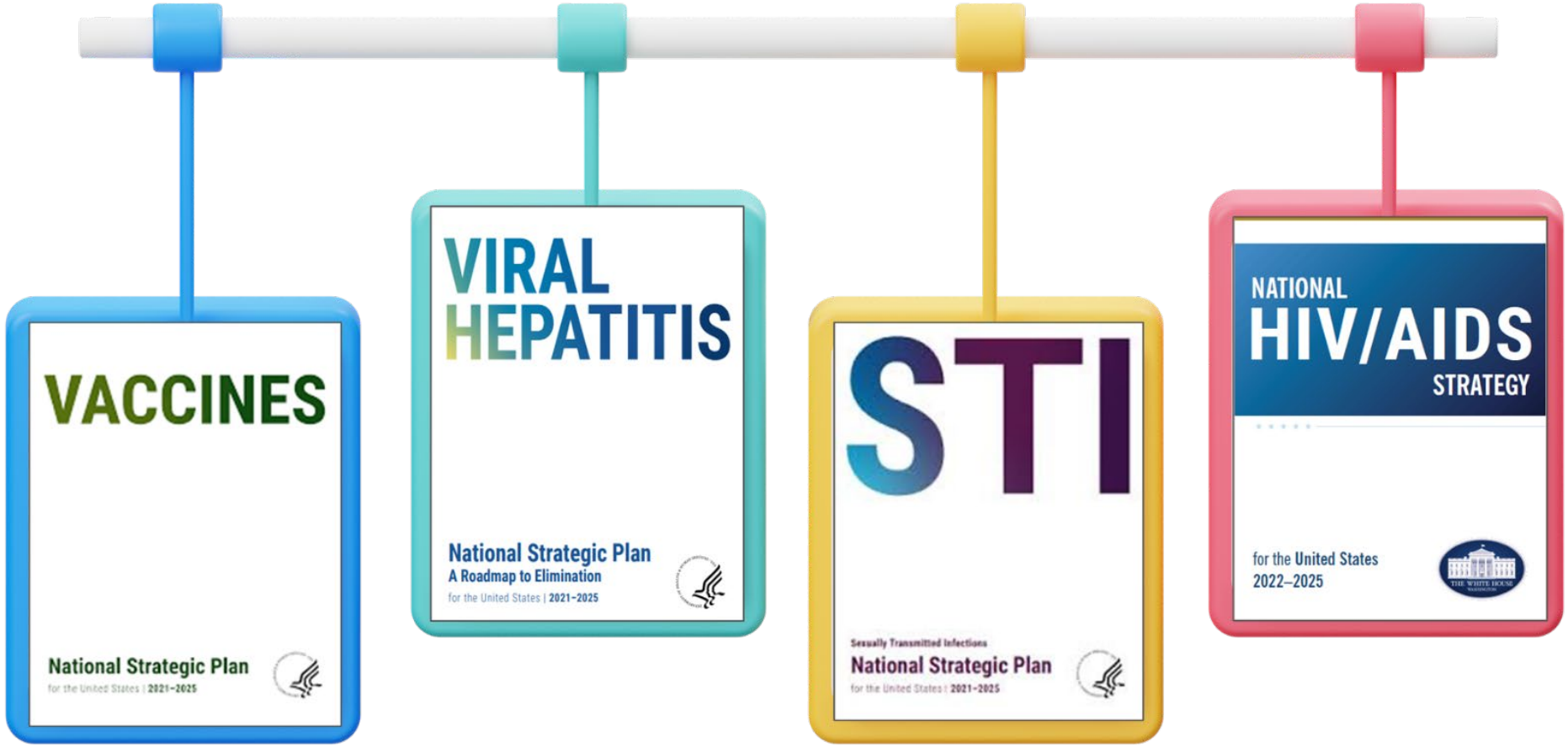
Write a short report for review and vote: **Feb 2025 NVAC meeting**

National Vaccine Strategic Plan 2026-2030 Timeline for Development Process

- Plan & Gather Data
  - Engagements
  - NVAC Report
    - Draft plan
- Clearances & Launch
  - Communications

- Communications
- Federal Implementation Plan
- Evaluation & Progress
- Course Correction(s) if needed
  - Look ahead

Current National Strategic Plans



Discussion

OASH | Office of the Assistant Secretary for Health

THANK YOU!

Towards an Updated National Strategy: Progress and Priorities

Discussion

NVAC

Public Comment

NVAC

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Meeting

NATIONAL VACCINE ADVISORY COMMITTEE

June 13-14, 2024

NVAC