Public Meeting

NATIONAL VACCINE ADVISORY COMMITTEE

February 22-23, 2024

NVAC

February 23, 2024

CHAIR'S WELCOME

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

NVAC

Housekeeping

- 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.

Public Comments

- Verbal comments are scheduled for 5:00 p.m., Eastern Time
  - Please limit all verbal comments to 3 minutes in length.
- Submit written comments to nvac@hhs.gov
  - Requests for public comment should be sent to NVAC@hhs.gov at least 5 days in advance of a scheduled public meeting.
  - Public comments made during the meeting will be limited to 3 minutes per person to ensure time is allotted for all those wishing to speak.
  - You may also submit written comments in advance. Written comments should not exceed 3 pages in length.

Meeting Highlights: February 22

- A 30-Fold Surge in Measles Cases in 2023: Protecting the Unvaccinated
- Innovation Insight: Analysis of the Pipeline and Industry Investment
- Innovation in Immunization Subcommittee Update
- Strong Supply Chains: Opportunities to Thwart Shortages
- A Cornerstone in Childhood Immunization: State Policies for School Entry
- Celebrating 30 Years of Saving Lives: The Vaccines for Children Program Now and in the Future
- Public Comment

Meeting Highlights: February 23

- Artificial Intelligence: Real Uses in Vaccine Development and Immunization Efforts
- Innovative Approaches to Improve Adult Immunization
- Immunization in Focus: Vaccinating Pregnant People
- Inclusion in Immunization: Special Practices for Special Needs
- Federal Agency and Liaison Member Updates
- Public Comments
- Adjourn 5:15 PM Eastern

Upcoming Meetings

- June 13-14, 2024
- September 12-13, 2024

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

Artificial Intelligence: Real Uses in Vaccine Development and Immunization Efforts

Greg Singleton
Dr. Justin Matthew
Ted Schenkelberg
Mark Langowski
Dr. Jimmy Gollihar
Demetris Zambas

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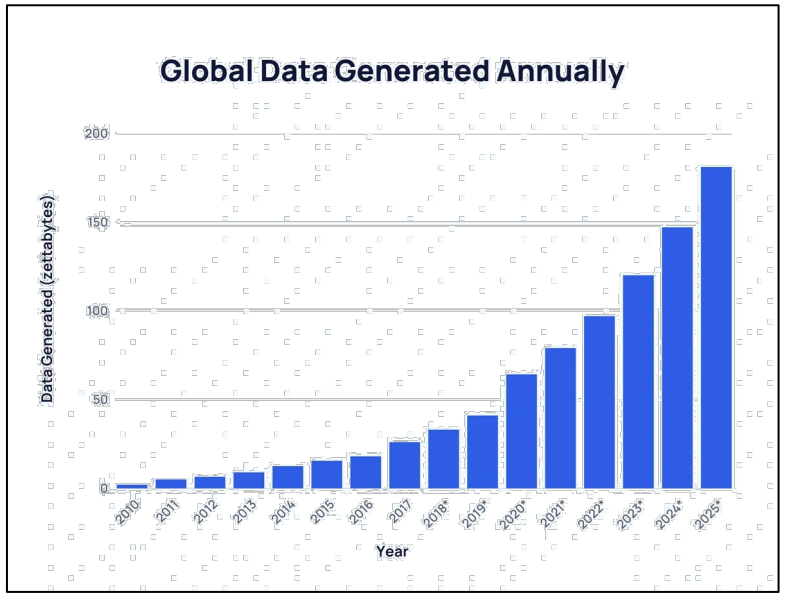
HHS ARTIFICIAL INTELLIGENCE PERSPECTIVES

Greg Singleton
Chief Artificial Intelligence Officer (CAIO)
Department of Health and Human Services

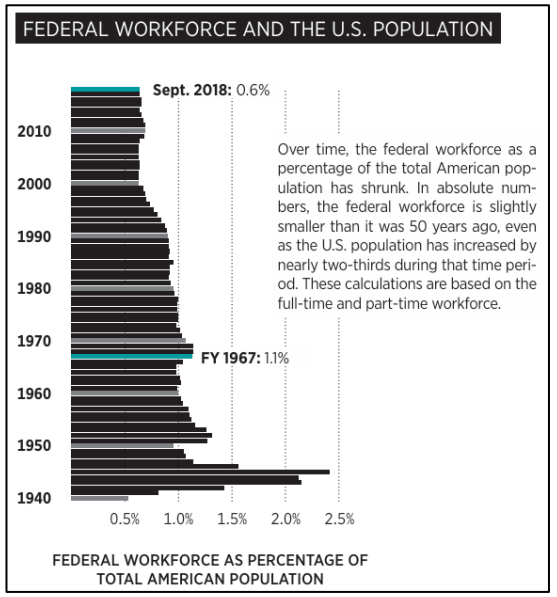
February 23, 2024

Why AI?

Data Generation



Workforce



Options ???

Framing AI

- AI technologies are not entirely new, but the capabilities and attention have increased
- AI approaches enable us to manage core challenges with information volume and the limits of attention
- AI applications are differentiated by application and use case, rather than by technique
- We are challenged to simultaneously deal with the practical present, and manage the theoretical future

HHS AI Approaches

- HHS has been working for many years in the space of artificial intelligence ("AI") to advance its mission across the health sector.
- Recently the pace and extent of advances in AI have accelerated, as has public attention to the transformational opportunities and potential risks.
- HHS has an opportunity to be a catalyst for successful advances and adoption of AI in the health sector but must match the pace and scale of AI developments.
- Pursuant to the AI Executive Order signed October 30, 2023, HHS is developing a new AI Strategy, an implementation roadmap, and implementing risk management activities through a Department-wide effort.

EO 14110 - Safe, Secure, and Trustworthy Development and Use of Artificial Intelligence

- As technology advances and America continues to strive to be a leader of the artificial intelligence (AI) space, there is a growing importance to manage the risks related to AI.
- The Biden-Harris administration has acted by implementing an executive order that directs actions related to the following themes related to those currently in/looking to enter the AI space and others who may be indirectly impacted.
- The following themes represent the main areas of action addressed within the executive order (EO):

New Standards for AI Safety and Security
- To direct "the most sweeping actions ever taken to protect Americans from the potential risks of AI systems"

Protecting Americans' Privacy
- "To better protect Americans' privacy, including from the risks from AI"

Advancing Equity and Civil Rights
- "To ensure that AI advances equity and civil rights, the President directs the following additional actions"

Standing Up for Consumers, Patients, and Students
- "Protect consumers and ensuring that AI can make Americans better off"

Supporting Workers
- "To mitigate these risks, support workers' ability to bargain collectively, and invest in workforce training and development accessible to all"

Promoting Innovation and Competition
- To ensure "that we lead the way in innovation and competition"

Advancing American Leadership Abroad
- To "continue working with other nations to support safe, secure, and trustworthy deployment and use of AI worldwide"

Responsible and Effective Government Use of AI
- "To ensure the responsible government deployment of AI and modernize federal AI infrastructure"

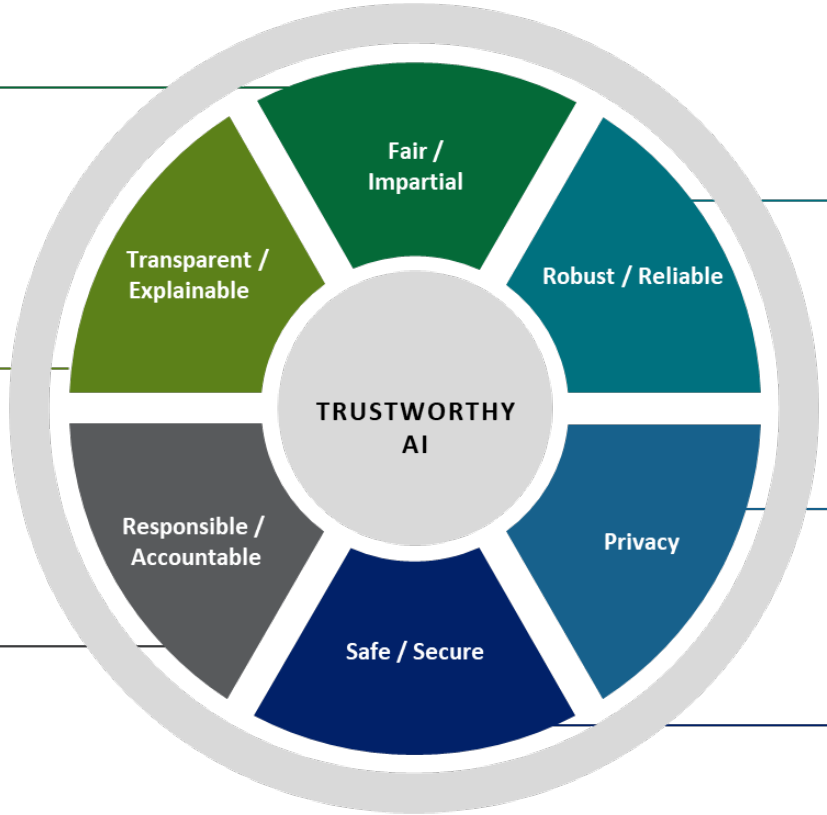
HHS Trustworthy AI Playbook – Overview of Principles

Trustworthy AI refers to the design, development, acquisition, and use of AI in a manner that **fosters public trust and confidence** while protecting privacy, civil rights, civil liberties, and American values, consistent with applicable laws

Fair / Impartial
AI applications should include checks from internal and external stakeholders to help ensure equitable application across all participants

Transparent / Explainable
All relevant individuals should understand how their data is being used and how AI systems make decisions; algorithms, attributes, and correlations should be open to inspection

Responsible / Accountable
Policies should outline governance and who is held responsible for all aspects of the AI solution (e.g., initiation, development, outputs, decommissioning)



Robust / Reliable
AI systems should have the ability to learn from humans and other systems and produce accurate and reliable outputs consistent with the original design

Privacy
Individual, group, or entity privacy should be respected, and their data should not be used beyond its intended and stated use; data used has been approved by the data owner or steward

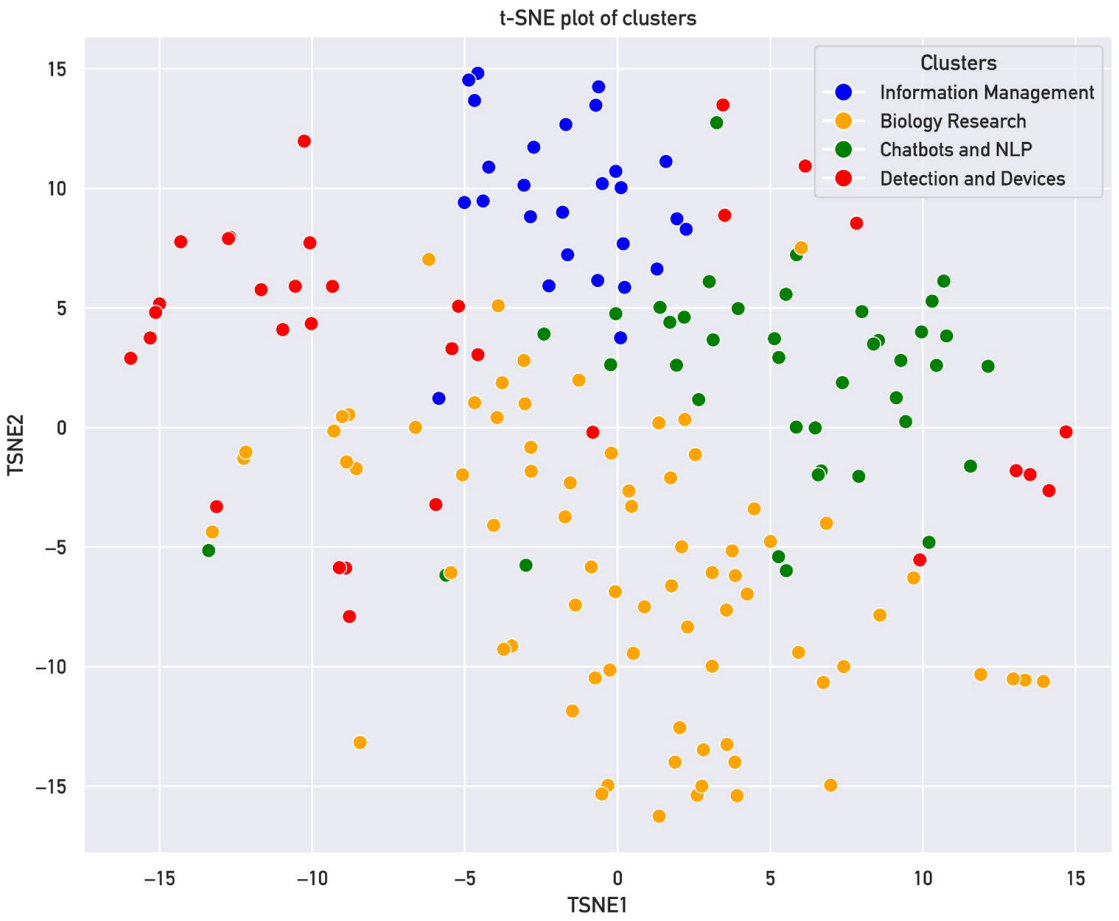
Safe / Secure
AI systems should be protected from risks (including Cyber) that may directly or indirectly cause physical and/or digital harm to any individual, group, or entity

TAI principles are not mutually exclusive, and tradeoffs often exist when applying them.

HHS AI Use Cases - Examples

- **Virtual animal models** for toxicology testing using AI-based generative adversarial network (GAN) architecture (FDA)
- AI to identify **drug repurposing candidates** (ASPR / BARDA)
- HaMLET uses computer vision models to **detect TB from chest x-rays** to improve the quality of overseas health screenings for immigrants and refugees seeking entry to the U.S. (CDC)
- Feedback Analysis - a system that uses CMS or other publicly available data (such as Regulations.Gov) to **review public comments** and/or analyze other information from internal and external stakeholders (CMS)
- **Stem Cell Coding**: uses natural language processing and machine learning to **predict the research subcategories** of an application: human embryonic, non-human embryonic, human induced pluripotent, non-human induced pluripotent, human non-embryonic, and non-human non-embryonic. (NIH)
- Document Examination - Text analytics portal allows personnel without an analytics background to quickly **examine text documents** through a related set of search, topic modeling, and entity recognition technologies (OIG)

HHS AI Use Cases



- Information Management:
  - **Keywords:** grants, indexing, information, document
  - **Examples:** NIH grant classification, FDA ASSIST4TOBACCO, AHRQ search
- Biology Research:
  - **Keywords:** public health, drugs, study
  - **Examples:** FDA adverse drug event prediction, HRSA community analysis, CDC 'nowcasting' suicide trends
- Chatbots and NLP:
  - **Keywords:** chatbot, NLP, public interface
  - **Examples:** CMS chatbot, ACF information gateway, OIG grant analytics portal
- Detection and Devices:
  - **Keywords:** detection, hardware, diagnosis
  - **Examples:** ASPR smartphone COVID-19 diagnosis, CDC TB detection, NIH PangoLearn

Way Forward

- The E.O. sets forth an assertive series of actions for HHS; specific emphasis on safety, rights, and responsibility.
- AI technologies have the potential to improve care, address health inequities, accelerate innovation, and increase market competition.
- Ensure we are approaching risk minimizing approaches that rely on core principles of trustworthiness.
- Vital for the nation to both seize the promise and manage the risks to enable progress.

U.S. FOOD & DRUG ADMINISTRATION

Responsive Regulation of Artificial Intelligence in Drug Development

LCDR Justin Mathew Pharm.D.

- The views expressed in this presentation do not necessarily represent the policies of the FDA
- Mentions are not endorsements
- Disclosures: None

Let’s start with definitions

EO 14110:

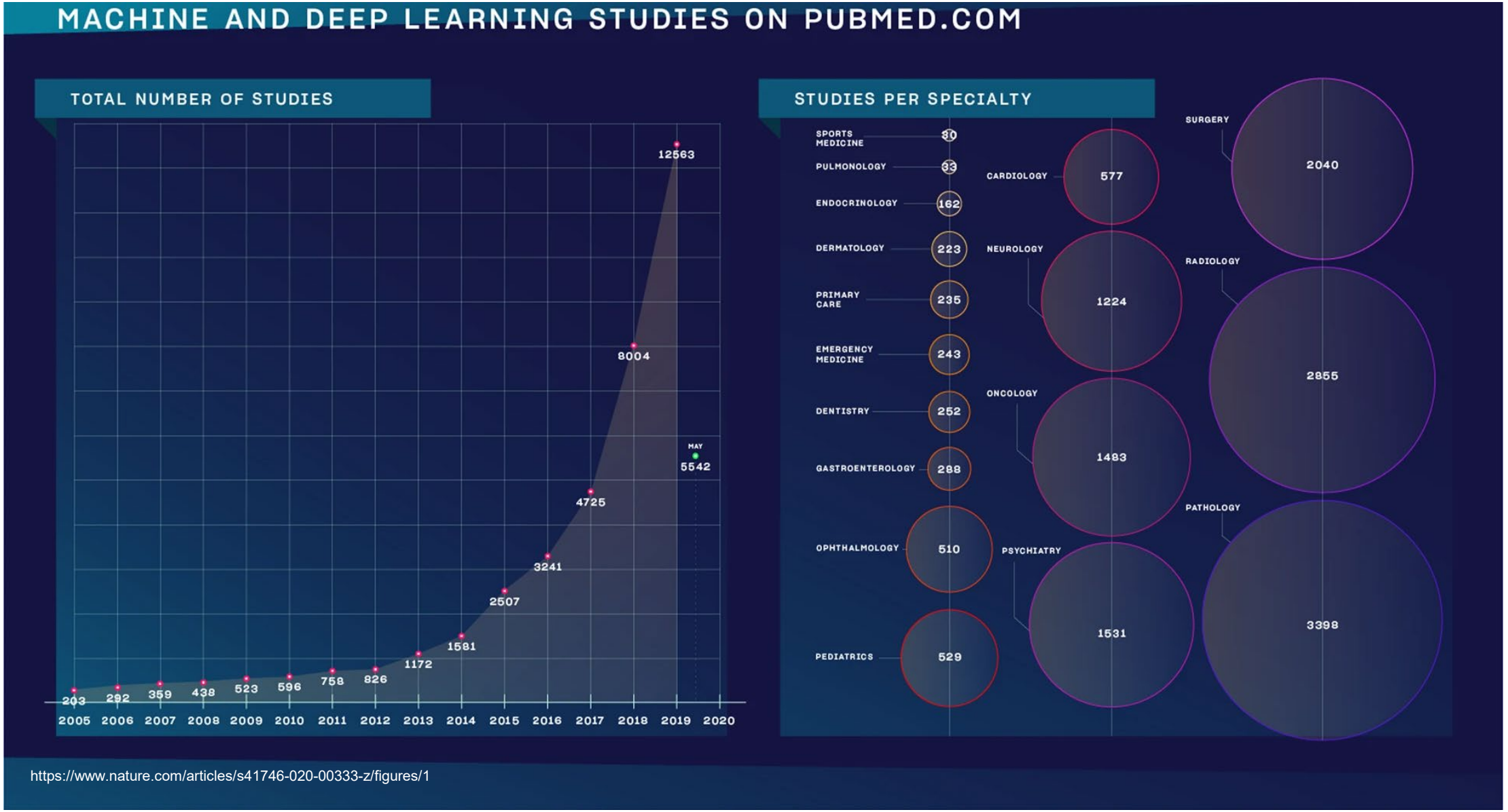
The term “artificial intelligence” or “AI” has the meaning set forth in 15 U.S.C. 9401(3): a machine-based system that can, for a given set of human-defined objectives, make predictions, recommendations, or decisions influencing real or virtual environments. Artificial intelligence systems use machine- and human-based inputs to perceive real and virtual environments; abstract such perceptions into models through analysis in an automated manner; and use model inference to formulate options for information or action.

EO 14110

Drivers behind the growth in AI health applications

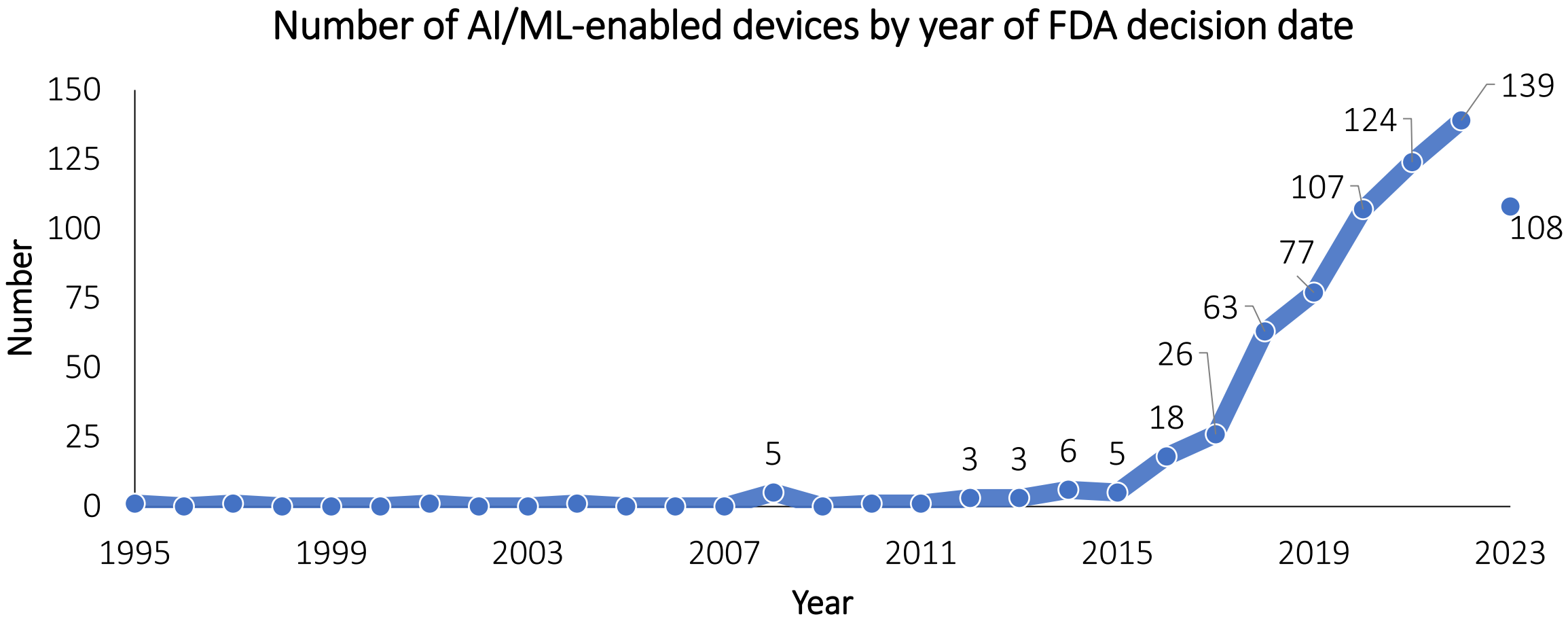
- Large datasets (e.g., administrative data, EHRs, registries, etc.)
- Diverse and multimodal datasets (e.g., DHTs, genomic, laboratory, imaging, etc.)
- Improvements in data standards (e.g., ICD-10, LOINC, NDCs, UMLS, FHIR/HL7, OHDSI/OMOP, etc.)
- Improved data interoperability and healthcare data exchange
- Increased computing power
- Advancements in data privacy persevering approaches
- Breakthroughs in methods (e.g., deep neural networks, reinforcement learning, generative adversarial networks, variational autoencoders, etc.) and causal inference approaches (e.g., structural causal models and causal Bayesian networks)

Number of medical AI studies by year from 2005 to 2020; and by medical specialties



https://www.nature.com/articles/s41746-020-00333-z/figures/1

FDA's Center for Devices and Radiological Health (CDRH) has authorized ~700 AI-enabled devices



SOURCE: https://www.fda.gov/medical-devices/software-medical-device-samd/artificial-intelligence-and-machine-learning-aiml-enabled-medical-devices

AI use across the drug and biologic development landscape

Discovery

- Drug Target Identification, Selection, and Prioritization
- Compound Screening and Design

Preclinical Research

- Pharmacokinetic (PK), pharmacodynamic (PD), and toxicologic studies
- Dose range finding

Clinical Research

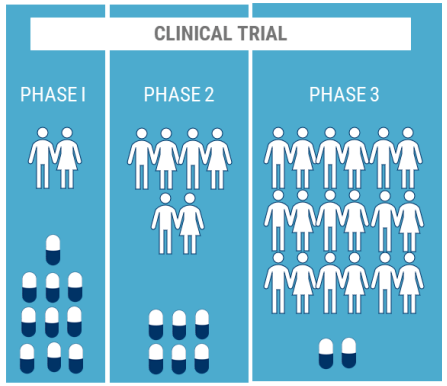


Image source: cbinsights.com

- Dose range finding
- Recruitment
- Adherence
- Retention
- Site selection
- Data collection, management, and analysis
- RWD analyses, “digital twins”, etc.
- Clinical endpoint assessment

Manufacturing and Post-Market Safety Monitoring

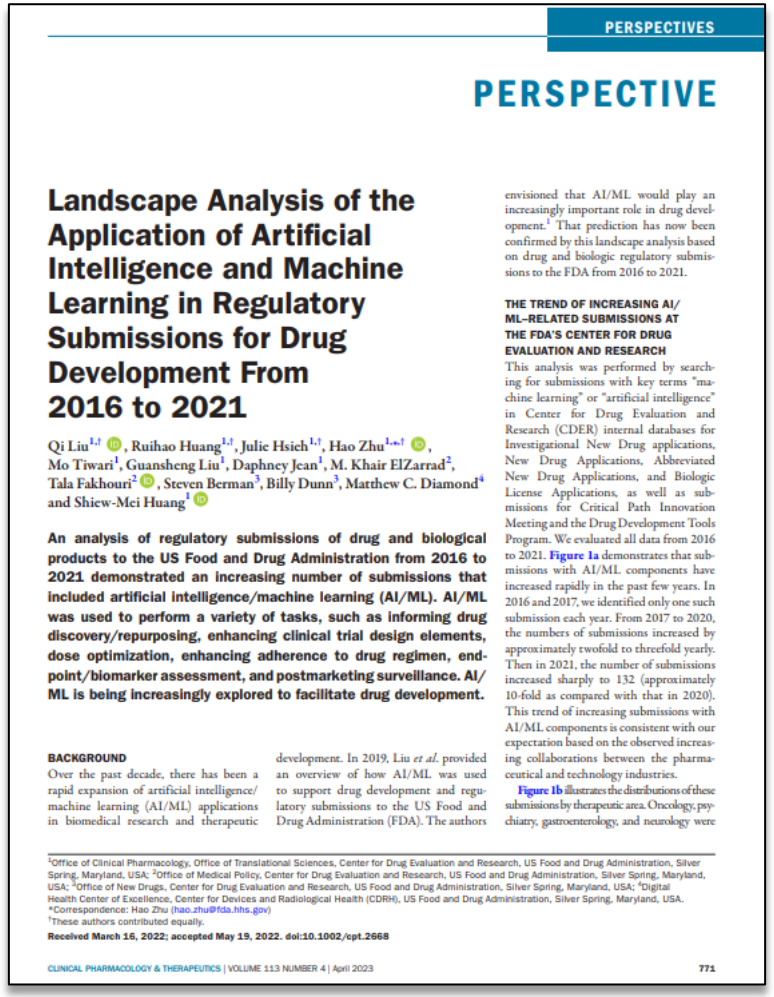
- Advanced pharmaceutical manufacturing
- Post-market safety surveillance or pharmacovigilance (PV)

FDA's Center for Drug Evaluation and Research (CDER) has received over 300 submissions with AI Components

	Year					
Drug Development Stage (n)	**2016**	**2017**	**2018**	**2019**	**2020**	**2021**
Discovery and Development	-	-	-	-	1	3
Preclinical Research	-	-	-	-	-	8
Clinical Research	1	1	3	5	12	118
Post-Market Safety Monitoring	-	-	-	2	1	3

ABBREVIATIONS: Investigational New Drug (IND); New Drug Application (NDA), Abbreviated New Drug Application (ANDA), Biologics License Application (BLA); Drug Development Tool (DDT) Qualification Programs, Critical Path Innovation Meeting (CPIM)

SOURCE: Internal databases maintained by the FDA Center for Drug Evaluation and Research (CDER)



PERSPECTIVES

PERSPECTIVE

Landscape Analysis of the Application of Artificial Intelligence and Machine Learning in Regulatory Submissions for Drug Development From 2016 to 2021

Qi Liu[1,†], Ruihao Huang[1,†], Julie Hsieh[1,†], Hao Zhu[1,*,†], Mo Tiwari[1], Guansheng Liu[1], Daphney Jean[1], M. Khair ElZarrad[2], Tala Fakhouri[2], Steven Berman[3], Billy Dunn[3], Matthew C. Diamond[4] and Shiew-Mei Huang[1]

An analysis of regulatory submissions of drug and biological products to the US Food and Drug Administration from 2016 to 2021 demonstrated an increasing number of submissions that included artificial intelligence/machine learning (AI/ML). AI/ML was used to perform a variety of tasks, such as informing drug discovery/repurposing, enhancing clinical trial design elements, dose optimization, enhancing adherence to drug regimen, endpoint/biomarker assessment, and postmarketing surveillance. AI/ML is being increasingly explored to facilitate drug development.

BACKGROUND

Over the past decade, there has been a rapid expansion of artificial intelligence/machine learning (AI/ML) applications in biomedical research and therapeutic development. In 2019, Liu *et al.* provided an overview of how AI/ML was used to support drug development and regulatory submissions to the US Food and Drug Administration (FDA). The authors envisioned that AI/ML would play an increasingly important role in drug development.[1] That prediction has now been confirmed by this landscape analysis based on drug and biologic regulatory submissions to the FDA from 2016 to 2021.

THE TREND OF INCREASING AI/ML-RELATED SUBMISSIONS AT THE FDA'S CENTER FOR DRUG EVALUATION AND RESEARCH

This analysis was performed by searching for submissions with key terms "machine learning" or "artificial intelligence" in Center for Drug Evaluation and Research (CDER) internal databases for Investigational New Drug applications, New Drug Applications, Abbreviated New Drug Applications, and Biologic License Applications, as well as submissions for Critical Path Innovation Meeting and the Drug Development Tools Program. We evaluated all data from 2016 to 2021. Figure 1a demonstrates that submissions with AI/ML components have increased rapidly in the past few years. In 2016 and 2017, we identified only one such submission each year. From 2017 to 2020, the numbers of submissions increased by approximately twofold to threefold yearly. Then in 2021, the number of submissions increased sharply to 132 (approximately 10-fold as compared with that in 2020). This trend of increasing submissions with AI/ML components is consistent with our expectation based on the observed increasing collaborations between the pharmaceutical and technology industries.

Figure 1b illustrates the distributions of these submissions by therapeutic area. Oncology, psychiatry, gastroenterology, and neurology were

[1]Office of Clinical Pharmacology, Office of Translational Sciences, Center for Drug Evaluation and Research, US Food and Drug Administration, Silver Spring, Maryland, USA; [2]Office of Medical Policy, Center for Drug Evaluation and Research, US Food and Drug Administration, Silver Spring, Maryland, USA; [3]Office of New Drugs, Center for Drug Evaluation and Research, US Food and Drug Administration, Silver Spring, Maryland, USA; [4]Digital Health Center of Excellence, Center for Devices and Radiological Health (CDRH), US Food and Drug Administration, Silver Spring, Maryland, USA.
*Correspondence: Hao Zhu (hao.zhu@fda.hhs.gov)
†These authors contributed equally.

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Source: https://ascpt.onlinelibrary.wiley.com/doi/epdf/10.1002/cpt.2668

Challenges with AI use for drug development

- AI or ML approach can only ever be as good as the underlying data:
  - Scarcity of high-quality, large-scale, and fit-for-purpose datasets for development and testing
  - Identification and mitigation of bias in datasets
  - poor generalization due to dataset shift, to overfitting, to confounders
- Opacity of some algorithms
- Ensuring transparency to users
- Data privacy and security
- Providing oversight/governance for adaptive algorithm

Center for Devices and Radiological Health (CDRH) has been leading the way

Published [AI/ML-SaMD Discussion Paper]

First joined [Collaborative Community] related to AI/ML

Public Workshop on [AI/ML in Radiological Imaging]

PEAC Mtg on [Patient Trust in AI/ML Devices]

[AI/ML Medical Device Software Action Plan]

[List of Currently Marketed AI/ML Devices]

[Public Workshop on Transparency of AI/ML Devices]

GMLP Guiding Principles

[Change Control Plan Guidance]

Slide Adapted from Dr. Matthew Diamond, Chief Medical Officer for Digital Health, CDRH

CDRH's Good Machine Learning Practice for Medical Device Development: Guiding Principles

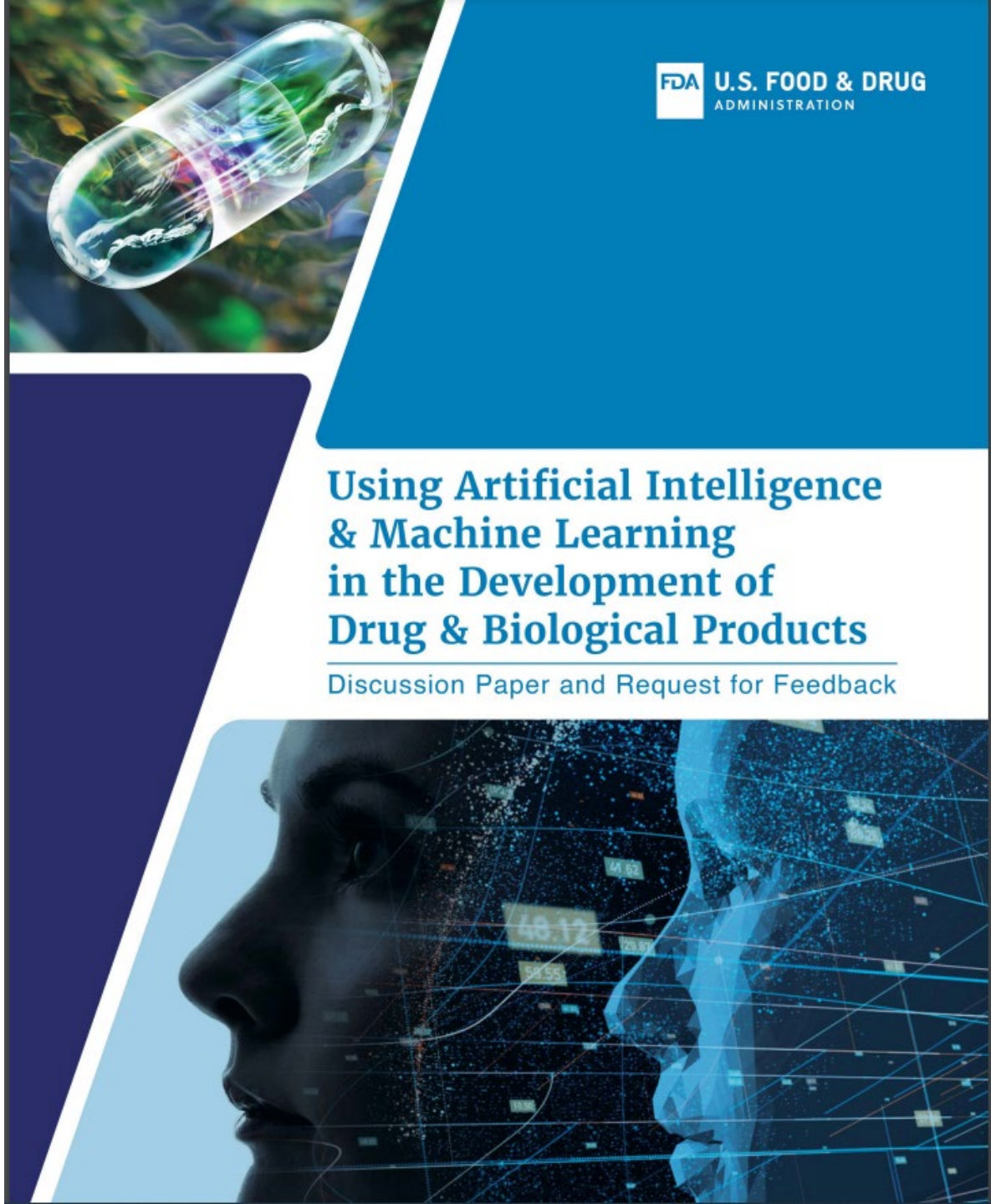
1. Multi-Disciplinary Expertise Is Leveraged Throughout the Total Product Life Cycle
2. Good Software Engineering and Security Practices Are Implemented
3. Clinical Study Participants and Data Sets Are Representative of the Intended Patient Population
4. Training Data Sets Are Independent of Test Sets
5. Selected Reference Datasets Are Based Upon Best Available Methods
6. Model Design Is Tailored to the Available Data and Reflects the Intended Use of the Device
7. Focus Is Placed on the Performance of the Human-AI Team
8. Testing Demonstrates Device Performance During Clinically Relevant Conditions
9. Users Are Provided Clear, Essential Information
10. Deployed Models Are Monitored for Performance and Re-training Risks Are Managed

https://www.fda.gov/medical-devices/software-medical-device-samd/good-machine-learning-practice-medical-device-development-guiding-principles

Engagement is key

Goal is to promote mutual learning around three main core issues:

- Human-led governance, accountability, and transparency
- Quality, reliability, and representativeness of data
- Model development, performance, monitoring, and validation



What's next?

- Leading the HHS "Device and Drug" working group which is tasked with implementing "device and drug" related activities in EO 14110
- Developing guidance and policy
- Advancing safety and security
- Leveraging HHS grants and funding
- Deploying AI within FDA
- Public education and engagement


SECURITY
SYSTEM-PREF.
CLOUD
SEARCH
PROFILE
SECtion
SUMMARY:
CAMERA-S.2
SEARCH
RESOURCE GATHERER SUPPORT

Thank you!

NVAC Panel: AI to Advance Immunization

February 23, 2024

AI/Advanced Computing and the Future of Vaccine Development

Ted Schenkelberg, MPH/MBA

Managing Partner, Next Frontier Advisors

Co-Founder/Former Chief Strategy Officer, Human Immunome Project

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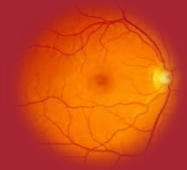
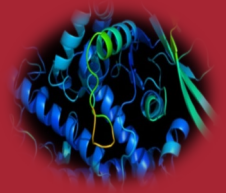
Context: AI is Increasingly Changing Biomedical Discovery

Computer Vision



Retinal scans identify disease from kidney, Alzheimer's to cardiovascular disease.

Protein Prediction



AlphaFold: Prediction Amino acid -- > Protein Structure for 200M known proteins.

Genomics

Huge datasets. Prediction of gene expression from DNA sequence.

Drug Discovery

Deep Learning identified first new class of antibiotics in a generation.

Large Language Models

Potential to synthesize data and information, hypothesis generation. Reliable?

Modified from an Eric Topol slide.

Historically Technological Advancements Have Driven Advances in Vaccine Development

Century	Technological Advance	Examples
18th	Vaccination	Smallpox
19th	Attenuation	Anthrax; Rabies
19th	Inactivation	Typhoid, Cholera, Plague
20th- First Half	Toxoids Egg Cultures	Diphtheria; Tetanus Influenza
20th- 2nd Half	Tissue Culture Protein-Conjugate Polysaccharides Recombinant Protein Genomics/Reverse Vaccinology	MMR Hemophilus Influenzae Hepatitis B; HPV Meningococcus B
21st Century	Structural biology, mRNA, synthetic biology	RSV, COVID-19, adjuvant design

Adapted from Plotkin's Vaccines, 7th ed.

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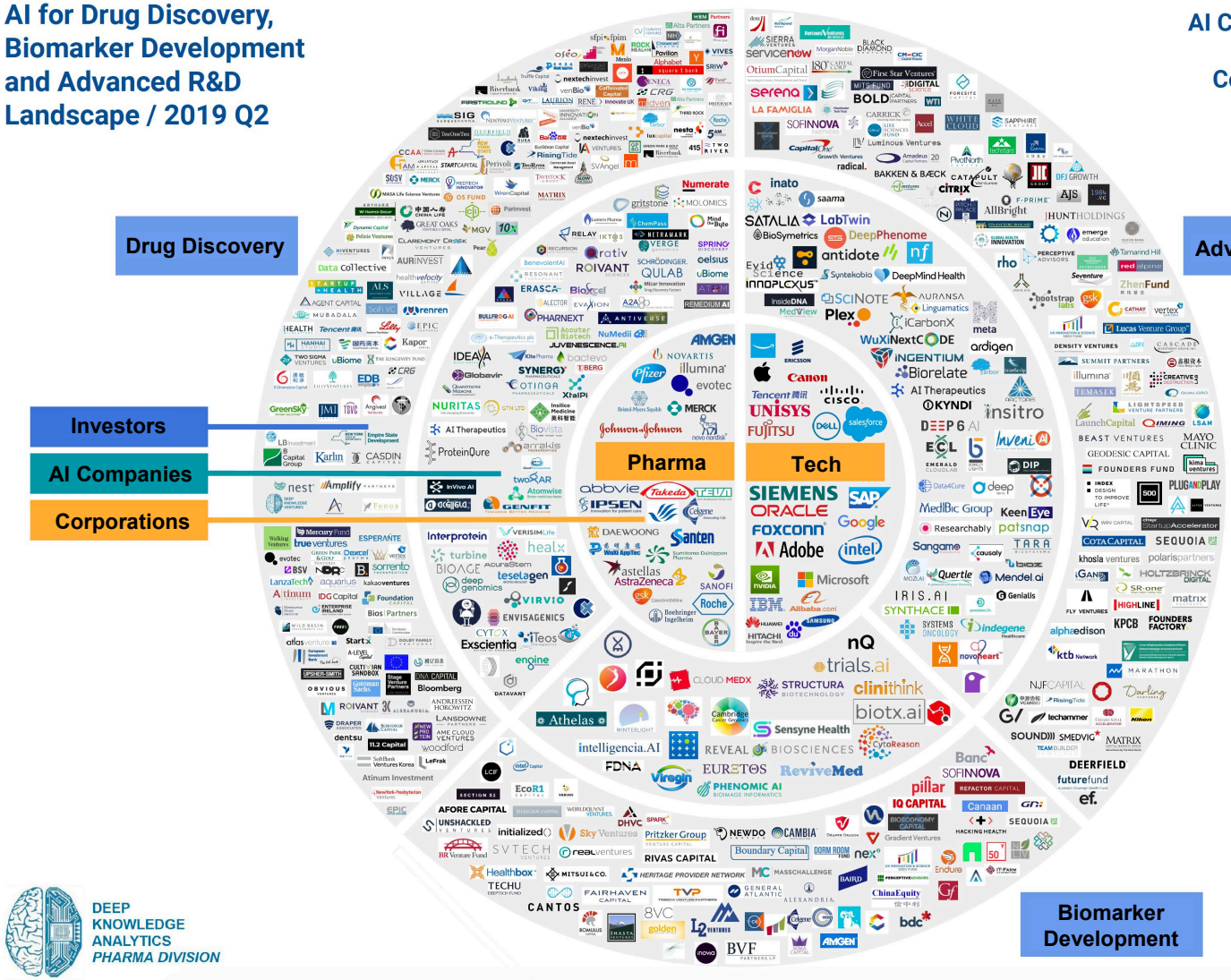
There is a Lot of Activity in the AI - Biomed Space

AI for Drug Discovery, Biomarker Development and Advanced R&D Landscape / 2019 Q2

AI Companies - 170
Investors - 400
Corporations - 50



AI Can Help Solve Major Problems Hindering Vaccine Development

1) **Lack of understanding of the how the immune system works**
   - Decoding/modeling effective immunity at component and system-wide level
2) **Lack of understanding of protective immunity in vulnerable populations**
   - Older adults, infants, immunocompromised, individuals living in LIMCs
3) **Antigen / immune receptor identification and design**
   - Major hurdle for complex infectious and non-communicable diseases
4) **Optimization of process and platforms**
5) **AI/computer assisted (Simulated ??) clinical trials**

Hype and Reality: These are the Very Early Days !

AI/Advanced computing offers great potential for biomed and vaccines.

This potential is far from realized.

Technologies are still nascent, and need to demonstrate impact, efficiency and effectiveness.

"It is still far faster and cheaper and more efficient to make a new antibody with preferred properties from the naturally occurring B cells of human immune subjects, for foreign antigens like viruses.

I think we all have a sense AI will eventually help us here. But at present, lab methods are still superior."

- **James Crowe**, Director, Vanderbilt Vaccine Center

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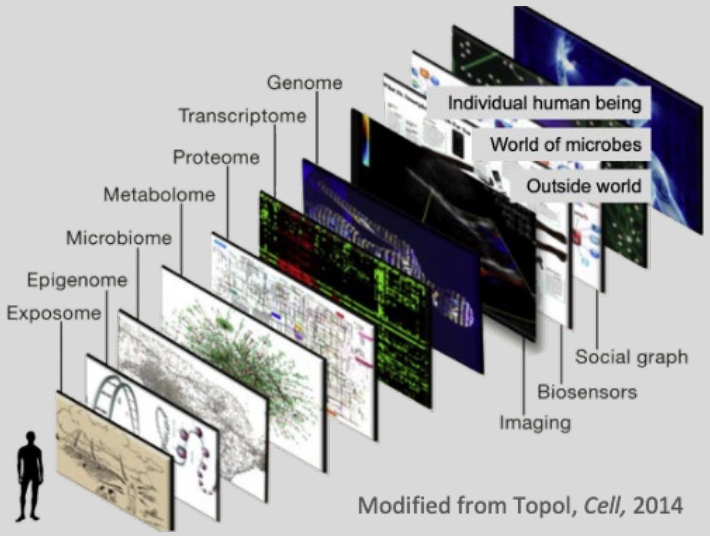
Data is the Fuel for AI.

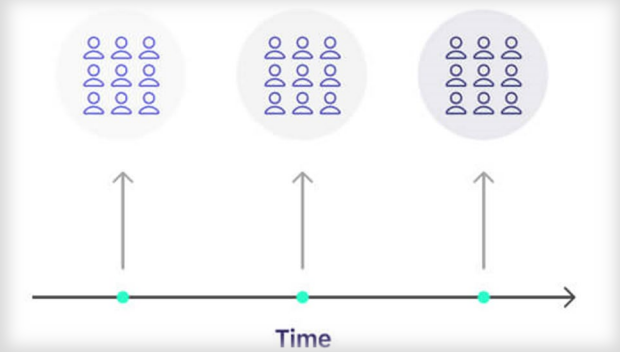
We now have more biological data than ever.

It can be generated at lower and lower costs.

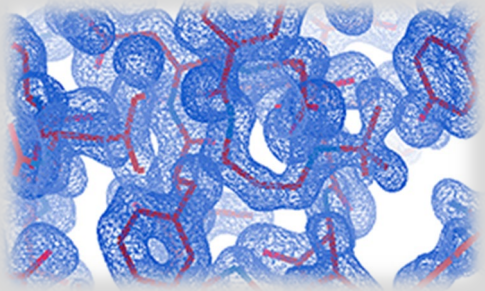
Systems Biology



Population Data: Longitudinal Studies



Structural and Other Molecular Data



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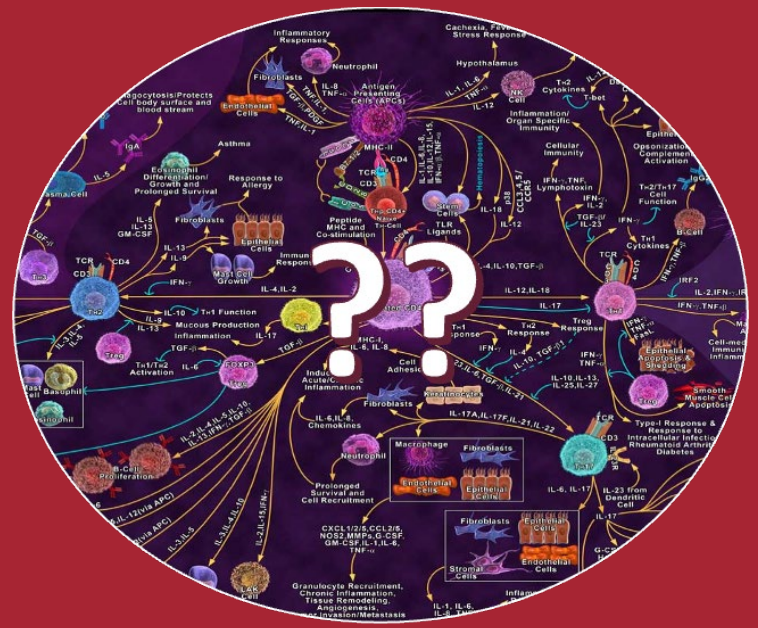
Problem #1: Decoding Effective Immunity

We don’t understand at a component or systemic level how effective human immunity is generated.



Can we model effective immunity at the component and system levels?

