NAIIS and ACP

mRNA Vaccines: Scientific Update and Overcoming Clinician and Patient Hesitation

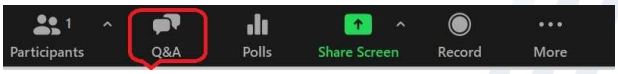
Thursday, August 22, 2024 - 3:00 p.m. (ET)

Audio broadcast available through your computer

- All participants will join the webinar in "listen only" mode. You should be able to hear through your computer audio. Please make sure your speakers are not on mute. You should have received dial in information with our invitation email.

Want to ask a question?

- Type your question into the "Q&A Box" in the lower area of your screen. Questions will be answered during the Q&A session, as time permits.



- Additional questions may be sent to info@izsummitpartners.org.

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- For assistance, please call 1-651-647-9009 or Zoom Technical Support at 1-888-799-9666 ext. 2

ACP American College of Physicians Leading Internal Medicine, Improving Lives

National Adult and Influenza Immunization Summit

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Agenda

- mRNA Vaccines: Scientific Update and Overcoming Clinician and Patient Hesitation
  - Jason M. Goldman, MD, FACP
    ACP President-Elect
  - LaTonya Washington, MD, MBA, FACP, FAAP

ACP American College of Physicians Leading Internal Medicine, Improving Lives

National Adult and Influenza Immunization Summit

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mRNA Vaccines: Scientific Update and Overcoming Clinician and Patient Hesitation

August 22, 2024

ACP
American College of Physicians
Leading Internal Medicine, Improving Lives

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ACP

Financial Disclosure

- Has no relationships with any entity producing, marketing, re-selling, or distributing health care goods or services consumed by, or used on, patients.

mRNA background and history

- In 1953 Watson and Crick propose DNA double helix
- In 1961 mRNA discovered by Jacques Monod, Francois Gros and Francois Jacob
- Normal protein synthesis
  - DNA unwinds and segment of mRNA is transcribed
  - Complementary base pairing
  - Linear polymer of four nucleotide subunits
  - Single strand, therefore can fold into different shapes
  - Protein can be produced by translation, triplets of base pairs on mRNA correspond to amino acids by using tRNA (transfer RNA)
  - Amino acids are bonded together and protein synthesized in ribosomes
  - Ribosomes exist in the cytoplasm where proteins are produced

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Alberts B, Johnson A, Lewis J, et al. Molecular Biology of the Cell. 4th edition. New York: Garland Science; 2002. From DNA to RNA. Available from: https://www.ncbi.nlm.nih.gov/books/NBK26887/
Alberts B, Johnson A, Lewis J, et al. Molecular Biology of the Cell. 4th edition. New York: Garland Science; 2002. From RNA to Protein. Available from: https://www.ncbi.nlm.nih.gov/books/NBK26829/

RNA as therapeutic

- Many uses of RNA
  - Antisense oligonucleotides module expression of target RNA
  - Small interfering RNA suppress the expression of target RNA
  - Aptamers bind specific proteins to module functions
  - mRNA allows production of functional proteins
- In 1990 mRNA injected into mice to produce protein
- 1995 mRNA vaccines designed as a cancer vaccine
- Early 2000's had many trials to create RNA drugs with different mechanism of action
- 2020 EUA of mRNA for COVID