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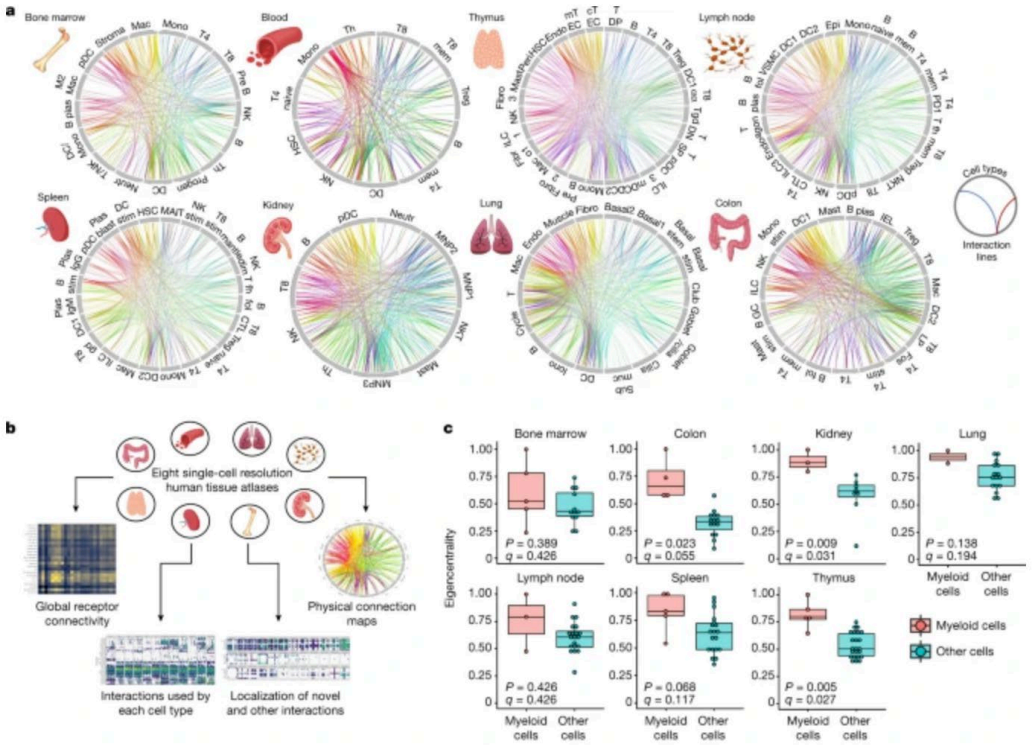
Early Modeling of Immunity as a System

A physical wiring diagram for the human immune system

Fig. 3: An interactive atlas of immune cell connections across the human body.



nature

- The Immune System is a distributed network characterized by response, communication and memory.
- How do these parts fit together from molecular to system level?
- Proof of concept mathematical model predicting intercellular wiring from systems-level principles of immune cell connectivity down to characterization of individual receptors.
- Bridges individual protein molecules to multicellular behavior.

Shilts, J., Severin, Y., Galaway, F. *et al.* A physical wiring diagram for the human immune system. *Nature* **608**, 397–404 (2022). https://doi.org/10.1038/s41586-022-05028-x

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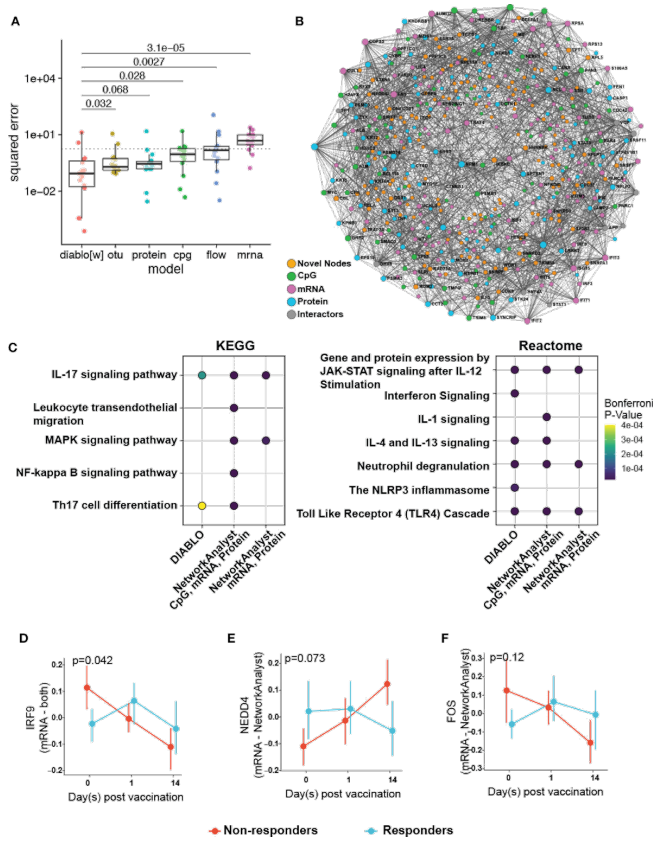
Systems Biology: Early Predictions of Vaccination Outcomes

Multi-Omic Data Integration Allows Baseline Immune Signatures to Predict Hepatitis B Vaccine Response in a Small Cohort



- Identification of predictive signatures for responders vs. non-responders to vaccination.
- Data integrated across cellular, epigenomic, transcriptomic, proteomic, and fecal microbiome profiles, and correlated to final HBV antibody titers.
- Baseline immune signatures able to predict who responds as well as antibody titer levels.
- Very small cohort applying machine learning.

Multi-Omic Data Integration Allows Baseline Immune Signatures to Predict Hepatitis B Vaccine Response in a Small Cohort Shannon CP etal, 2020.
https://www.frontiersin.org/articles/10.3389/fimmu.2020.578801/full

Problem #2: Immunity and Vaccine Response Varies by Population

We don’t know how to protect groups with greatest burden of disease:

- Older adults
- Infants
- Immunocompromised
- Individuals in LIMCs

Can we develop a predictive understanding of immunity in key groups ?

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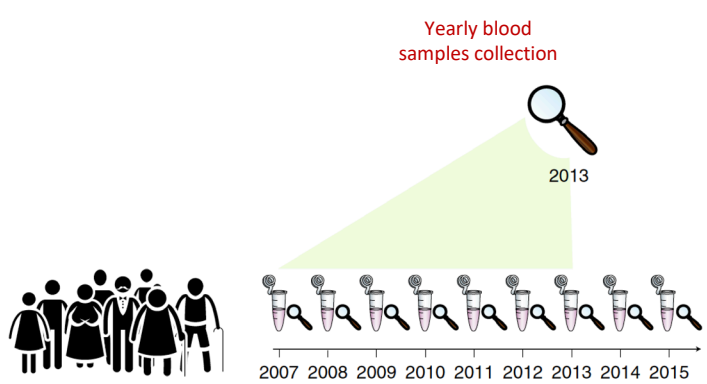
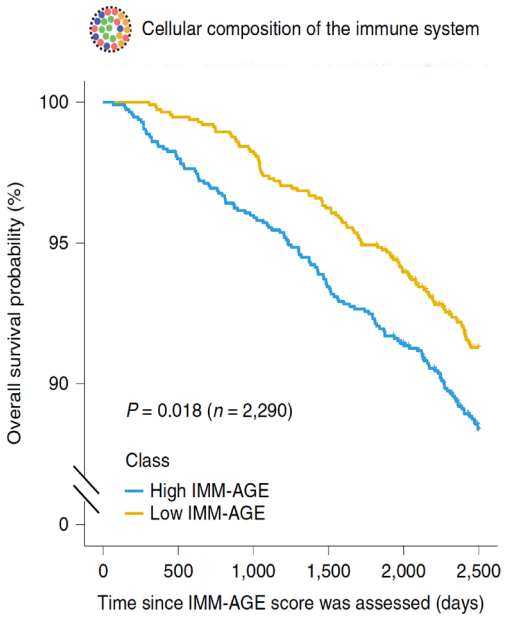
Prediction of Immune Health and Mortality in Older Adults

A clinically meaningful metric of immune age derived from high-dimensional longitudinal monitoring



Ongoing profiling	Cellular phenotyping
72 older adults (60–96)	Cytokine responses
63 young adults (20–31)	Gene expression



nature medicine

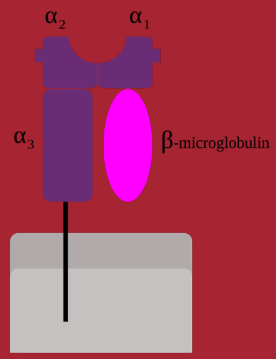
- Immunosenescence is a major issue in responses to vaccination and infection, health span and life span.
- Predicted all-cause mortality beyond well-established risk factors in the Framingham Heart Study.
- *IMM-AGE* describes a person's immune status better than chronological age.

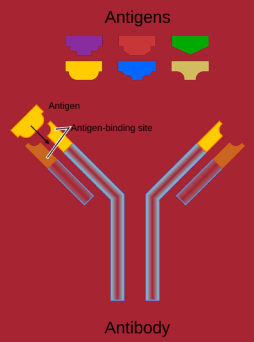
Alpert, A., Pickman, Y., Leipold, M. *et al.* A clinically meaningful metric of immune age derived from high-dimensional longitudinal monitoring. *Nat Med* **25**, 487–495 (2019). https://doi.org/10.1038/s41591-019-0381-y

NFA NEXT FRONTIER IN AGING
HUMAN VACCINES PROJECT
DECODING THE IMMUNE SYSTEM

Problem #3: Antigen / Immune Receptor Prediction and Identification

Antigen / immune receptor identification is a major limitation for successful immunotherapy and vaccine development.





Predictive models would accelerate therapeutic and preventative vaccines across diseases, from infectious to non-communicable diseases like cancers.

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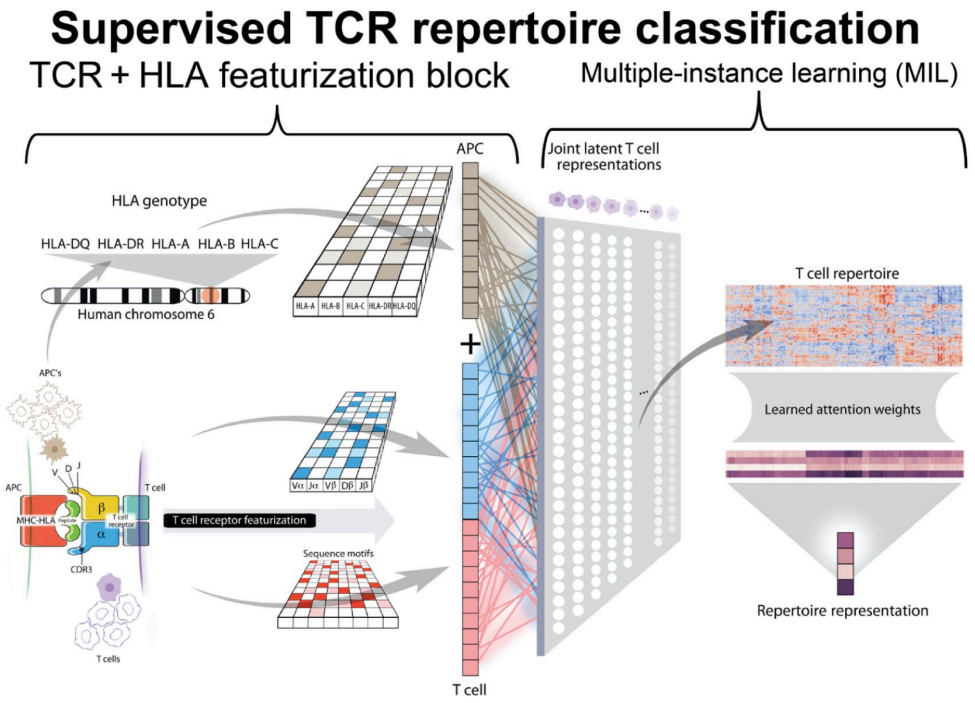
Predicting Effective TCR Immune Repertoires

Deep learning reveals predictive sequence concepts within immune repertoires to immunotherapy



- Most patients still do not respond to cancer immunotherapy.
- Using DeepTCR, a deep learning algorithm, identified T cell receptors that predict response to immunotherapy.
- Concept highly applicable to vaccines.

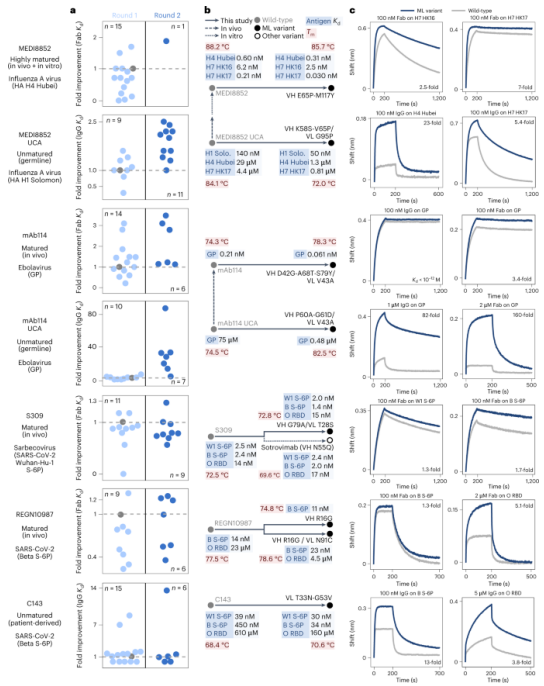
ScienceAdvances

John-William Sidhom *et al.* Deep learning reveals predictive sequence concepts within immune repertoires to immunotherapy. *Sci. Adv.* **8**, eabq5089 (2022). DOI: 10.1126/sciadv.abq5089

NFA NEXT FRONTIERS IN HUMAN VACCINES PROJECT DECODING THE IMMUNE SYSTEM

Efficient Evolution of Human Antibodies from General Protein Language Models

Efficient evolution of human antibodies from general protein language models



nature biotechnology

- Natural antibody evolution / affinity maturation greatly improves antibody binding and neutralization. It is hard to accomplish in a lab.
- General language models suggested evolutionarily plausible mutations to improve antibody fitness and binding.
- Evolved seven human IgG antibodies from coronavirus, ebolavirus and influenza A virus.
- Improved antibody affinity across all in two rounds of evolution.

Hie, B.L. *Nat Biotechnol* (2023). https://doi.org/10.1038/s41587-023-01763-2

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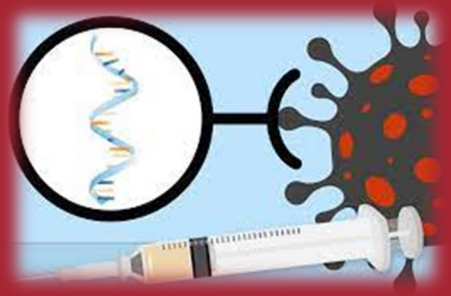
Problem #4: Vaccine Development Is Not Fully Optimized

Lack of optimization across vaccine platforms hinder efficacy, efficiency and distribution—and our ability to respond to pandemics.



Computational design and iteration has potential to rapidly improve vaccine design at key steps.

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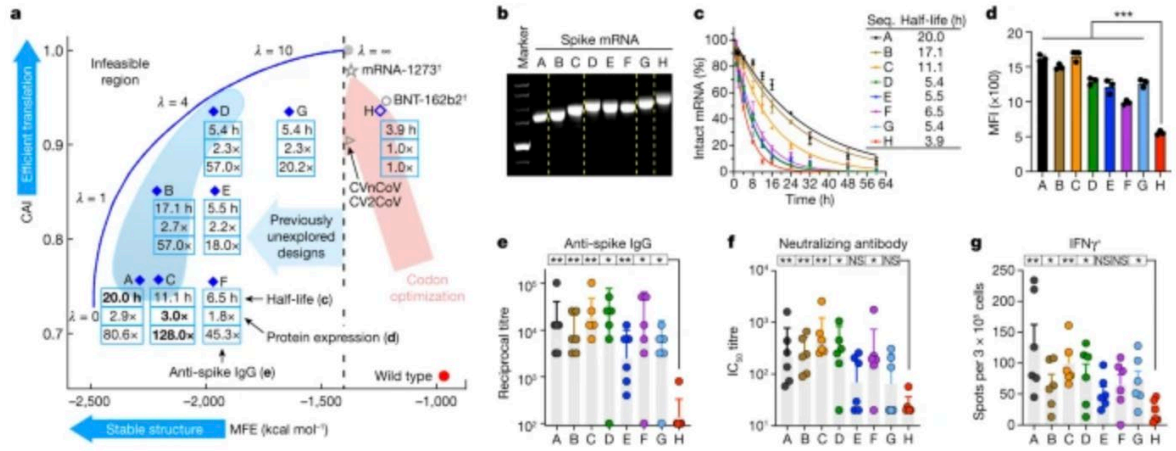
Computational Optimization of mRNA Vaccines

Algorithm for optimized mRNA design improves stability and immunogenicity

Fig. 4: Experimental evaluation of LinearDesign-generated mRNA sequences encoding SARS-CoV-2 spike protein.



nature

- Instability and protein expression for mRNA vaccines are major obstacles to storage, distribution and efficacy.
- LinearDesign is a program that uses approaches in computational linguistics to improve vaccine design.
- Algorithm can design an optimal mRNA encoding the SARS-CoV-2 spike protein in 11 min.
- Improved chemical stability, protein translation and in vivo immunogenicity.

Zhang, H., Zhang, L., Lin, A. *et al.* Algorithm for optimized mRNA design improves stability and immunogenicity. *Nature* **621**, 396–403 (2023). https://doi.org/10.1038/s41586-023-06127-z

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Problem #5: Optimizing Clinical Studies

Clinical trials are expensive, time consuming, and especially in the early stages, not highly predictive of success.

Predictive signatures in clinical studies offers potential for smaller, faster, safer, more efficient clinical studies, that include key immunological subgroups.

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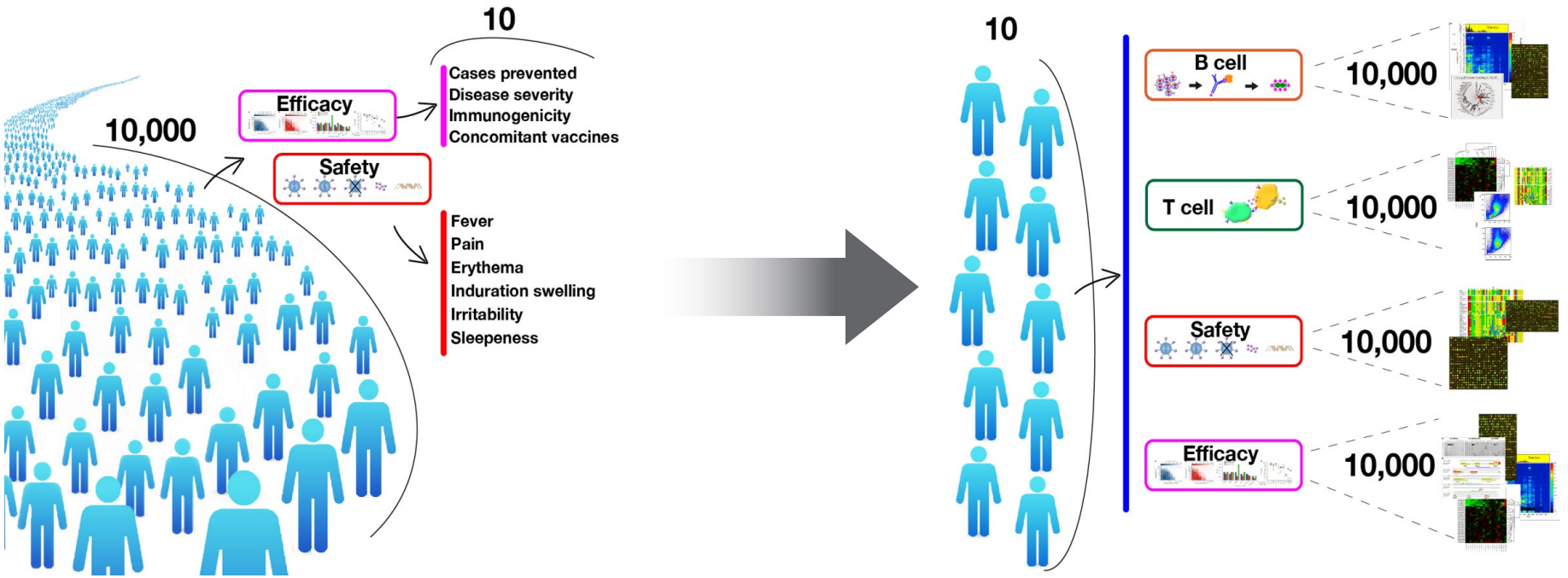
Integration of Systems Vaccinology with Clinical Design



Smaller Trials	Big Data	Predictive Signatures	Greater Probability of Success

Slide adapted from Rino Rappuoli

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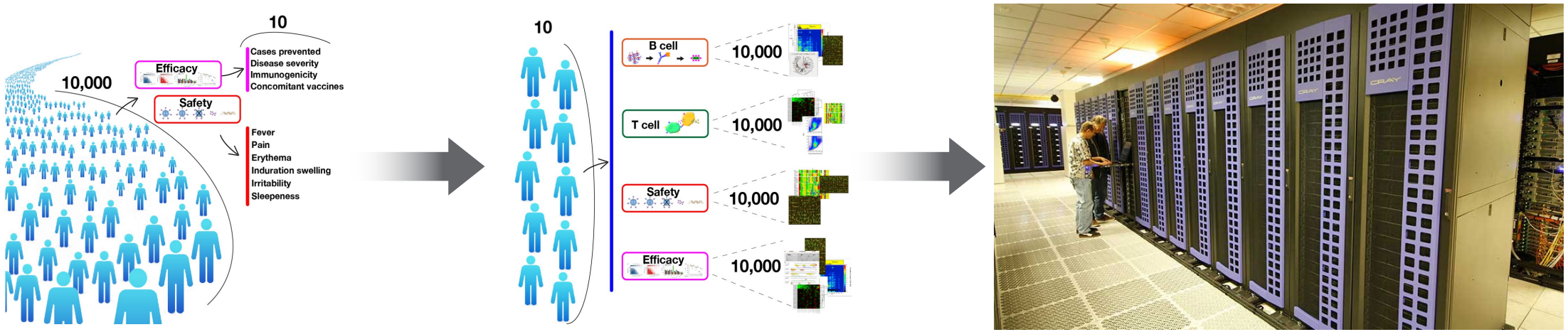
The Future?: Towards AI-Simulated Vaccine Trials



- Exponential leaps in scale of data being generated
- It is now estimated that 1 trillion terabytes (1 yottabyte) would give a complete picture of human biology per individual
- Artificial intelligence and machine learning will be central for analysis of “big data” and will transform the future of vaccine development

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AI Will Transform Vaccine Development…
But These are the Early Days …

- **New Technology has been historical driver in advances of vaccines.**
- **Artificial Intelligence is revolutionizing other industries:** Investment banking, media, cybersecurity, weather modelling, driverless cars, imaging.
- **Tools Just Beginning to be Applied to Biomed and Vaccines:** In molecular biology, LLMs will likely change that more: excellent at predicting outcomes from the statistical properties of intricate, noisy sequential data.
- **Proof is in the Pudding:** Must show clinical efficacy and improvement/efficiency over existing lab approaches.

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Acknowledgements

Next Frontier Advisors, the Human Immunome Project, participants at the Human Immunome Project AI Summit, Eric Topol, Shai Shen Orr, John Tsang, Rino Rappuoli, Wayne Koff.

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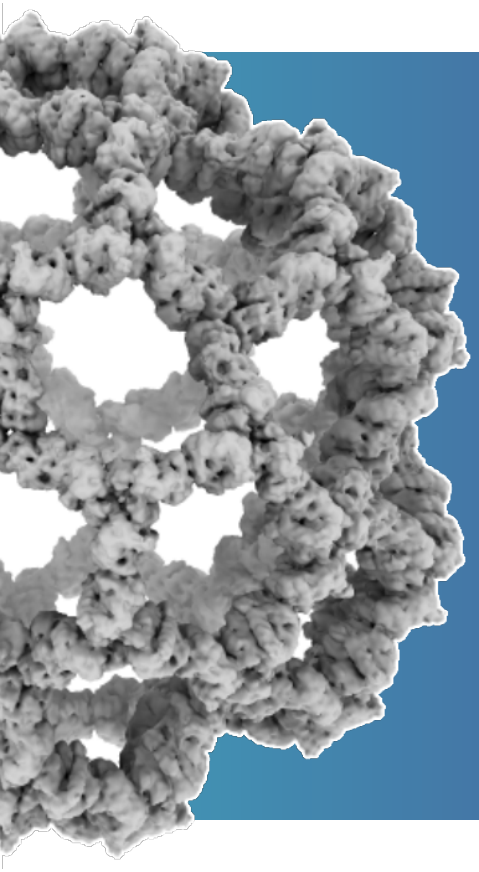


Artificial Intelligence (AI) assisted vaccine design

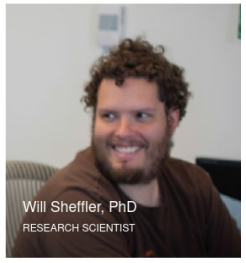
Mark Langowski

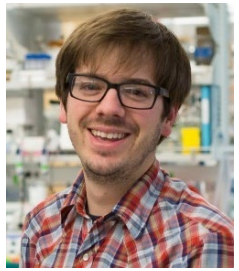
King Lab

23 February 2024

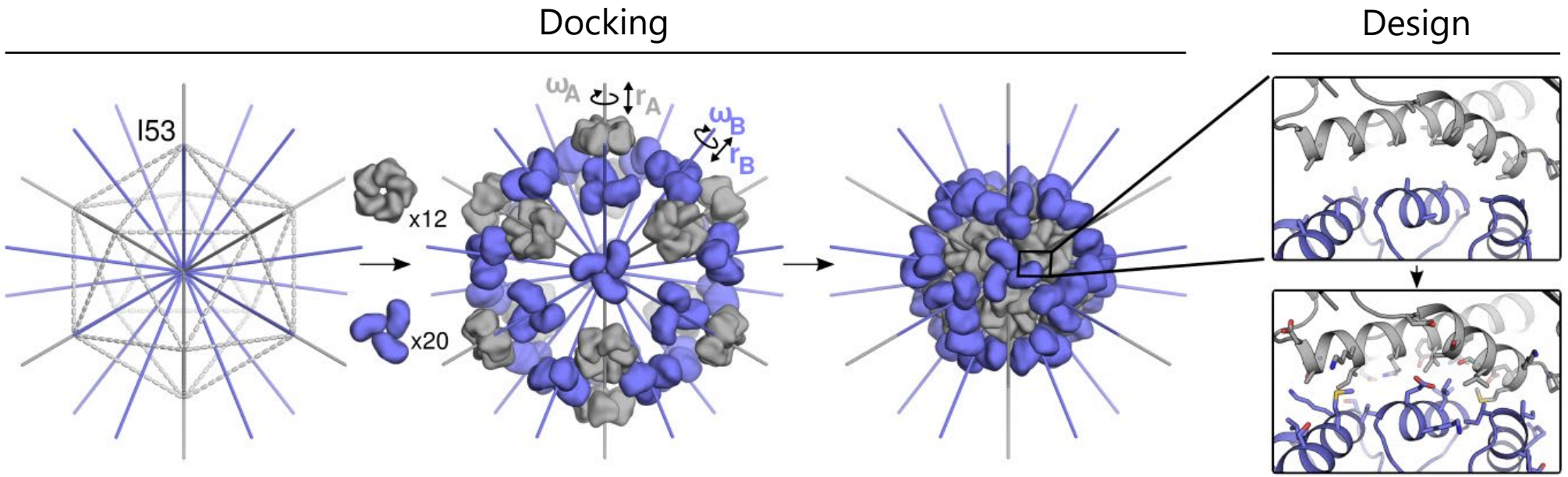
INSTITUTE FOR
Protein Design
UNIVERSITY of WASHINGTON

We previously developed a general computational method for designing new self-assembling protein nanomaterials



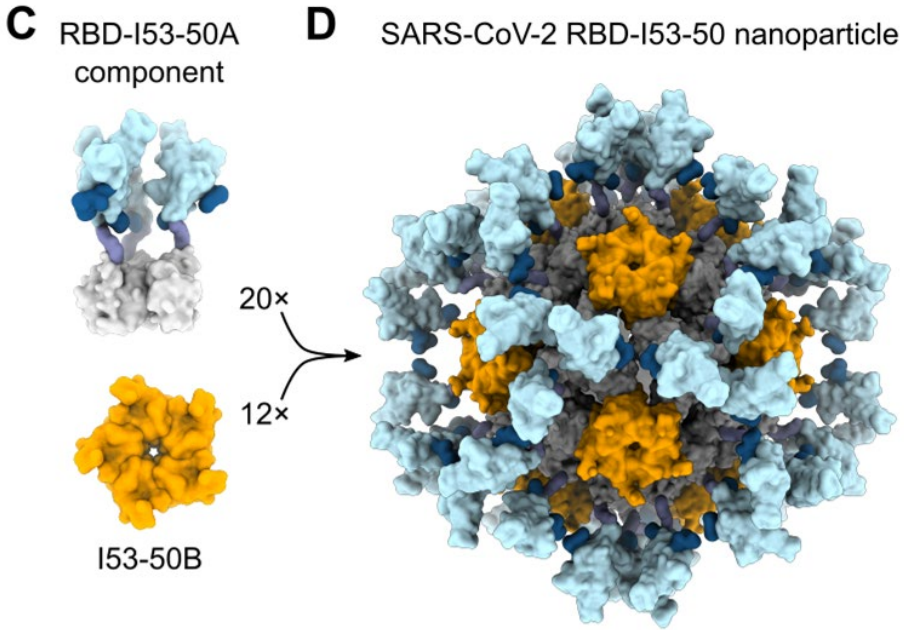


Jacob Bale



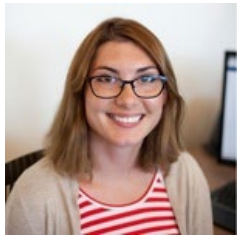
King NP, et al. (2012) *Science* **336**: 1171-4.
King NP, et al. (2014) *Nature* **510**: 103-8.
Hsia Y et al. (2016) *Nature* **535**: 136-9.
Bale J, et al. (2016) *Science* **353**: 389-94.
Ueda G & Antanasijevic A, et al. (2020) *eLife* **9**: e57659.
Wang JW & Khmelinskaia et al. (2022) *PNAS* **120**: e2214556120.
de Haas RJ, et al. (2023) *bioRxiv* 2023.08.04.551935.

The world's first computationally designed protein medicine is licensed for use in multiple jurisdictions

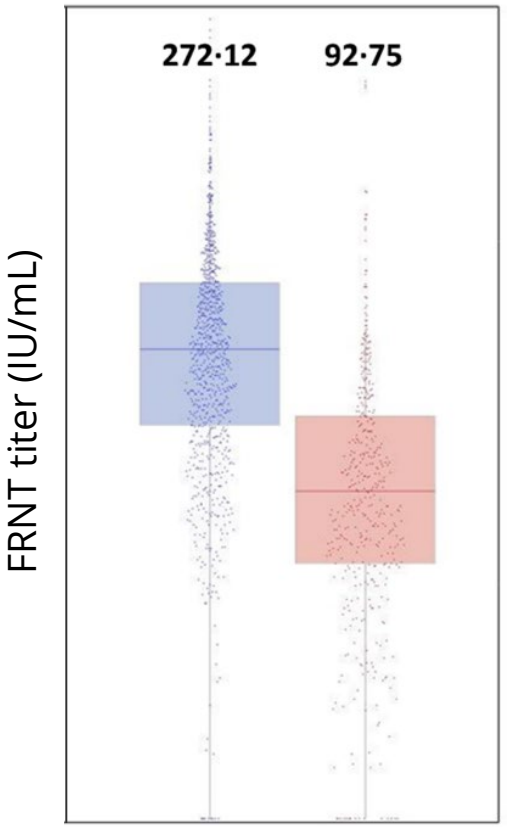


Lexi Walls

Brooke Fiala



David Veesler



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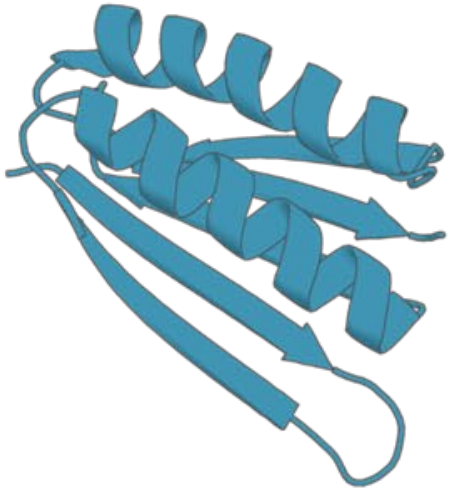
SK bioscience

gsk

Walls AC & Fiala B et al. (2020) *Cell* **183**: 1367-82.
Song JY et al. (2023) *EClinicalMedicine* **64**: 102140.

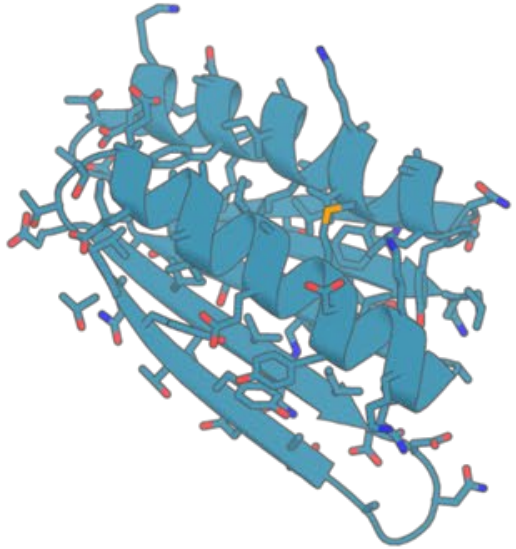
AI-assisted protein design

Protein backbone generation



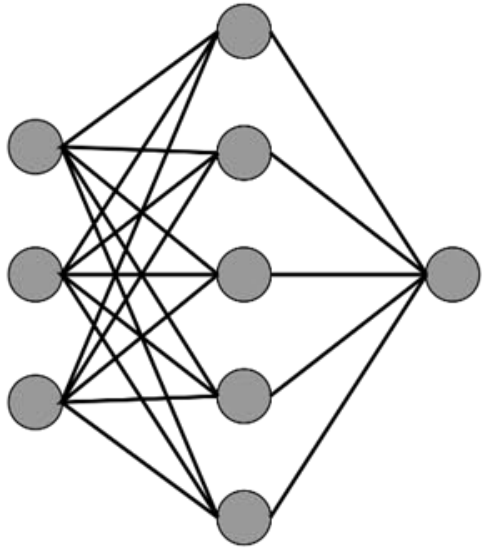
What features do we want?

Sequence design



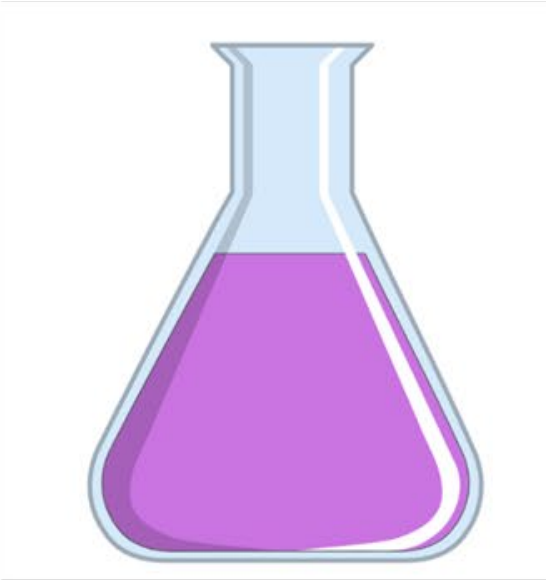
What sequence will fold into this protein?

Structure prediction



Is this protein predicted to fold?

Experimentation



Does this protein "work"?

Machine learning is revolutionizing protein design

1 **Hallucination, Inpainting, RFdiffusion**
Generates new protein structures

Wang et al. *Science* 2022
Watson et al., *Nature* 2023

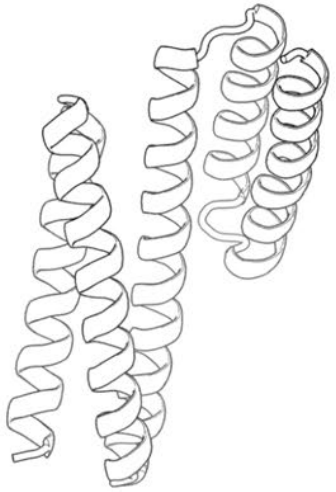
2 **ProteinMPNN**
Assigns amino acids to protein structures

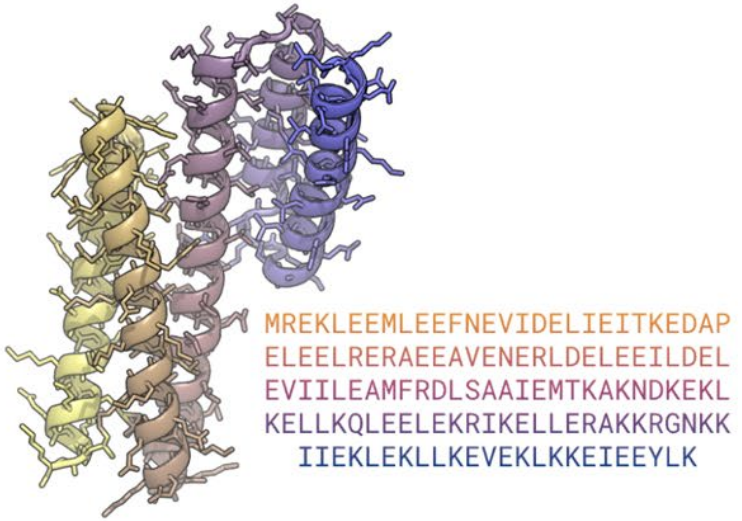
Dauparas et al., *Science* 2021

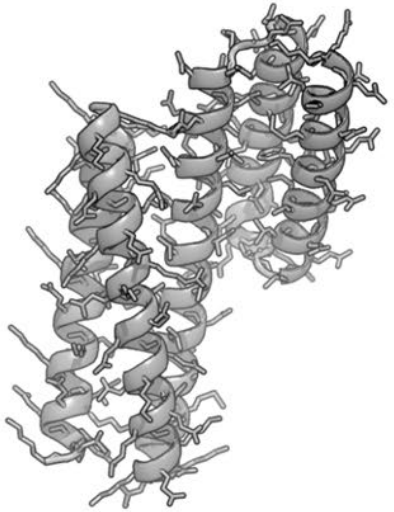
3 **RoseTTAFold / AlphaFold**
Predicts structures from sequence

BREAKTHROUGH OF THE YEAR
Baek et al., *Science* 2021

David Baker

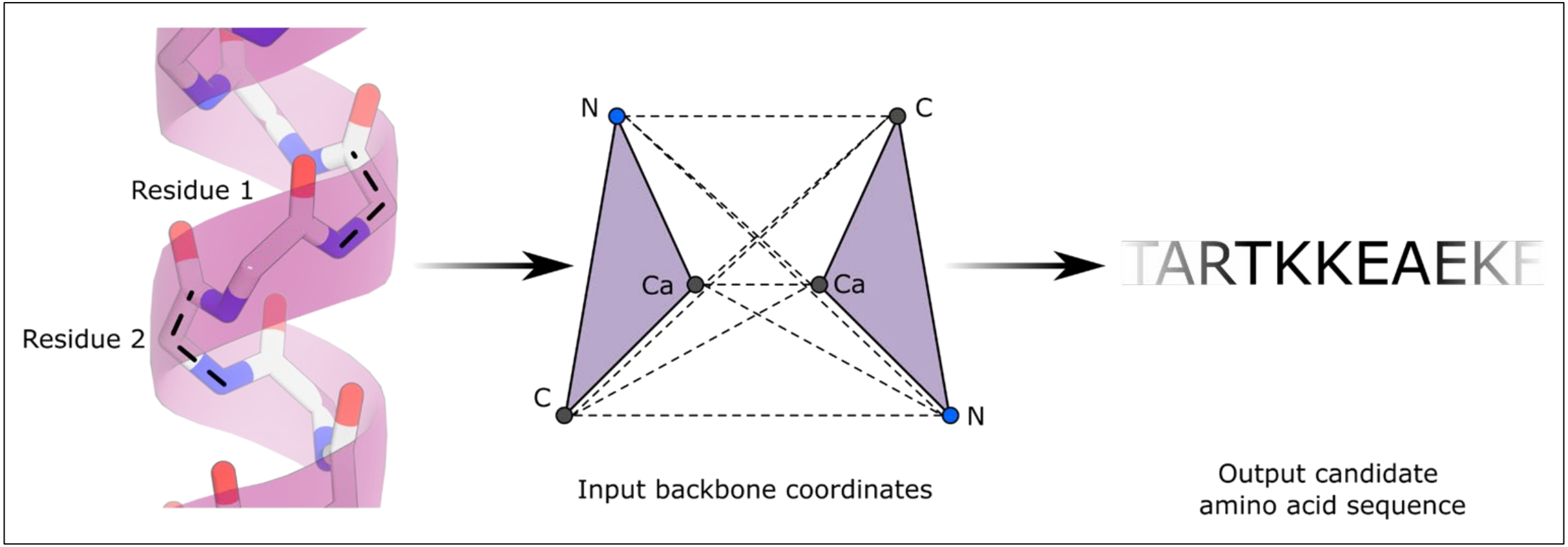






Sequence design improved with *ProteinMPNN*

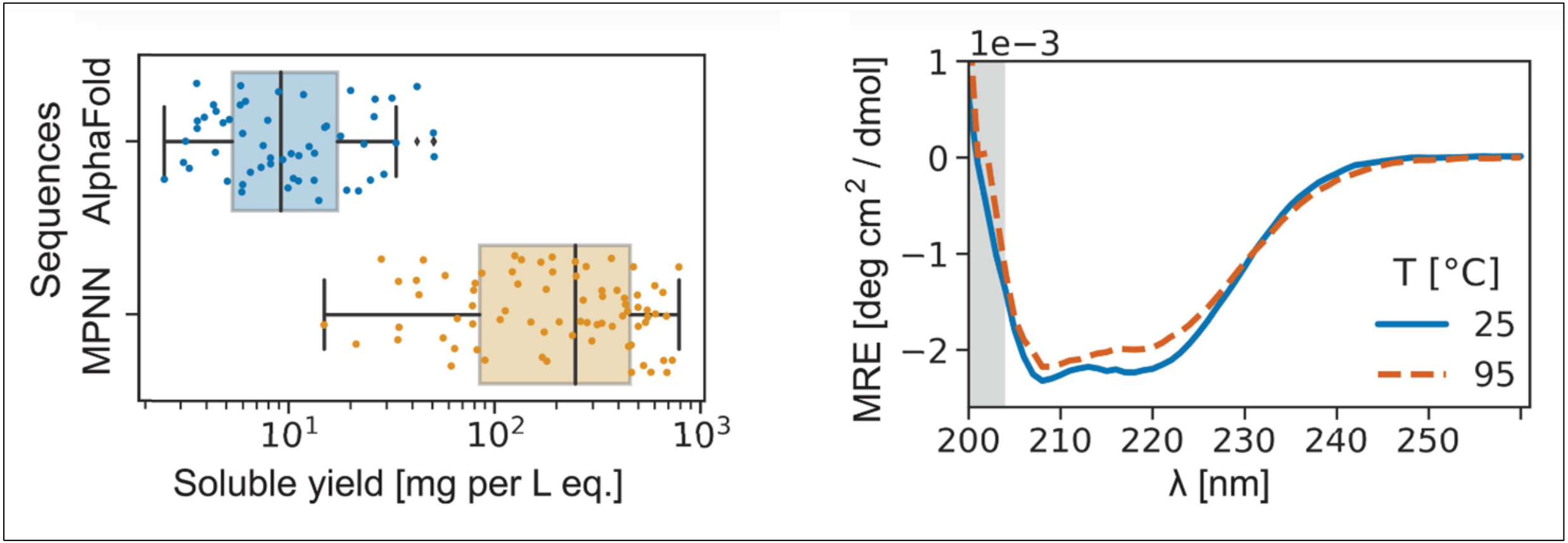
ProteinMPNN takes in a backbone and returns a candidate sequence.



Dauparas, et al., 2022

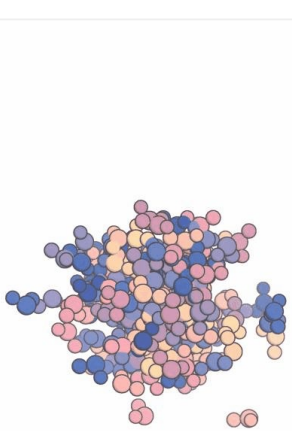
Sequence design improved with *ProteinMPNN*

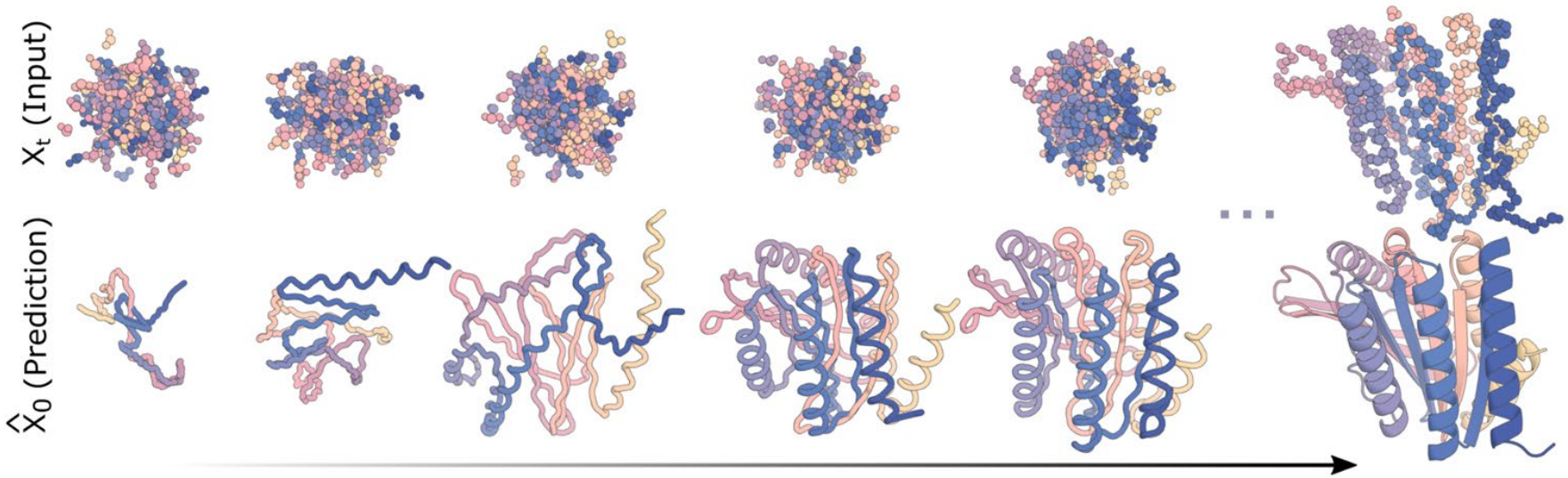
Sequences designed with ProteinMPNN tend to be highly soluble and thermostable.



Dauparas, et al., 2022

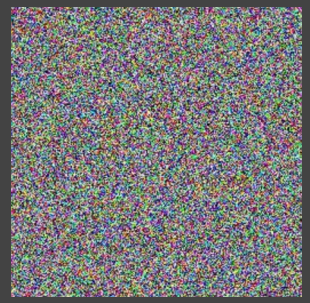
RFdiffusion generates new protein structures via progressive denoising

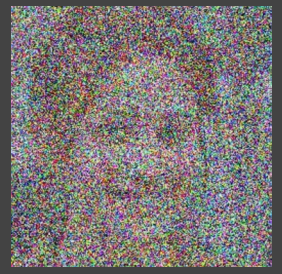




Inspired by deep-learning methods for generating synthetic images

e.g. DALL-E

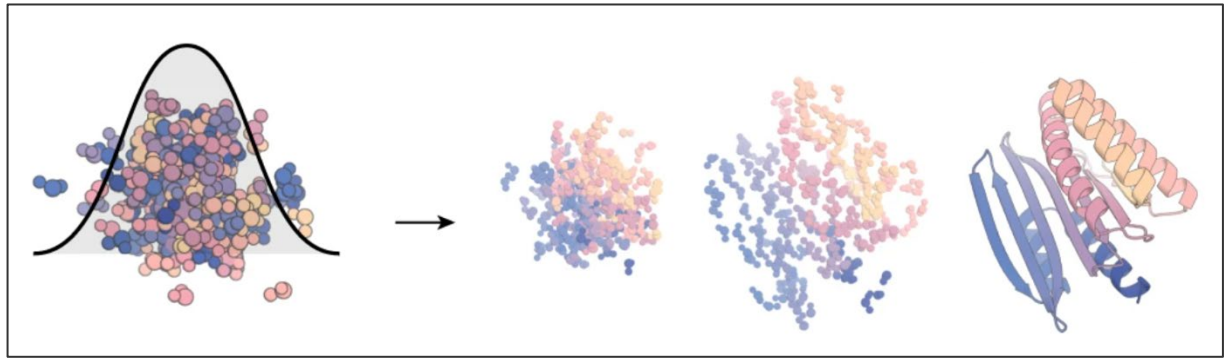




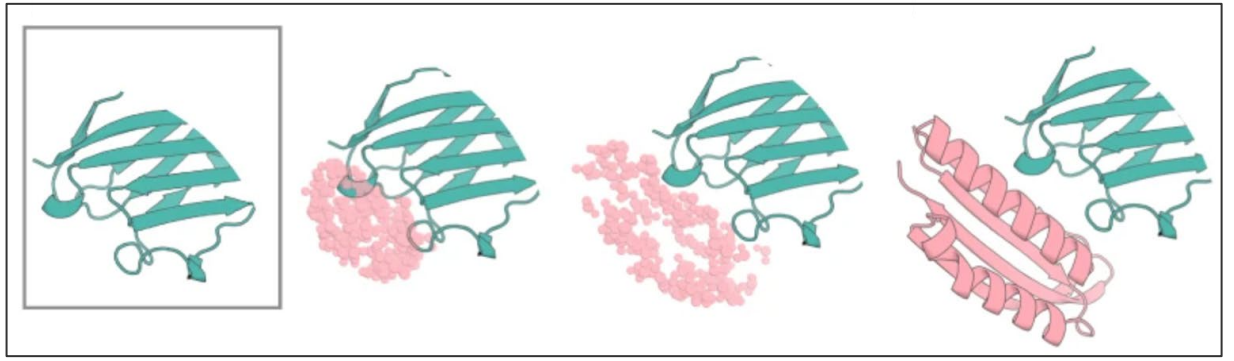
Watson J. et al. (2023) *Nature* **620**: 1089–1100.
Synthetic image trajectory from Lugmayr et al., ETH Zürich

RFdiffusion accommodates a wide variety of design tasks

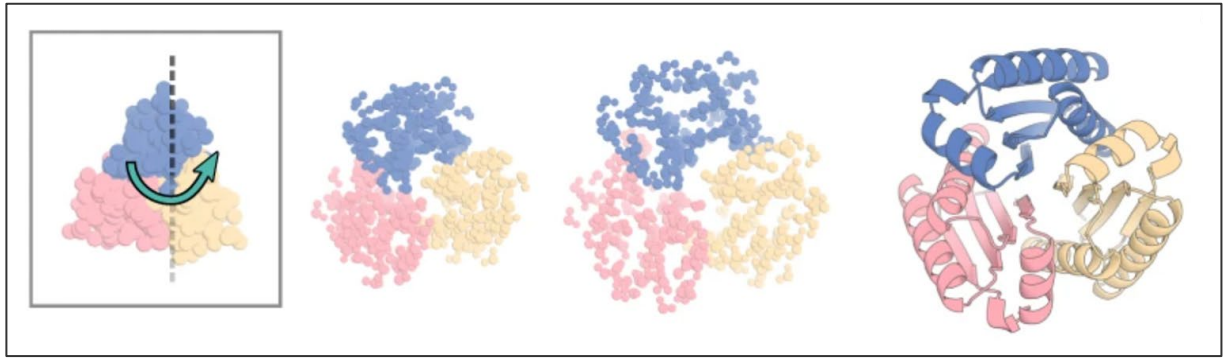
Unconditional generation



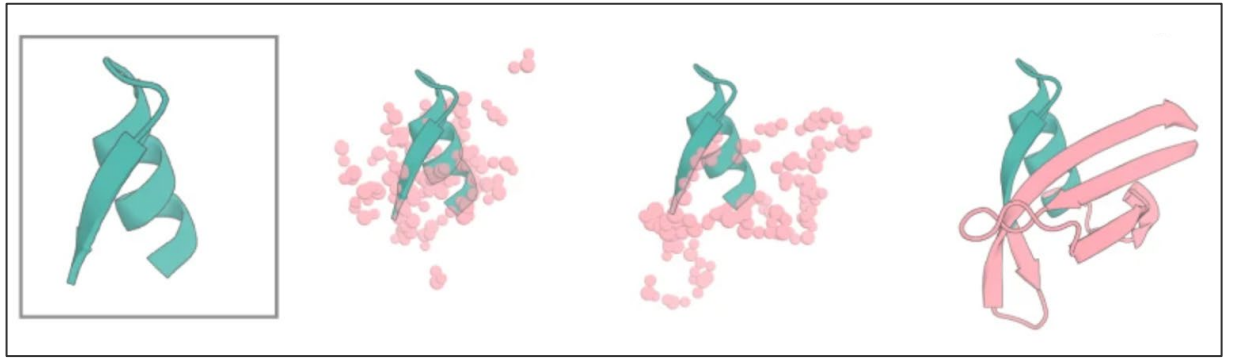
Protein binders



Symmetric oligomers

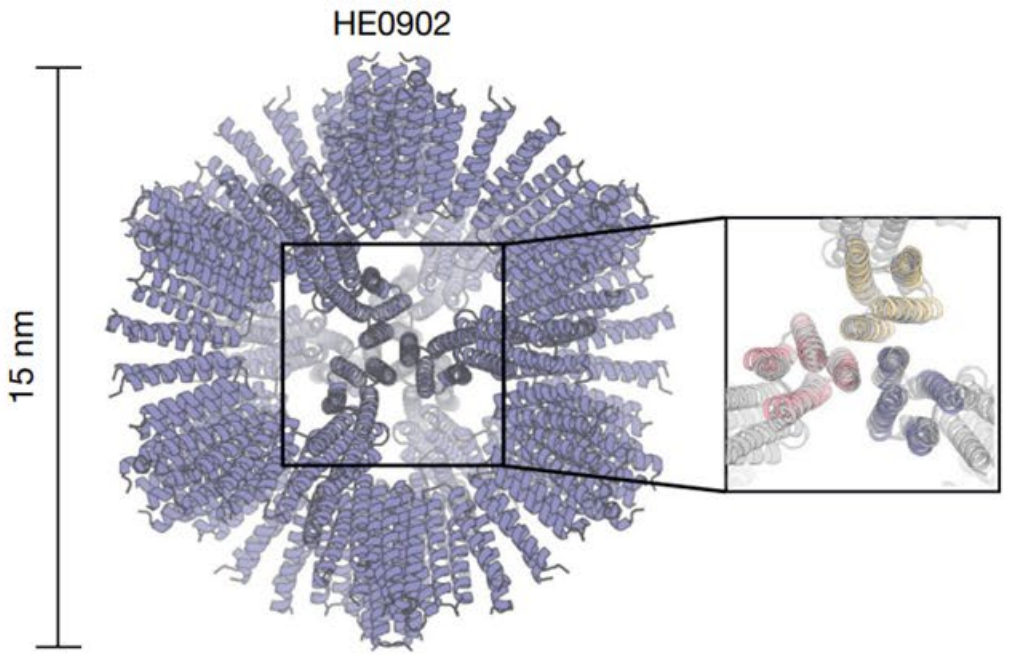


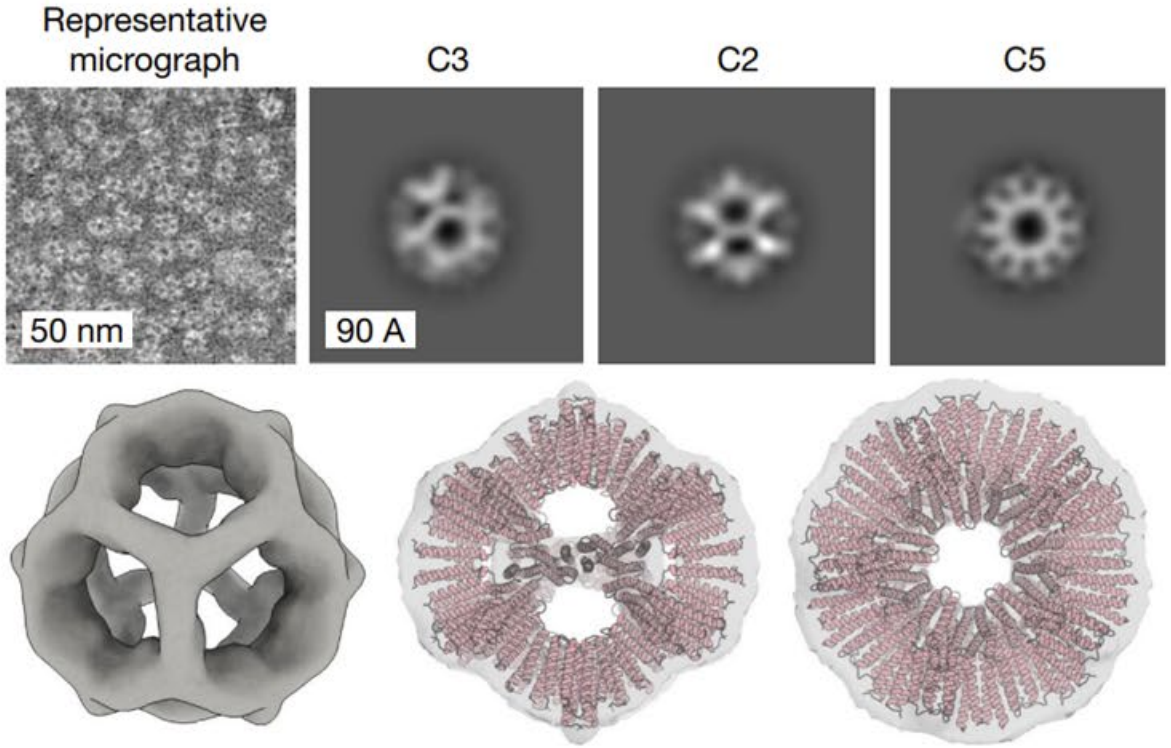
Functional motif scaffolding



Watson, et al., 2023

RFdiffusion can generate novel self-assembling proteins completely *de novo*



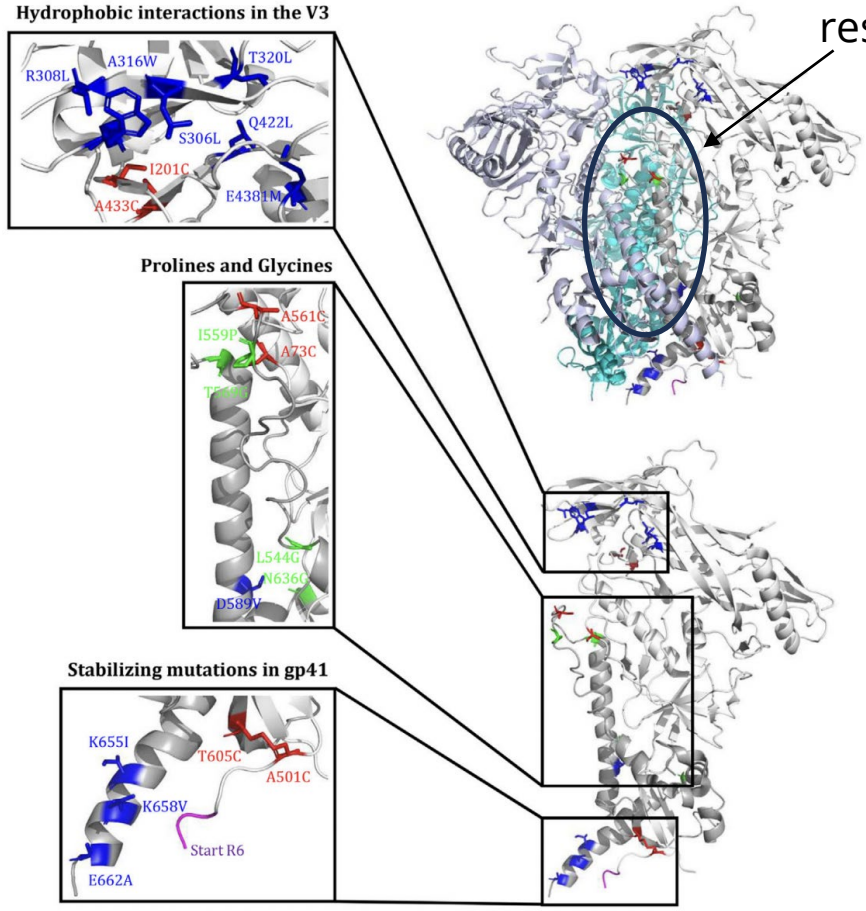


Helen Eisenach

Watson J. et al. (2023) *Nature* **620**: 1089–1100.

Can we replace gp41 to make hyperstable native-like pre-fusion Env trimers?

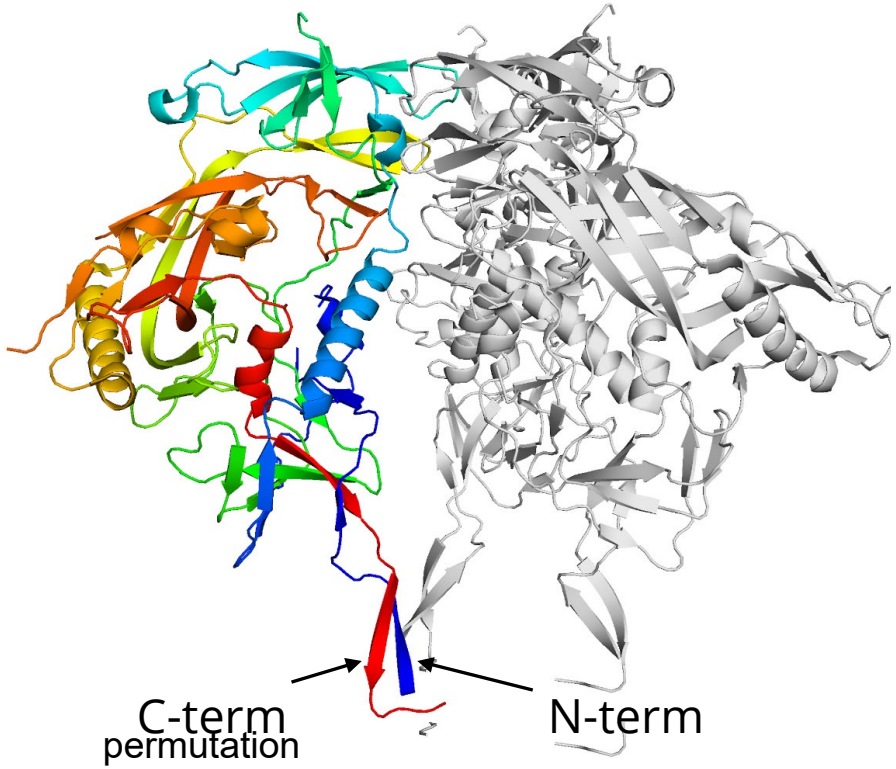
Metastable core; structure not fully resolved



From Derking R. and Sanders R.W., *JIAS*, 2021

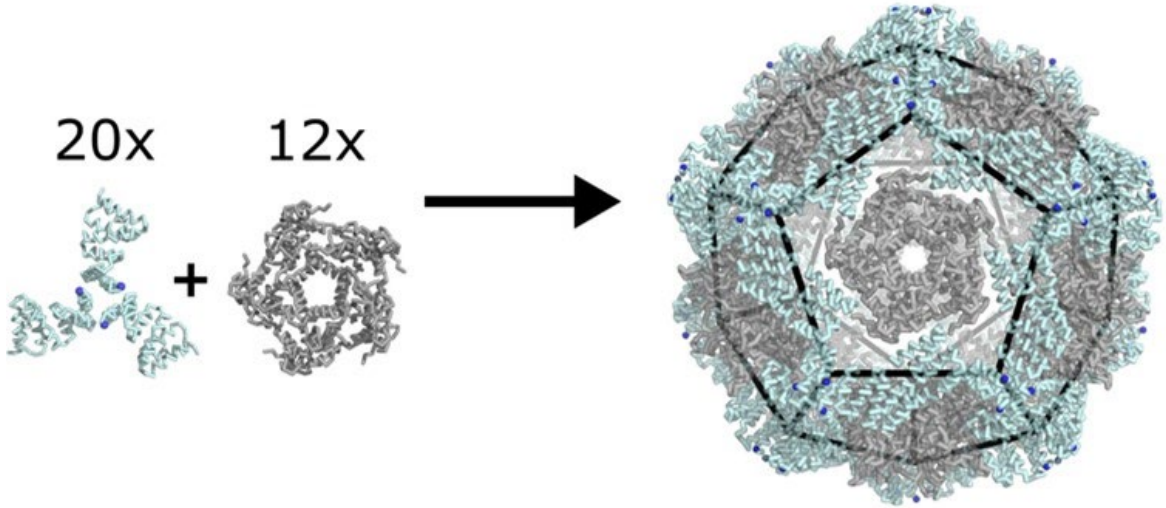
Majority of stabilization mutations focus on the gp41/gp120 interface and gp41 stability

How to accommodate new core?



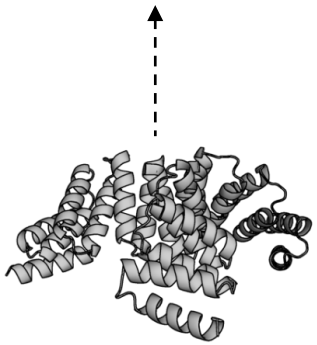
- Remove gp41
- New gp120 permutation
- New supporting structure
- Target epitopes in proper trimer context

Using AI-assisted methods to generate a new gp120 trimer core and fusion to a nanoparticle



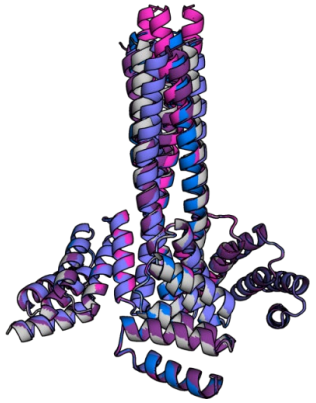
I53_dn5

Yoann Aldon

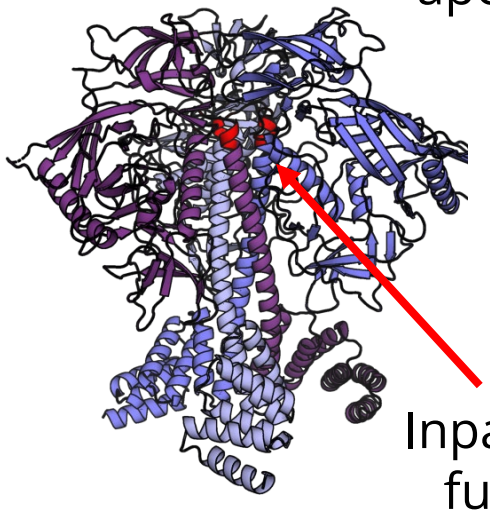


I53_dn5B

Oligomeric hallucination to generate a helix bundle

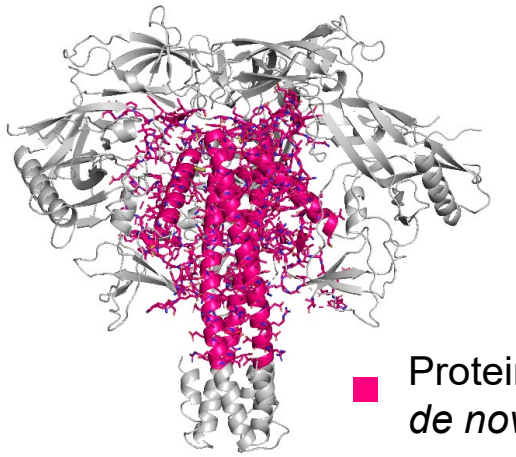


Dock gp120 trimer and inpaint new connection

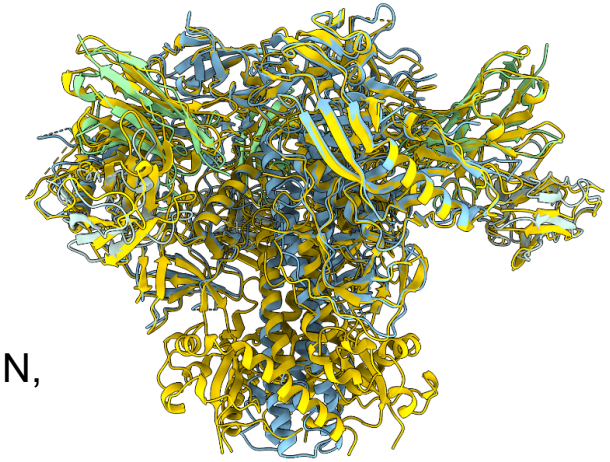


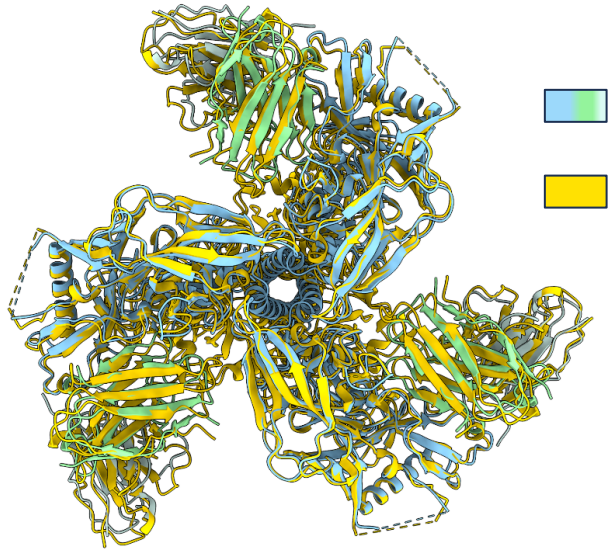
Ueda G & Antanasijevic A, et al. (2020) *eLife* **9**: e57659.

High-resolution cryo-EM structure of a gp41-free native-like trimer shows high fidelity to the native Env trimer



ProteinMPNN, *de novo*

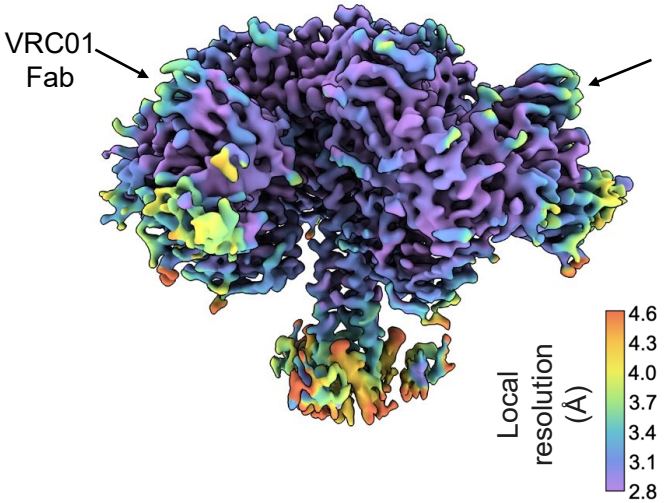




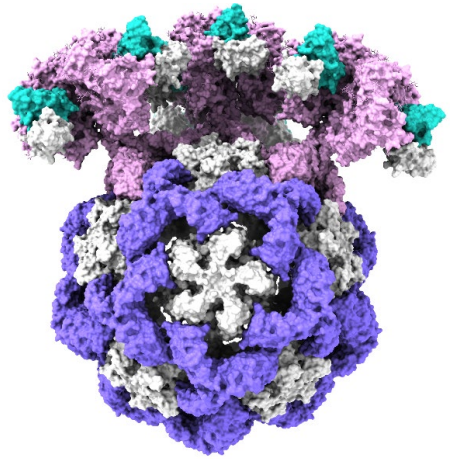
38G trimer + VRC01 (cryo-EM)

SOSIP trimer + 3BNC117 (PDB 5v8m)

38G trimer + VRC01 Fab
3.31 Å resolution



38G on I53_dn5 nanoparticle



- **Closely matches design model**
- **VRC01-class angle of approach identical to native SOSIP**
- **Full Fab to nanoparticle stoichiometry (60 Fabs:1 NP)**

G. Jo, A. Tran, G. Ozorowski, A. Ward

Summary and outlook

Computationally designed protein vaccines are now a reality

AI is revolutionizing protein design – dramatically expanding what we can make and how quickly we can make it

AI protein design is a positive force in designing better protein medicines

Acknowledgements

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Universitair Medische Centra

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INSTITUTE FOR Protein Design
UNIVERSITY of WASHINGTON

AI/ML Immunogen Design

Jimmy Gollihar, PhD

02/23/2024

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Workflow for traditional vaccine design

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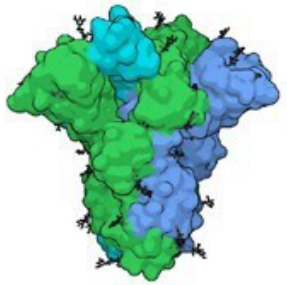
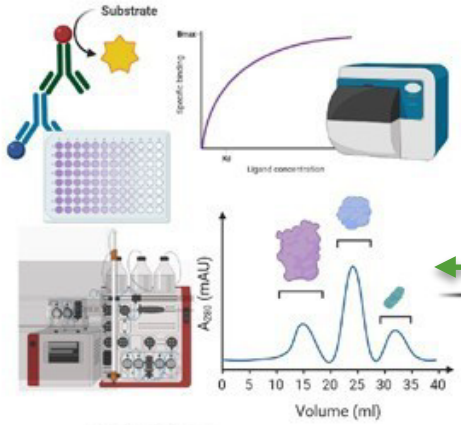
antigen design



- rational design
- directed evolution
- computational design

in vitro experiments



- stability
- epitope display
- expression
- antibody binding
- structural biology

pre-clinical work

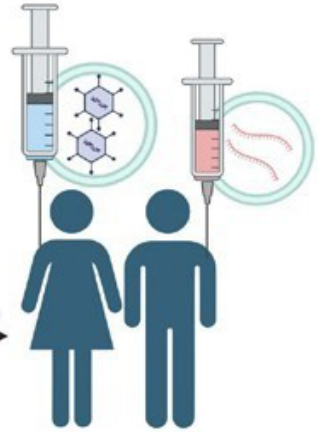
early animal work

- immunization
- toxicity

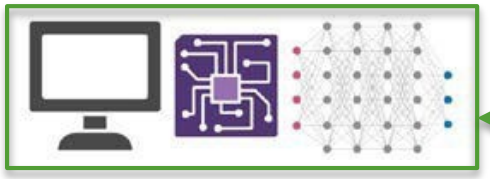
late-stage animal work

- challenge
- immunization
- toxicity

clinical studies



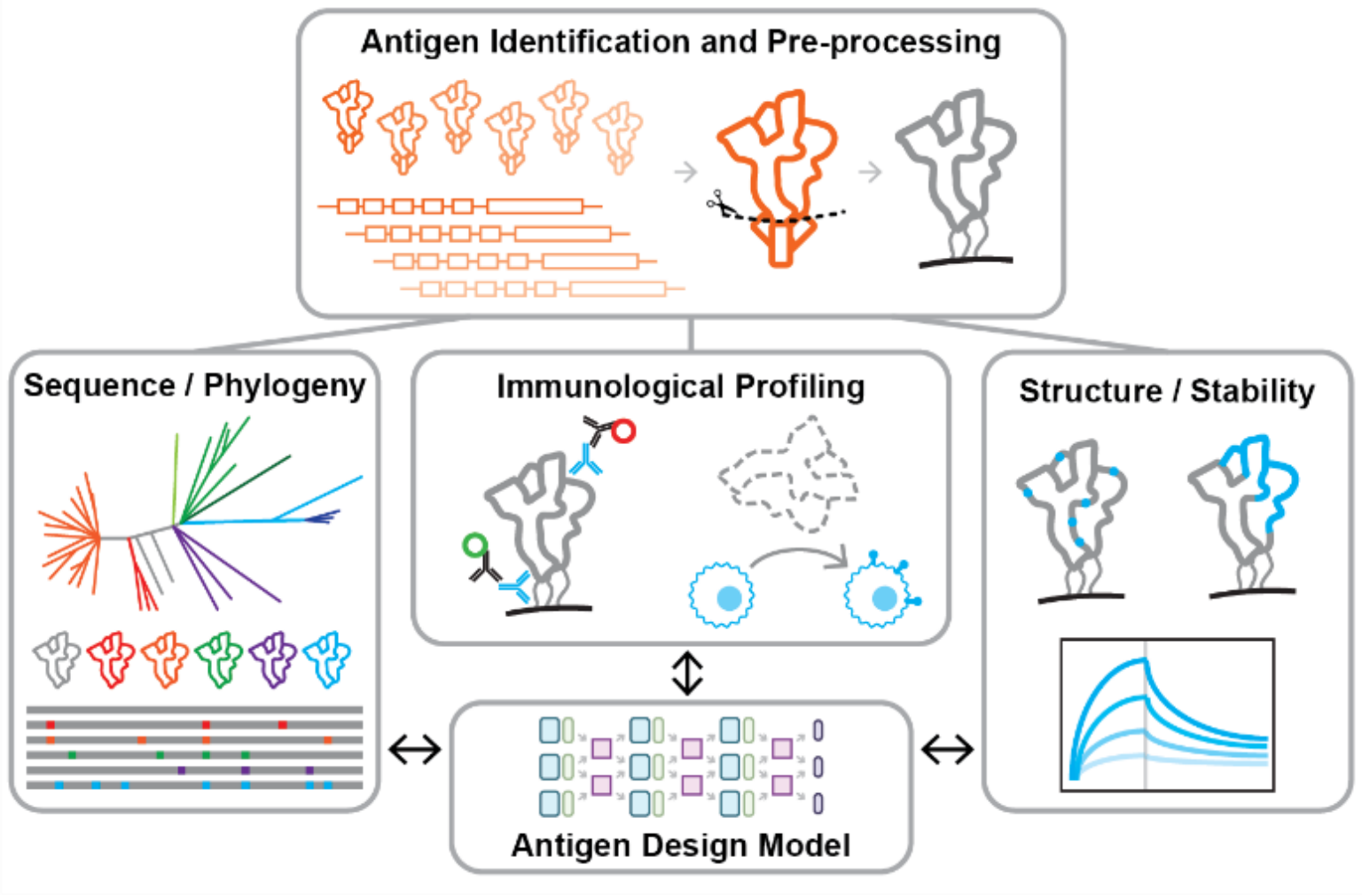
- platform-agnostic
- easily to be combined with mRNA, adenovirus vectors, etc.
- protein level



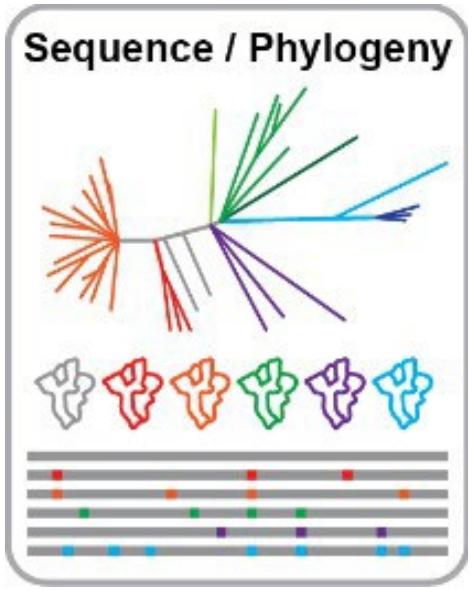
abstract concepts, learn from data, optimize methods

AG Schoeder, Institute for Drug Discovery

AI/ML immunogen design tools



Sequence & phylogeny



Training Phase

Language Model (GPT-2)

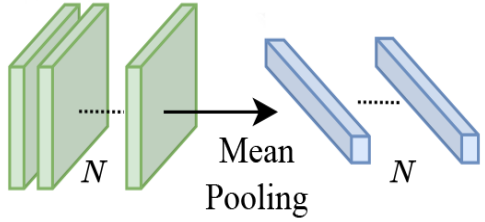
$$p(x) = \prod_{i=1}^{n} p(s_n | s_1, ..., s_{n-1})$$

1. Train on a fixed protein family
2. Learn the families latent sequence distribution

Generation Phase

1. Autoregressive generation of N sequences
2. Latent embeddings

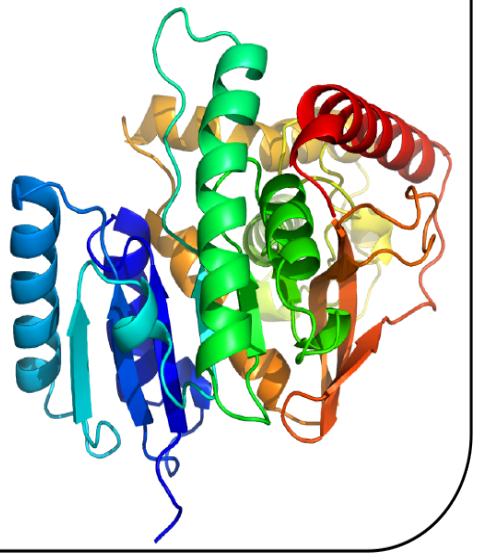
$h_{ij}\ \varepsilon\ r^{512\times d}$ $z_j\ \varepsilon\ r^{d}$



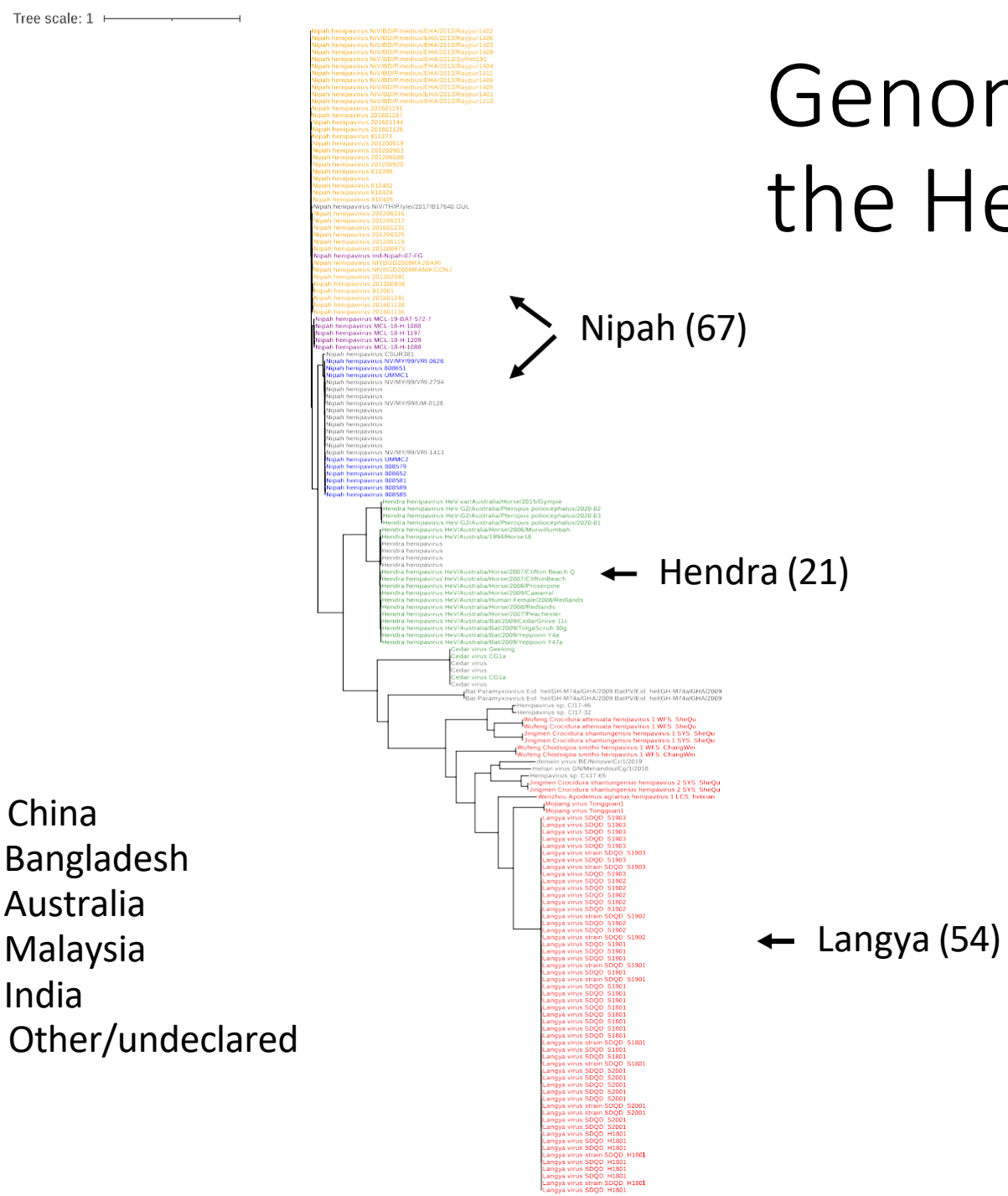
3. k-means clustering and prototype selection

Folding Phase

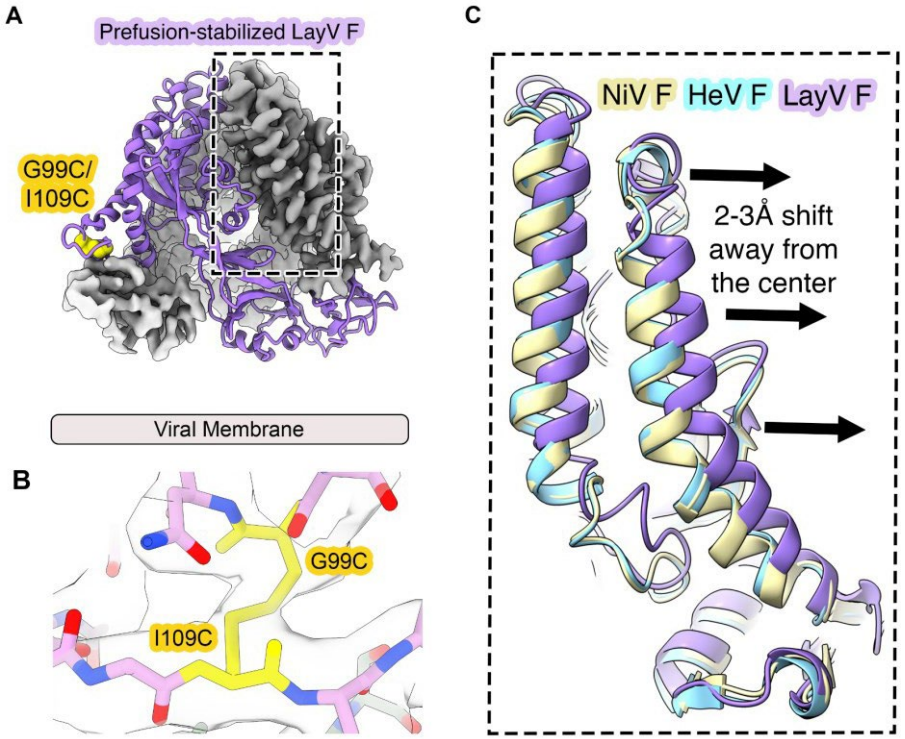
AlphaFold2



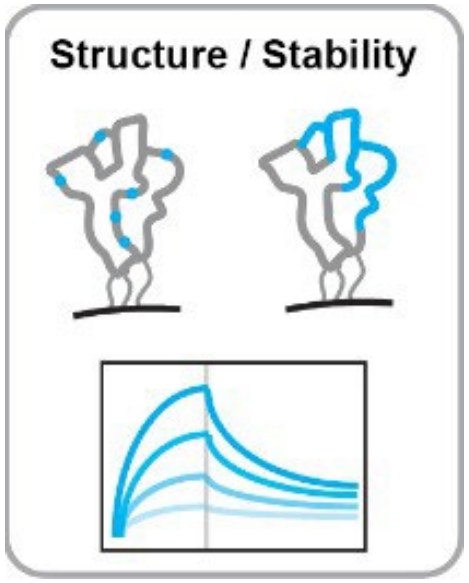
Genomes and Diversity in the Henipa branch (BV-BRC)

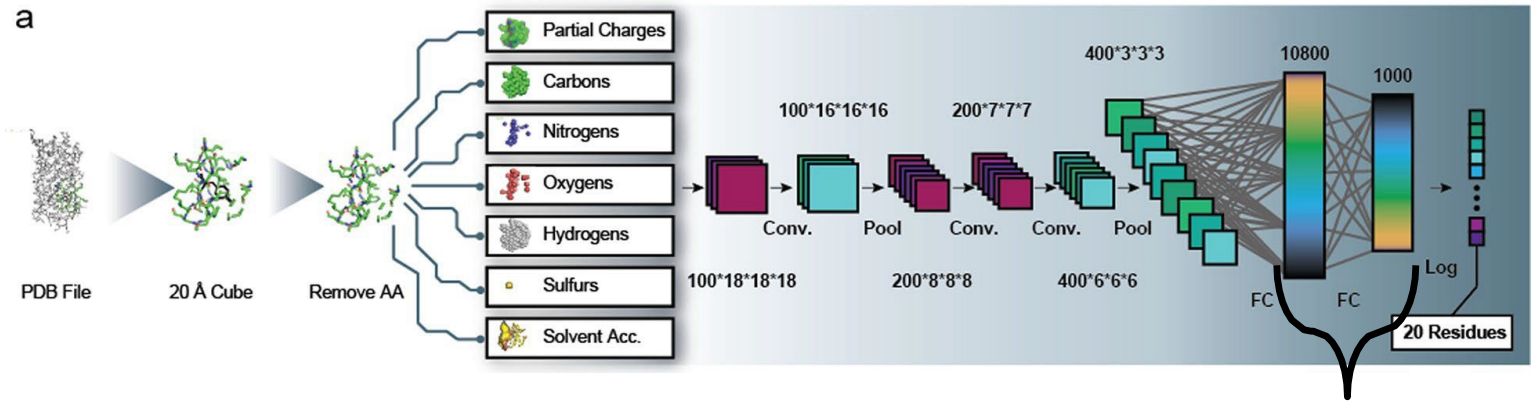


How far do stabilizing mutations reach??

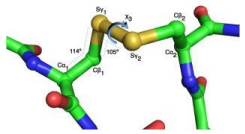


Structure & stability

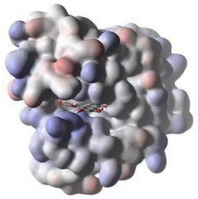




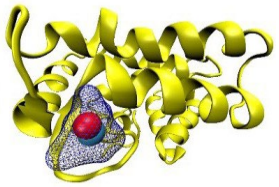
Transfer learn for specific chemistries:



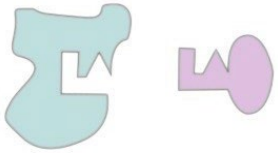
Disulfide bonds



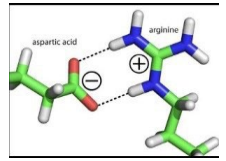
Solvent Inaccessible Regions



Cavity Filling



Lock-and-key indels



Salt bridges

Cavity filling mutations

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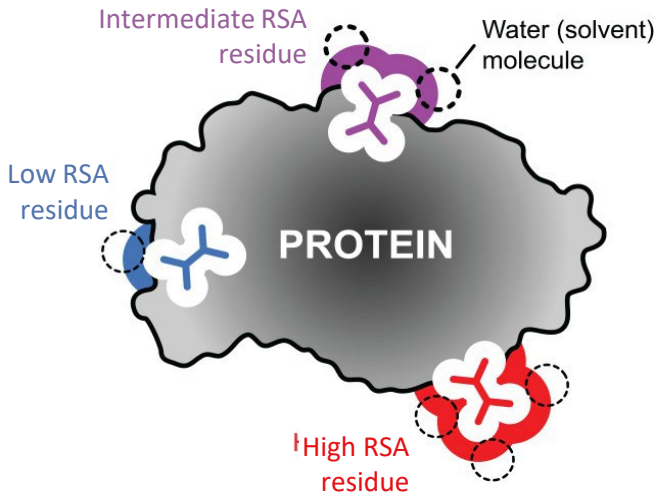
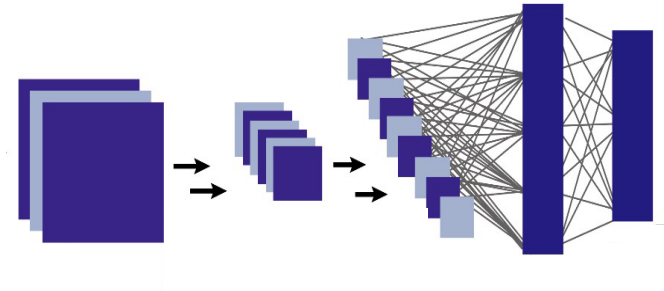
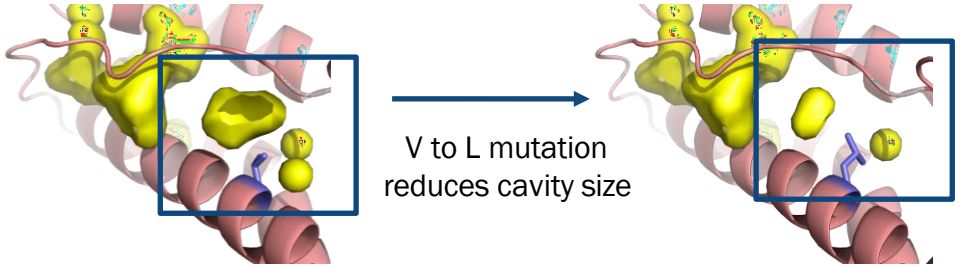
Solvent Accessibility → Net → Cavity calculation





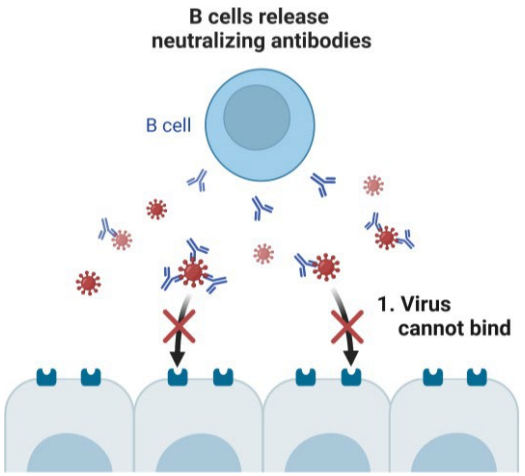


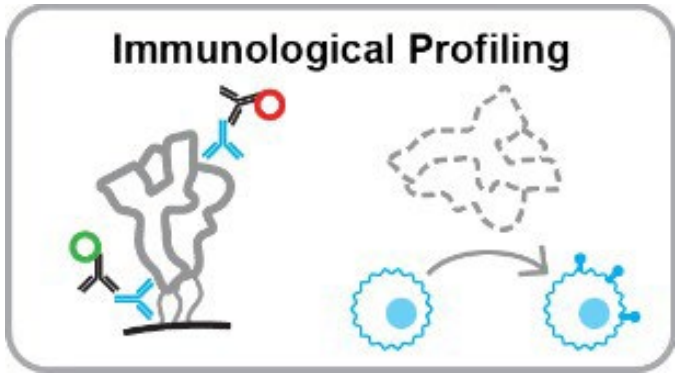
Scan protein and calculate solvent accessibility to identify buried residues

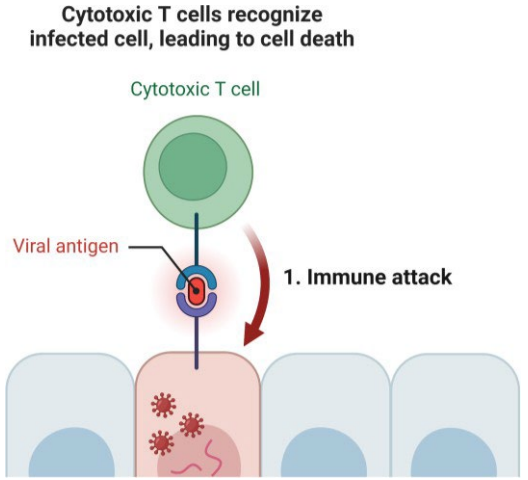
Target and downselect specific amino acid substitutions (I,V,L,M,F)

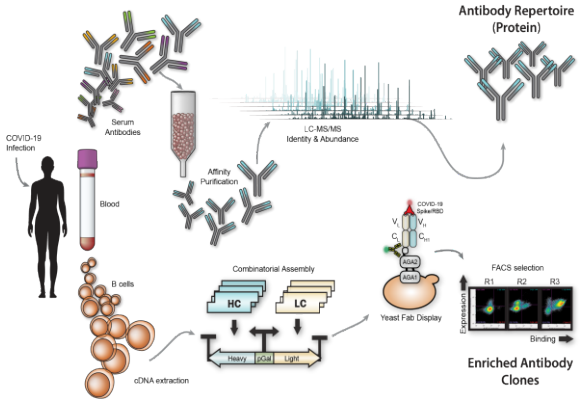
Build variant structures with DLPacker and calculate cavity volume to ensure reduction

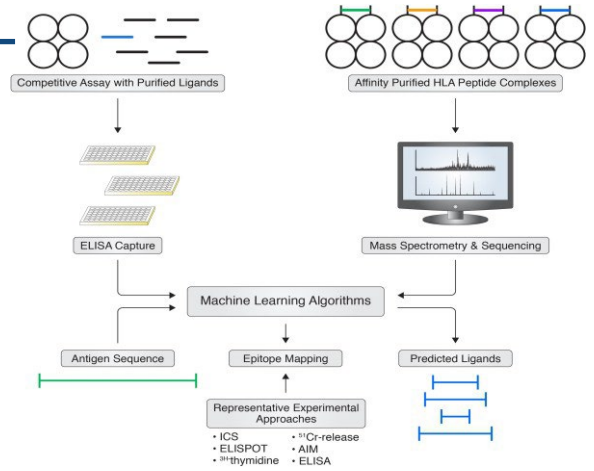
Immune Repertoire Profiling











Conserved immunodominant T cell targets

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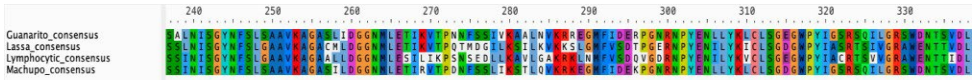
J. Craig Venter INSTITUTE

La Jolla Institute FOR IMMUNOLOGY | Life Without Disease.®

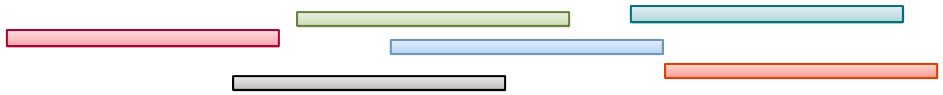
ViPR Virus Pathogen Resource

BV-BRC

Initial choices of target virus taxonomic groups



Determine if there are conserved regions of priority viruses and their close relatives



Meta-analysis of known T cell epitopes

IMMUNE EPITOPE DATABASE AND ANALYSIS RESOURCE

Predict epitopes in conserved antigen regions using ML-based algorithms

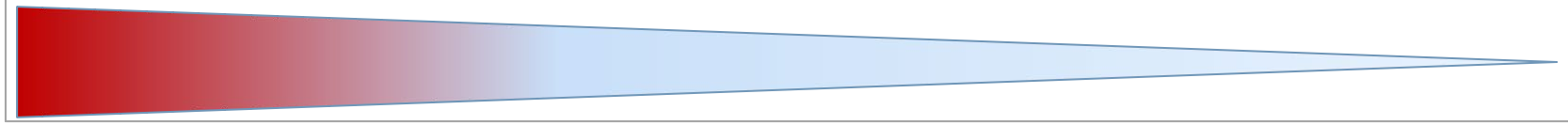
Step 1.