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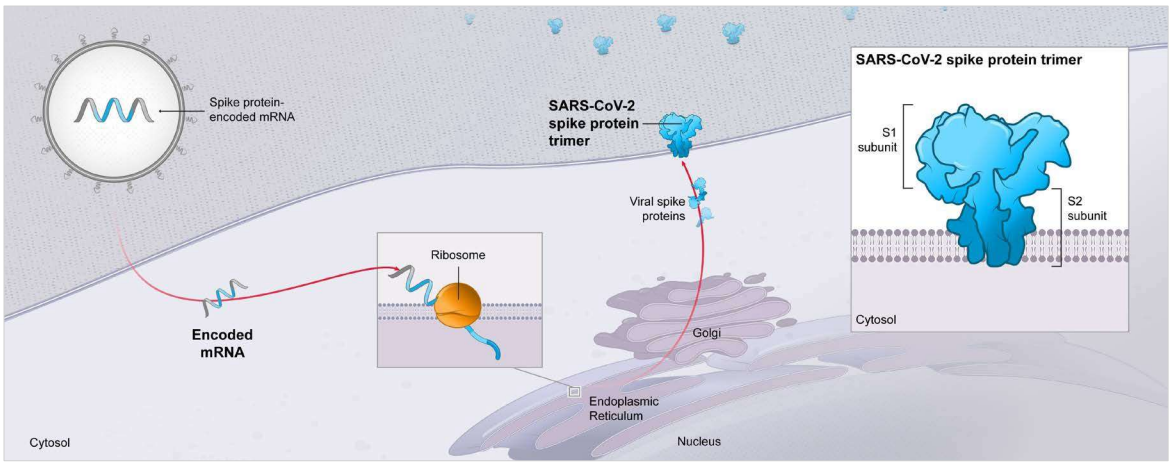
mRNA-1273 encodes for the full-length Spike Protein in the Pre-fusion Conformation (S-2P)

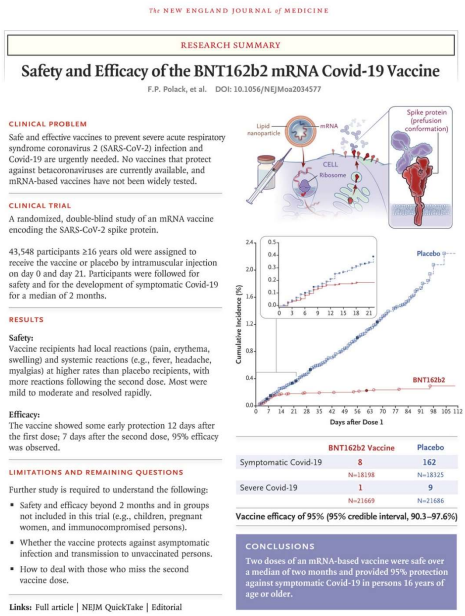


moderna

Advantages and Disadvantages

- Advantages
  - Quick production of treatments
  - Treatment of rare disease
  - Targeted therapy of many different diseases
  - No risk of genotoxicity. Does not integrate into DNA
  - Only works in cell cytoplasm and then degraded
- Disadvantages
  - Unstable molecule making delivery difficult
  - Many requires encapsulation with lipid nanoparticles
  - Vaccines are stored in ultra cold temp -50 degree Celsius to -15 degrees Celsius
    - Moderna
      - Up to 30 days in refrigerator once thawed
      - Punctured vials 8 hours for bivalent
      - 12 hours for all other Moderna
    - Pfizer
      - Refrigerator up to 10 weeks once thawed
      - Punctured vials 12 hours

Kim YK. RNA therapy: rich history, various applications and unlimited future prospects. Exp Mol Med. 2022 Apr;54(5):455-465. Doi:10.1038/s12276-022-00757-5. Epub 2022 Apr 19. PMID: 35440755; PMCID: PMC9016686



The NEW ENGLAND JOURNAL of MEDICINE

RESEARCH SUMMARY

Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine

F.P. Polack, et al. DOI: 10.1056/NEJMoa2034577

CLINICAL PROBLEM

Safe and effective vaccines to prevent severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and Covid-19 are urgently needed. No vaccines that protect against betacoronaviruses are currently available, and mRNA-based vaccines have not been widely tested.

CLINICAL TRIAL

A randomized, double-blind study of an mRNA vaccine encoding the SARS-CoV-2 spike protein.

43,548 participants ≥16 years old were assigned to receive the vaccine or placebo by intramuscular injection on day 0 and day 21. Participants were followed for safety and for the development of symptomatic Covid-19 for a median of 2 months.

RESULTS

Safety:
Vaccine recipients had local reactions (pain, erythema, swelling) and systemic reactions (e.g., fever, headache, myalgias) at higher rates than placebo recipients, with more reactions following the second dose. Most were mild to moderate and resolved rapidly.