Evaluate if known T cell epitopes could elicit cross-protective immune response for other related viruses and supplement those regions by predicting epitopes in conserved antigen regions

High Immunogenicity
High Conservation

Moderate Immunogenicity
High Conservation

High Immunogenicity
Moderate Conservation

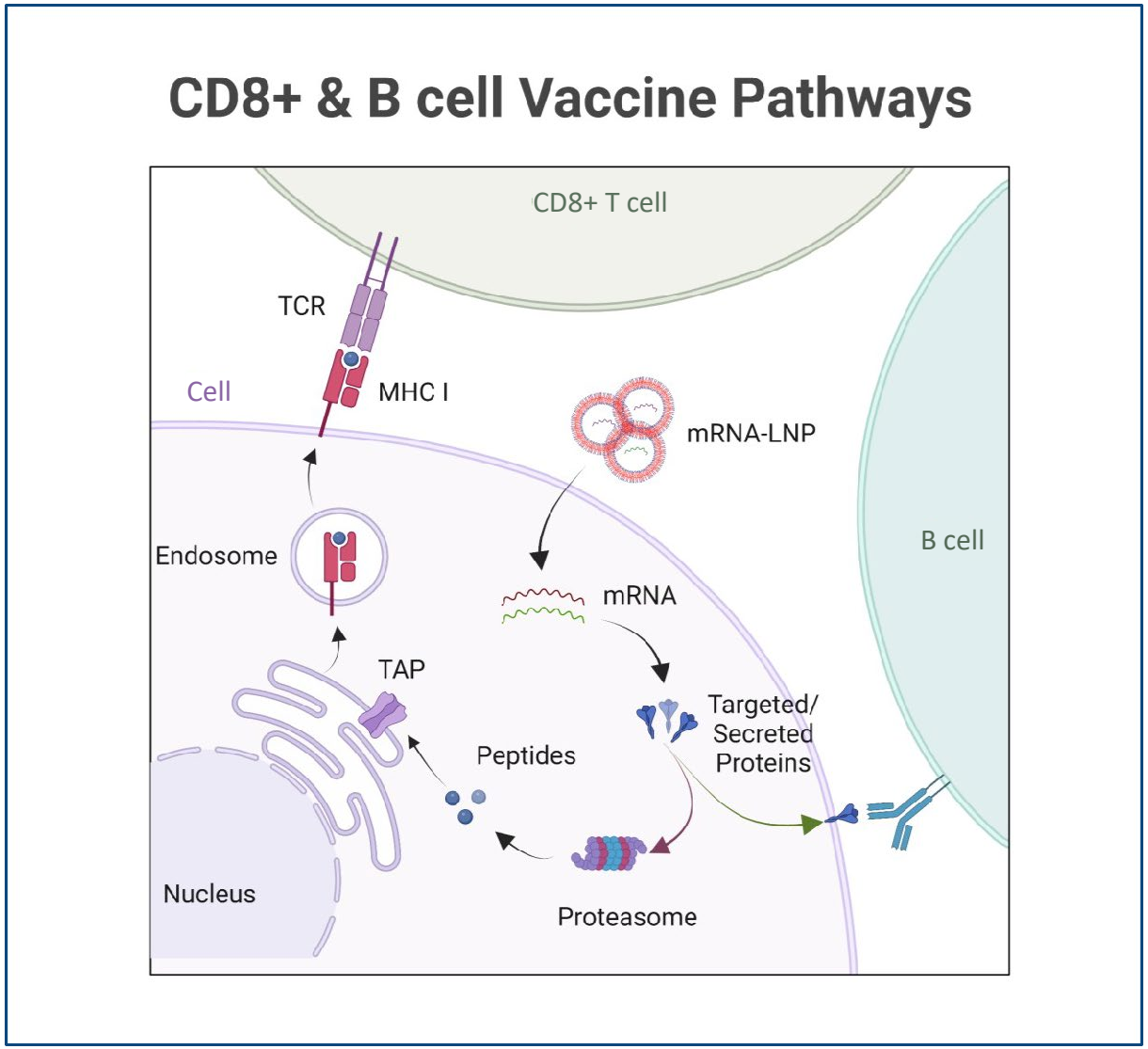


Step 2.

Integrate the results from the above two approaches to select a set of candidates for experimental evaluations

Gene Tan & Alex Sette

Targeting distinct immune cells



From silicon to carbon

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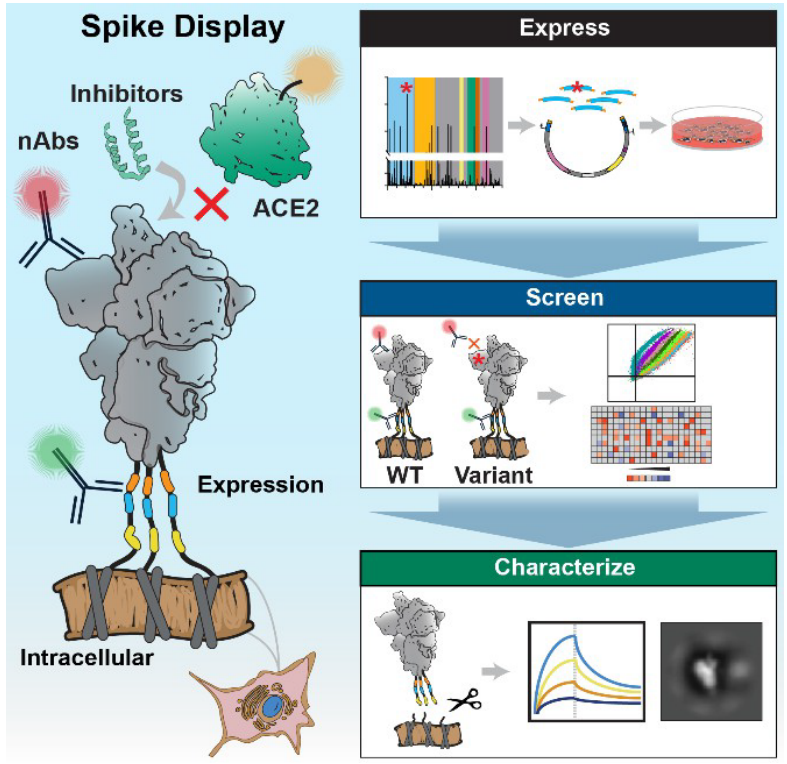
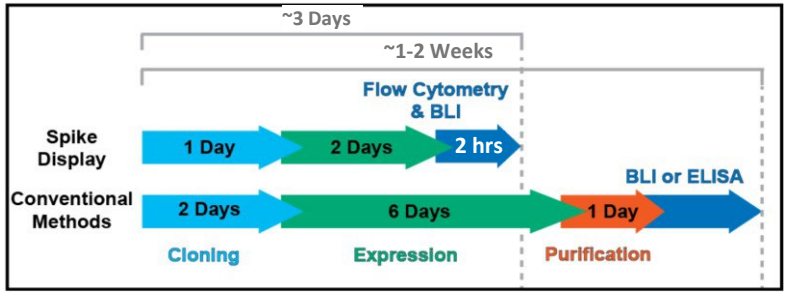
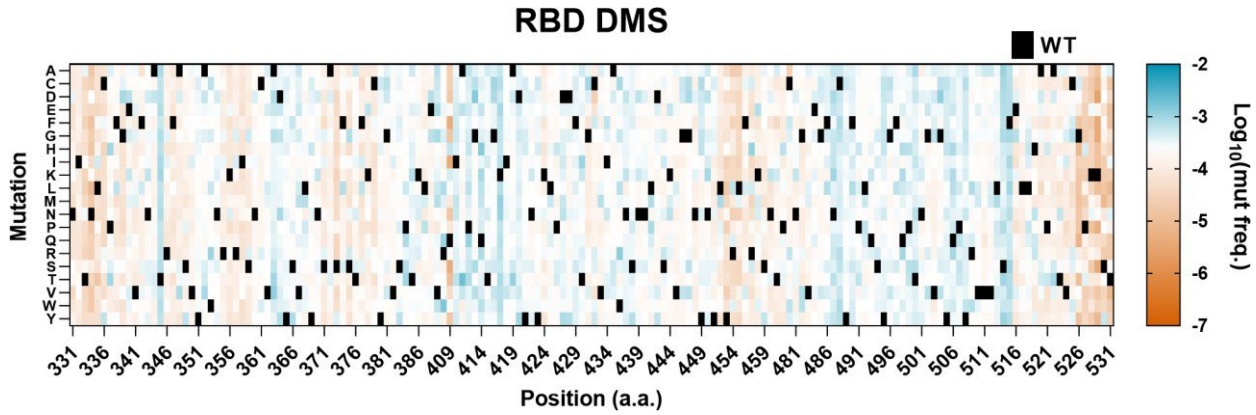
Gen 1: Rapid Characterization



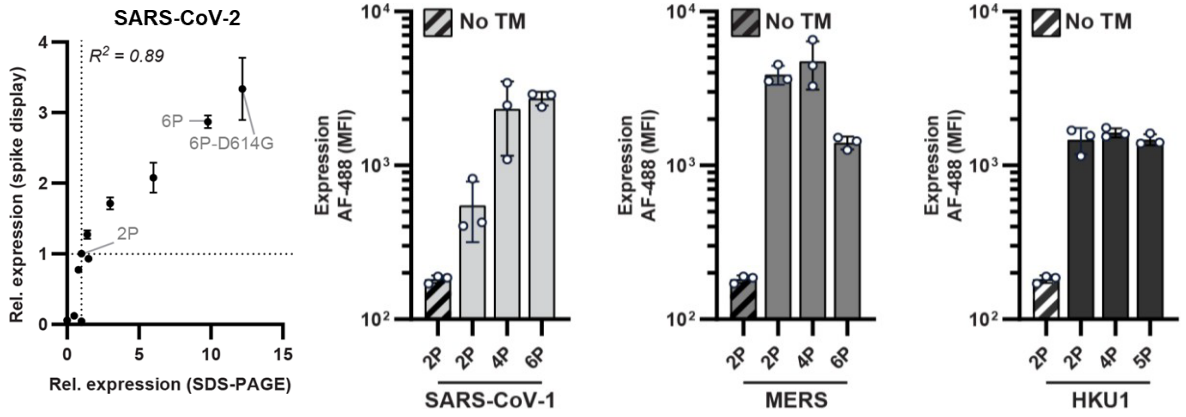


Gen 2: High Throughput Screening

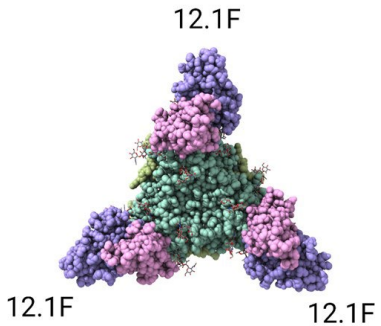
Deep mutational scanning

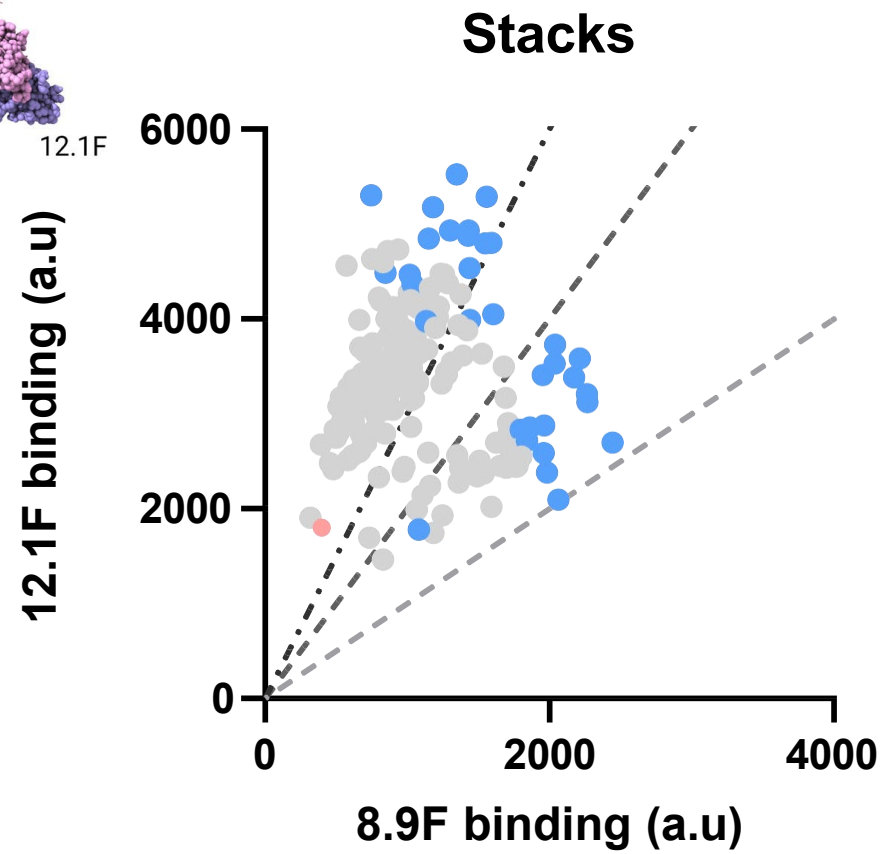


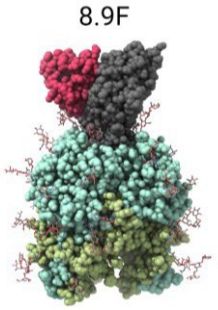
Antigen engineering



mAbs as conformational probes







S2	A328P,I15P
S13	A330P,Q331P,I15P
S22	Q331P,S171P,I15P
S35	Q331P,I15P,H93C,A195C
S37	A328P,I15P,H93C,A195C
S39	S171P,I15P,H93C,A195C
S49	A330P,Q331P,S171P,I15P
S57	A328P,I15P,M192C,G198C
S60	A330P,Q331P,M192C,G198C
S67	S27C,S437C,A330P,Q331P,I15P
S75	A330P,Q331P,I15P,H93C,A195C
S80	Q331P,A328P,I15P,H93C,A195C
S82	Q331P,S171P,I15P,H93C,A195C
S84	A328P,S171P,I15P,H93C,A195C
S1	Q331P,I15P
S8	I15P,H93C,A195C
S21	Q331P,A328P,I15P
S43	A330P,Q331P,H93C,A195C
S59	Q331P,A328P,S171P,I15P
S69	S27C,S437C,Q331P,T87C,G197C
S101	Q331P,S171P,I15P,M192C,G198C
S102	A328P,S171P,I15P,M192C,G198C
S130	Q331P,A328P,S171P,I15P,H93C,A195C
S139	A330P,Q331P,A328P,I15P,M192C,G198C
S162	A330P,Q331P,A328P,S171P,I15P,H93C,A195C

Highlighted variants were selected for further characterization against a larger panel of

Rapid characterization of mutations

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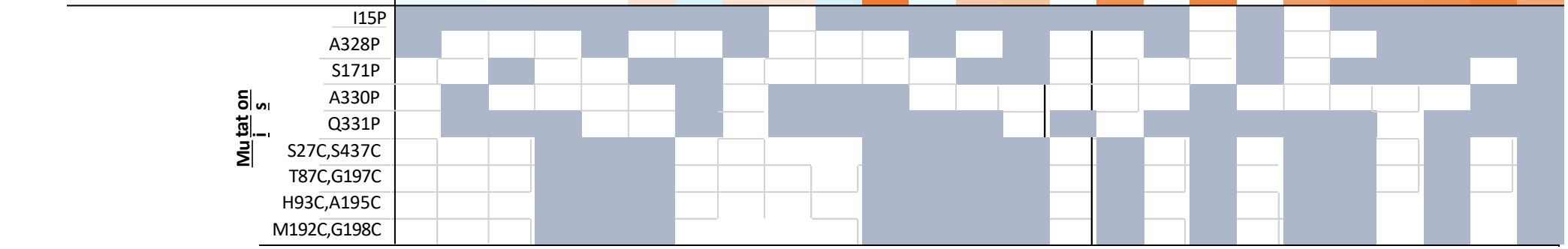
ind	Name	mAb	epitope group	S2	S13	S22	S35	S37	S39	S49	S57	S60	S67	S75	S80	S82	S84	S1	S8	S21	S43	S59	S69	S101	S102	S130	S139	S162
1	**10.4B**	**1**	GP1-A	4.77	6.31	5.17	8.44	12.5	8.01	5.52	2.05	2.62	5.89	4.43	7.71	4.81	6.61	2.02	4.37	2.79	5.73	1.8	1.84	2.77	3.23	3.48	3.9	6.84
2	**12.1F**	**2**	GP1-A	**2.68**	**2.77**	**2.78**	**1.84**	**2.17**	**1.19**	**2.23**	**1.56**	**1.57**	**2.13**	**0.67**	**1.91**	**0.86**	**1.05**	**1.77**	**0.95**	**1.47**	**0.67**	**1.69**	**1.17**	**1.85**	**1.32**	**1.04**	**1.82**	**1.22**
3	**19.7E**	**5**	GP1-A	2.55	2.73	2.64	2.85	3.01	2.29	2.3	1.16	1.65	1.94	1.29	2.92	1.47	1.81	1.31	1.9	1.67	1.91	1.64	1.61	1.78	1.75	1.93	2.29	2.3
4	**25.10C-FNQI**	**24**	GPC-A	3.39	3.75	3.96	2.51	3.19	2.05	2.9	1.55	2.02	2.64	1.59	3.21	1.76	2.5	1.18	2.5	2.05	1.63	1.72	1.95	2.21	1.8	1.91	2.88	2.56
5	**36.1F**	**9**	GPC-A	2.52	2.2	2.24	2.46	2.39	1.75	1.91	1.32	1.49	1.83	1.05	2.27	1.05	1.5	1.49	1.28	1.43	1.23	1.64	1.47	1.64	1.64	1.23	1.97	1.61
6	**8.11G**	**14**	GPC-A	2.73	2.6	2.59	3.37	3.92	2.94	2.36	2.17	2.24	1.75	1.57	3.2	1.93	2.5	1.82	2.14	1.72	1.84	1.75	1.7	2.31	2.37	2.21	2.41	2.56
7	**18.5C**	**3**	GPC-B	2.76	2.72	2.83	3.21	3.63	3.61	4.41	1.91	1.78	3.86	1.85	3.68	2.31	3.22	1.21	1.52	1.91	0.84	1.45	1	2.27	1.43	1.65	2.72	3.31
8	**37.7H**	**13**	GPC-B	2.02	2.64	2.19	2.95	1.64	2.02	2.07	1.41	1.56	2.37	1.08	2.98	1.57	1.93	1.94	1.51	1.31	1.4	1.93	0.92	1.86	1.58	1.83	2.21	2.21
9	**25.6A**	**8**	GPC-B	1.85	2.27	2.52	2.41	2.41	2.24	2.88	1.39	1.38	2.22	1.51	2.29	1.57	2	1.12	1.84	1.71	1.21	1.41	1.24	1.97	1.33	1.46	2.21	2.36
10	**37.2D**	**11**	GPC-B	1.26	1.3	1.24	1.33	1.53	1.31	1.31	1.25	1.19	1.15	0.86	1.36	2.07	1.36	1.4	0.79	0.85	0.7	0.72	0.73	0.91	0.71	0.67	0.83	0.83
11	**37.2G**	**12**	GPC-B	2	1.54	1.58	2.31	3.54	2.17	1.94	1.72	1.96	1.87	1.24	2.63	2.36	2.69	1.16	0.95	1.12	0.7	1.16	0.82	1.34	1.26	1.46	1.38	1.98
12	**9.8A**	**16**	GPC-B	3.02	2.85	2.96	3.85	3.63	2.66	4.21	1.57	1.5	3.34	1.45	3.45	2.09	2.28	2.13	1.26	1.81	1.12	2.04	0.7	1.86	1.71	1.55	2	2.29
13	**NE13**	**17**	GPC-B	1.62	1.36	1.46	2.39	5.16	1.84	1.68	1.57	1.46	1.58	1.14	3.12	1.68	1.85	1.48	1.02	1.32	0.86	1.57	0.72	1.55	1.27	1.7	1.62	2.03
14	**8.9F**	**15**	GPC-C	**8.99**	**9.77**	**10.7**	**9.36**	**9.99**	**6.93**	**7.9**	**3.88**	**5.09**	**6.46**	**4.23**	**9.08**	**4.77**	**5.22**	**3.79**	**3.71**	**3.43**	**4.28**	**3.44**	**2.46**	**4.36**	**3.62**	**4.21**	**4.97**	**4.65**
15	**8.9F-pdb**	**26**	GPC-C	8.25	8.44	9.9	6.84	10.1	8.25	7.04	3.74	4.99	7.23	4.69	12.4	6.44	6.5	3.45	4.84	3.54	5.75	3.21	2.14	4.65	3.41	5.54	4.57	6.39
16	**LAVA01**	**19**		1.72	1.71	1.38	1.13	1.03	0.9	2.76	0.89	0.9	2.94	0.47	1.88	0.79	0.76	1.32	0.56	1.2	0.51	1.11	0.62	0.55	0.56	0.55	0.49	0.65



It takes a village...

HOUSTON Methodist LEADING MEDICINE

Jason McLellan, PhD

UT Austin

- Structural virology
- Protein engineering

Scott Weaver, PhD

UTMB

- Virology
- Animal models

Alessandro Sette, PhD

La Jolla Institute for Immunology

- Immunology
- T cell epitope prediction

Alba Grifoni, PhD

La Jolla Institute for Immunology

- Immunology
- T cell epitope prediction

Gene Tan, PhD

J. Craig Venter Institute

- Molecular immunology
- Bioinformatics

James Davis, PhD

University of Chicago

- Bioinformatics
- AI/ML

Alexander Freiberg, PhD

UTMB

- Virology
- BSL-3 & BSL-4

Arvind Ramanathan, PhD

University of Chicago

- Bioinformatics
- AI/ML

Clara Schoeder, PhD

IDDL

- Biologics
- Protein engineering

Jimmy Gollihar, PhD

HMRI

- Protein engineering
- Synthetic biology

CEPI

Antibody Discovery & Accelerated Protein Therapeutics

HOUSTON Methodist LEADING MEDICINE

Jimmy Gollihar, PhD

Head of ADAPT

- Protein engineering
- Synthetic biology

Raghav Shroff, PhD

AI/ML

- Neural networks
- Protein engineering

Daniel Boutz, PhD

Protein biochemistry

- Antibody discovery
- Structure & proteomics

Andrew Horton, PhD

Systems biology & informatics

- Antibody methods
- Pipeline automation

Thomas Segall-Shapiro, PhD

Synthetic biology

- Genetic circuit design
- Synthetic biology

Kameka Johnson, PhD

Program Coordinator

- Antibody characterization
- Protein biochemistry

Michell Byrom

Laboratory Supervisor

- Molecular biology
- Protein expression

Shaunak Kar, PhD

Synthetic biology

- Synthetic biology
- Genetic circuit design

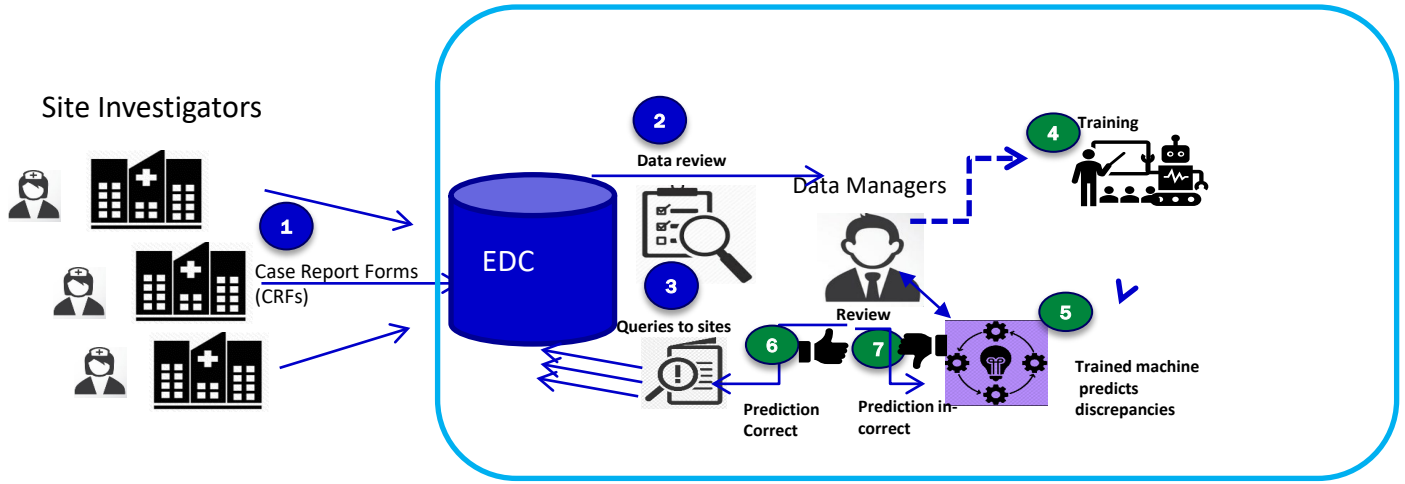
ADAPT

Smart Data Query

Demetris N. Zambas

VP Global Head, Clinical Data Sciences
Pfizer Research & Development

Smart Data Query (AI driven data reconciliation used in Pfizer's COVID vaccine Study)

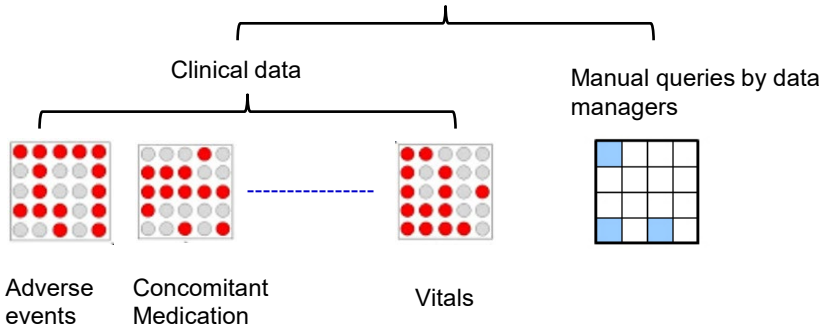


- Data Managers **manually review** and reconcile clinical data using reports.
- '**Query**' is raised to alert the site to review data.
- **Labor intensive**, often same discrepancy propagates across sites

- ✓ High volume data reconciliation (**105+ Million** data point reconciliation performed in **4 months**)
- ✓ More than **1 Million** free text phrases/sentences processed to detect unique adverse event signs or symptoms to reconcile with Medical history and other relevant CRFs
- ✓ Total time saved in reviewing data and automating of query text is estimated to be between **2800 and 3500 hours***

How was AI/ML applied?

Pattern Recognition

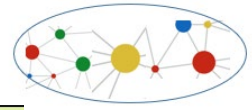


- Supervised Machine Learning
- “Teach Cycles” provide ‘Ground Truth’ to recognize data patterns
- Deep Learning models (Tabnet) developed for machines to learn from training data
- Model predictions for new clinical data points
- Human-in-the-loop feedback for evaluating predictions providing feedback
- Natural Language Processing for processing textual data as well as query text generation
- GPU based state-of-the-art computing

+

Clinical Inference

WHO Drug Dictionary

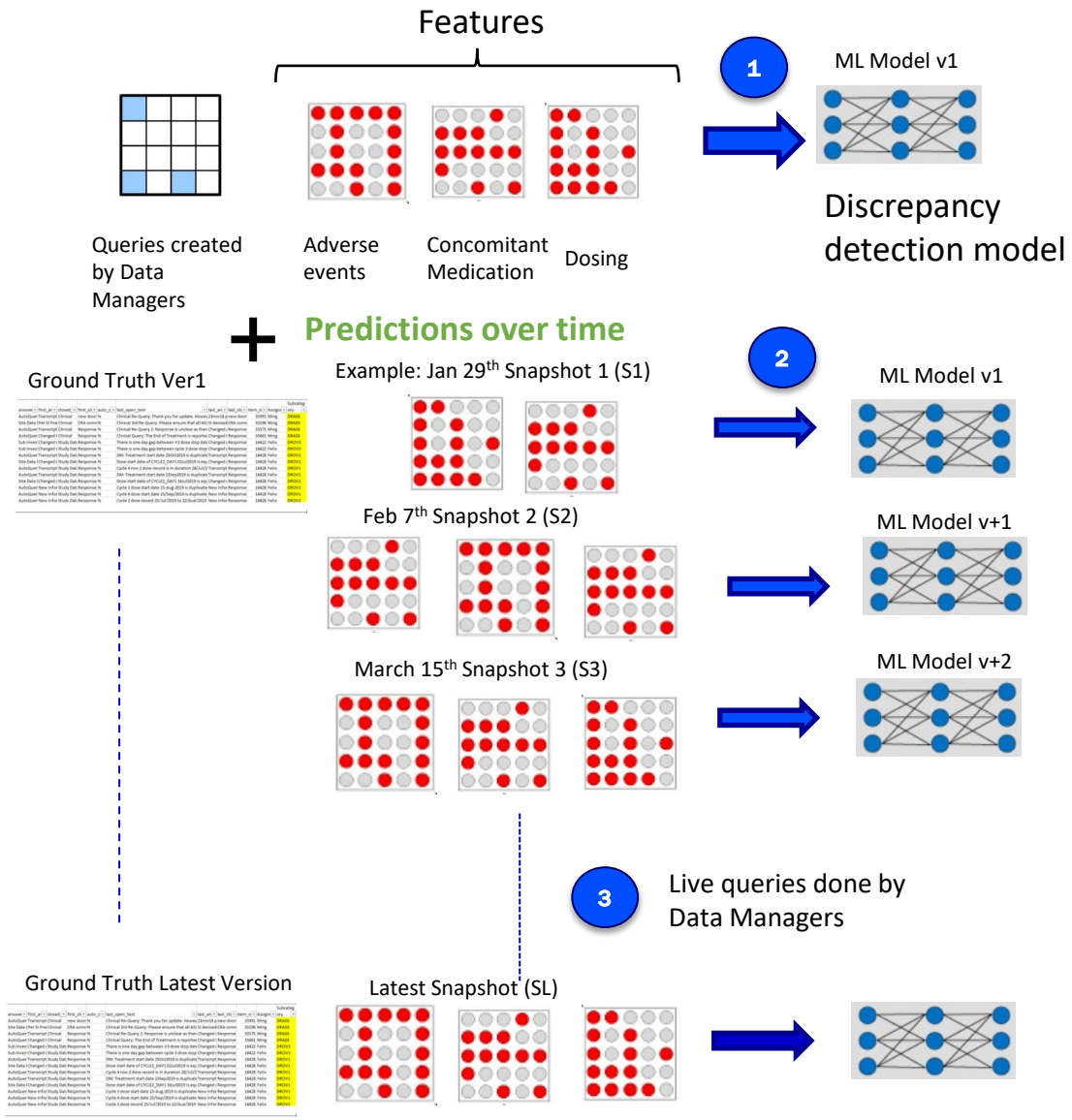


FDA U.S. FOOD & DRUG ADMINISTRATION

openFDA

1. Start with Medication drug name
2. Standardize drug name using WHO Drug dictionary
3. Generate Knowledge base by extracting all possible Indications from FDA open label content
4. Associate the correct indication for the given drug name from FDA open label content
5. Apply Clinical NER Model to extract all diagnosis
6. Compare with Adverse event term hierarchy for logical consistency between this term and drug name

Training ML models for Pattern recognition



1

- Use historical data for studies that are reviewed by data managers
- Extract “features” or input to the ML models to train models on discrepancy detection by comparing discrepant data with queries created by data managers

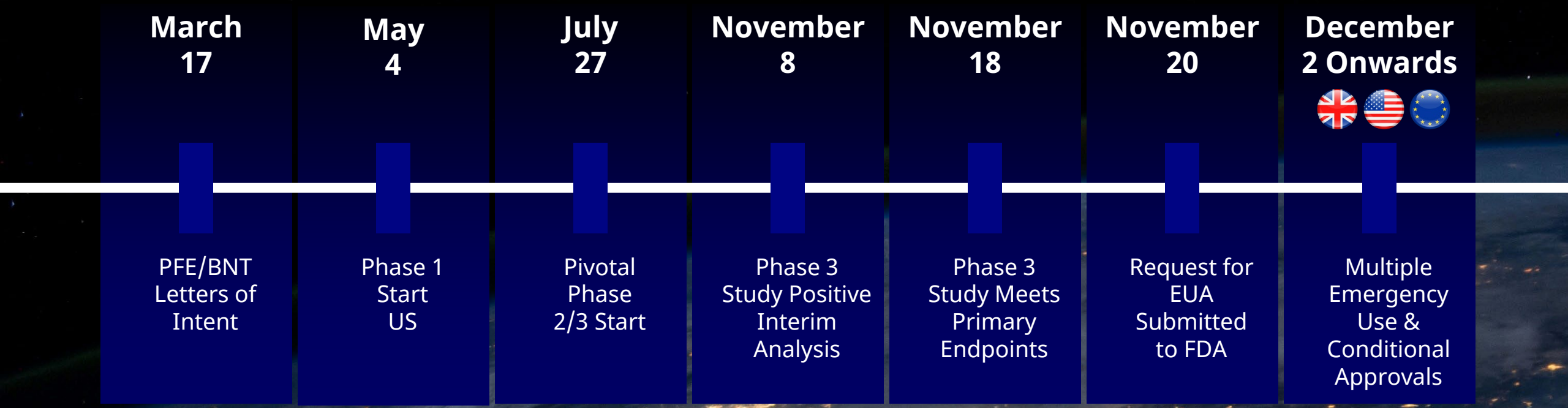
2

- Machine training was done with iterative snapshots of data to predict discrepancies
- Ground truth was provided to classify discrepancies as different sub-categories

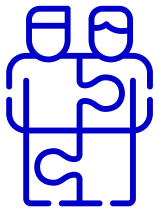
3

- Machine predictions were compared with “human queries” done over time by data managers
- For each snapshot, accuracy between machine predictions and human queries in a Confusion Matrix
  - True Positives (Machine prediction matches human query)
  - False Positives (Machine prediction is deemed incorrect)
  - False Negatives (Machine missed predicting a discrepancy)
  - True Negatives (Not applicable for this use case)

The challenge: Operationalizing a study that is a program



Each site and each participant are critically important



over
46,000
participants

154
Investigators plus their staff members

over **1,000**
colleagues and vendor partners in clinical development

ONE
COVID-19 vaccine

Leading with science

- Speed, quality, and flexibility in study design
- Site selection led by analytics of future cases
- Agility in anticipating multiple amendments
- Real-time dialogue with regulators
- Real time aggregate blinded safety data review
- Weekly DMC review
- Segregation of blinded and unblinded teams

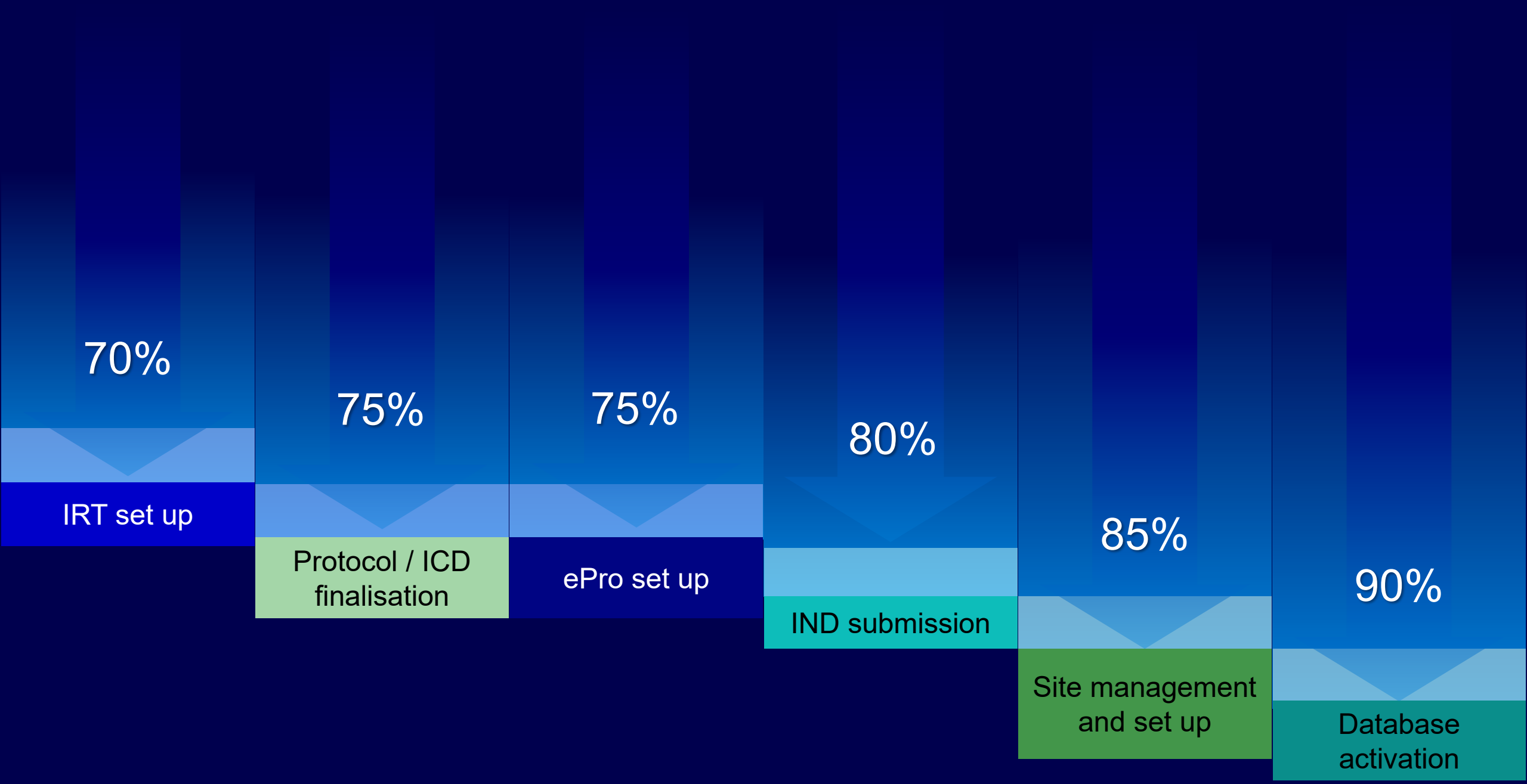
Nearly 500 colleagues working in synchrony to drive efficiencies

20

Vendor Collaborations

18

Pfizer functional lines


70%
IRT set up
75%
Protocol / ICD finalisation
75%
ePro set up
80%
IND submission
85%
Site management and set up
90%
Database activation

Accelerating Clinical Data Review Processes

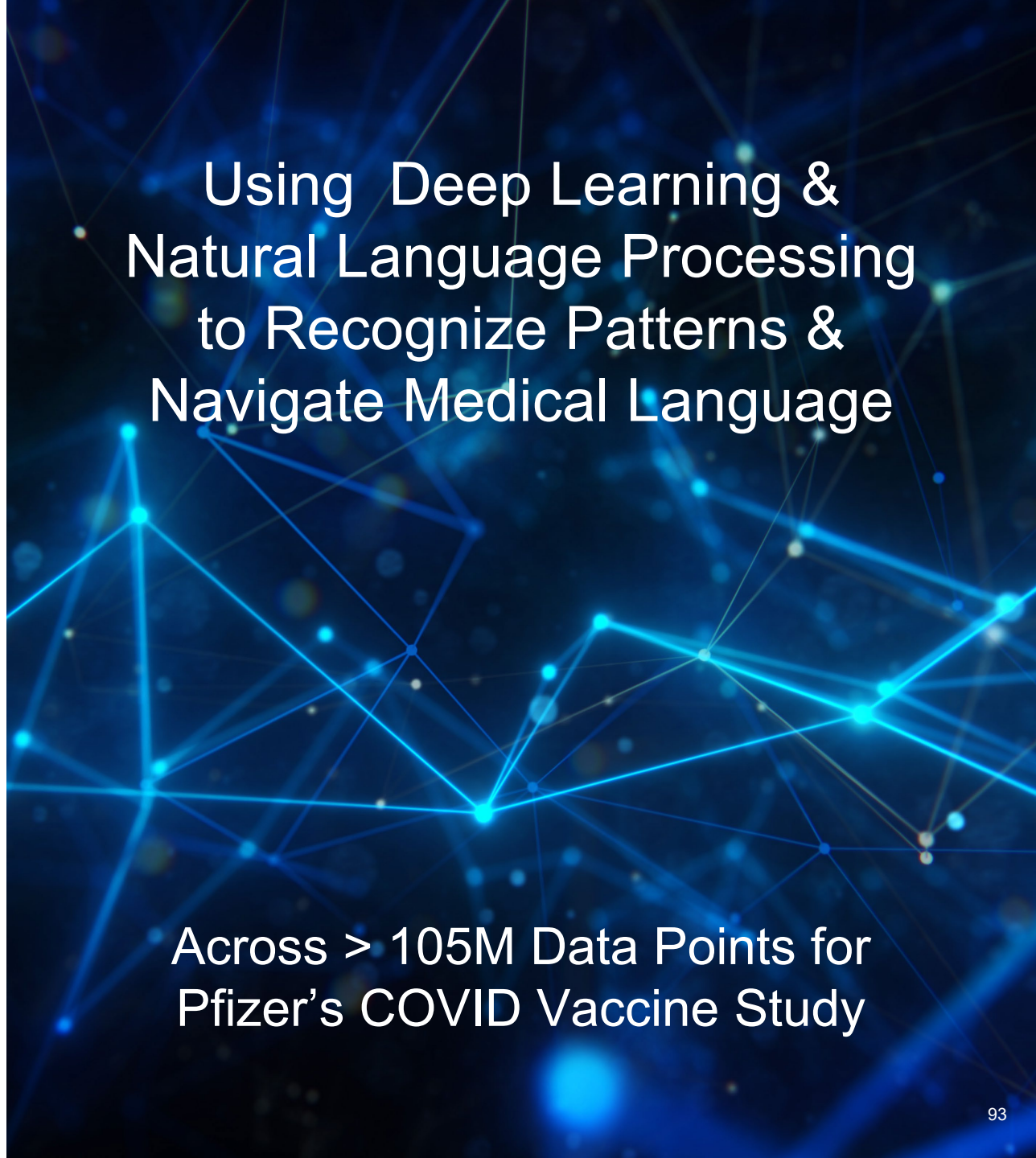
Days Required to Navigate from Data Capture to Query Generation

25.4 » 1.7

Median Calendar Days All Vaccine Studies

Median Calendar Days COVID Vaccine Study

Eliminating an estimated 2,800 to 3,500 hours required to reconcile..



Contributors to the Accelerated EUA Submission

1. Dedicated focus programming teams
2. Programming standards
3. Limiting/controlling output
4. Leveraging technology
5. Regulatory engagement
6. Ensuring high quality
7. Planning & cross-functional alignment

Thank You

Artificial Intelligence: Real Uses in Vaccine Development and Immunization Efforts

Discussion

NVAC

Innovative Approaches to Improve Adult Immunization

Nandini Selvam
Marquisha Johns
Elizabeth Sobczyk

NVAC

Adult and Maternal Annual Vaccination Trends in the US (data as of Sep 2023)

National Vaccine Advisory Council

Nandini Selvam, PhD, MPH
VP & GM, IQVIA, Inc.

Feb 23, 2024

Executive Summary

Objectives

Understand the impact of COVID19 on routine adult (Influenza, Pneumococcal, Shingles) and Maternal (Tdap) vaccinations

Data Sources

Patient level data* representing both private (commercial) and public (Medicare FFS, Medicare Advantage, Medicaid FFS, Managed Medicaid, and cash) insurers across all 50 states of the US

Study Population

Population of ~258M adults (age 18+); cohort of eligible patients of ~60M for tracking vaccinations.
Vx rate calculated as number of adults who received each vaccine out of eligible adults, and aligned with US population[1]

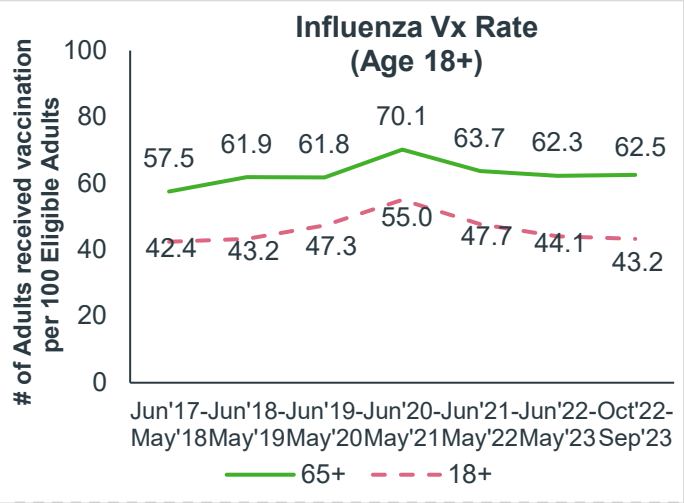
Key Findings and Insights

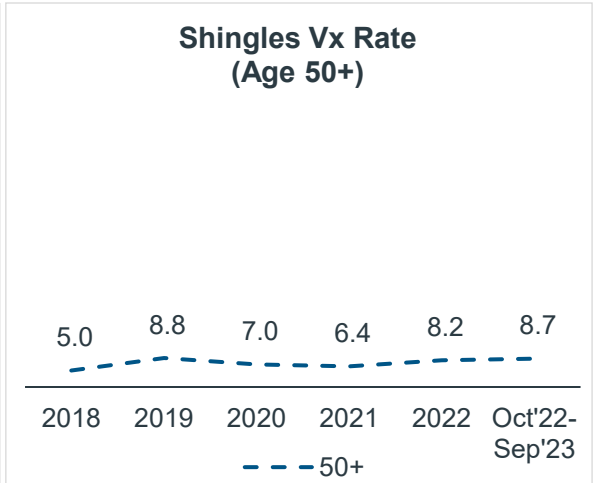
- Influenza Annual Vx rates declined post 2021, while Pneumococcal and Shingrix improved in 2022, and is reaching/exceeding pre-pandemic levels (2019)
- Overall reduction in Influenza Annual Vx across age groups, especially age 65+ and public insurance, with trends widening among Black/Hispanic vs. White/Asian and lower income groups
- Shingles Annual Vx rates for age 65+ increased in H1'2023 coinciding with the implementation of the Inflation Reduction Act
- Pneumococcal Annual Vx among age 65+ declined during the pandemic, but now catching up to pre-pandemic levels, with trends widening among Public vs Private channel
- Tdap Annual Vx in pregnancy significantly lower among public insured, with trends widening among Black/Hispanic vs. White/Asian and lower income groups

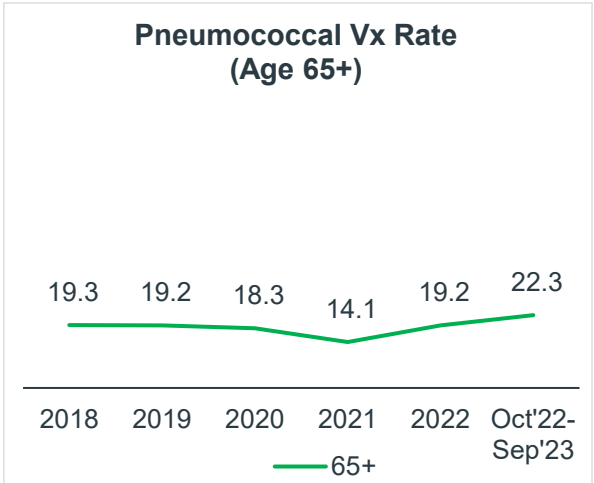
*IQVIA Administrative claims data and Experian consumer data with access to social determinants of health variables
[1]Pregnant women vaccination is based on IQVIA claims sample and not aligned to US population

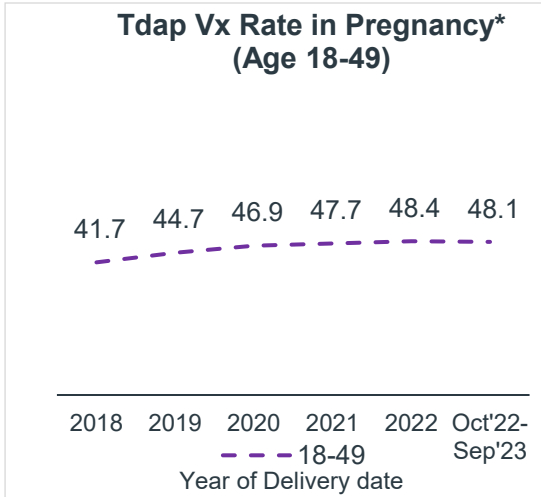
Summary of Adult and Maternal Annual Vaccinations (as of Sep 2023)

Annual Vx rate = # of Adults who received a per 100 Eligible Adults









- Across the board declines of ~1% during Jun'22-May'23 vs. Oct'22-Sep'23
  - Blacks (-0.2%) and Hispanics (-0.2%) had lowest Annual Vx rates vs. national average
  - Annual Vx rates among individuals with private payors had an additional decline of 1.2% vs. public payors

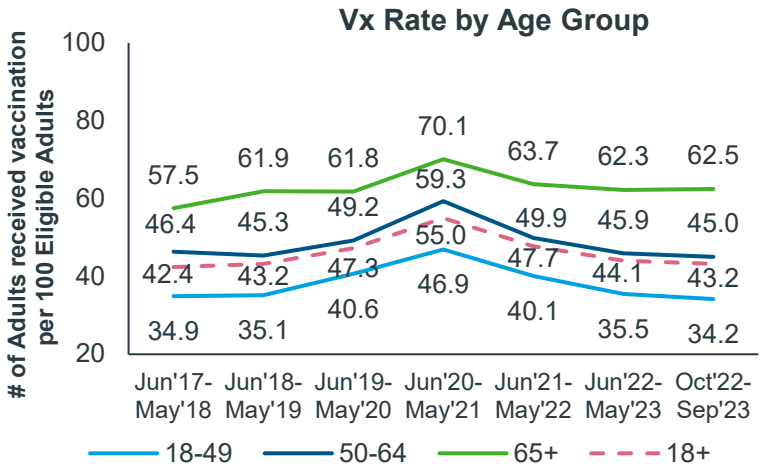
- Shingles Annual Vx rate has shown 0.5% increase during Oct'22-Sep'23 vs 2022
- Annual Vx rates among individuals with public payors has not recovered post pandemic (10.1% in 2019 vs 9.1% in Oct'22-Sep'23)

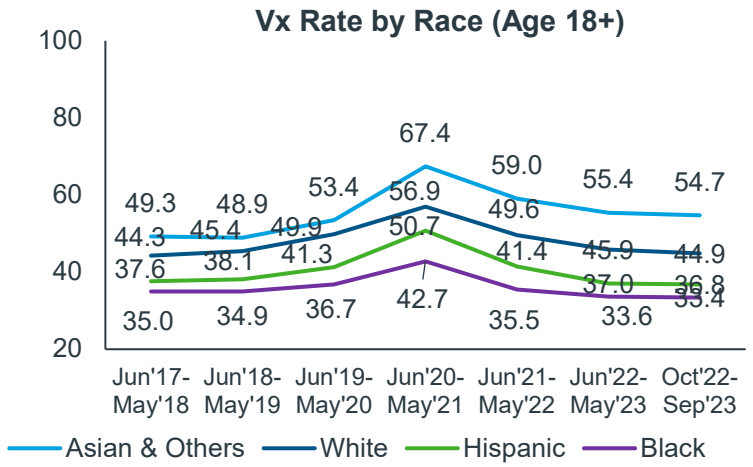
- Improvements in Pneumococcal Annual Vx rates in the most recent year, primarily driven by
  - Age based recommendation vs shared clinical decision making
  - Increased options, given launch of 2 newer vaccines
  - Increases in both public and private channel

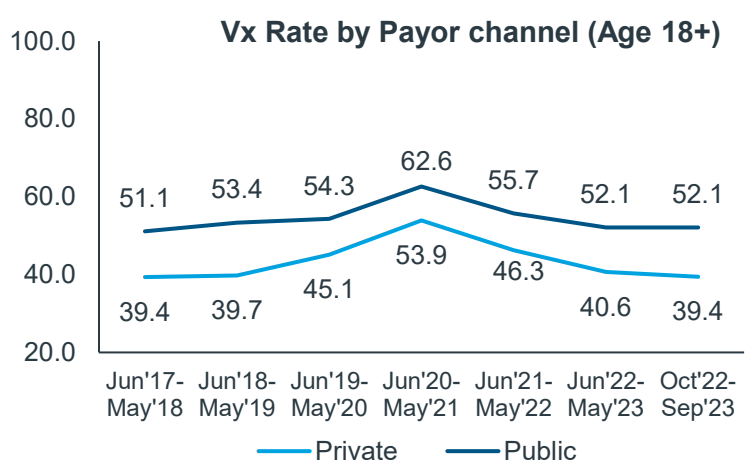
- Tdap Annual Vx among Pregnant Women* has increased except small drop in latest quarter / MAT
- Rates have decreased slightly during Oct'22-Sep'23, with drop of ~0.3% compared to 2022 driven by drop in 35-49 age group

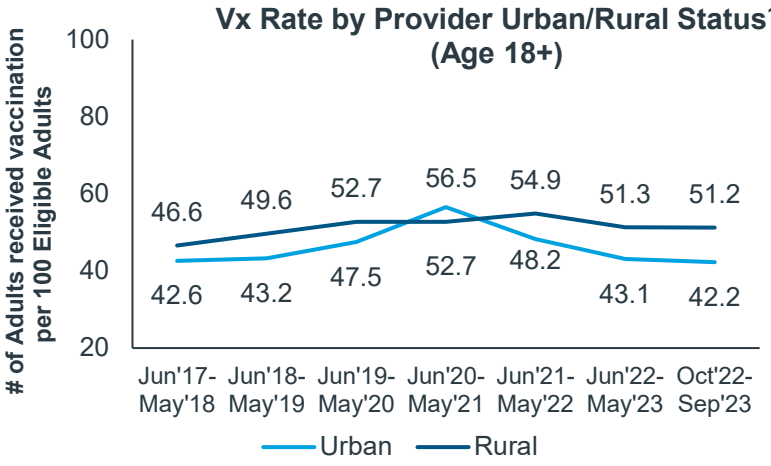
Sources: IQVIA LAAD and Experian Data. Annual Vx rate = Population received vaccination/Eligible Population
*Pregnant Women (PW) cohort is based on 'Delivery date';

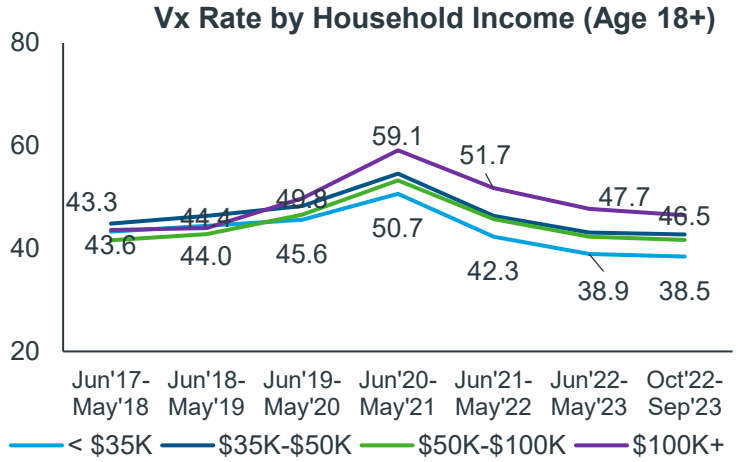
Influenza vaccination decreased in Oct'22-Sep'23 vs season ending May'23 except for 65+ age. Black and Hispanic population remained least vaccinated.











Key Insights

- Uptake in initial months of Influenza 2024 season is lower compared to Season 2023
- There is a larger decline in the private payors vs. public payors
- Lower rates among Black and Hispanic vs. White and Asian/Others

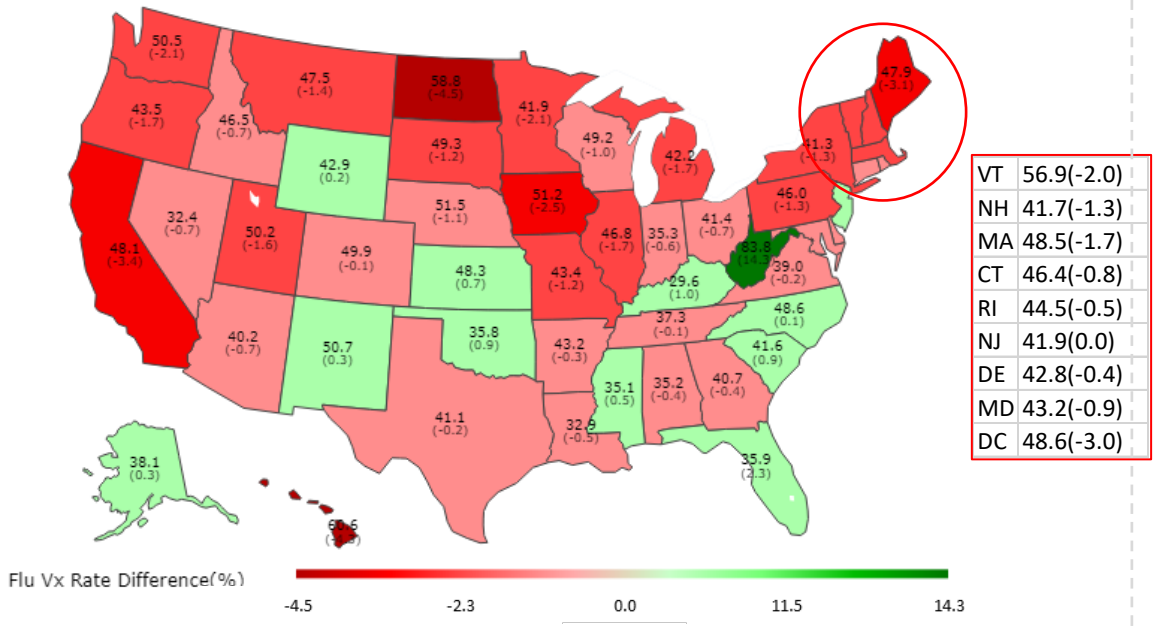
Influenza

Sources: IQVIA LAAD and Experian Data. Annual vaccination = Population received vaccination/Eligible Population
*2% patients did not have race info and not included
Private channel includes Commercial. Public channel includes Medicare (FFS and Medicare Advantage), Medicaid (FFS and Managed) and Cash
[1]Rural population represent only 5% in IQVIA claims

Influenza vaccination decreased in 39 states for 18+, and 20 states for 65+ in Oct'22 - Sep'23 vs. season ending May'23

Age group : 18+

Flu Vx Rate(%) Oct'22-Sep'23 (Oct'22-Sep'23 - Jun'22-May'23)

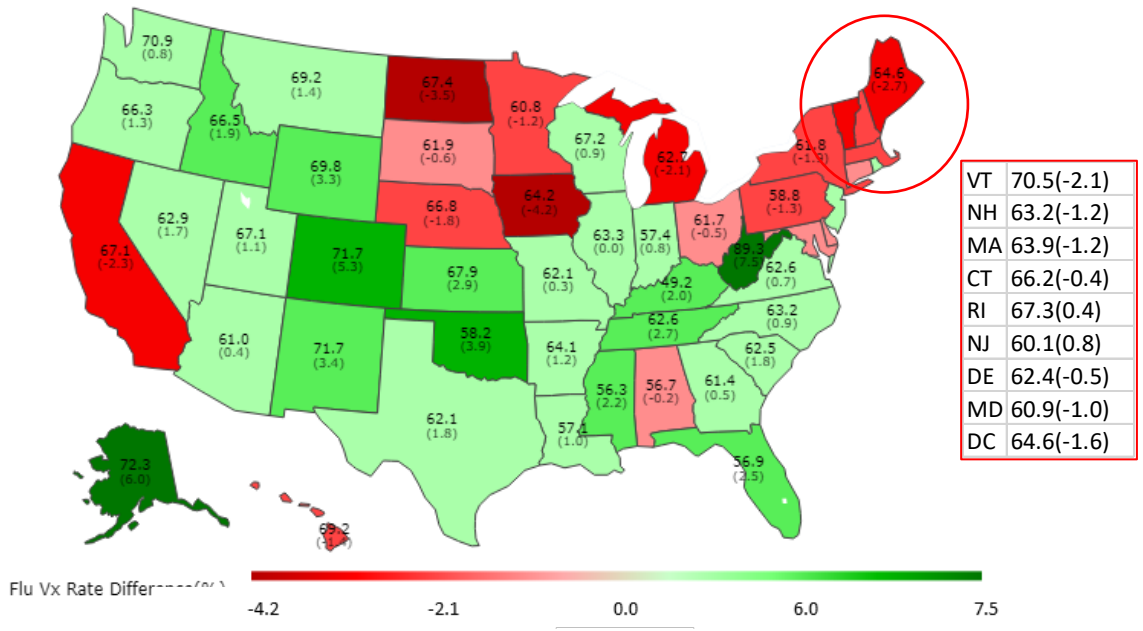


VT	56.9(-2.0)
NH	41.7(-1.3)
MA	48.5(-1.7)
CT	46.4(-0.8)
RI	44.5(-0.5)
NJ	41.9(0.0)
DE	42.8(-0.4)
MD	43.2(-0.9)
DC	48.6(-3.0)

WV, FL, KY showed highest increases in Oct'22 - Sep'23 vs Jun'22 - May'23
ND, HI, CA showed highest drops in Oct'22 - Sep'23 vs Jun'22 - May'23

Age group : 65+

Flu Vx Rate(%) Oct'22-Sep'23 (Oct'22-Sep'23 - Jun'22-May'23)



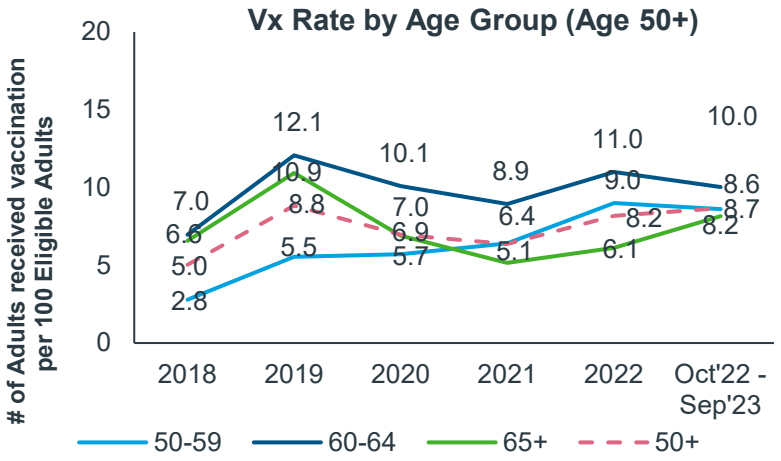
VT	70.5(-2.1)
NH	63.2(-1.2)
MA	63.9(-1.2)
CT	66.2(-0.4)
RI	67.3(0.4)
NJ	60.1(0.8)
DE	62.4(-0.5)
MD	60.9(-1.0)
DC	64.6(-1.6)

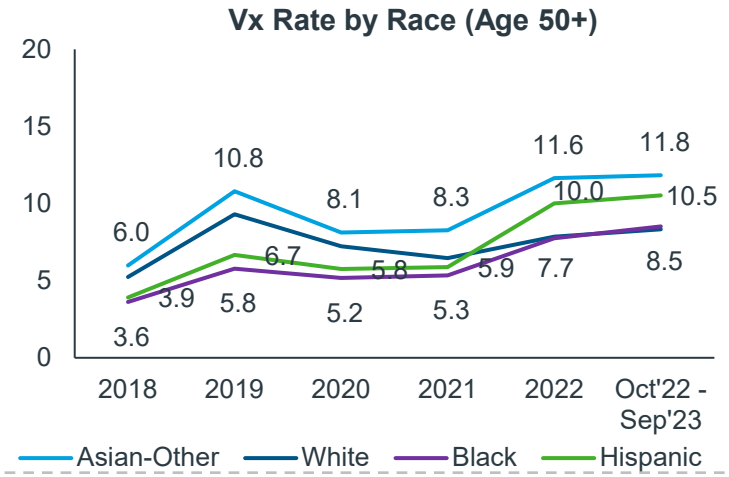
WV, AK, CO showed highest increases in Oct'22 - Sep'23 vs Jun'22 - May'23
IA, ND, ME showed highest drops in Oct'22 - Sep'23 vs Jun'22 - May'23

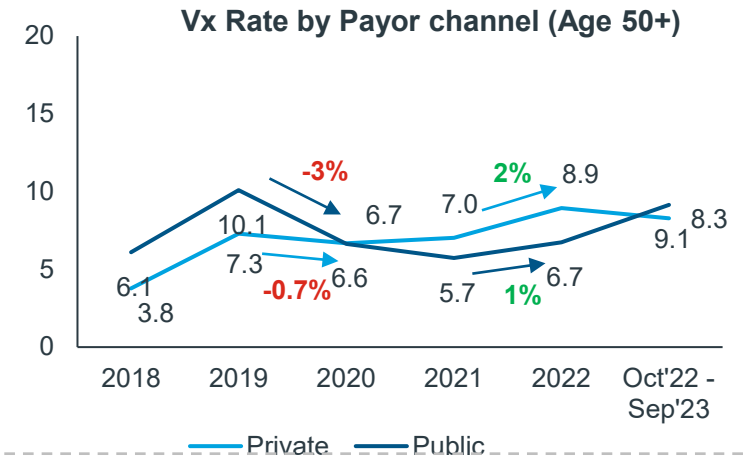
Sources: IQVIA LAAD and Experian Data; Annual vaccination = Population received vaccination/Population eligible for vaccination

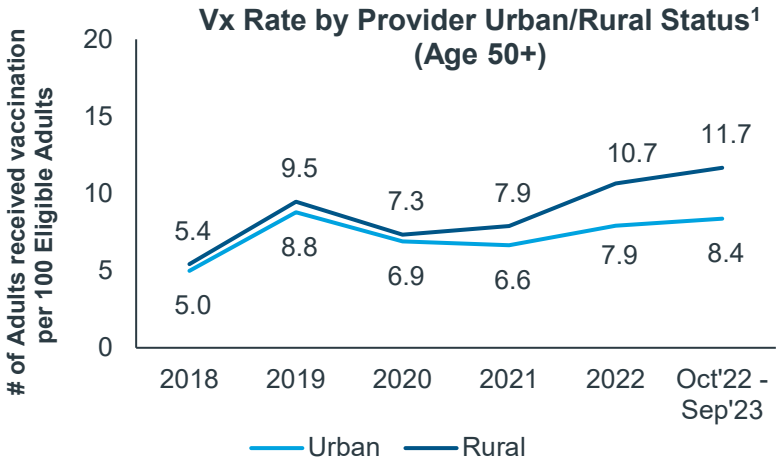
Shingles vaccination rates are improving in 65+ age groups. Vx rates in all population groups improved

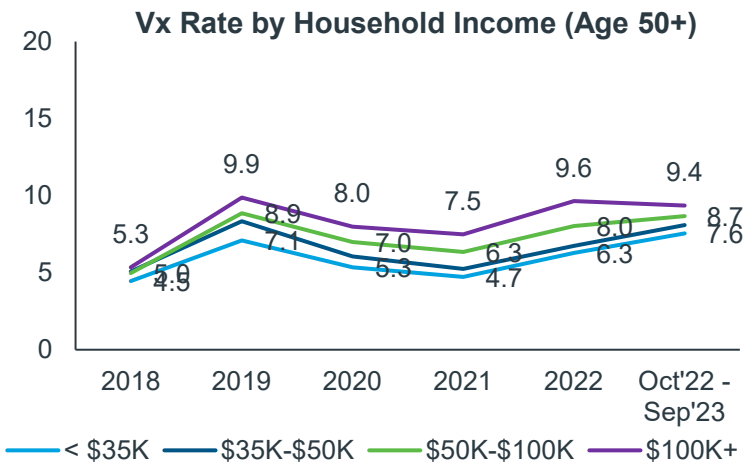
Recommended for 50+ years, not required annually











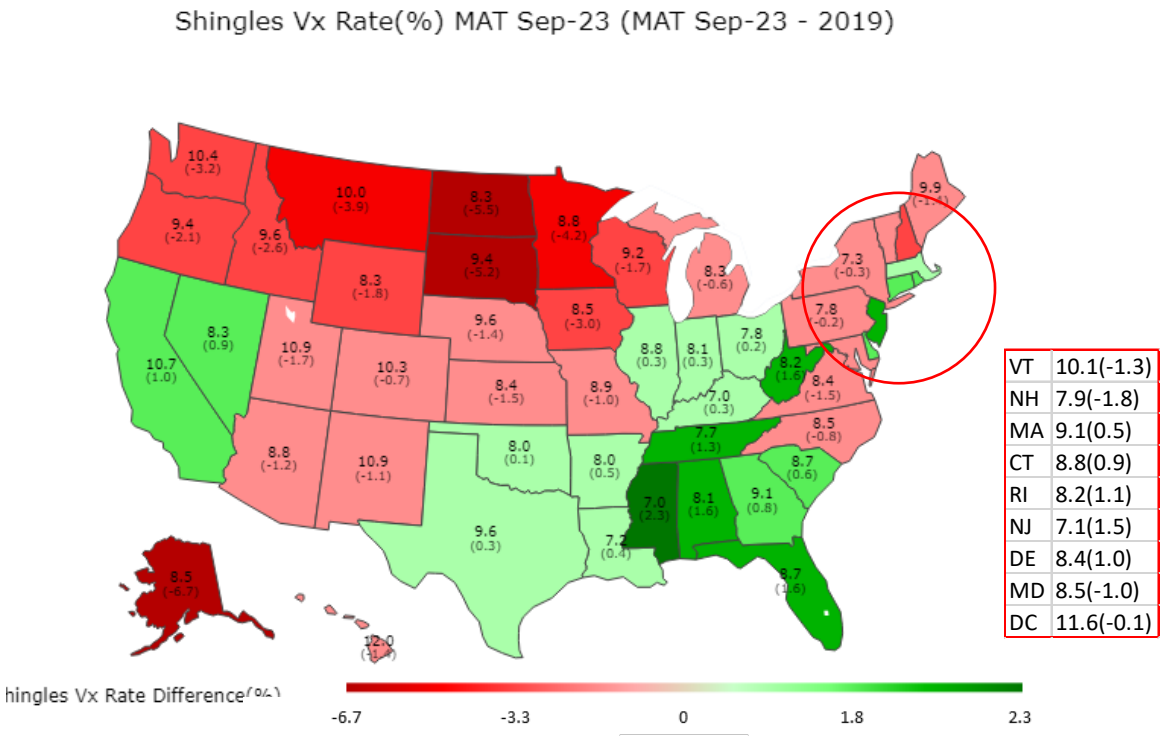
Key Insights

- Shingles Annual vaccination rate has shown an increase in 2022 compared to 2021
- Shingles Annual vaccination rate had a better recovery among those with Private (commercial) vs. public insurance (Medicare/Medicaid/Cash) in latest year
- Shingrix entered the market in 2018, followed by supply chain issues, increase in 2019 may be reflective of that

Sources: IQVIA LAAD and Experian Data; *2% patients did not have race info
Annual vaccination = Population received vaccination/Population eligible for vaccination
Private channel includes Commercial. Public channel includes Medicare (FFS and Medicare Advantage), Medicaid (FFS and Managed Medicaid) and Cash
1. Rural population represent only 5% in IQVIA claims

Improvement in Shingles vaccinations in 22 states for 50+ but decreased in 48 states for 65+ age group, between Oct'22 – Sep'23 vs 2019.

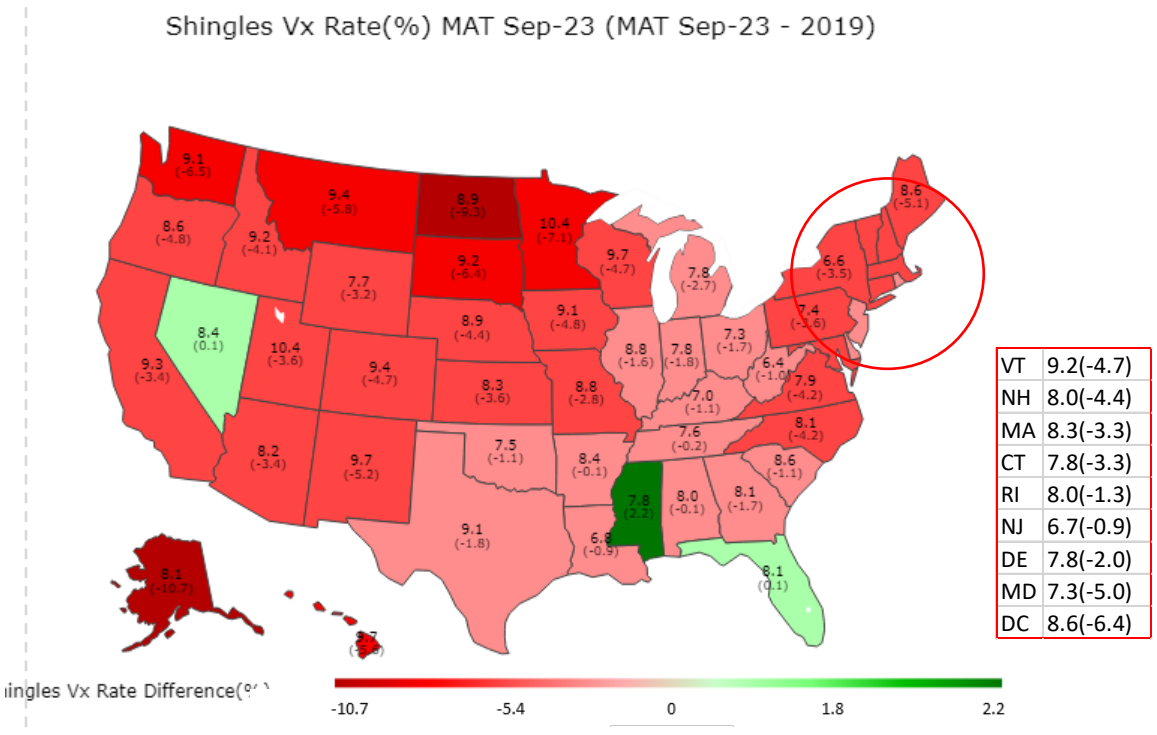
Age group : 50+



VT	10.1(-1.3)
NH	7.9(-1.8)
MA	9.1(0.5)
CT	8.8(0.9)
RI	8.2(1.1)
NJ	7.1(1.5)
DE	8.4(1.0)
MD	8.5(-1.0)
DC	11.6(-0.1)

MS, FL, AL showed highest increases in Oct'22 - Sep'23 vs 2019
AK, ND, SD showed highest drops in Oct'22 - Sep'23 vs 2019

Age group : 65+



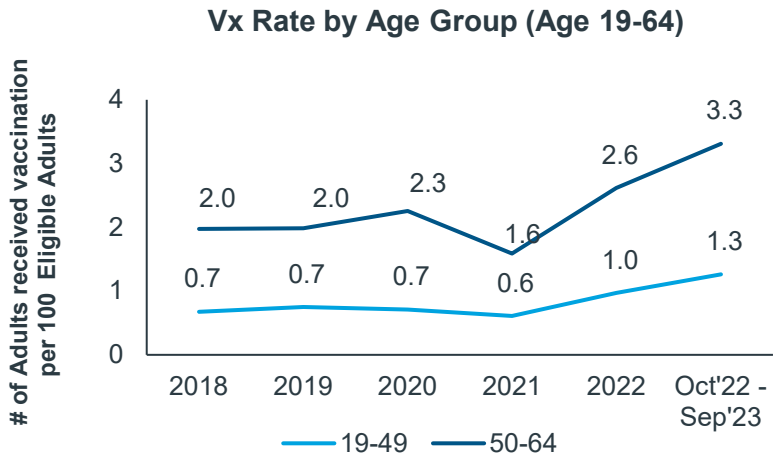
VT	9.2(-4.7)
NH	8.0(-4.4)
MA	8.3(-3.3)
CT	7.8(-3.3)
RI	8.0(-1.3)
NJ	6.7(-0.9)
DE	7.8(-2.0)
MD	7.3(-5.0)
DC	8.6(-6.4)

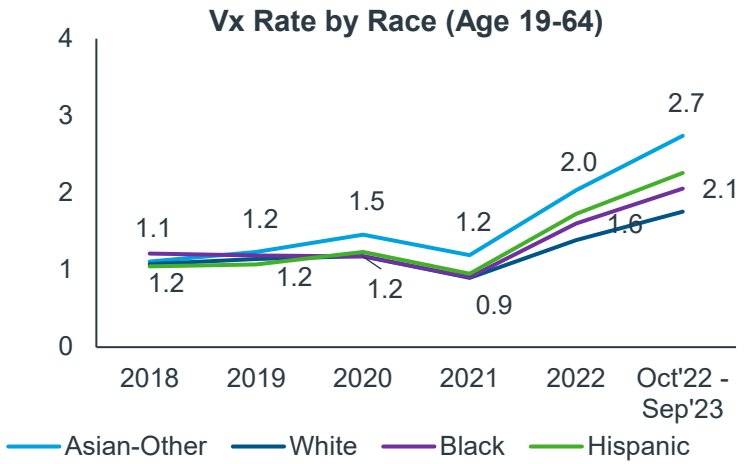
MS, FL, NV showed highest increases in Oct'22 - Sep'23 vs 2019
AK, ND, MN showed highest drops in Oct'22 - Sep'23 vs 2019

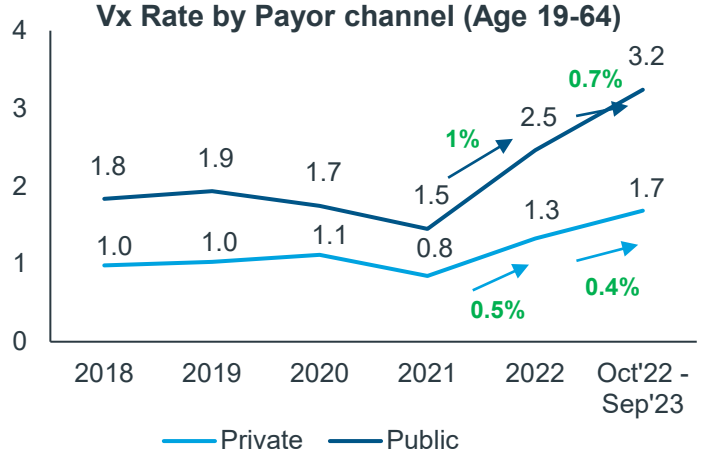
Sources: IQVIA LAAD and Experian Data; Annual vaccination = Population received vaccination/Population eligible for vaccination

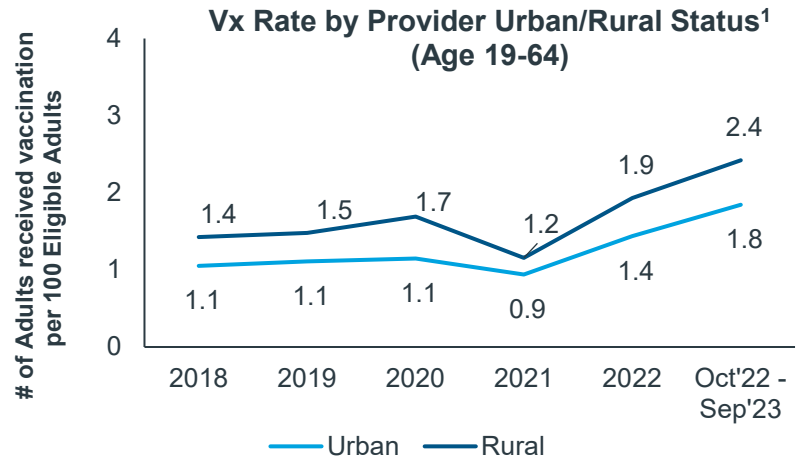
Pneumococcal vaccination bounced back since 2021, driven by improvement in Public channel. Black and White population remain least vaccinated – 19-64 years

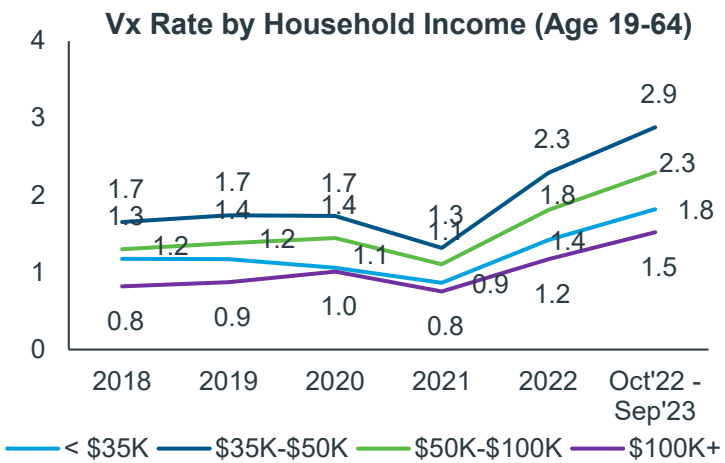
Recommended for 50+ years for Pneumovax, and 65+ for Prevnar











Key Insights

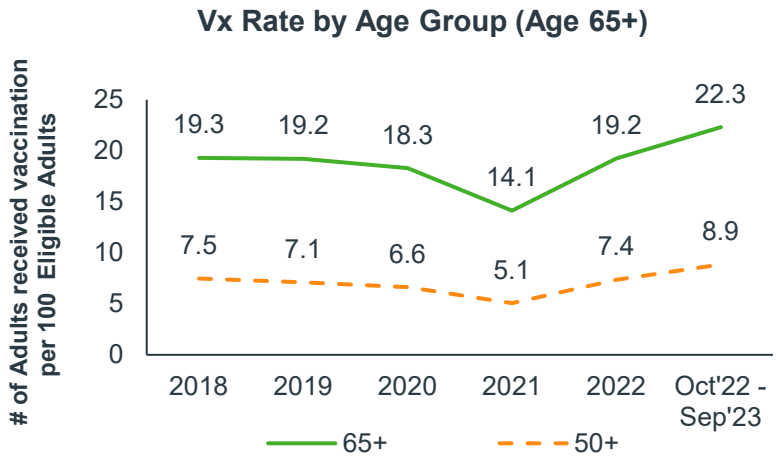
- Pneumococcal Annual vaccination rate declined for age 50-64 until 2021, shows increase in 2022.and Oct'22 - Sep'23
- Black and White adults' Pneumococcal Annual vaccination rates are relatively lower compared to Hispanic and Asian/Others.
- Pneumococcal Annual vaccination rate is higher with Rural Providers
- Pneumococcal Annual vaccination rate is higher for Income Group 35K-50K

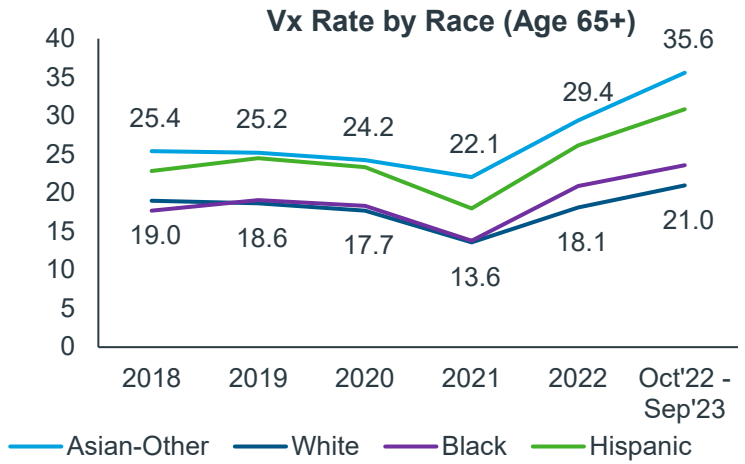
Pneumococcal

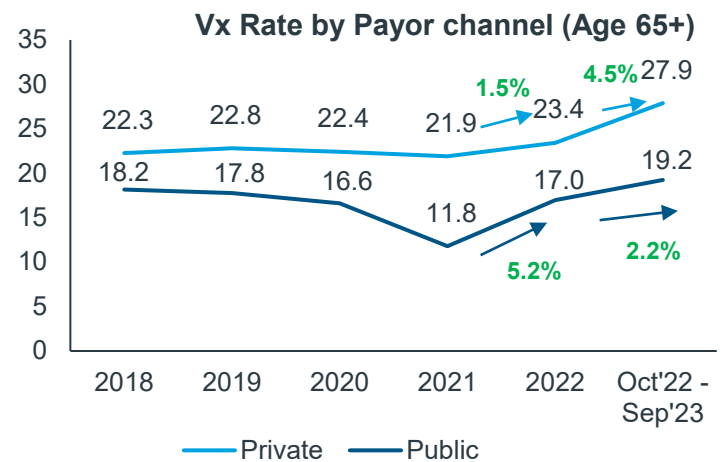
Sources: IQVIA LAAD and Experian Data; *2% patients did not have race info
Annual vaccination = Population received vaccination/Population eligible for vaccination
Private channel includes Commercial and Medicare Advantage. Public channel includes Medicare (Medicare FFS), Medicaid (FFS and Managed Medicaid) and Cash
1. Rural population represent only 5% in IQVIA claims

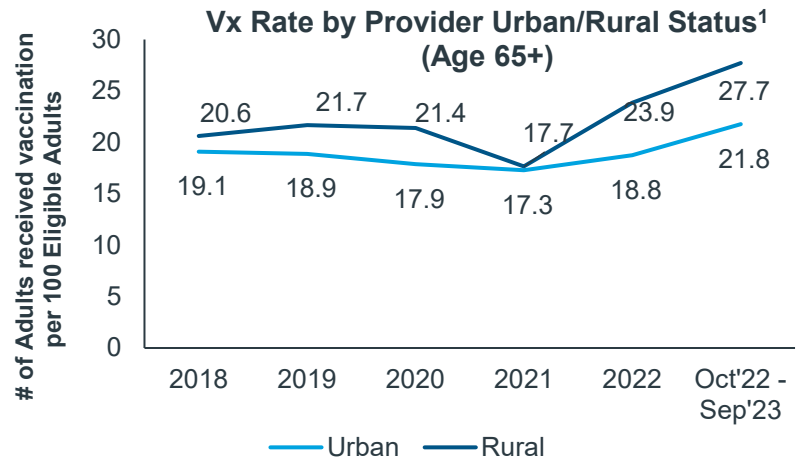
Pneumococcal vaccination has bounced back post COVID season driven by improvement in Public channel. Black and White population remained least vaccinated – 65+ years

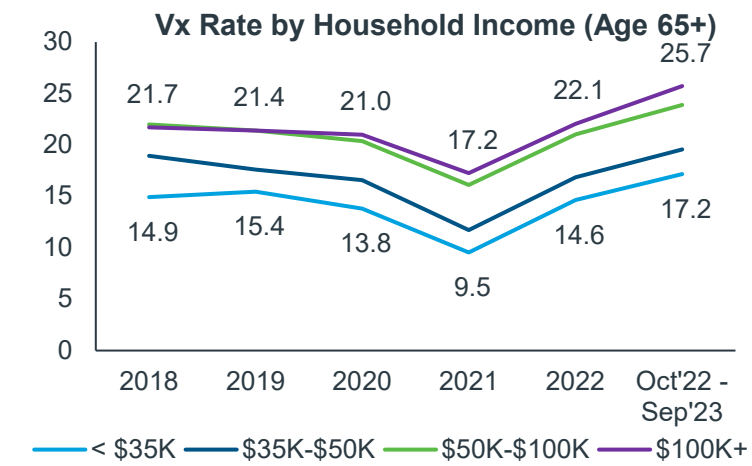
Recommended for 50+ years for Pneumovax, and 65+ for Prevnar











Key Insights

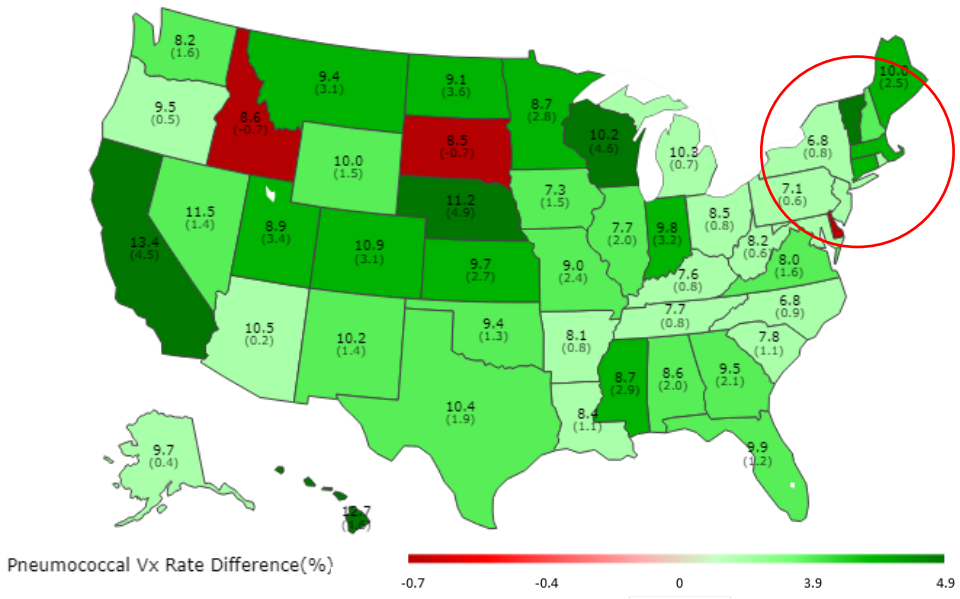
- Pneumococcal Annual vaccination rate declined for age 65+ until 2021, shows increase in 2022 and Oct'22 - Sep'23
- Black and White adults' Pneumococcal Annual vaccination rates are relatively lower compared to Hispanic and Asian/Others.
- Pneumococcal Annual vaccination rate is higher with Rural Providers
- Pneumococcal Annual vaccination rate is higher for Income Group 100K+

Sources: IQVIA LAAD and Experian Data; *2% patients did not have race info
Annual vaccination = Population received vaccination/Population eligible for vaccination
Private channel includes Commercial and Medicare Advantage. Public channel includes Medicare (Medicare FFS), Medicaid (FFS and Managed Medicaid) and Cash
1. Rural population represent only 5% in IQVIA claims

Overall, Pneumococcal Vaccination* has increased in 48 states for 50+ and 42 states for 65+ age groups in Oct'22 – Sep'23 compared to 2019.