Efficacy:
The vaccine showed some early protection 12 days after the first dose; 7 days after the second dose, 95% efficacy was observed.

LIMITATIONS AND REMAINING QUESTIONS

Further study is required to understand the following:

- Safety and efficacy beyond 2 months and in groups not included in this trial (e.g., children, pregnant women, and immunocompromised persons).
- Whether the vaccine protects against asymptomatic infection and transmission to unvaccinated persons.
- How to deal with those who miss the second vaccine dose.

Links: Full article | NEJM QuickTake | Editorial

	BNT162b2 Vaccine	Placebo
Symptomatic Covid-19	8	162
	N=18198	N=18325
Severe Covid-19	1	9
	N=21669	N=21686

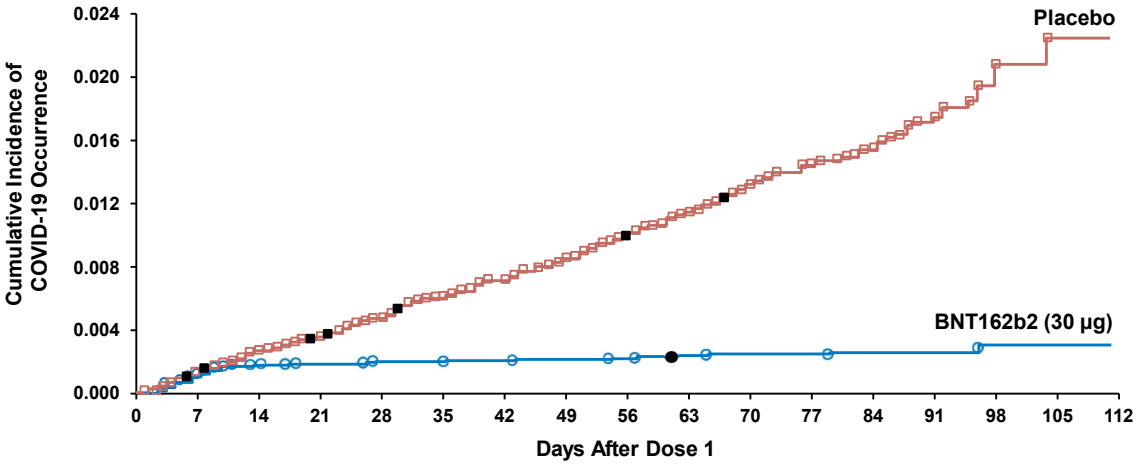
Vaccine efficacy of 95% (95% credible interval, 90.3–97.6%)

CONCLUSIONS

Two doses of an mRNA-based vaccine were safe over a median of two months and provided 95% protection against symptomatic Covid-19 in persons 16 years of age or older.

FP Polack et al. N Engl J Med 2020. DOI: 10.1056/NEJMoa2034577

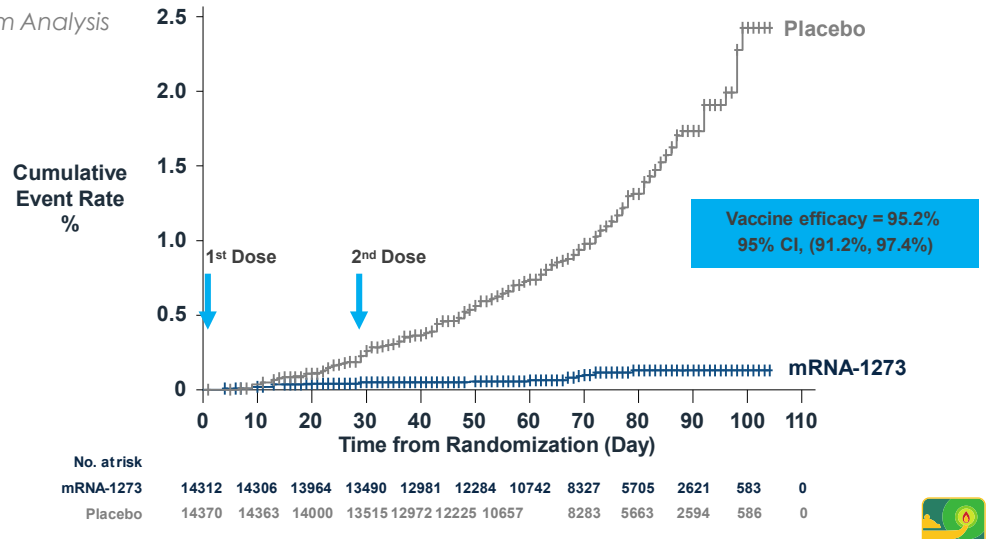
Cumulative Incidence of COVID-19 After Dose 1