Age Group : 50+

Pneumococcal Vx Rate(%) MAT Sep-23 (MAT Sep-23 - 2019)

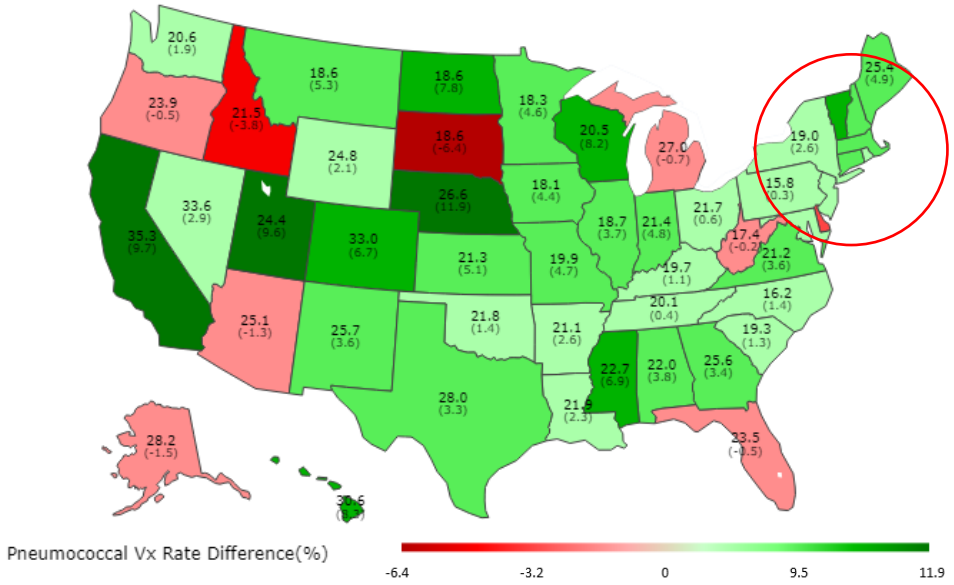


VT	11.1(4.2)
NH	8.8(2.2)
MA	7.1(2.8)
CT	8.2(3.0)
RI	6.6(0.4)
NJ	6.6(1.0)
DE	8.8(-0.6)
MD	6.8(0.2)
DC	8.5(1.4)

NE, WI, HI showed highest increases in Oct'22 - Sep'23 vs 2019
SD, ID, DE showed highest drops in Oct'22 - Sep'23 vs 2019

Age Group : 65+

Pneumococcal Vx Rate(%) MAT Sep-23 (MAT Sep-23 - 2019)



VT	24.1(7.7)
NH	20.9(4.4)
MA	15.8(4.9)
CT	23.0(5.4)
RI	22.6(1.0)
NJ	20.3(0.8)
DE	25.3(-2.1)
MD	19.9(0.8)
DC	27.6(6.3)

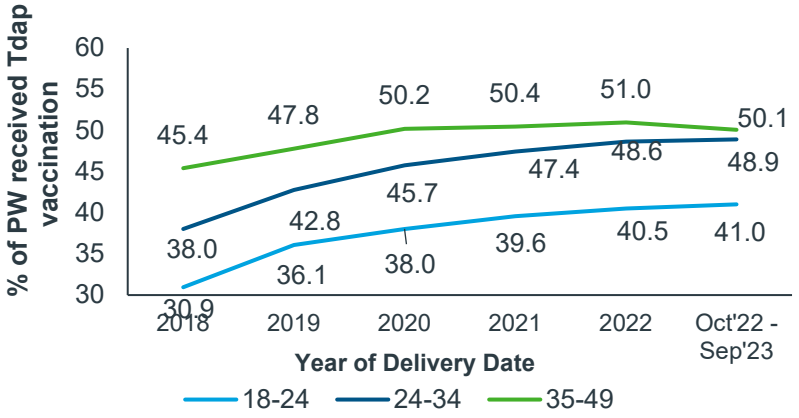
NE, CA, UT showed highest increases in Oct'22 - Sep'23 vs 2019
SD, ID, DE showed highest drops in Oct'22 - Sep'23 vs 2019

Pneumococcal

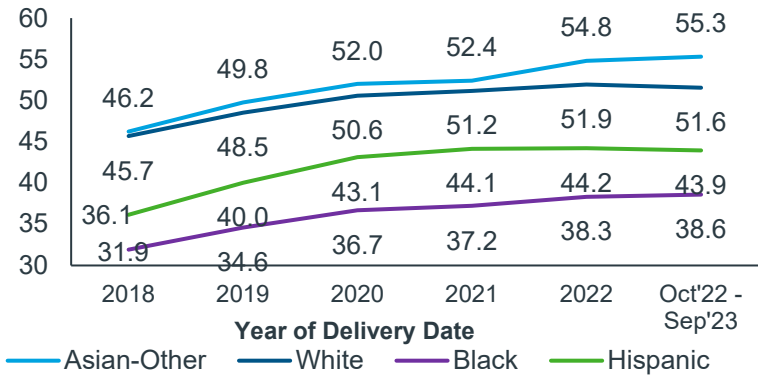
Sources: IQVIA LAAD and Experian Data; Annual vaccination = Population received vaccination/Population eligible for vaccination
*Considered PCV 13 (Prevnar 13), PCV 15 (Vaxneuvance), PCV 20 (Prevnar 20) and PPSV23 (Pneumovax 23) for Pneumococcal vaccinations

Tdap vaccination in Pregnant Women(PW) is similar in Oct'22 – Sep'23 as compared to 2022

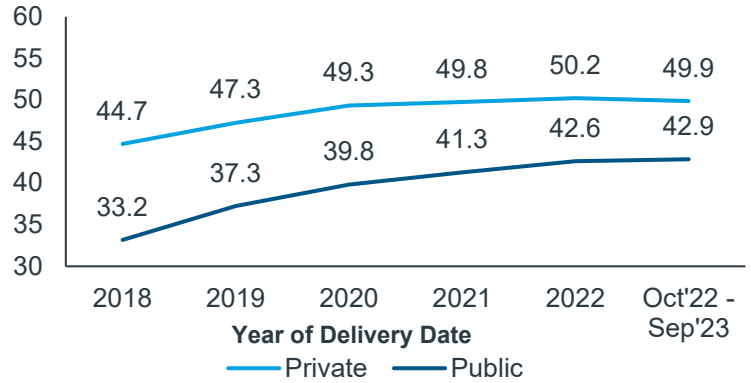
Vx Rate by Age Group (Age 18-49)



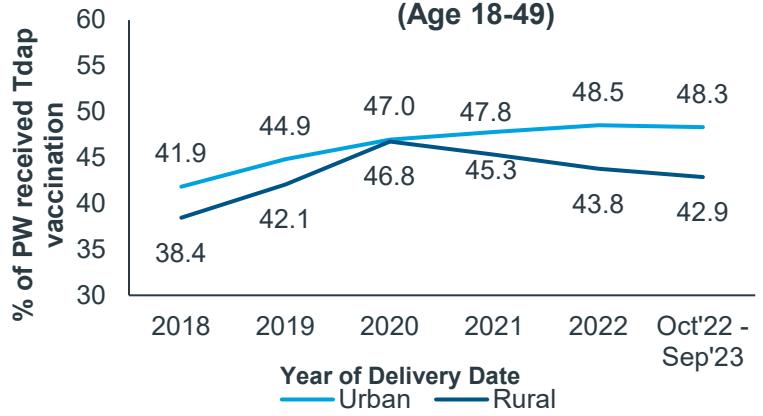
Vx Rate by Race (Age 18-49)



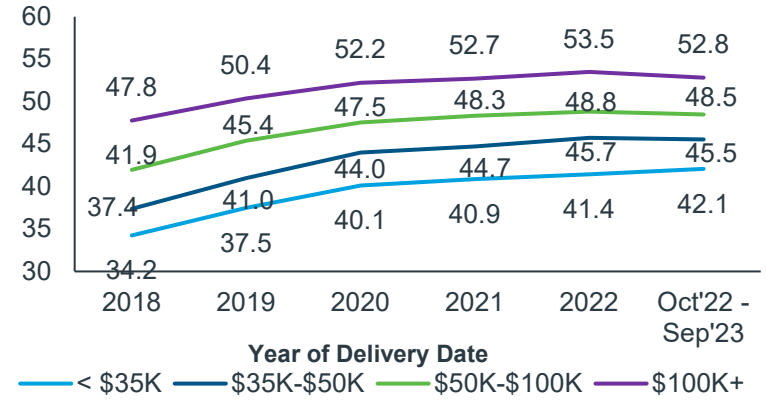
Vx Rate by Payor channel (Age 18-49)



Vx Rate by Provider Urban/Rural[1] Status (Age 18-49)



Vx Rate by Household Income (Age 18-49)



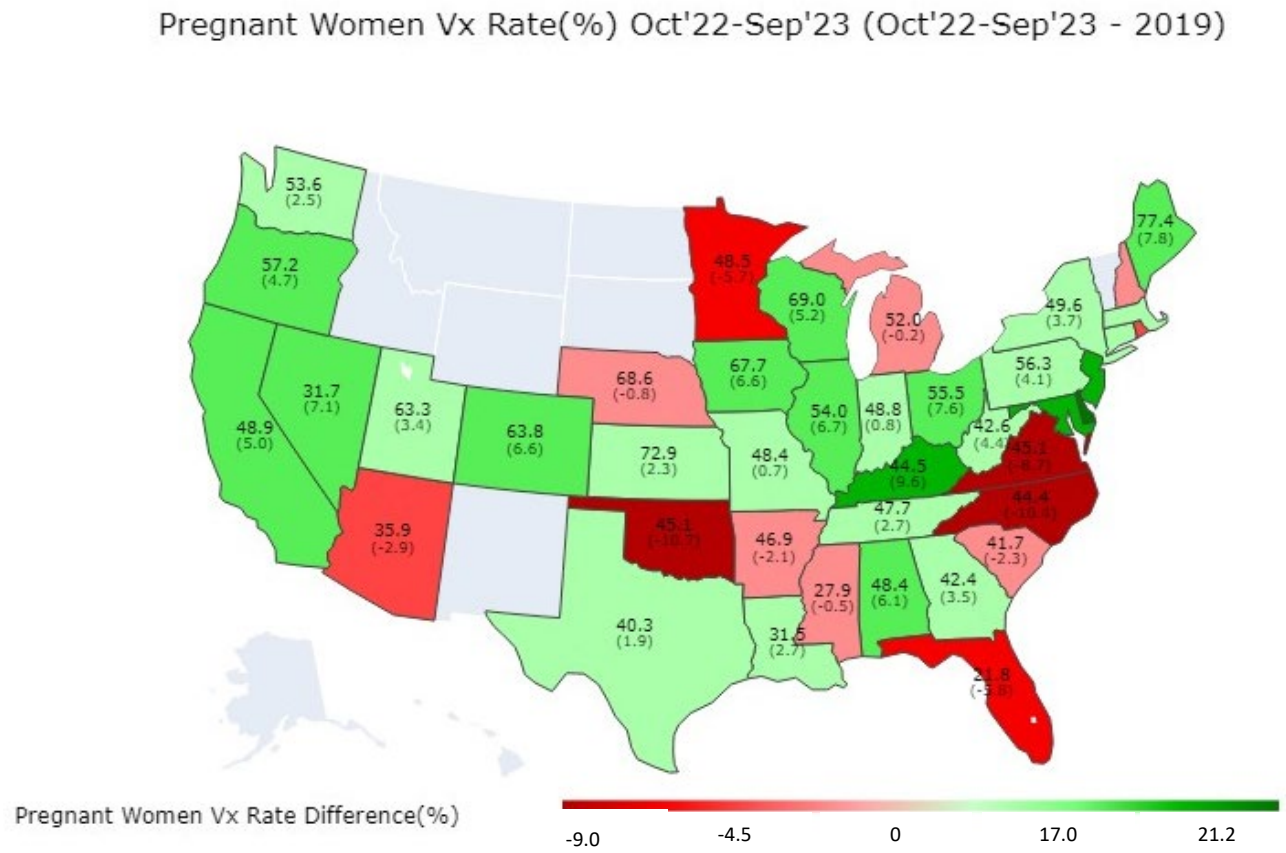
Key Insights

- Tdap Vx rate for Pregnant Women increased by 0.7% in Oct'22 - Sep'23 as compared to 2022 for < $35K Income group patients
- Tdap Vx rate for Pregnant Women has increased by 0.3% in Public setting and Private setting in Oct'22 - Sep'23 as compared to 2022
- Tdap Vx rate for Pregnant Women has increased for Asian and Black ethnicities in Oct'22 - Sep'23 as compared to 2022

Sources: IQVIA LAAD and Experian Data; Annual vaccination = Pregnant women received vaccination/Total eligible Pregnant Women Indexed at year of Delivery Date ;
Private channel includes Commercial and Medicare Advantage. Public channel includes Medicare (Medicare FFS), Medicaid (FFS and Managed Medicaid) and Cash
For Tdap vaccination was administered between up to 180 days before Last Menstrual Period and up to delivery date
1. Rural population represent only 5% in IQVIA claims

Overall, Tdap Vaccination for Pregnant Women has increased in 28 states in Oct'22-Sep'23 compared to 2019 for 18-49 age group.

Age group:18-49 years



Delaware shows highest increase from previous year (18.2%)
Washington DC shows 2nd highest increase from previous year (17.1%)
Maryland shows 3rd highest increase from previous year (13.2%)

Oklahoma shows highest drop from previous year (-10.7%)
North Carolina shows 2nd highest drop from previous year (-10.4%)
Virginia shows 3rd highest drop from previous year (-8.7%)

Sources: IQVIA LAAD and Experian Data; Annual vaccination = Pregnant women received vaccination/Total eligible Pregnant Women; States with a small sample size have been greyed out
Indexed at year of Delivery Date; Private channel includes Commercial and Medicare Advantage. Public channel includes Medicare (Medicare FFS), Medicaid (FFS and Managed Medicaid) and Cash
For Tdap vaccination was administered between up to 180 days before Last Menstrual Period and up to delivery date;


CAP

The U.S. Needs a Federal Program To Expand Vaccine Access and Equity for Adults

Marquisha Johns
Center for American Progress
February 23, 2024

CAP

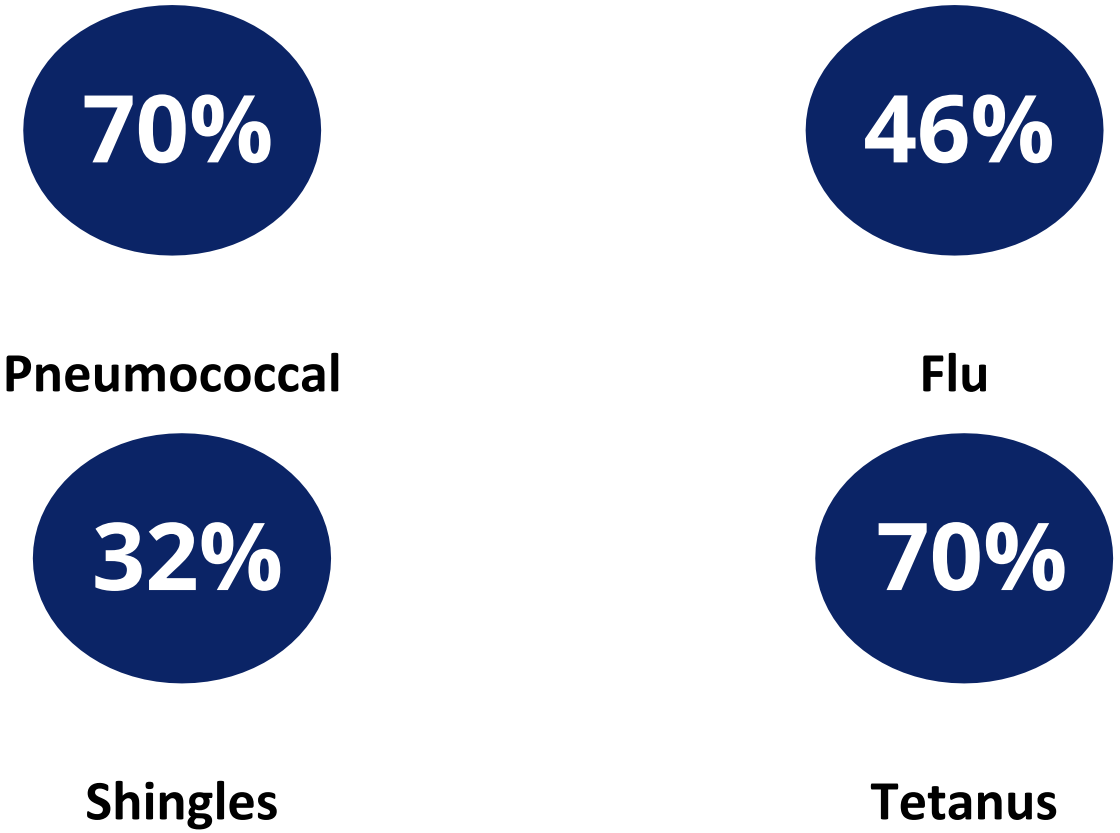
Vaccine Coverage in the U.S.

- Private Insurance
- Public Insurance (Medicaid/CHIP, Medicare)
- Vaccines for Children

However, this leaves nearly 23.7 million non-elderly uninsured adults without comprehensive, no-cost vaccine access.

In both its FY 2023 and FY 2024 budget proposals, the Biden Administration requested a Vaccine for Adults program be established and funded.

Vaccination Rates Among Adults



Source: GAO Analysis of 2019 -2020 BFSS data

The impact of vaccine-preventable disease among adults is significant.

> More than 50,000 adults die from vaccine-preventable diseases or their complications each year, not including COVID-19, and the economic burden among adults (the cost of medical treatment and lost productivity) is an estimated $9 billion to $26.5 billion each year.

A program for uninsured adult vaccine coverage

Section 317

- Public health infrastructure funding, including:
  - vaccine education and communication
  - immunization data systems
  - vaccine administration and distribution
  - disease outbreak monitoring and response
  - research on vaccine, recommendations, safety, and effectiveness
  - limited uninsured adult vaccine purchase

Vaccines for Adults (VFA)

- Vaccine purchase, including advanced contracting that can help improve vaccine supply
- Vaccine administration and distribution
- Expanded provider networks and partnerships to include other care settings (pharmacies, urgent care, etc.)
- More expansive vaccine availability
- Mandatory funding model

Political Landscape for VFA

- Important health priority for the Biden Administration
- Some congressional champions, but more education is needed on “why VFA” *
- Lack of appetite for vaccine work or additional mandatory spending (congressional gridlock)
  - Would need to be attached to another moving policy vehicle
- Preventative services/public health interventions are a hard sell in general *
- Need to reestablish CDC authority and trust

**this is where providers can be especially impactful*

Other Policy Options:

- Expand 317 funding or establish another discretionary program
- Address misinformation and disinformation
- Bridge Access Program *(ends December 2024)*

Questions?

Marquisha Johns
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Moving Needles

A CDC FUNDED INITIATIVE

Improving Adult Immunization Rates in PALTC

A five-year, CDC-funded cooperative agreement with AMDA

amda The Society For Post-Acute And Long-Term Care Medicine™

WWW.MOVINGNEEDLES.ORG

Objectives

- Provide context for immunization in a long-term care setting
- Share a project overview, findings, and progress
  - Quality improvement pilots
  - Frontline staff survey
  - EHR/IIS interoperability efforts
- Identify key opportunities for improving rates among staff and residents

Understanding the Environment

- Regulations
  - One of the most heavily regulated industries
  - Different regulations for skilled nursing, assisted living, home based care
- Short staffing
  - Generally low wage work with high need residents
  - Shortage across the healthcare system
  - Those who stay are burned out more quickly
  - High turnover
- More complex resident needs
- Real estate investment trusts (REITs) are purchasing buildings and profit margins are slim
- Immunizations are dependent on leaders championing and setting the vision, as well as directors of nursing and/or infection preventionists executing amidst many other immediate job needs

AMDA – The Society for Post-Acute and Long-Term Care Medicine, Inc.

- The only medical specialty society representing the community of medical directors, physicians, nurse practitioners, physician assistants, and other practitioners working in the various post-acute and long-term care (PALTC) settings.
- Formed in 1977 to help standardize the role of the medical director; have since expanded
- 3500 members currently
- Started a board and offer a certificate of medical direction (CMD)
- Received the Moving Needles cooperative agreement in fall 2021

Project Overview

Overview

Goal

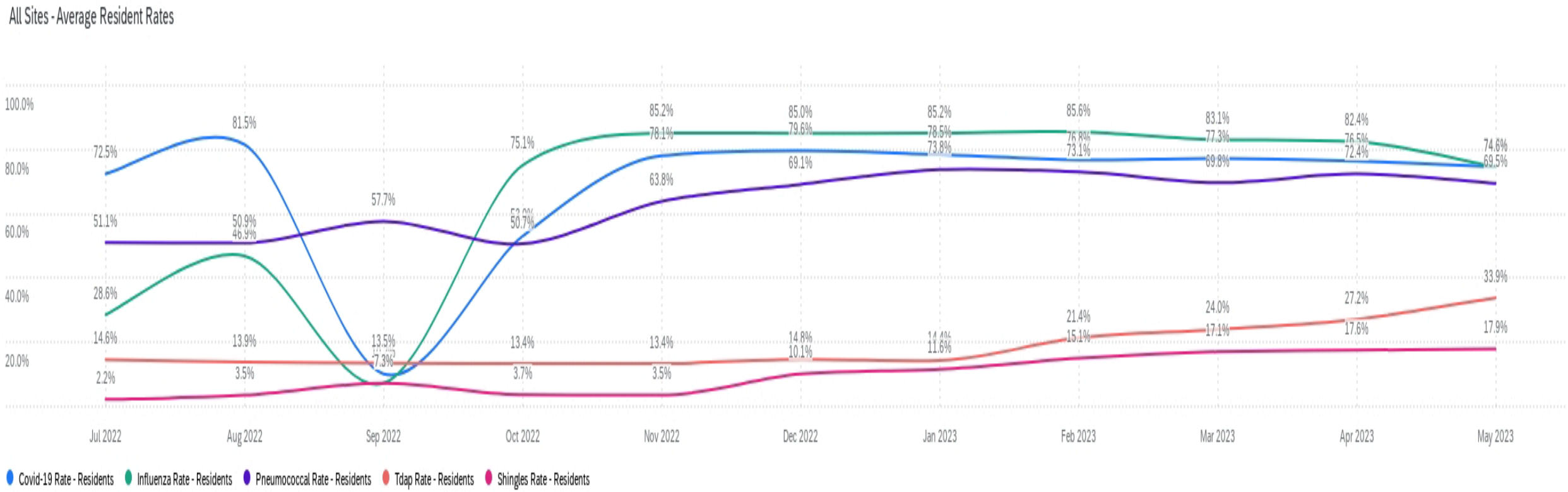
Make routine adult immunizations a standard of care for PALTC residents and an expectation for employees.

Main Components

- Develop pilot programs to test standardized routine adult immunizations across all PALTC settings, for both residents and staff
- Establish baseline data and measure improvement
- Support facilities in immunizing staff with responsive training
- Integrate routine immunization and reporting to state IISs into workflows and EHR systems for both staff and residents
- Demonstrate both clinical benefits and operational/cost benefits to implementation
- Establish a permanent resource on PALTC immunization

Quality Improvement Pilots

Residents: Average Vaccination Rates All 9 Facilities



Notes

- Average Vaccination Rates for all 9 facilities that participated in Round 1 of the QI Project.
- Upward trend for all of the vaccination rates during the period of the project – even for Tdap and shingles.

Residents: The Takeaways

- In many facilities, COVID-19 bivalent booster rates reached same or higher than the facilities' primary series rates at the start of the pilot.
- In almost every facility, influenza vaccination rates increased.
- In many facilities, pneumococcal vaccination rates were significantly higher than the start of the pilot.

- What Worked?
  - Facilities implemented structured processes and procedures because of the pilot. They routinized offerings and expanded which vaccines they provided.
  - Checked status on admission or used reminder-recall systems.
  - Organized vaccine availability outside of clinic times.
  - Assigned someone and/or a team to be responsible for the process.
  - Used the state Immunization Information System (IIS) to get data on resident history.

Residents: The Pain Points

- Facility billing during Part A stay for Medicare – pharmacies were able to direct bill Medicare and Medicaid on behalf of facilities during public health emergency; now facilities must bill directly
- Confusing around billing procedures for Part D vaccines
- Finding histories without an IIS is difficult
- Getting consent from family members for residents unable to assent themselves

Residents: The Pain Points

Residents

Influenza, pneumococcal, and COVID-19 vaccines

Influenza, pneumococcal, and COVID-19 vaccines are billed as part of **Medicare Part B**. Hepatitis B vaccine is covered under Part B only if an individual is considered to be at high risk – residents of long term care are considered high risk.

Part A Stay Resident

- **FACILITY**: Vaccine product and administration fee must be billed by facility using roster billing on a Part B claim
- **PHARMACY**: The LTC pharmacy is not allowed to bill directly for Part B vaccines for residents in their Part A stay

Non-Part A/Long-term Stay Resident

- **FACILITY**: Facility can use roster billing for both the vaccine cost and the administration fee on a Part B claim
- **PHARMACY**: Pharmacy can bill directly for both the vaccine cost and the administration fee

If the facility staff administered the vaccine, they can ask the pharmacy to bill the administration fee and provide it back to the facility. This should be written into contracts between facilities and pharmacies.

Hospice

Because vaccinations are not part of the Medicare hospice benefit, hospice claims *(type of bill 81X or 82X)* for vaccine services must be billed on a separate institutional claim and must only include charges for the vaccine and their administration.

COVID-19: For hospice patients under Part B only, include the GW modifier on COVID-19 vaccine administration claims if either of these apply:

1. **The vaccine isn't related to the patient's terminal condition.**
2. **The attending physician administered the vaccine.**

Tdap, shingles, and RSV vaccine

Tdap, shingles, and RSV are billed through **Medicare Part D**. Hepatitis B vaccine is covered under Part D if an individual is not at high risk.

Part A Stay Resident

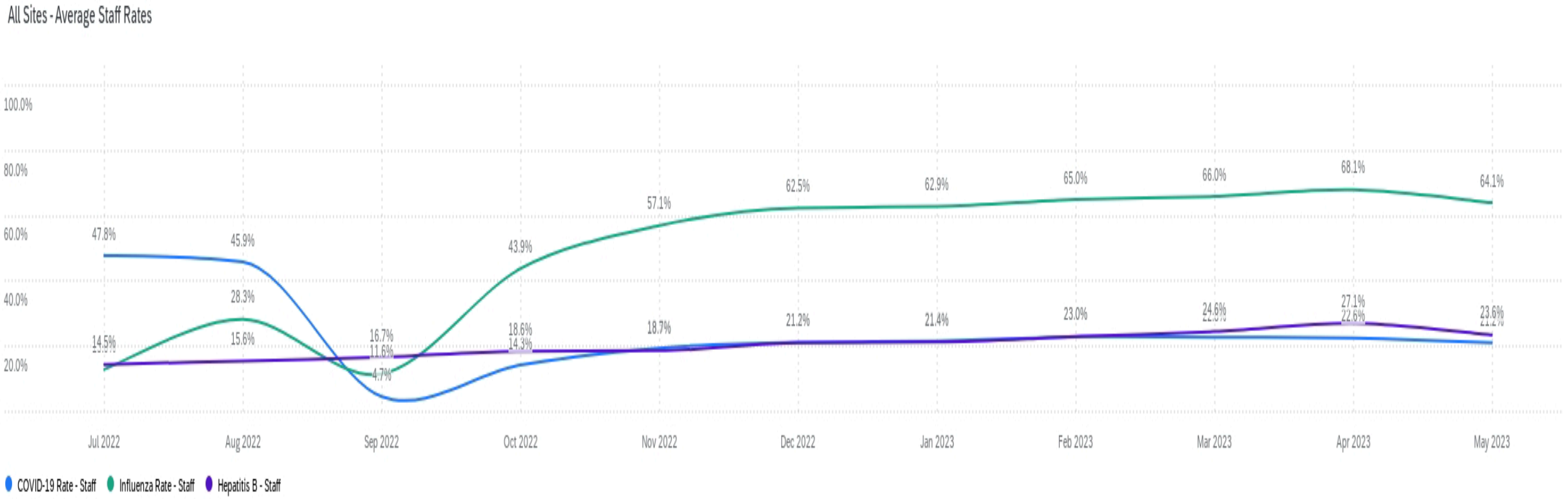
- **PHARMACY**: Pharmacies must provide and bill for the cost of the vaccine product and may bill for the administration fee

Non-Part A/Long-term Stay Resident

- **PHARMACY**: Pharmacies must provide and bill for the cost of the vaccine product and may bill for the administration fee

If the facility staff administered the vaccine, they can ask the pharmacy to bill the administration fee and provide it back to the facility. This should be written into contracts between facilities and pharmacies.

Staff: Average Vaccination Rates for All 9 Facilities



Notes

- Average Vaccination Rates for all 9 facilities that participated in Round 1 of the QI Project.
- Upward trend for Influenza and a slight upward trend for COVID-19 and Hepatitis B as well.

Staff: The Takeaways

- All facilities struggled with COVID-19 bivalent booster rates.
- Vaccine fatigue spilled over to influenza in some facilities.
- Strategies must be tailored to individual circumstances. Success occurred when:
  - Facilities made vaccine more accessible;
  - Facilities addressed staff in cohorts; and
  - Facilities persistently offered the vaccine.

- What Worked?
  - Identifying reason for lack of vaccination – sometimes it was a lack of a convenient time or location, needing to offer 3x from a trusted peer or staff person, or more traditional hesitancy.
  - Stepping back if continued offering pushed staff further away. Focusing on building trust.
  - Making vaccines accessible and provide reasons for staff provide records.
  - Building community.

Staff: The Pain Points

- Data collection for staff is challenging, particularly Hepatitis B.
- There is not an allowable use case for finding staff vaccination history in the IIS.
- All facilities struggled with COVID-19 bivalent booster rates.
- Vaccine fatigue spilled over to influenza in some facilities.
- Hesitancy is reflective of the communities from which staff come.
- With commercialization, facilities are unable to offer the vaccine on-site. LTC pharmacies are considered out of network with commercial insurance.

Year 2 Pilot

- Started Round 2 July 2023:
  - 4 chains participating, with 3 facilities from each chain – total of 12 facilities
  - Geographically diverse:
    - From the East, Mid-West, South, and West
  - Skilled Nursing and Assisted Living
  - For profit and non-profit
- Changes from Year 1
  - A more directed process around the Standards for Adult Immunization
  - Strong focus on standardization and operating procedures
- Goal is to understand what works and why to create a change package, likely based on stages of readiness for change

Frontline Staff Survey and In-Service

Frontline Staff Survey Goals

- Survey frontline PALTC staff in summer 2023 to understand:
  - What types of information they would like to receive regarding immunization
  - Trusted sources for vaccine information
  - Preferred modalities, sources, and formats for professional development
- AMDA using survey findings to develop a training module and distribution plan to encourage vaccine uptake among staff

Key Take-Aways

- Respondents are motivated to protect selves and others from illness
  - Half accept vaccination as a responsibility or requirement for LTC staff
- Respondents' confidence in protection through vaccination is low
- Many respondents view vaccination as a personal decision
  - Want balanced information to make own health decisions
  - Want information from healthcare providers, government agencies, co-workers with medical training
- For training, respondents preferred brief (<1 hour) paid in-service by a direct supervisor or administrator
- AMDA has developed an in-service slide deck and supervisor training that incorporate the findings

EHR/IIS Interoperability

EHR/IIS White Papers

Technical mapping document

- 5 keys to connectivity
- Workbook for self assessment
- Based on responses and interviews with multiple LTC EHRs

Implementation considerations

- Sustainable funding is critical
- Ensure awareness and understanding of connectivity benefits to strengthen and monitor collaborative action
- Positively incentivize connectivity
- Reduce the operational and technical burden of connectivity

Key Opportunities for Innovation

Opportunities

1. Think expansively about solutions to increase on-site accessibility, especially addressing billing challenges for residents and staff
2. Provide structural support and sustained technical assistance for implementation of standard operating procedures
3. Embed leadership training for medical directors, DONs, nurse practitioners and other clinical leaders in facilities, including how to build trust
4. Focus on interactive education opportunities that address the true concerns of staff, namely perceived low vaccine efficacy, from sources they trust (eg, personal healthcare provider, CDC, clinical supervisors)
5. Consider incentives to further EHR/IIS interoperability. Support increased awareness and understanding of the benefits of connectivity. Work towards reduction of operational and technical burdens.
6. Consider additional connections between the LTC and immunization communities (eg, representation at NVAC or ACIP, more systems that are built on adult vs pediatric infrastructure)

Thank You!

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Heather Roney hroney@paltc.org

www.movingneedles.org

Innovative Approaches to Improve Adult Immunization

Discussion

NVAC

Public Meeting

NATIONAL VACCINE ADVISORY COMMITTEE

February 22-23, 2024

Break

NVAC

Immunization in Focus: Vaccinating Pregnant People

Dr. Geeta Swamy
Dr. Flor Munoz-Rivas
Dr. Courtney Olson-Chen
Dr. Kevin Ault

NVAC

Dr. Geeta Swamy

Immunization in Focus: Vaccinating Pregnant People

NVAC

IMMUNIZATION IN FOCUS: PREGNANT PEOPLE QUALITY IMPROVEMENT AND SYSTEMIC STRATEGIES

NVAC PANEL - 23.FEB.2024

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Disclosures

- **Research Funding**
  - NIH / VTEU (PI Observational study vaccines in pregnancy – Momi-Vax; AFM)
  - CDC / Abt (Influenza and SARS CoV-2 burden in pregnancy)
  - Gilead (Remdesivir pediatric study)
  - Pfizer (COVID vaccines children)

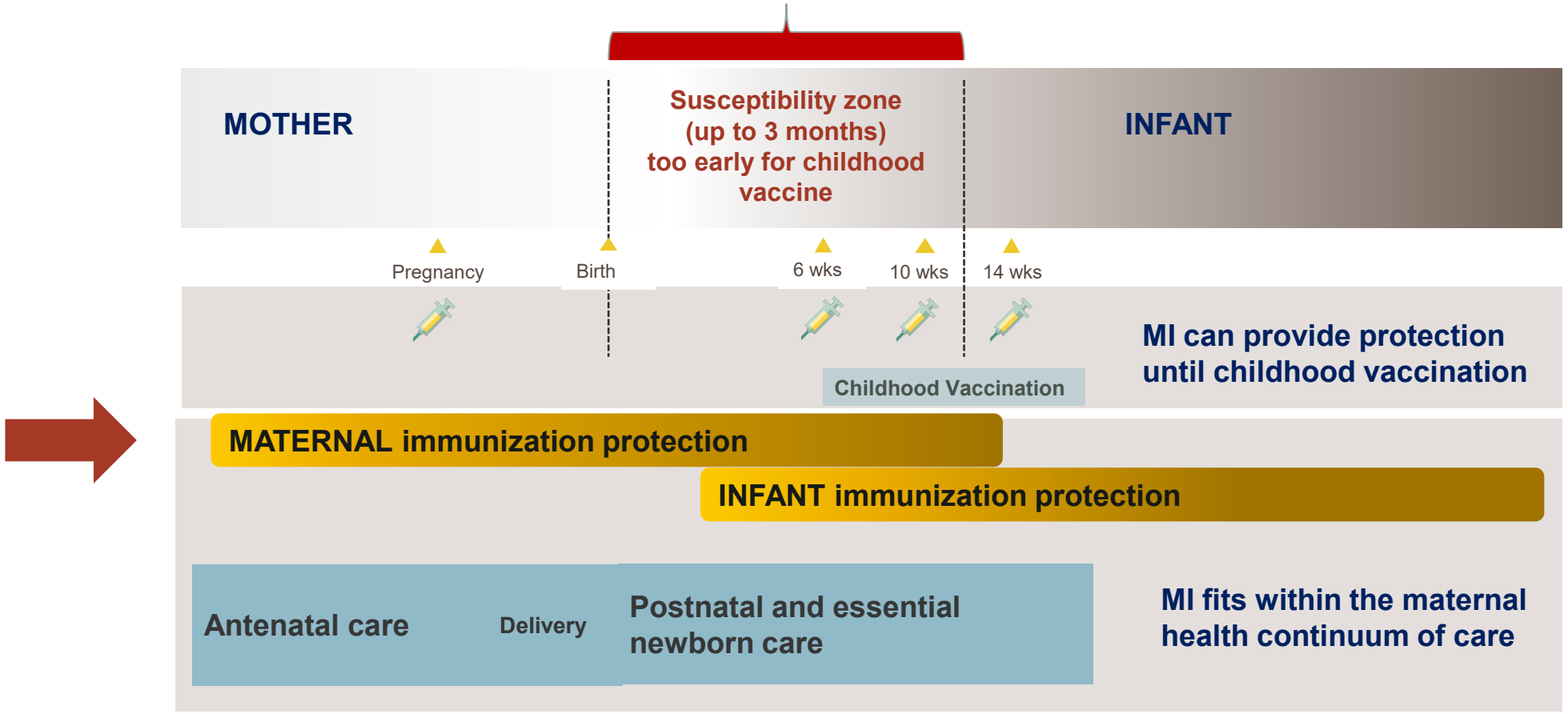
- **Special Groups**
  - AAP-COID (2015-2021) – Outbreaks Committee (2023-) - SOID (2021-current)
  - ACIP Mpox working group
  - ACOG Immunization Expert Group
  - COVAX-CEPI-MI WG (2020-22)
  - CEPI – SPEAC – Brighton Collaboration
  - GVDN – vaccine safety in pregnancy
  - NFID – Board Member
  - WHO – Vaccines in pregnancy/safety

- **Data Safety Monitoring Board**
  - NIH (Malaria, azythromycin)
  - Pfizer (RSV)
  - Moderna (various vaccines)
  - Meissa (RSV)
  - Virometix (RSV)
  - Dynavax (plague)

- **Advisory Groups**

  GSK
  Astra-Zeneca
  Regeneron
  Sanofi
  Merck
  Novavax
  Moderna
  Seqirus

The Continuum of Maternal and Infant Immunization



Adapted from: Maternal Newborn Child Health; Source: Every Newborn: An action plan to end preventable deaths (2013)

Vaccines for pregnant women and their infants

Vaccines in Development for Pregnancy

Phase I | Phase II | Phase III

GBS

Existing Recommended Vaccines

Recommended in specific situations | Generally recommended

Recommended in specific situations	Generally recommended
HAV, HBV	Tetanus (Td)
Meningococcal	Pertussis (Tdap)
Pneumococcal	Influenza
Polio	SARS-CoV-2
Typhoid	RSV
Rabies virus	
Cholera	
Yellow fever	
Japanese encephalitis	
Anthrax	

World Health Organization

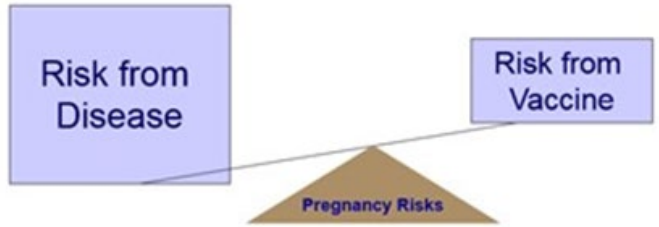
ACOG The American College of Obstetricians and Gynecologists

CDC Centers for Disease Control and Prevention

Advisory Committee on Immunization Practices (ACIP)

Opportunities for Maternal Immunization

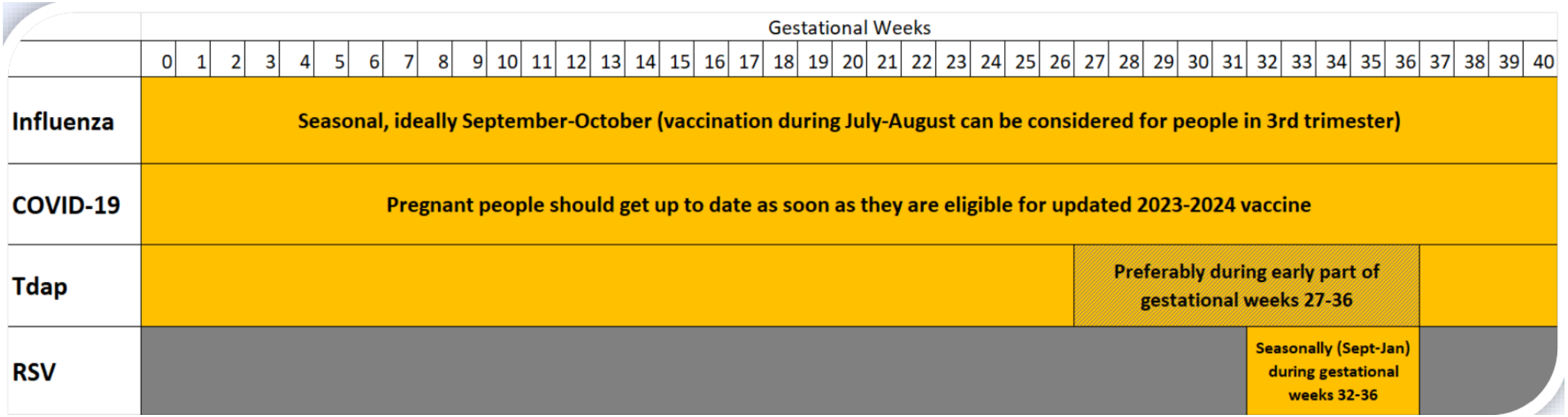
- **CMV**
- HSV
- **Malaria**
- **Ebola** (rVSV-ZEBOV vaccine)
- **Hepatitis E** (Genotype 1 subunit vaccines)
- **Lassa fever**
- Zika, **Chikungunya**
- Yellow fever
- Nipah virus
- Cholera, *E.coli,* Listeria
- Malaria



Adapted from : Philipp Lambach, World Health Organization. "Integration of infant and maternal immunization – A global challenge!" INMIS 2017, Brussels, Belgium.

Recommendations and Implementation Challenges

- Increasingly complex maternal immunization schedule, with different timing of **vaccines based on season and/or gestational age** (with seasonal timing varying by location)
- **Limited window for vaccine administration** increases risk of missing dose, especially in some vulnerable populations (equity), and of delivery occurring shortly after vaccination
- Unclear **willingness** of pregnant people **to accept multiple vaccines** in pregnancy
- **Burden on Obstetric Providers**

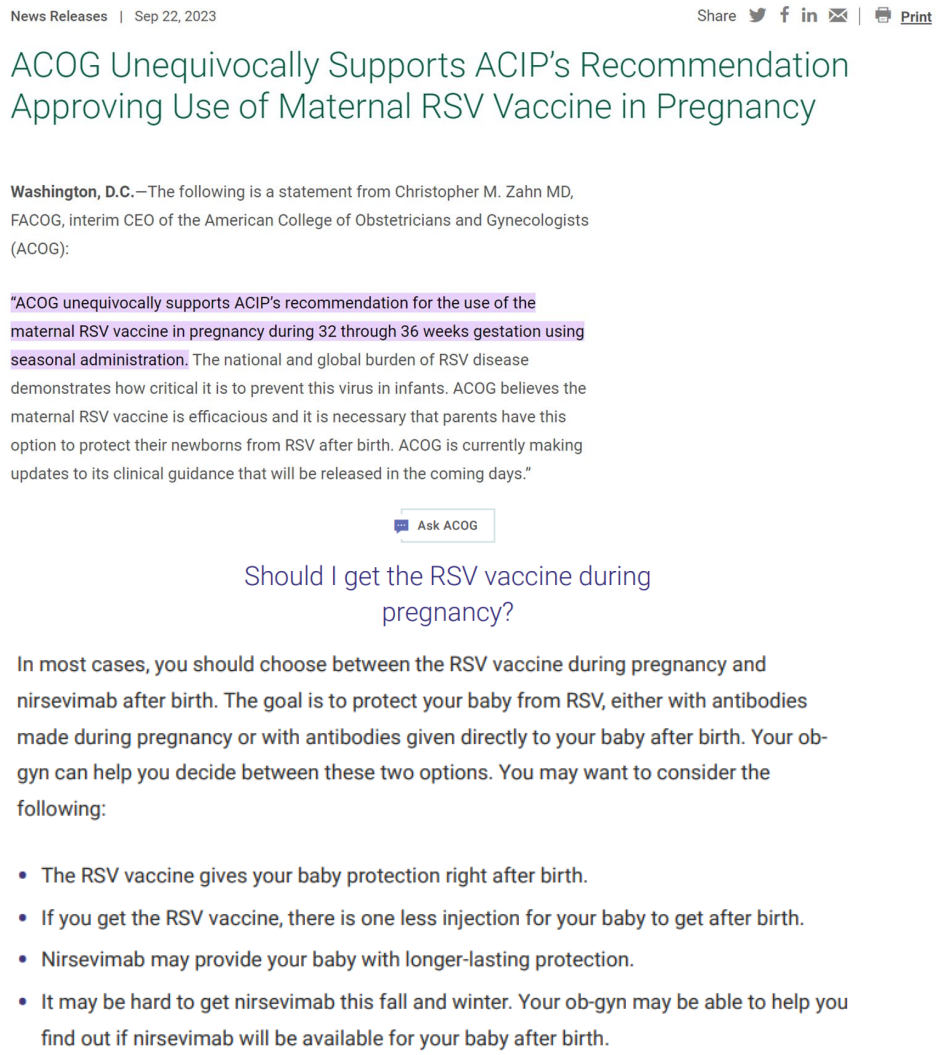


Source: ACIP meeting 22 SEP 2023

Maternal vaccine vs. Nirsevimab (ACIP)

- **Either maternal vaccination or use of nirsevimab in the infant is recommended to prevent RSV LRTI**
- **Both products are safe and effective in preventing RSV LRTI in infants**
- **Both provide passive immunity to the infant for 5-6 mo**
- **Administration of both products is not needed for most infants**
  - Nirsevimab is not needed for most infants born ≥14 days after maternal vaccination
- **Healthcare providers *of pregnant people*** should **provide information on both products** and consider **patient preferences** when determining whether to vaccinate the pregnant patient or to not vaccinate and rely on administration of nirsevimab to the infant after birth (choice)

https://www.cdc.gov/vaccines/vpd/rsv/index.html



News Releases | Sep 22, 2023

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ACOG Unequivocally Supports ACIP's Recommendation Approving Use of Maternal RSV Vaccine in Pregnancy

Washington, D.C.—The following is a statement from Christopher M. Zahn MD, FACOG, interim CEO of the American College of Obstetricians and Gynecologists (ACOG):

"ACOG unequivocally supports ACIP's recommendation for the use of the maternal RSV vaccine in pregnancy during 32 through 36 weeks gestation using seasonal administration. The national and global burden of RSV disease demonstrates how critical it is to prevent this virus in infants. ACOG believes the maternal RSV vaccine is efficacious and it is necessary that parents have this option to protect their newborns from RSV after birth. ACOG is currently making updates to its clinical guidance that will be released in the coming days."

Ask ACOG

Should I get the RSV vaccine during pregnancy?

In most cases, you should choose between the RSV vaccine during pregnancy and nirsevimab after birth. The goal is to protect your baby from RSV, either with antibodies made during pregnancy or with antibodies given directly to your baby after birth. Your ob-gyn can help you decide between these two options. You may want to consider the following:

- The RSV vaccine gives your baby protection right after birth.
- If you get the RSV vaccine, there is one less injection for your baby to get after birth.
- Nirsevimab may provide your baby with longer-lasting protection.
- It may be hard to get nirsevimab this fall and winter. Your ob-gyn may be able to help you find out if nirsevimab will be available for your baby after birth.

https://www.acog.org/news/news-releases/2023/09/

Patient Education and Counseling Maternal Vaccine

- Prenatal providers should **discuss both products** with pregnant people to aid in their decision-making, taking into account:
  - Relative advantages and disadvantages of each product
  - Patient preferences
  - Local availability of nirsevimab
- Prenatal providers who do not offer the maternal RSV vaccine in their practice should **refer patients elsewhere for vaccination**
  - Proactively provide a prescription if required by state law for vaccination in a pharmacy
- **Documentation of vaccination**
  - Critically important to document receipt of maternal RSV vaccine as most infants of vaccinated mothers not recommended to receive nirsevimab (Eg: Immunization Information Systems (IIS); Electronic Health Records (EHRs); Written documentation for patient to bring to birthing hospital and pediatric provider visits

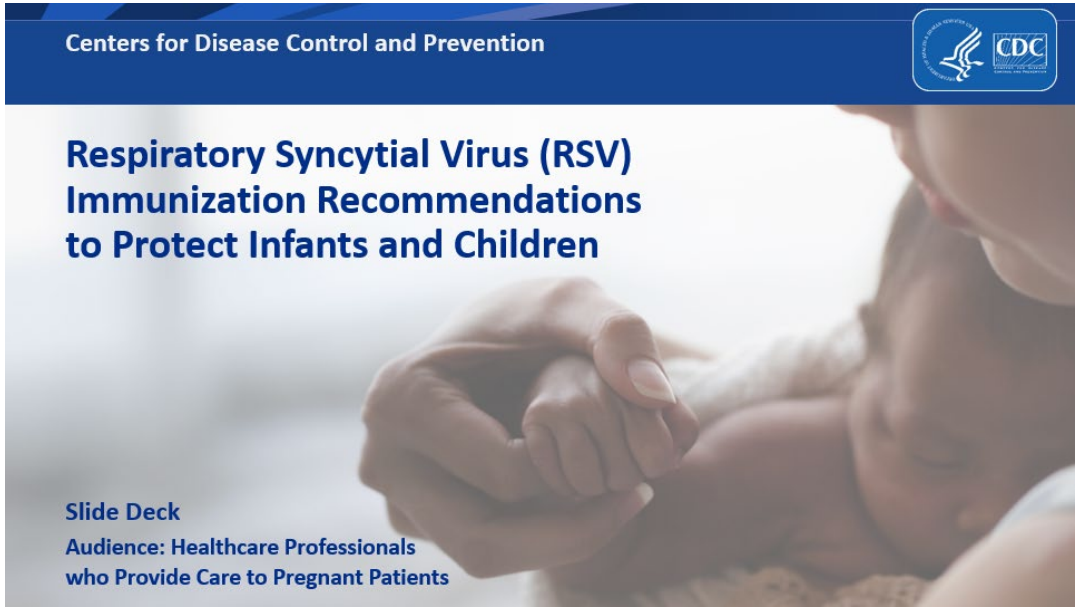
https://www.cdc.gov/vaccines/vpd/rsv/index.html

Progress in Research and Implementation of Vaccines in Pregnancy

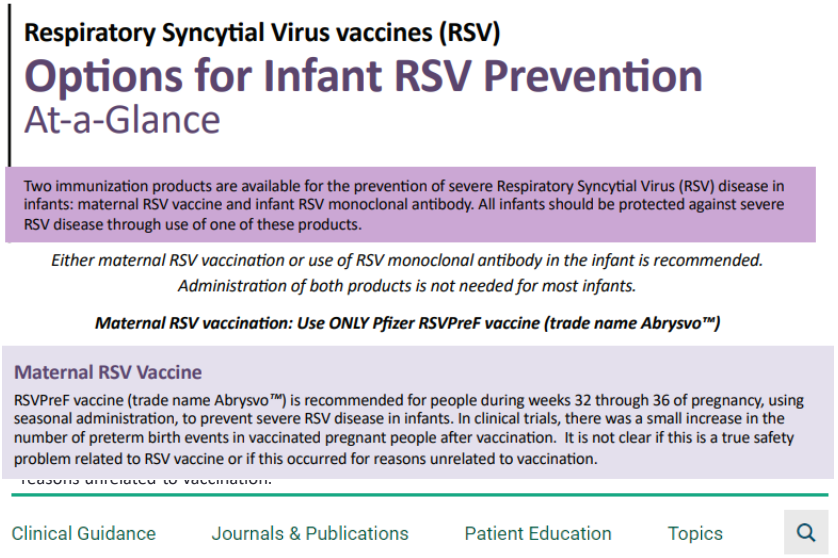
- **Paradigm shift: Inclusion of pregnant women in clinical trials**
- Design of vaccines and clinical research for pregnancy – research and regulatory pathway
- Assessment of **safety** (case definitions and surveillance systems), **efficacy and effectiveness** (outcomes)
- **Implementation Guidance**
- **Knowledge and Communication strategies**

Pregnancy and Lactation Labeling Rule (PLLR)
VRBAC Meeting 2015
NVAC 2015-16 MI group
Common Rule Update 2016
21 Century Cures Act 2017
CIOMS

CDC / ACOG Resources

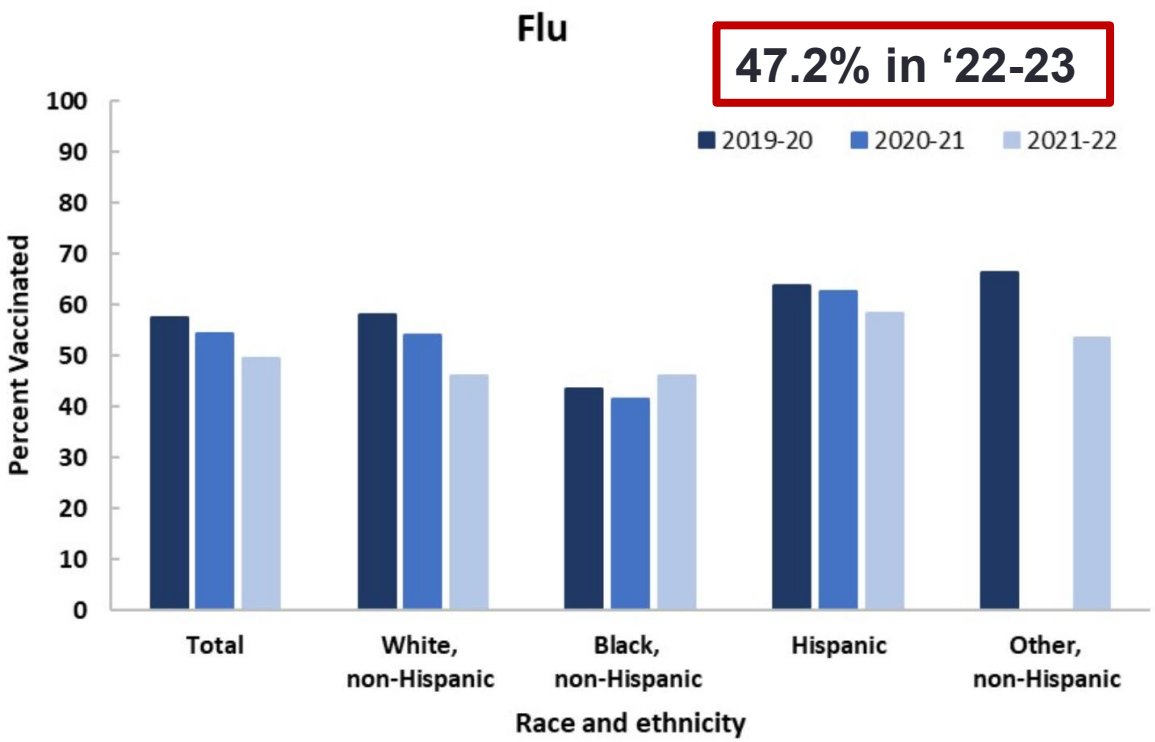


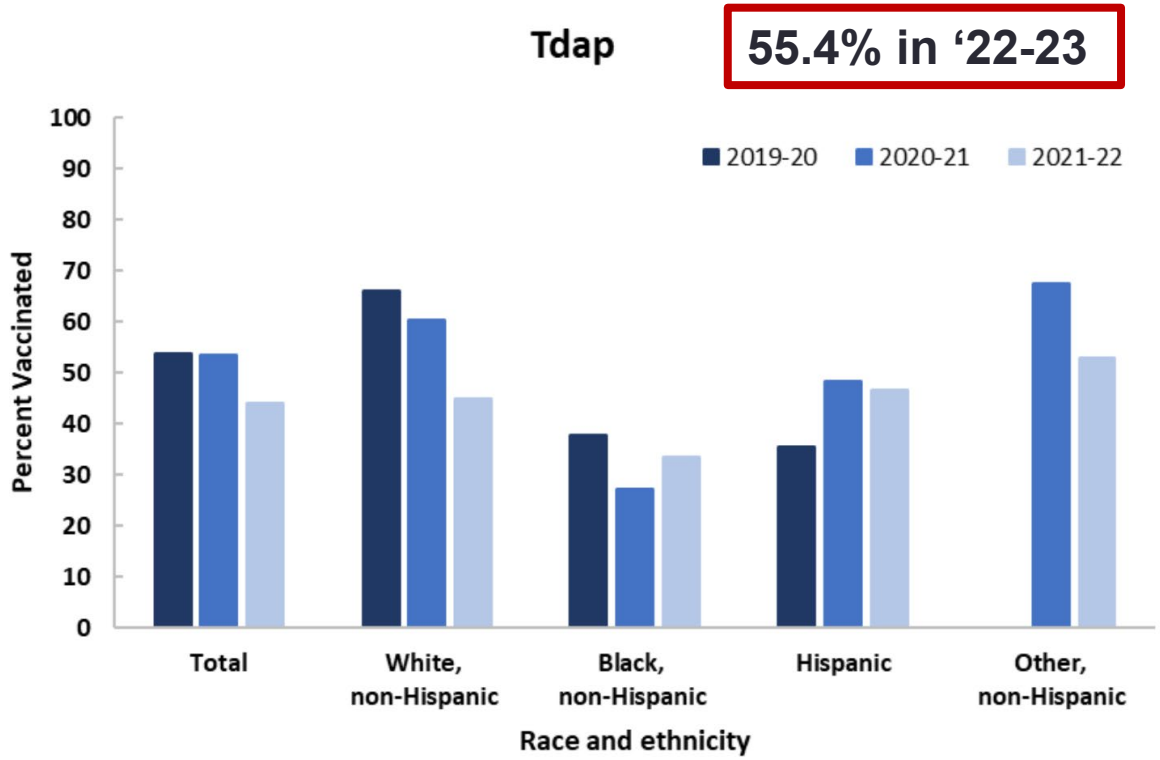
ACOG | Clinical



https://www.cdc.gov/vaccines/vpd/rsv/hcp/pregnant-people.html
https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2023/09/maternal-respiratory-syncytial-virus-vaccination

Pregnancy vaccination coverage remains low US April 2020-April 2022 ; 2023 (Internet panel survey)

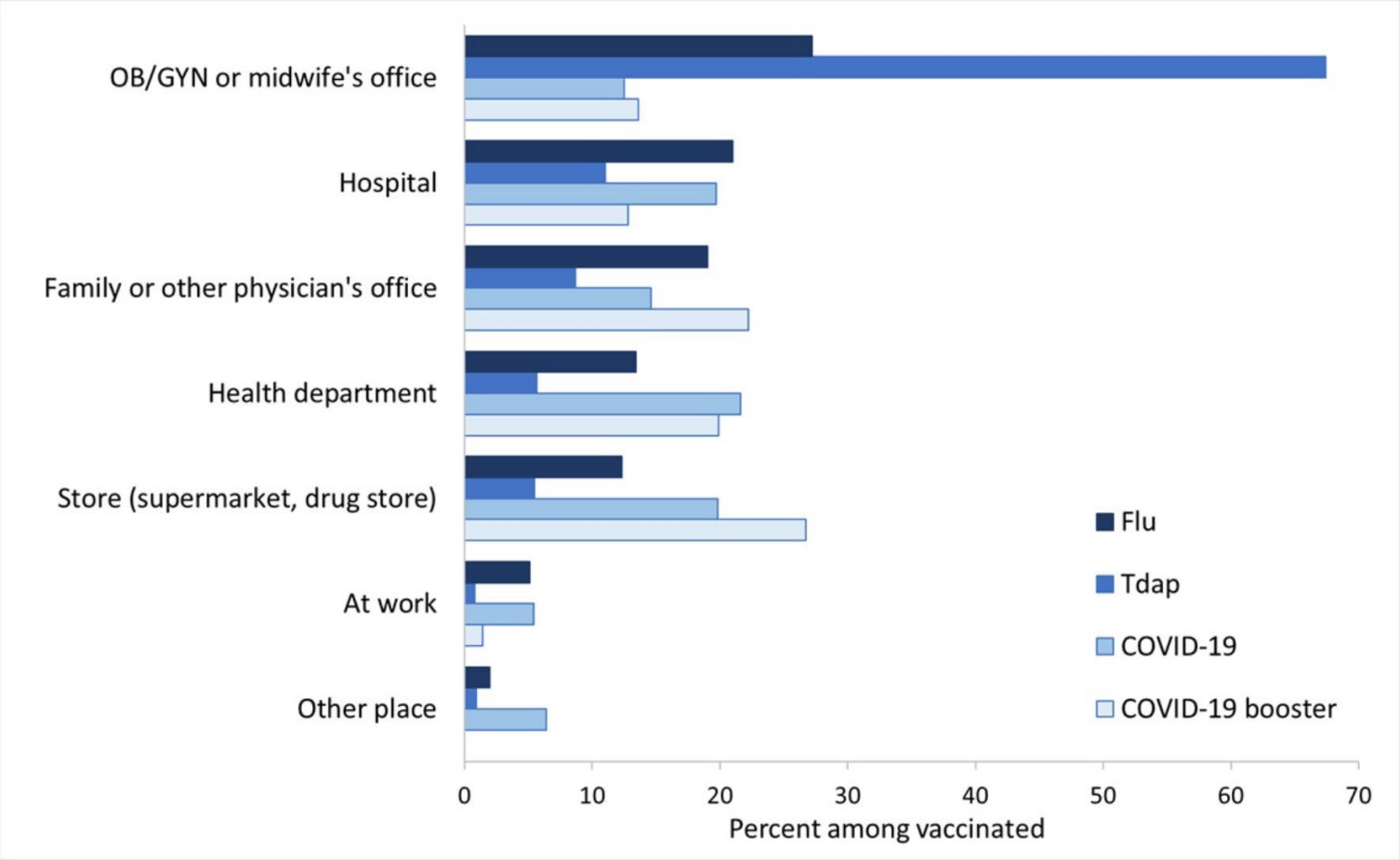




https://www.cdc.gov/flu/fluvaxview/pregnant-women-apr2022.htm
https://www.cdc.gov/mmwr/volumes/72/wr/pdfs/mm7239a4-H.pdf

25.6 % received both influenza and Tdap
Only 32.7 % of pregnant women were vaccinated with COVID-19 vaccines by end of 2021, 27.3% received Bivalent booster 2022-23

Factors contributing to vaccine acceptance among pregnant women



Place of Vaccination Among Pregnant Women, US
Internet Panel Survey, April 2022

Patient Perspective:
Most important maternal **concern**: **SAFETY** of the Baby

Most important factor for **acceptance**: **Provider Recommendation**

Other contributing factors:
Access, Perception of risk

Provider Perspective:
Time, Infrastructure, Reimbursement, Liability

https://www.cdc.gov/flu/fluvaxview/pregnant-women-apr2022.htm
https://www.cdc.gov/mmwr/volumes/72/wr/pdfs/mm7239a4-H.pdf

Systemic Strategies and QI are Necessary

- “Culture” of Maternal Immunization among antenatal care providers and staff
- Best interest of mother AND infant in mind – Planning and coordination
- Need for provider education and up to date information / resources for patients and their support system
- Vaccination in office vs. outside source: Infrastructure to order, store, manage vaccines within practice, wastage, error prevention, etc. vs. pro-active prescription
- Time within the antenatal care visit to discuss maternal vaccines / who should discuss?
- Dedicated personnel for MI? Standard order sets? Best practice advisories (BPA)?
- Documentation of vaccination, EHR vs. personal immunization records, reduce confusion about which vaccine was received
- Linkage of maternal and infant records
- Communication with and between providers (OB, neonatal, pediatric)
- Risk Management - assessment of safety / management of adverse events / reporting
- Vaccine acceptance - hesitancy
- Reimbursement (public vs. private)

Vaccine Hesitancy in Pregnancy

Courtney Olson-Chen, MD, MSCI

Associate Professor of Ob/Gyn

Division of Maternal-Fetal Medicine

Vaccine Hesitancy

A behavior, influenced by a number of factors including issues of

1) **confidence** [lack of trust in vaccine or provider]

2) **complacency** [do not perceive a vaccine need or value]

3) **convenience** [access]

- Complex issue with a continuum between vaccine acceptance and refusal
- Complicated by rise in available vaccines and modes of communication
- Not all predictive factors have been identified

Understanding vaccine hesitancy around vaccines and vaccination from a global perspective: A systematic review of published literature, 2007-2012. Larson, et al. Vaccine 2014.

Understanding vaccine hesitancy around vaccines and vaccination from a global perspective: A systematic review of published literature, 2007-2012. Larson, et al. Vaccine 2014.

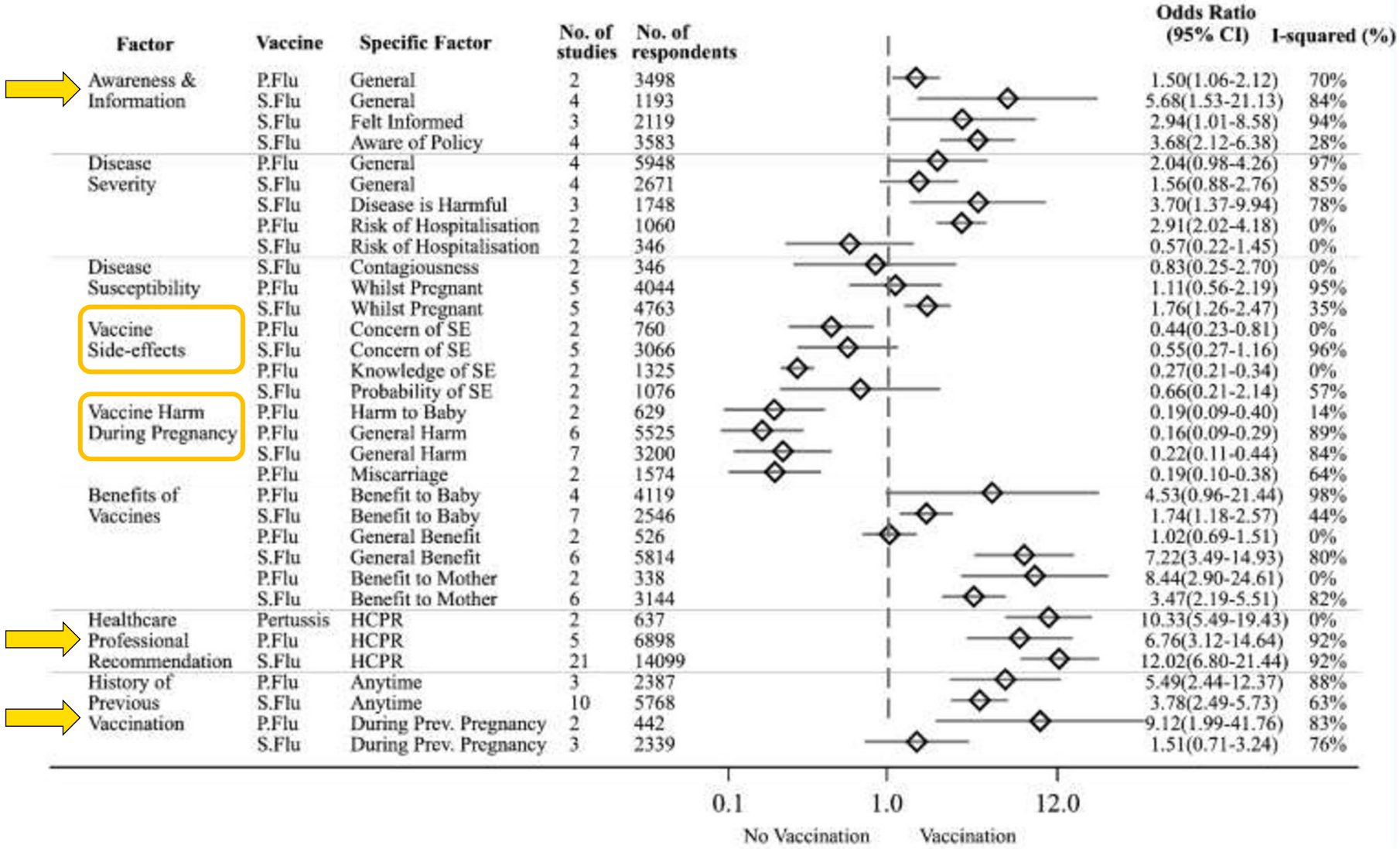
Vaccine Hesitancy in Pregnant People

- Most common barriers to acceptance are related to safety concerns
- Other factors:
  - Not perceiving themselves to be at risk of the disease
  - Lack of healthcare provider recommendation

Vaccine	Acceptance Rate (Oct 2021- Jan 2022)
Influenza	48.4%
Tdap	45.8%
COVID-19 (≥1 dose)	60.5%

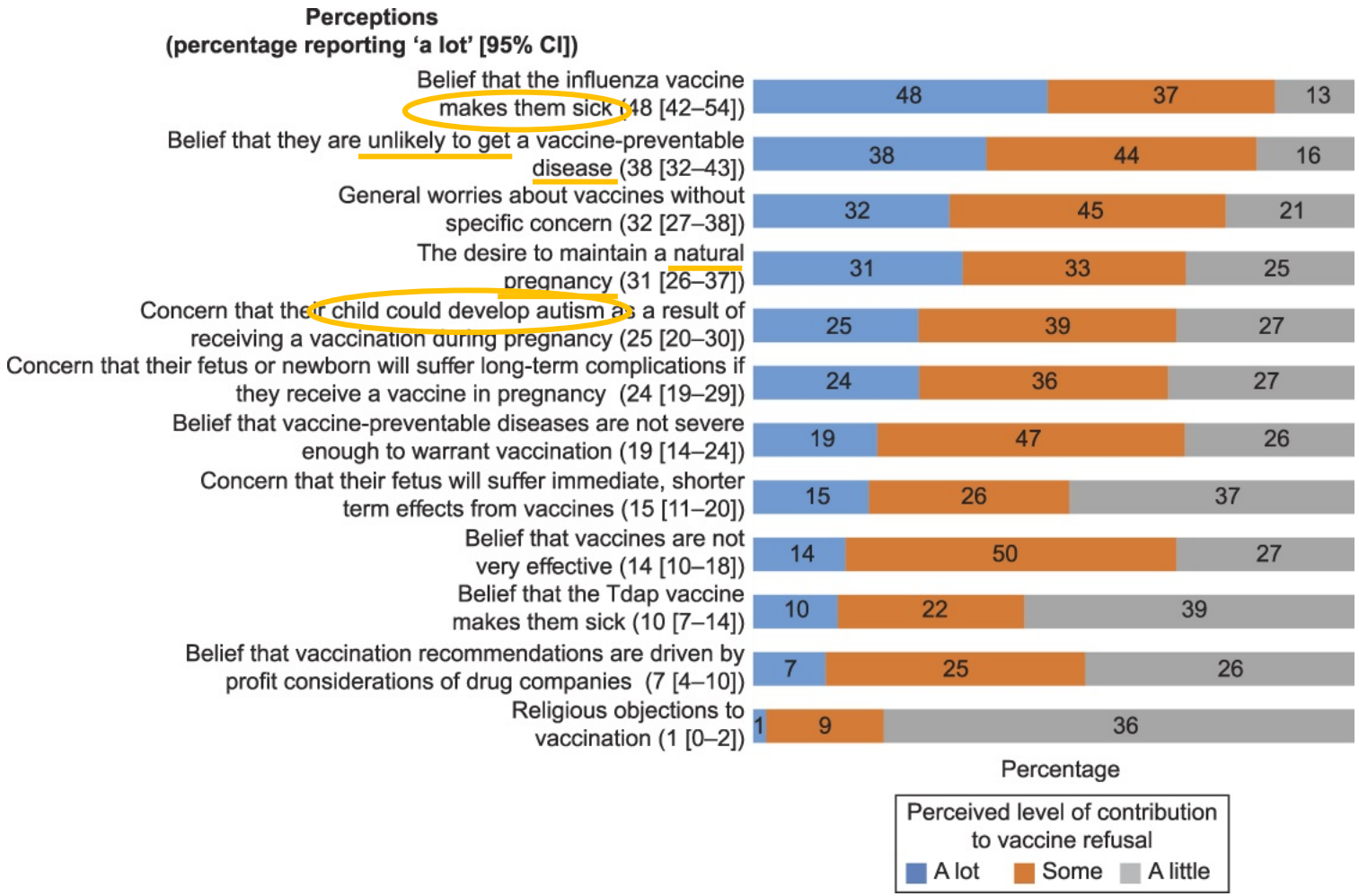
Understanding barriers and predictors of maternal immunization: Identifying gaps through an exploratory literature review. Lutz, et al. Vaccine 2018.

Kahn, et al. National Center for Immunization and Respiratory Diseases, CDC 2022.



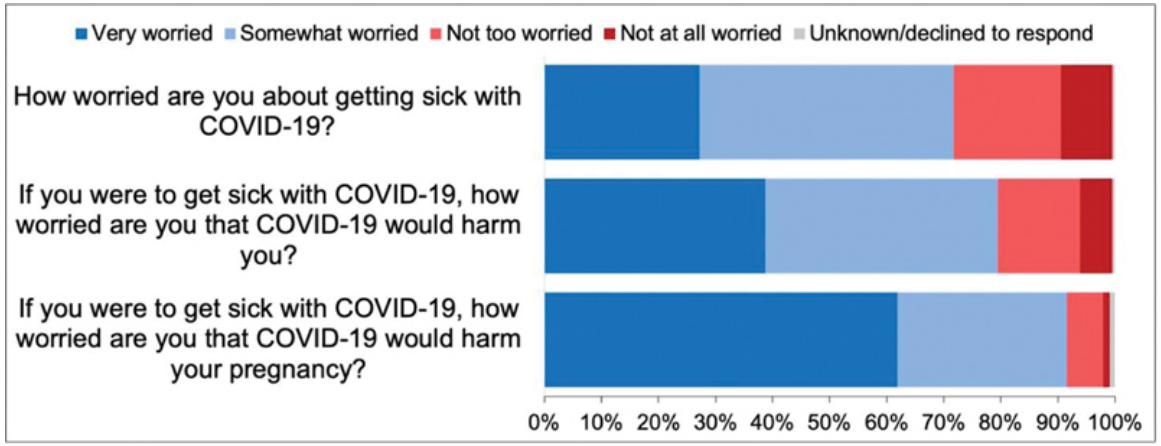
Factors that influence vaccination decision-making among pregnant women: A systematic review and meta-analysis. Kilich, et al. PLOS One 2020.

Influenza Vaccine Hesitancy



Obstetrician–gynecologists' attitudes about vaccination of pregnant patients. Tdap, tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis.O'Leary. Obstetrician–Gynecologists and Vaccination. Obstet Gynecol 2019.

COVID-19 Vaccine Hesitancy



41% of people said they would get the COVID-19 vaccine if one became available during their pregnancy.

Most common concerns:

- Vaccine safety for pregnancy (82%)
- Vaccine safety for themselves (68%)
- Vaccine effectiveness (52%)
- Lack of need for vaccine (22%)

Attitudes toward COVID-19 Illness and COVID-19 Vaccination among Pregnant Women: A Cross-Sectional Multicenter Study during August-December 2020. Battarbee, et al. Am J Perinatol 2022.

Table 2. Reasons for COVID-19 Vaccine Hesitancy among Pregnant Californians.

Reason for Hesitancy	Average Endorsement (1–4) *Strong Disagree* to *Strong Agree*	Average Importance (1–5) *Not at all* to *Most Important*
I don't know enough about the vaccine	3.1	4.3
Vaccine is not safe	2.3	3.7
Some other reason	2.7	3.6
Vaccine is not effective	2.0	3.3
COVID-19 isn't a serious illness	1.4	3.1
Others should get the vaccine, but I should not	2.3	3.0
I do not trust the vaccine makers	2.0	2.8
I do not want authorities telling me what to do	1.9	2.5
Immunizations are not good for anyone	1.5	2.5
Fear of needles or injections	1.6	2.0

Factors Associated with Vaccine Hesitancy:

- Younger Age
- Living in a less urban context
- Essential worker status
- History of COVID-19 infection
- Lack of seasonal Flu Vaccine

Understanding COVID-19 vaccine uptake during pregnancy: 'Hesitance', knowledge, and evidence-based decision-making. Simmons, et al. Vaccine 2022.

Figure 1. Themes for Vaccine Hesitancy

Too Rushed/ Too New/ Needs More Research

- "I personally do not feel that [the vaccine has] been developed enough for me to be putting it in my body." (Participant 13)

Safety/Potential Side Effects for Fetus

- "I'm worried that they could affect the baby. I don't care, like, after, if I get it done... to me. It's fine. But since I have the baby, I don't want to get it right now." (Participant 17)

Safety/Potential Side Effects for Self

- "I have so many health conditions, I'm like really worried about getting sick with it or having complications…" (Participant 27)

Long Term Side Effects

- "I think that, yes, it might be safe right now, but it could be 5,10 years down the line and 'if your family member got this… call this number, blah, blah, blah'" (Participant 25)

Conflicting Expert Recommendations/ Messaging Changes

- "I just feel like they change their guidelines so often, that I feel like they don't know much about the vaccine, either. So, I'm skeptical." (Participant 16)

Not Fully FDA Approved

- "I [won't get it] because it's not fully FDA approved yet." (Participant 28)

Not Fully Effective

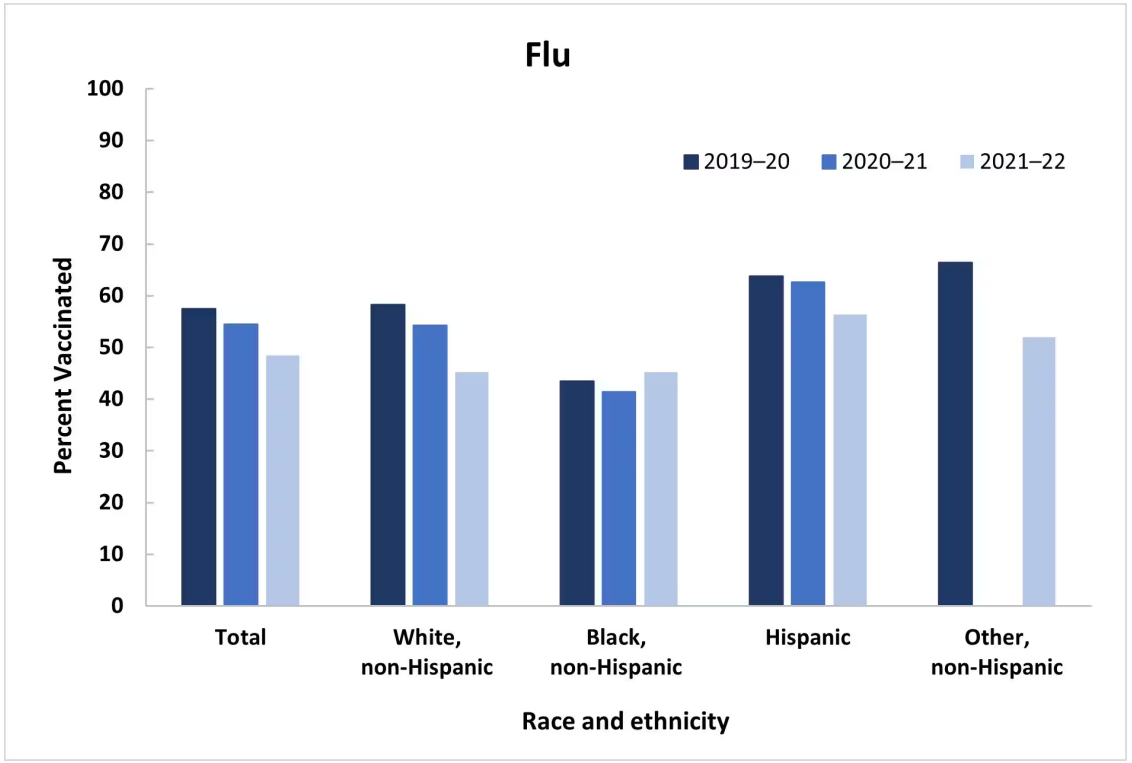
- "Not saying that it's not working, but it doesn't protect you against all strains. So, it's just, if it's something that's not going to protect you completely then I don't see the point of it." (Participant 24)

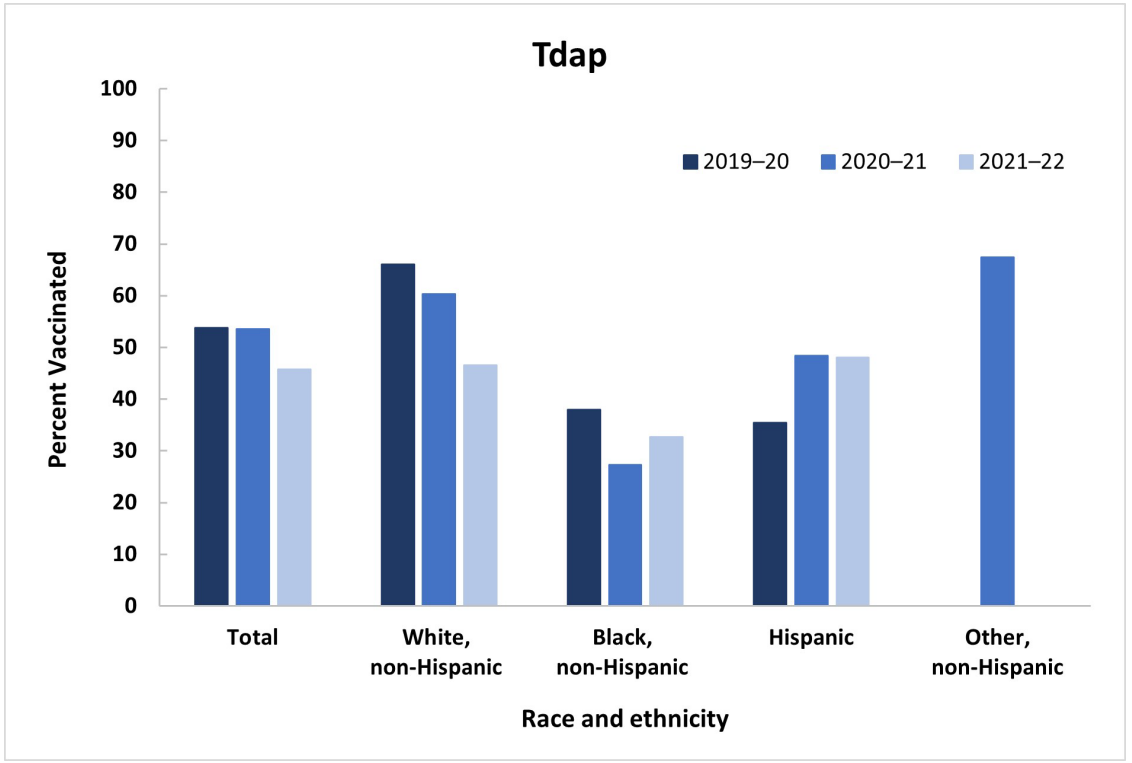
Future Fertility Concerns

- "I want to have more children, and then there's just not enough studies for me. With all my [miscarriages], that plays a big part. I don't want to cause anything that could harm my future kids." (Participant 20)

Attitudes toward COVID-19 vaccination among pregnant persons in urban hospital-affiliated practices: exploring themes in vaccine hesitancy. Gibson, et al. Maternal and Child Health Journal 2023.

Vaccine Coverage Disparities in Pregnancy

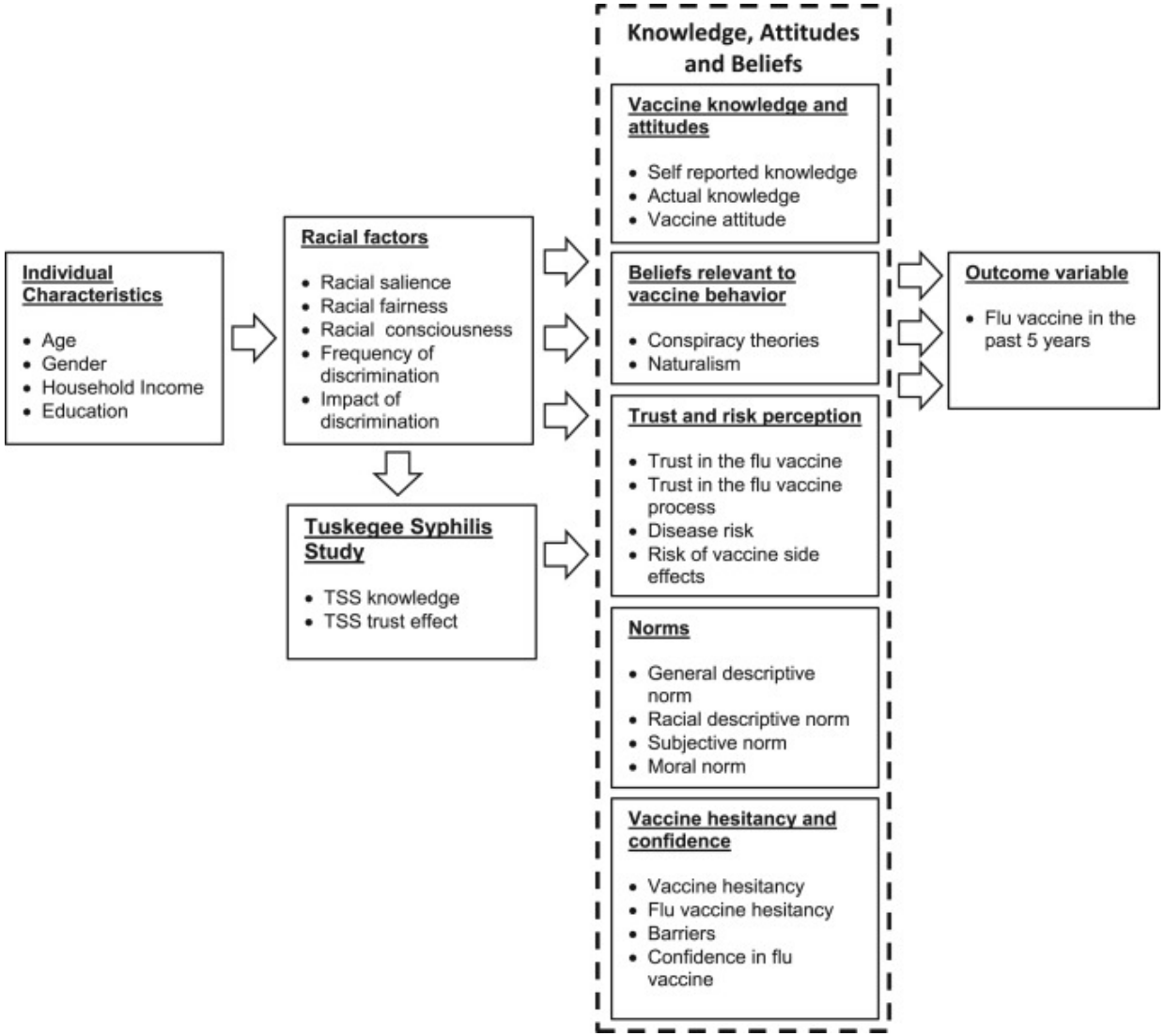




Kahn, et al. National Center for Immunization and Respiratory Diseases, CDC 2022.

Vaccine Statements among Black Pregnant People	OR (95% CI)
Confident in safety of influenza vaccine	0.37 (0.27-0.49)
Confident in safety of Tdap vaccine	0.32 (0.24-0.44)
Worry about getting influenza	0.40 (0.29-0.55)
Worry about getting pertussis	0.47 (0.33-0.67)
Trust in the information provided by obstetric healthcare providers about vaccines	0.59 (0.36-0.99)
Trust in the information provided by federal agencies like CDC about vaccines	0.54 (0.39-0.75)
Friends and family would receive vaccines in pregnancy	0.45 (0.33-0.60)

Racial/Ethnic Disparities in Maternal Vaccine Knowledge, Attitudes and Intentions. Dudley, et al. Public Health Reports 2021.



Breaking down the monolith: Understanding flu vaccine uptake among African Americans. Quinn, et al. SSM – Population Health 2018.

Addressing Vaccine Hesitancy in Pregnancy

Frequent office visits allow for provider recommendation and counseling, vaccine access and continued offer of vaccine.

Table 1. Evidence for interventions to increase maternal vaccination rates

Intervention	Evidence
Provider recommendation	++
Stocking vaccines in practice	++
Standing orders	+
Group prenatal care	+
Offering vaccination more than once	+
Provider prompt	+
Multifaceted QI intervention	+
Patient education	+/−
Patient reminders	+/−

Strong evidence (++); Some evidence (+); No evidence (−).

Maternal vaccination and Vaccine hesitancy. Rand, et al. Pediatric Clinics of North America 2023.

UNIVERSITY of ROCHESTER MEDICAL CENTER

MEDICINE of THE HIGHEST ORDER

Provider strategies and practical tips for medical practices

Kevin A. Ault MD FACOG FIDSA
Professor and Chair, Department of Obstetrics and Gynecology

Disclosures

Consultant to Parexel

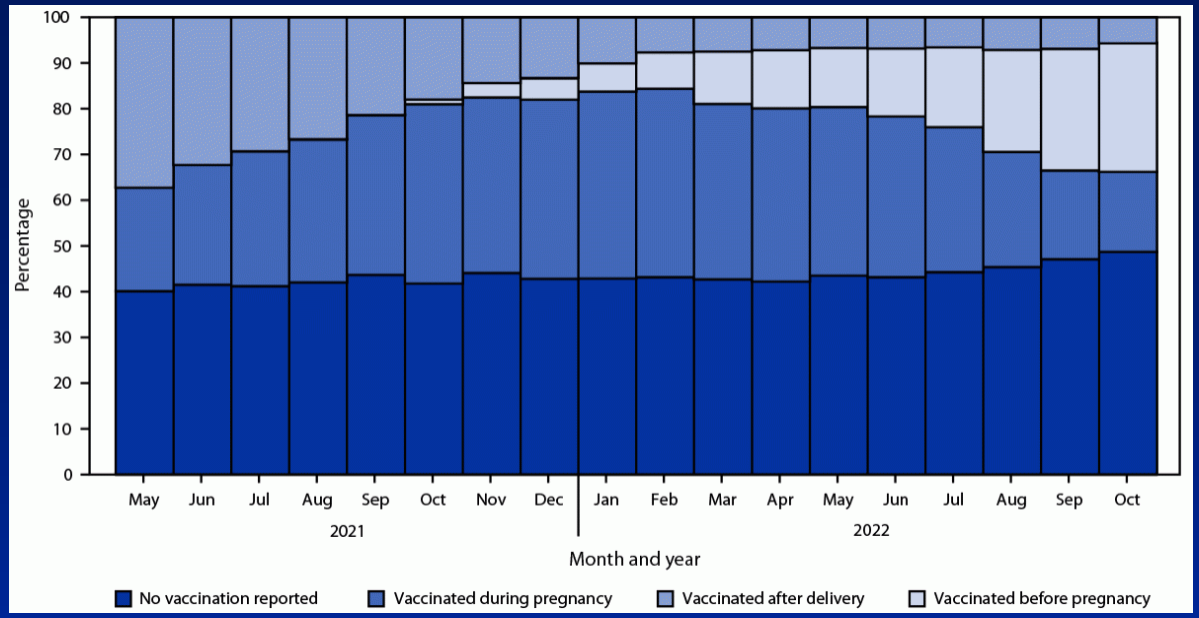
ACOG – member of immunization “working group”

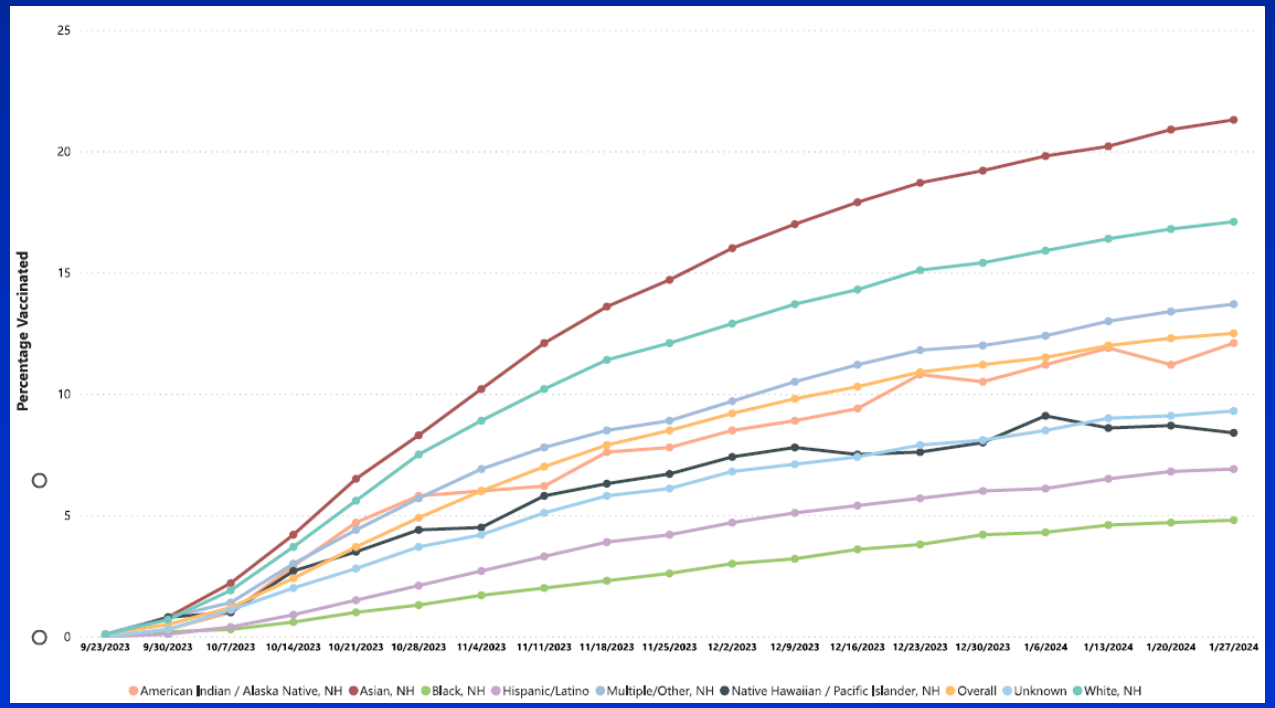
NFID – Board of Directors

ACIP – multiple working groups including influenza

Uptake of recommended COVID vaccination during pregnancy

2021 - 2024



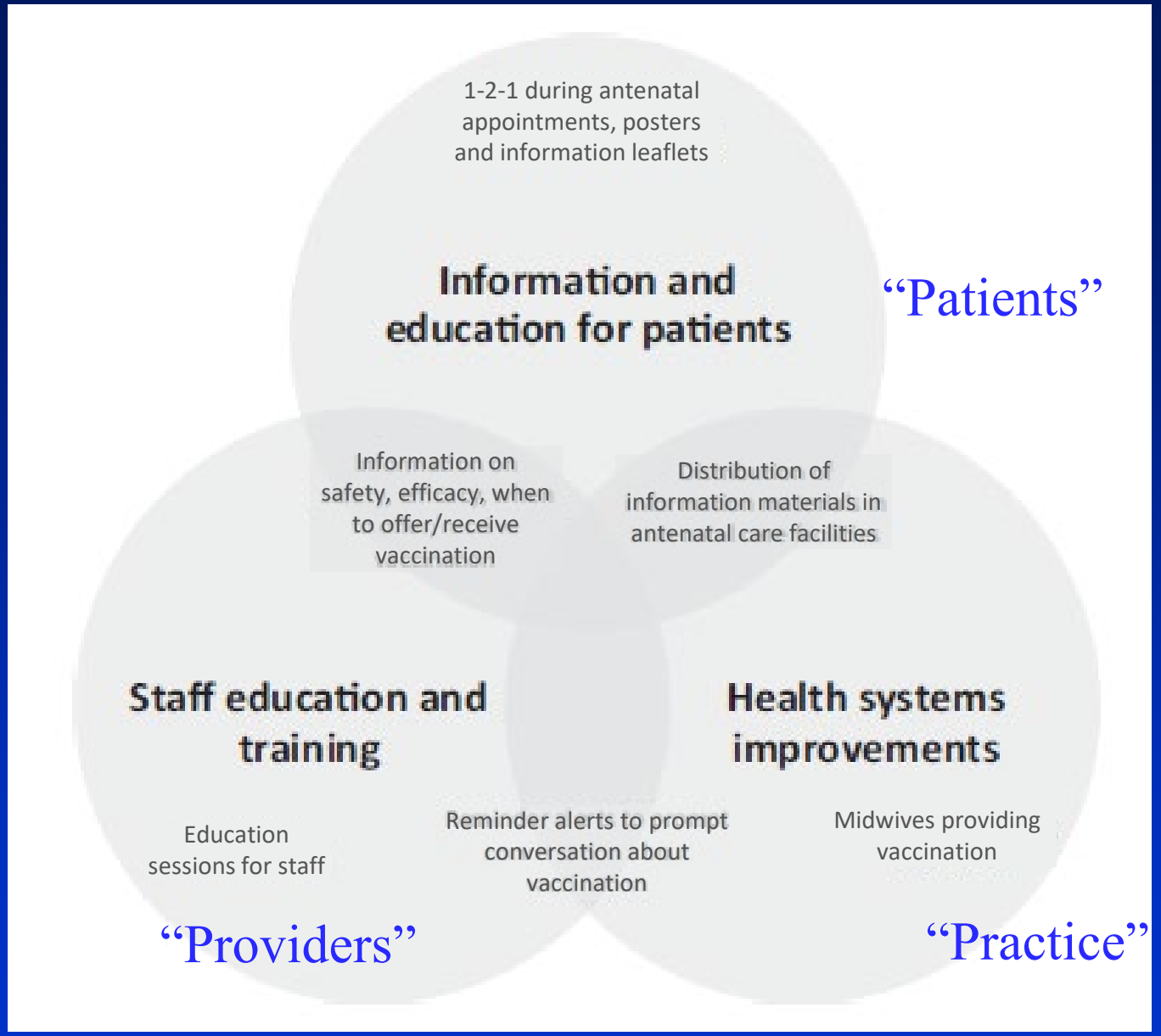


Sources:
MMWR 2023
and COVID
Vax View (VSD)

Improving Vaccine Uptake

- Strong provider recommendation
- Access to prenatal care
- Focus on vaccine safety
- Infant benefits

Geoghegan *et al* 2022



Bisset and Paterson 2018

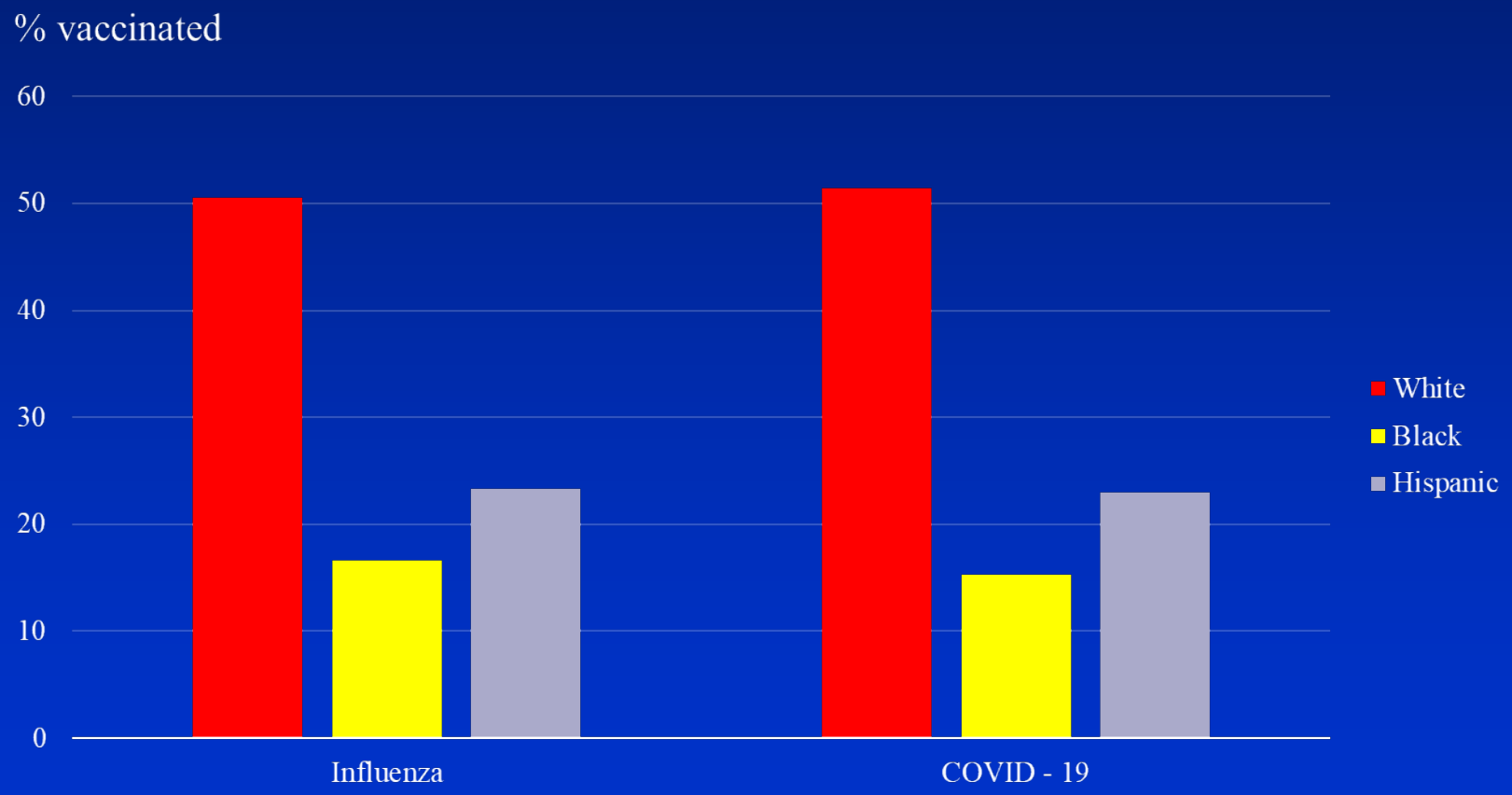
Multi-component antenatal vaccine “package”

- Office vaccine “champions”
- Talking points / “Tool kits”
- Brochures, posters, lapel buttons
- Videos

Results – increased vaccine knowledge, trust in information from providers, reduced safety concerns.

Chamberlain *et al* 2015, Healey *et al* 2015, Mohammed *et al* 2019, Dudley *et al* 2022

Uptake of Recommended Maternal Vaccines - 2023



MMWR Sept 29, 2023

Improving Vaccine Confidence

Table 1. Vaccine-related challenges and potential solutions among pregnant minority women.

Challenges	Solutions
Safety concerns and side effects for themselves and for their babies	Peer to peer communications to improve vaccine confidence and uptake
Distrust of medical providers and the government	Town hall meetings with pregnant minority women and medical providers of vaccines of the same race and ethnicity
Misinformation about the COVID-19 vaccine effects on fertility	Open discussions on social media platforms with medical providers and pregnant women to discuss vaccine safety regarding fertility
Unaware of the benefits of being vaccinated for COVID-19 during pregnancy	Community engagement health forums with pregnant women and OBGYN medical providers
Fear due to lack of research on the vaccines and its potential harm specific to minority communities	Community based focus groups with vaccinated and unvaccinated pregnant women that includes OBGYN medical providers providing culturally competent information

Alcendor *et al* 2022

"Thank you ever so much" –
Any questions?

IMMUNIZATION OF PREGNANT WOMEN WITH A POLYSACCHARIDE VACCINE OF GROUP B STREPTOCOCCUS

CAROL J. BAKER, M.D., MARCIA A. RENCH, B.S., R.N., MORVEN S. EDWARDS, M.D., ROBERT J. CARPENTER, M.D., BETHANY M. HAYS, M.D., AND DENNIS L. KASPER, M.D.

Abstract Immunization of pregnant women with a polysaccharide vaccine of group B streptococcus is a promising strategy for the prevention of perinatal infections caused by group B streptococci. To explore the feasibility of this strategy, we vaccinated 40 pregnant women at a mean gestation of 31 weeks with a single 50-μg dose of the Type III capsular polysaccharide of group B streptococcus.

The only adverse effect detected was a mild local reaction in nine women (22 percent). Of the 35 women with low or unprotective antibody levels before immunization (<2 μg per milliliter), 20 (57 percent) responded to the vaccine. The geometric mean antibody level rose from 1.3 to 7.1 μg per milliliter four weeks after vaccination ($P<0.02$), and these levels persisted at delivery and three months post partum. Sixty-two percent of the vaccine-induced immunoglobulin in the mothers was IgG, which readily crosses the placenta. Infant antibody levels in cord serum correlated directly with maternal antibody levels at delivery ($r = 0.913$, $P<0.001$). Of the 25 infants born to women who responded to the vaccine, 80 percent continued to have protective levels of antibody at one month of age and 64 percent had protective levels at three months. Serum samples from infants with ≥2 μg of antibody to Type III group B streptococcus per milliliter uniformly promoted efficient opsonization, phagocytosis, and bacterial killing in vitro of Type III strains. This effect could be mediated exclusively by the alternative complement pathway.

Although this vaccine with an overall response rate of 63 percent is not optimally immunogenic, we conclude that maternal immunization is feasible and can provide passive immunity against systemic infection with Type III group B streptococcus in the majority of newborns. Larger trials with better vaccines will be required to evaluate the safety and clinical effectiveness of this strategy. (N Engl J Med 1988; 319:1180-5.)

Immunization in Focus: Vaccinating Pregnant People

Discussion

NVAC

Inclusion in Immunization: Special Practices for Special Needs

Dr. Allison Bray
Dr. Jessica Peck
Dr. Anna Taddio
Melanie Hoynoski
Eden Barker
Allison Tappon

NVAC


Baylor University

Immunization Inclusion:
Children with Special Needs

Dr. Alison Bray, DNP, APRN, CPNP-PC
Dr. Jessica Peck, DNP, APRN, CPNP-PC, CNE, CNL, FAANP, FAAN

Baylor University

Pediatric Healthcare Goals

- Meet holistic healthcare needs
- Provide a safe, trusting environment
- Recognize physical and cognitive differences
- Consider physical and psychosocial barriers
- “Identity first” language

General Challenges to Vaccinating in Pediatric Primary Care

- Less than ½ of parents lack trust in their local health departments, the CDC, the American Academy of Pediatrics (AAP), or the whole vaccine development process (Szilagyi et al., 2021)
- Less than ½ of U.S. parents are likely to have their children vaccinated against Covid-19
- 1/3 of parents are unlikely to have their children vaccinated against Covid-19 (Szilagyi et al., 2021)
- 95% of healthcare providers report that the **excess time** it takes to discuss parental vaccine concerns is a significant barrier to practice (Kempe et al., 2011)

Special Considerations

- Children with physical disabilities, neurologic and neurodevelopmental disorders, and autism
- Physical: about 3 million children have a disability (4.8% of children under 18 years), 53% more likely to have allergies to food, latex, and microbials (Stone et al., 2019; Xu et al., 2018)
- Psychosocial: changes related to the Covid-19 global pandemic, increased use of personal protective equipment (PPE)- cause fear or anxiety in children with special needs
- AAP- recommends children with special needs be vaccinated following the same CDC immunization schedule as healthy children, unless medically contraindicated (Langkamp et al., 2020)

Physical Challenges- Children with Special Needs

- egg allergy- no longer contraindication
- gelatin found in MMR, MMRV, & Varicella may cause hypersensitivity
- severe cow's milk allergy problem in DTaP, Tdap, OPV, or Hep B
- latex concerns

(Magista et al., 2020)

Psychosocial Challenges- Children with Special Needs

- Increased use of personal protective equipment (PPE) in hospitals and clinics has reduced communication and increased patient anxiety, particularly among children with special needs
- Patients and parents base initial perceptions of pediatric providers on attire, facial expressions, and body language, which can affect the patient's comfort level and ability to cooperate, exacerbated by increased use of PPE. (Hampton et al., 2020; Krmar, 2019)
- Children with special needs are more likely to externalize the behavioral manifestations of anxiety than children without disabilities (O' Neill et al., 2019)

Minimizing Stress of Immunizations

- Develop a trustworthy and honest relationship
- Distraction techniques- blowing bubbles or pinwheels, deep breathing, or music therapy (Sirtin et al., 2020)
- Social Assistive Robots (SAR)- captures the child's attention and redirects attention towards interesting objects, some may show empathy (Rossi et al., 2020)
- Squeezing a ball
- Thermomechanical regulation- cold and vibration therapy
- Streaming movies or music

Positioning Considerations

- Upright, sitting position- fosters child's sense of control
- Parent's/Caregiver's lap- facing or away
- Use least amount of force possible- minimal time

(Trottier et al., 2019)

Pharmacist Considerations

- Access (most of the US population lives within 5 miles of a pharmacy)
- History (small pox 1800s; first formal training in 1994)
- 1996- American Pharmacists Association initiates first certificate program
- 2020- PREP Act authorized pharmacists and technicians to give flu and COVID vaccines
  - Varies by state law
- Training Program
  - 20 hours covering various topics
  - Lack of content addressing children with special health needs
  - Opportunity exists to collaborate with local pediatric providers
  - Respect family as experts

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PLAYING YOUR CARDs:

Improving vaccination experiences and equity of care

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UNIVERSITY OF TORONTO
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SickKids

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OUTLINE

1. **WHY ADDRESSING VACCINATION PAIN IS IMPORTANT**

2. **HOW TO PLAY YOUR CARDS TO IMPROVE VACCINATION DELIVERY**

OUTLINE

1. **WHY ADDRESSING VACCINATION PAIN IS IMPORTANT**

2. **HOW TO PLAY YOUR CARDS TO IMPROVE VACCINATION DELIVERY**

PAIN AT THE TIME OF VACCINATION

- **Unpleasant sensation** associated with needle injection
- **Subjective experience, very variable** among individuals
- **Children perceive needles as more painful** and are more bothered by them
- **Anticipation** of pain can increase fear and anxiety
- Fear can lead to **dizziness and fainting**
- Fear and pain can **escalate over time**
- Concerns about pain/fear contribute to **vaccine refusal across the lifespan**

Pain during vaccination is expected and normal, but it can be modified. Current practice uses a ‘one size fits all’ (or provider-centered) model of care. A practice model called the CARD system turns the research into action and improves equity.

OUTLINE

1. **WHY ADDRESSING VACCINATION PAIN IS IMPORANT**

2. **HOW TO PLAY YOUR CARDS TO IMPROVE VACCINATION DELIVERY**

The CARD System

(**C**OMFORT, **A**SK, **R**ELAX, **D**ISTRACT)

- A practice model for vaccination delivery based on clinical practice guidelines (CPG)
  - Systematic approach; turns research evidence into 'action'
- User-friendly and intuitive tool
  - All users *'play their CARDs'*
- Achieves patient-centered care for vaccination
  - All patients actively participate, and coping preferences are honored
- Effective across all vaccination settings including diverse populations
  - Schools, clinics, pharmacies, hospitals

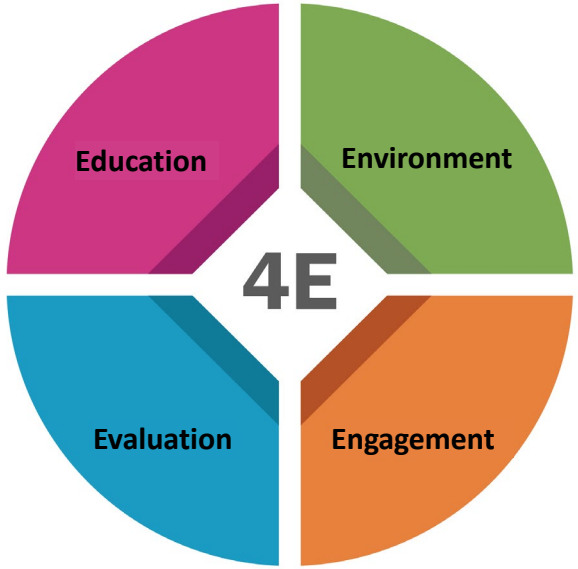
https://academic.oup.com/pch/issue/24/Supplement_1

CARD PLAYBOOK FOR PATIENTS AND PROVIDERS

For Patients…

1. An easy acronym that identifies coping strategy categories patients can choose from to help manage stressful procedures and improve their experiences
2. A participatory approach whereby patients are decision makers and lead their coping

For Providers…

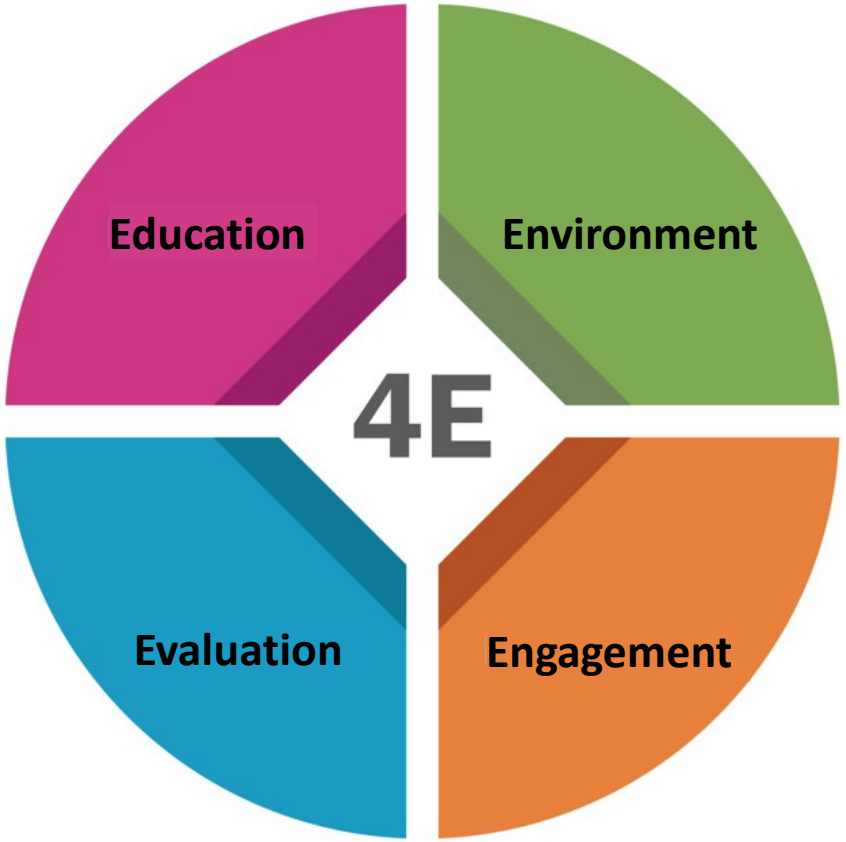


1. A protocol for planning and performing needle procedures that incorporates research in a systematic way and leads to equitable care
2. A tool-kit of resources to operationalize patient centered care beyond theory

HOW THE PROVIDER *PLAYS*: THE 4E MODEL

- Health care providers
- Patients
- Parents/caregivers
- Others/onlookers
- **Ahead of time**
- **Procedure day**

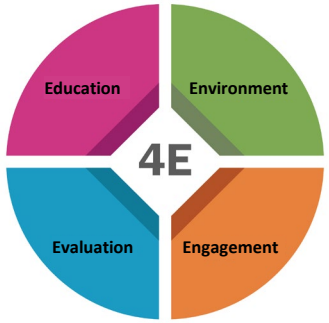
- Patients
- Parents/caregivers
- Health care providers



- Separate all clinic areas
- Seating available
- Distractions
- Space for support person
- Privacy
- Minimize fear cues (visual and auditory)

- Be calm, positive, promote coping
- Assess symptoms (fear, pain, dizziness, fainting)
- Invite participation, answer questions
- Support CARD (coping) choices
- Minimize injection pain

CARD IN ACTION!



Education

- Providers learn about CARD
- Patients and caregivers learn about CARD (ahead of time and/or on appointment day)

Engagement and Environment

- CARD Checklist completed by the patient
- Providers review and support choices during the needle procedure

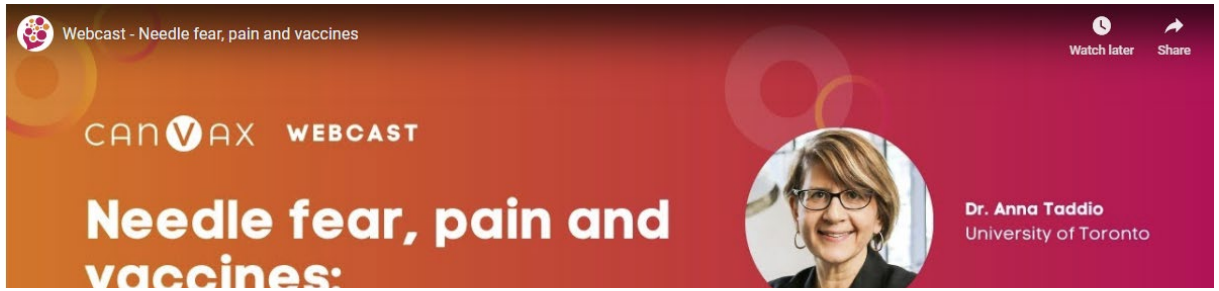
Facilitators

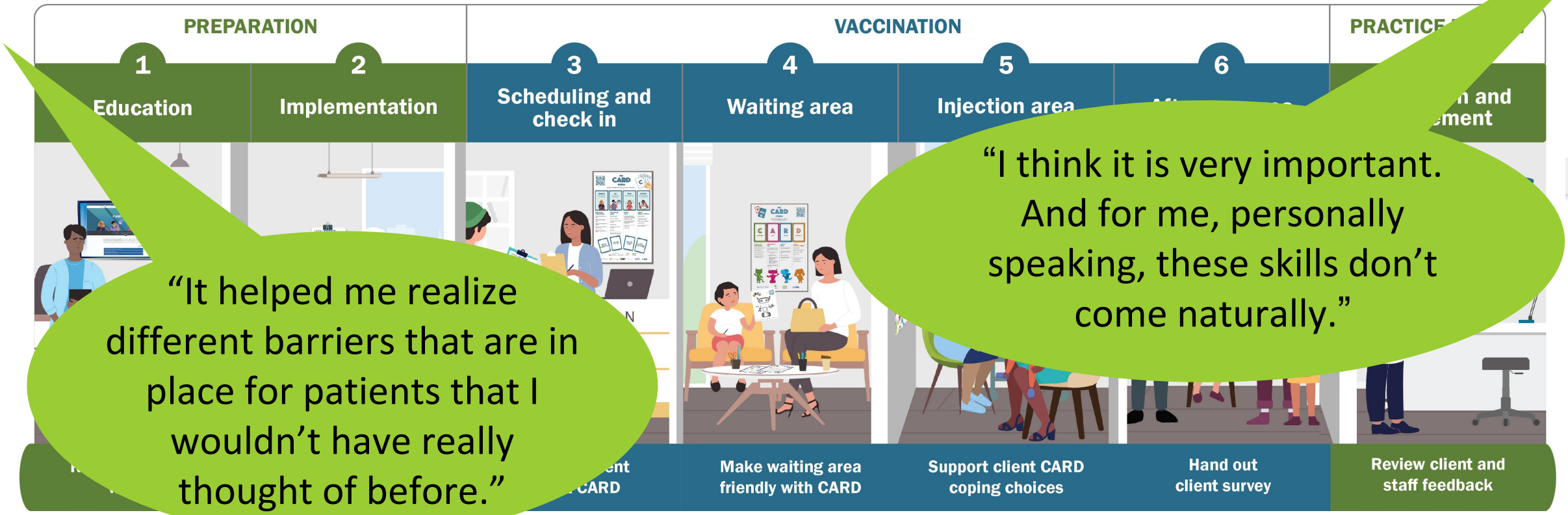
- CARD resources (communication, topical anesthetic, muscle tension etc)
- Distraction carts
- Environmental changes to reduce fear cues and increase comfort

Evaluation

- Pain and fear assessment completed
- Patient and family experience survey completed
- Staff debriefs and review of patient and family feedback

PROVIDER EDUCATION





"It helped me realize different barriers that are in place for patients that I wouldn't have really thought of before."

"I think it is very important. And for me, personally speaking, these skills don't come naturally."

CARD educational resources support providers and trainees; embedded in curricula/vaccine programs.

PATIENT EDUCATION: CARD web game (5-12yrs)

I learned needles aren't as bad as they seem and it's easy to distract yourself.

I can tell my friends, "Hey, there's this game, and it really helped me."

I liked the games because they were simple but fun and really distracting.

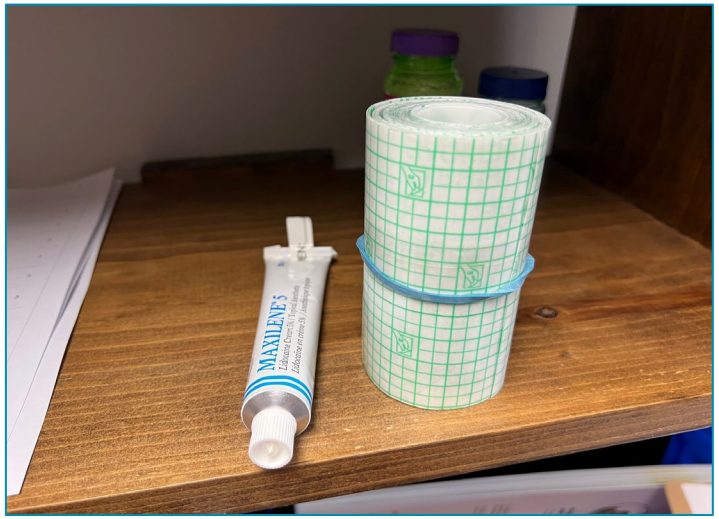
It helped me be less afraid because you can just breathe in and out.

https://immunize.ca/card-game-kids

Patients can play ahead of time and on the day of vaccination.

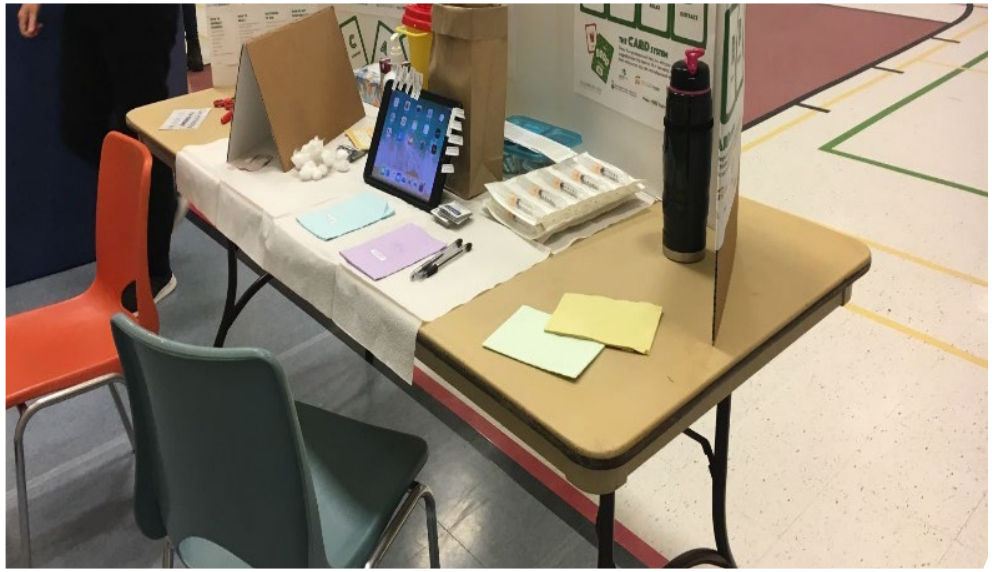
ENVIRONMENT: DISTRACTION ITEMS (all areas)

Distraction cart with items and activities



Numbing cream and transparent film

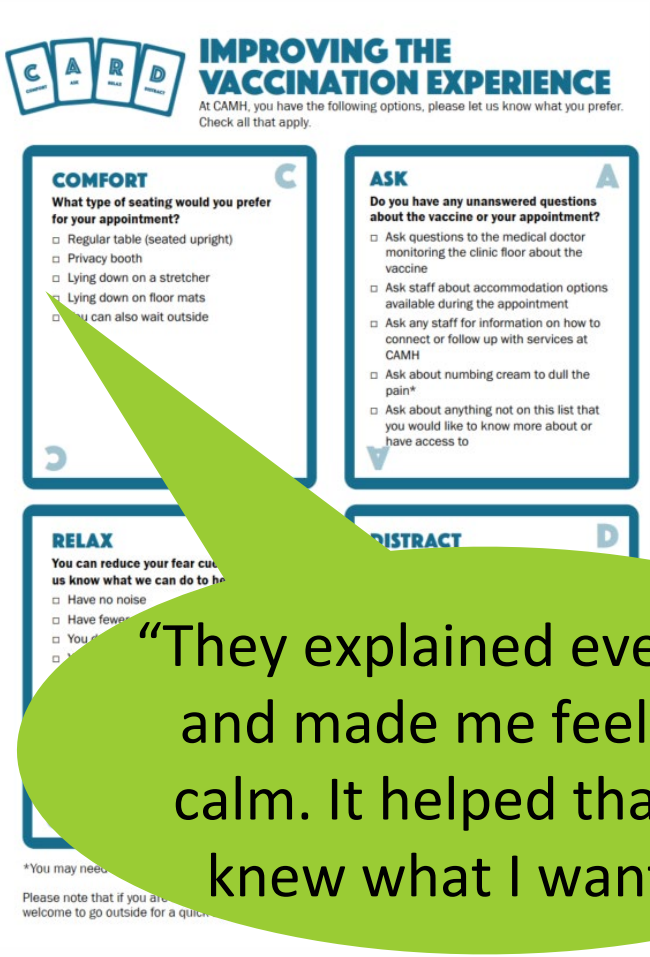
ENVIRONMENT: VACCINATION SPACES

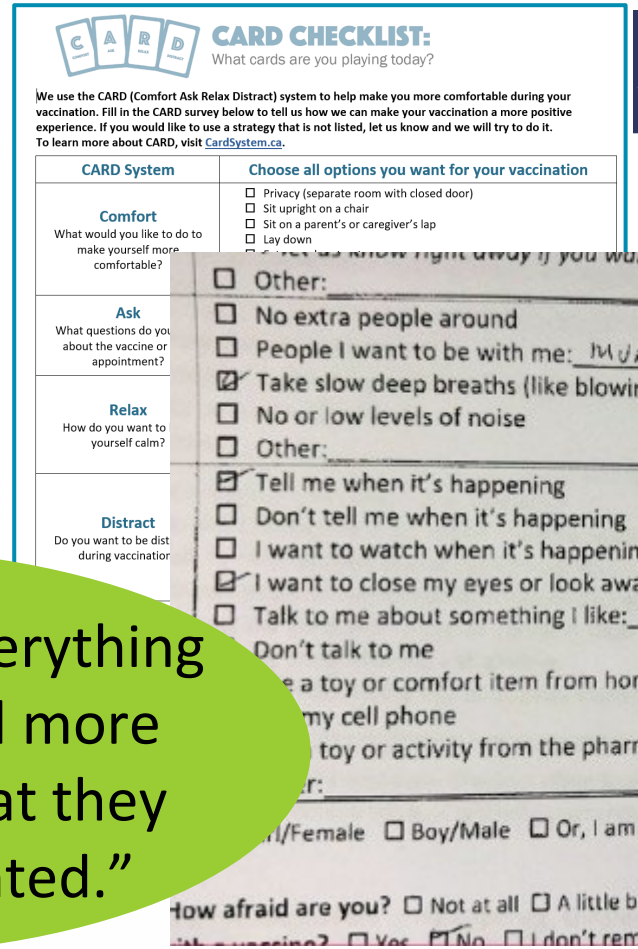


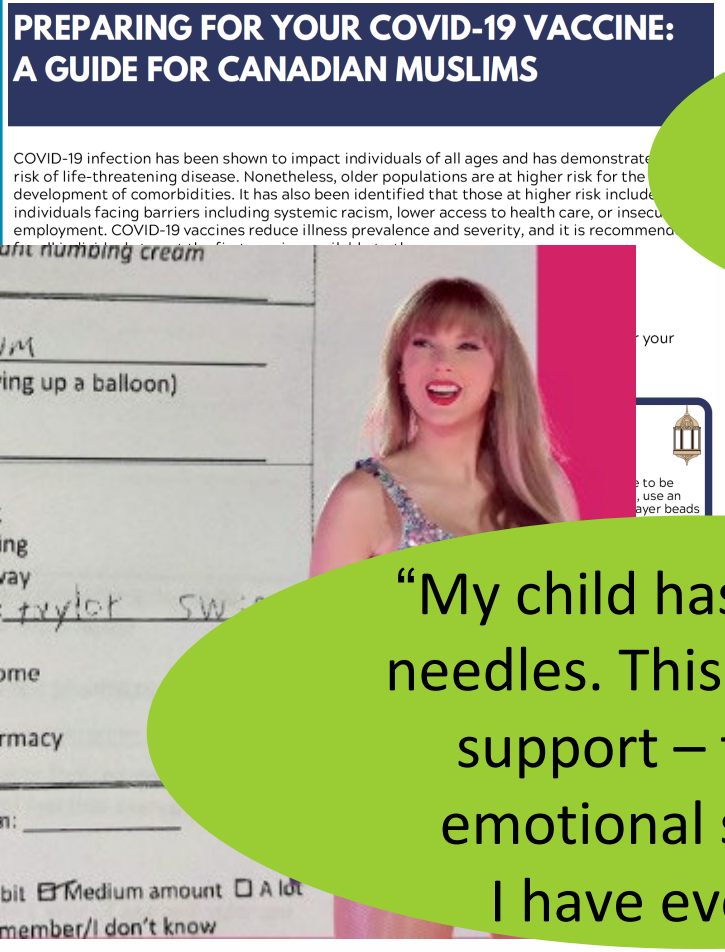
Purposeful positioning of items and furniture to minimize fear cues

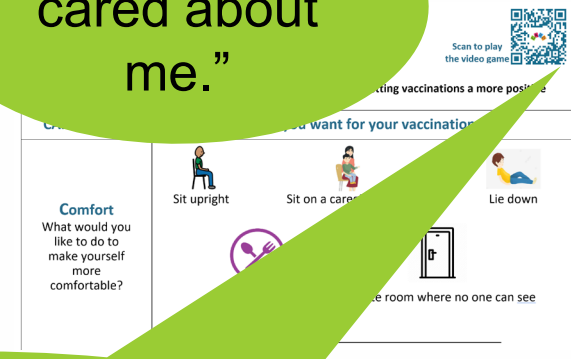
Separate room with the ability to close the door to allow for privacy

ENGAGEMENT: CARD CHECKLIST (*customizable)*









"They really cared about me."

"They explained everything and made me feel more calm. It helped that they knew what I wanted."

"My child has had many needles. This is the most support – the most emotional support – I have ever felt!"

All patients are invited to participate (play their CARDs). Involving patients in their care improves patient-centeredness and equity. Note that caregivers can help younger children.

EVALUATION: PATIENT FEEDBACK SURVEYS

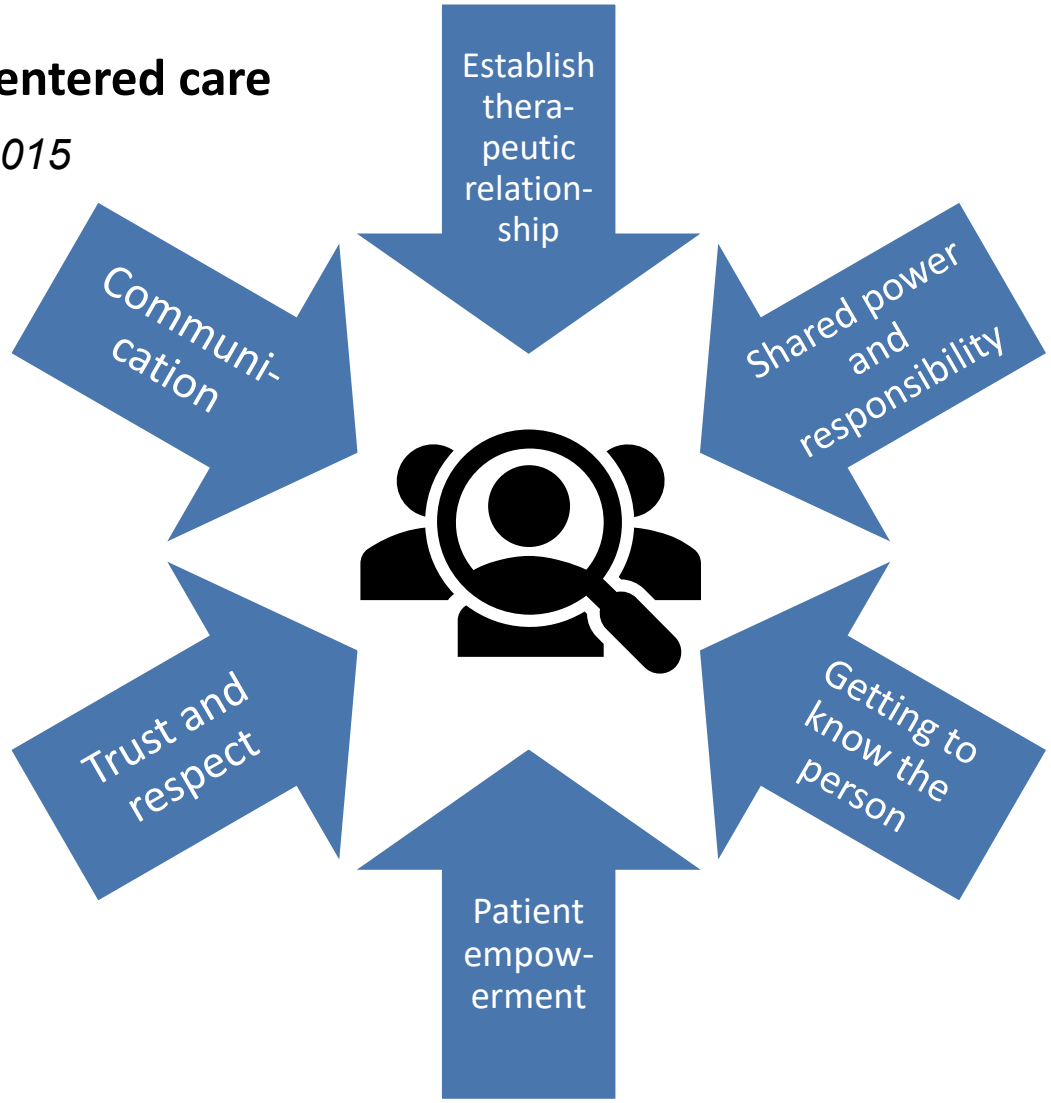
Surveys allow patients and families to provide feedback about symptoms (e.g., fear, pain, dizziness) and satisfaction

Staff debriefs and discussions about implementation should incorporate this feedback to ensure activities align with expected outcomes.

CARD ENABLES INDIVIDUALIZED AND EQUITABLE CARE

Person-centered care

Sharma, 2015



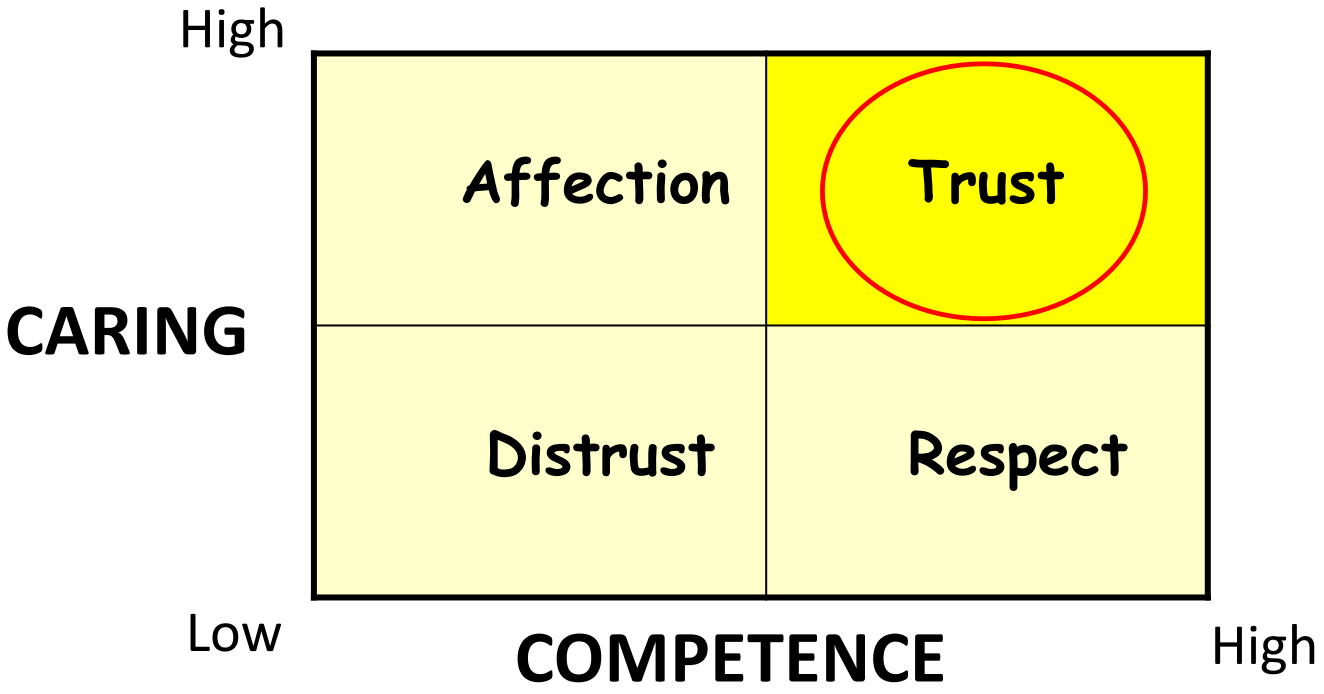
Consider how vaccinations are delivered to incorporate needs and preferences of sub-populations:

- gender
- age
- culture
- neurodevelopmental diversity

CARD incorporates evidence in vaccination delivery that supports patient-centered care across populations and settings

HOW CARD BUILDS TRUST (AND VACCINE CONFIDENCE)

TRUST = Competence + Caring



Paling J. BMJ 2003; 327-745

ACROSS VACCINATION SETTINGS, CARD IMPROVES:

Attitudes

Knowledge

Equity

Safety

Experiences

[equity vs equality picture - Search Images (bing.com)]

Taddio et al. (2019)
Taddio et al. (2022)
Tetui et al. (2022)
Taddio et al. (2022)
Taddio et al. (2023)
Gudzak et al. (in prep'n)

CARD STUDIES: PATIENT SYMPTOMS DURING VACCINATION

Study	Target	Setting	Design	Sample size	Impact
Freedman et al. (2019)	Providers, children 12 years, parents, educators	Schools	Controlled Clinical Trial	323	↓ fear, dizziness
Taddio et al. (2022)	Providers, children 12 years, parents, educators	Schools	Randomized Controlled Trial	1919	↓ fear, pain, fainting
Tetui et al. (2022)	Providers, patients ≥12 years	Mass vaccination clinics	Before and After Trial	2488	↓ fear, pain, dizziness
Taddio et al. (2022)	Providers, parents, children 5-11 years	Community pharmacies	Before and After Trial	153	↓ fear, pain
Taddio et al. (2023)	Providers, parents, children 12-14 years	Schools (urban)	Randomized Controlled Trial	8839	↓ fear
Gudzak et al. (in prep'n)	Providers, adults ≥18 years	University vaccination pop-up clinics	Before and After Trial	476	↓ fear, pain

CARD STUDIES: PATIENT ATTITUDES (CARD education ahead of time)

	Hospital[1] 2021	Pop-up[2] 2022	Pop-up[3] 2023	Pharmacy[4] 2023-24
No. that reviewed CARD information before attending (%)	(n=116) 75 (65%)	(n=86) 37 (43%)	(n=544) 326 (60%)	(n=938) 49 (5%)
No. reporting CARD influenced decision to attend clinic (%)	(n=71) 64 (90%)	(n=44) 15 (34%)	(n=387) 204 (53%)	(n=49) 34 (69%)
No. reporting CARD helped (%)	(n=103) 95 (92%)	(n=86) 68 (79%)	(n=543) 445 (82%)	(n=49) 40 (82%)
No. reporting experience better compared to last needle (%)	(n=61) 43 (71%)	(n=82) 55 (67%)	(n=511) 313 (61%)	(n=49) 23 (47%)

[1] Centre for Addiction and Mental Health Hospital: speciality COVID-19 vaccine clinics for children and adults with needle fear and anxiety
[2] University of Toronto campus influenza vaccination popups for adults
[3] University of Toronto campus influenza and COVID-19 vaccination popups for adults
[4] Community pharmacies across southern Ontario: influenza and COVID-19 vaccinations for children and adults

RECOMMENDATIONS FOR CARD IMPLEMENTATION

INTEGRATE

Providers and health systems

– integrate into vaccine policies and procedures, provider training

Patients and caregivers

– educate and invite participation (websites, providers, schools)

EVALUATE

– adverse events following immunization, experiences, vaccine acceptance

– patient symptoms and satisfaction are quality indicators; use to increase accountability for the delivery of high-quality vaccination services

CONCLUSION

- Pain **hurts** vaccination
- CARD turns the evidence into **actionable steps**
  - Customizable to any population and setting
- Learn more at **cardsystem.ca** and start playing!

National Vaccine Advisory Committee's
Panel Presentation

Child Life in Primary Care

Eden Barker, MS, CCLS
Melanie Hoynoski, MPH, CCLS, CTRS
Ali Tappon, MS, CCLS

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Child Life, Education & Creative Arts Therapy

WHAT IS A CHILD LIFE SPECIALIST?

Child development experts who address the psychosocial concerns that accompany stressful or traumatic events by promoting optimal child development and minimizing adverse effects.

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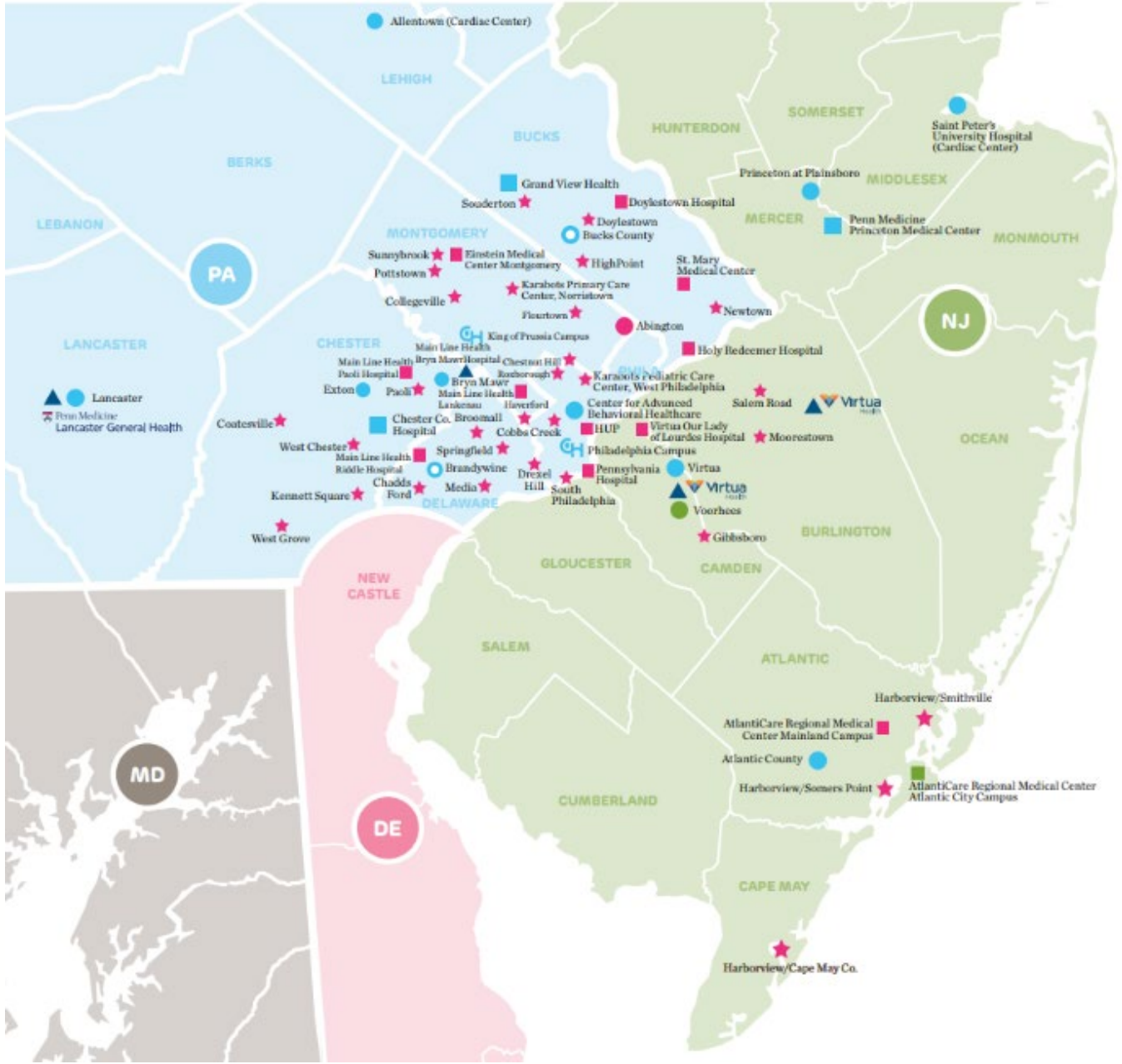
AMBULATORY MAP



32 Primary Care Sites
15 Specialty Care Sites
15 Hospital Partners

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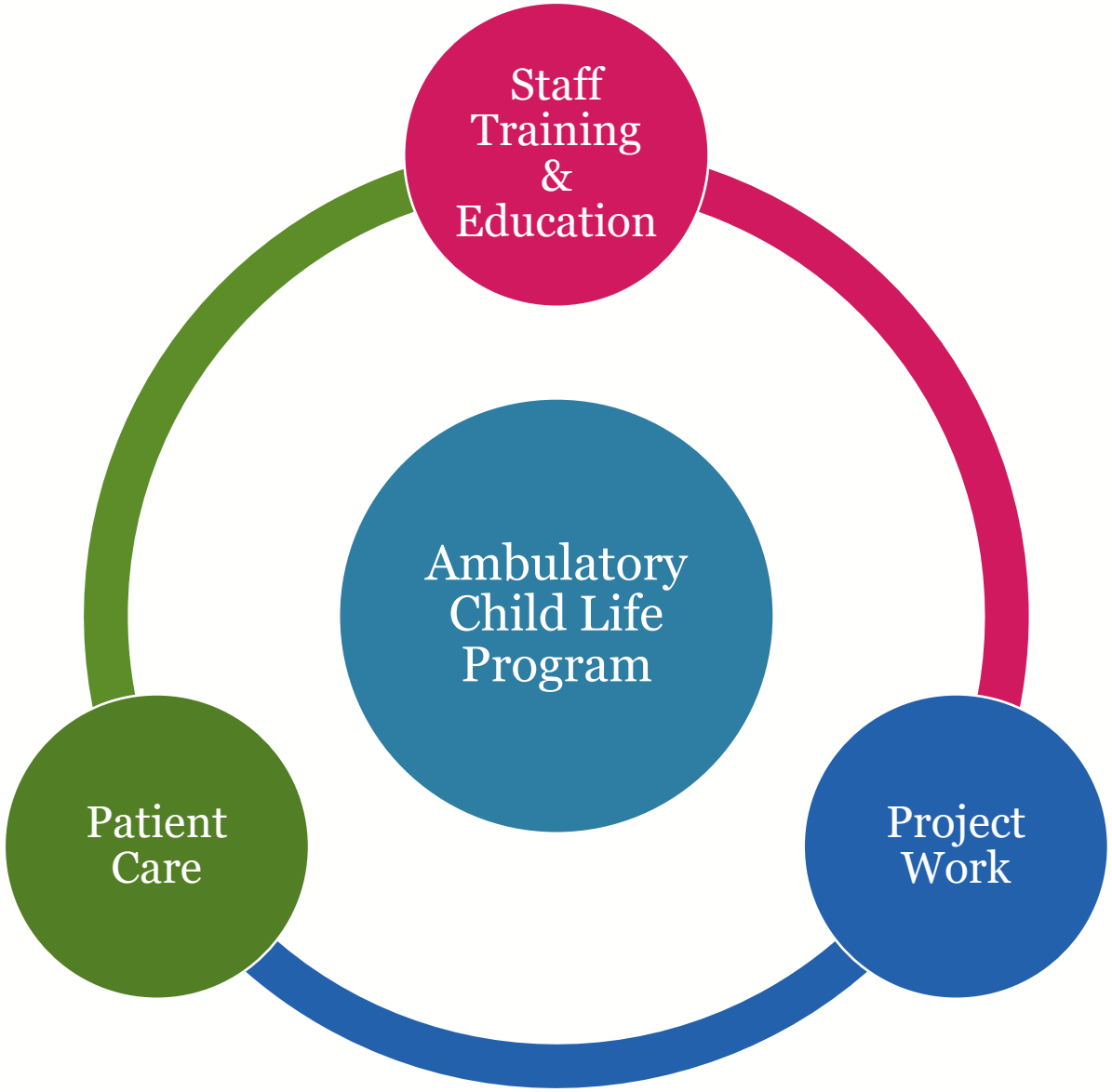
AMBULATORY CHILD LIFE CLINICAL ADVISOR: SCOPE OF SERVICE



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CALL TO ACTION

INTERACTIVE VACCINE RESOURCE

[Prepare Your Child for a Vaccine | Children's Hospital of Philadelphia (chop.edu)]

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PREPARE YOUR CHILD FOR A VACCINE

CHOOSE PREPARATION RESOURCE

Here are some ways you can prepare for a vaccine visit.

Click one of the buttons below to choose how you would like to prepare.

PRINTABLE VISUAL SCHEDULE

INTERACTIVE SLIDE SHOW

ANIMATED VIDEO

SCAN CODE

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VACCINE PAIN MANAGEMENT PROJECT

Problem

- Despite evidence supporting the use of pediatric vaccine pain management interventions and the availability of such interventions, the utilization of these tools is not standard practice within this primary care network.

Project Goal

- A multidisciplinary team will develop a framework to increase utilization of pediatric vaccine pain management strategies based on the results of a literature review, a primary care nursing survey, and a patient/family survey.

SMARTIE Aim

- Utilization of VPM strategies will increase by 25%, as evidenced by survey feedback, at CHOP Primary Care _____ and _____, regardless of clinician and patient factors such as age, race/ethnicity, and language.

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COMMUNITY PROJECTS

- Philadelphia Department of Public Health Initiative
  - *"Improving the Primary Care Experience for Children with Autism"*
- Vaccine Education Center Initiative for Providers and Caregivers
  - *"Improving the Vaccine Experience for Neurodiverse People"*
- Medical Assistant Fellowship Program for Philadelphia High School Students
- Community-based Covid Testing: open access learning module
- School-based Covid Testing Initiative
- Community Covid Vaccine Clinics

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Inclusion in Immunization: Special Practices for Special Needs

Discussion

NVAC

Federal Agency and Liaison Representative Updates

NVAC

Public Comment

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Meeting

NATIONAL VACCINE ADVISORY COMMITTEE

February 22-23, 2024

NVAC