Solid fill marker indicates subjects with severe COVID-19

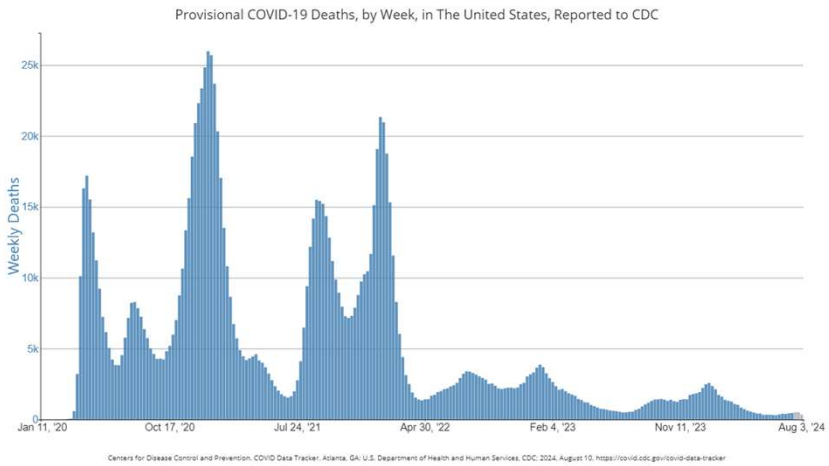
Kaplan-Meier Estimates of Time to First Occurrence of COVID-19 Starting After Randomization

mITT – Interim Analysis



No. at risk												
mRNA-1273	14312	14306	13964	13490	12981	12284	10742	8327	5705	2621	583	0
Placebo	14370	14363	14000	13515	12972	12225	10657	8283	5663	2594	586	0

COVID-19 weekly deaths as of August 10, 2024



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Current Guidelines

- Two types of Covid Vaccines available
  - mRNA
    - Pfizer-BioNTech (Comirnaty)
    - Moderna (Spikevax)
  - Protein subunit
    - Novavax adjuvanted
- No preference on which is used
- Should use same formulation in series when possible
- Recommended for all individuals 6 months of age and older
  - 65 and older should received 1 dose of updated vaccine, at least 4 months apart
  - 12 years and older 1 dose of mRNA or 2 doses of Novavax if unvaccinated, 1 dose if vaccinated
  - 5-11 one dose of mRNA
  - 6 months to 4 years
    - If up to date then receive 1 dose
    - If incomplete series then 1 or 2 doses of same vaccine
    - Unvaccinated receive 2 or 3 of same vaccine
  - Moderate to Severe immunocompromised may receive 1, 2, or 3 doses depending on previous vaccine status
- Consider 8 week interval to possible decrease myocarditis risk but risk of myocarditis is rare
- More likely to get myocarditis from infection then vaccine

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Summary

- mRNA technology has been available for decades
- mRNA technology is safe and effective
- mRNA vaccines have greatly impacted the course of the pandemic
- COVID-19 is still circulating and causing significant hospitalization and death
- COVID-19 deaths can be preventable with vaccination
- New variants will continue
- Updated vaccines being considered as new information becomes available

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Questions?

LaTonya Washington, *MD, MBA, FACP, FAAP*

Vice President and Chief Medical Officer
Methodist North Hospital
Clinical Assistant Professor of Medicine
University of Tennessee Health Science Center

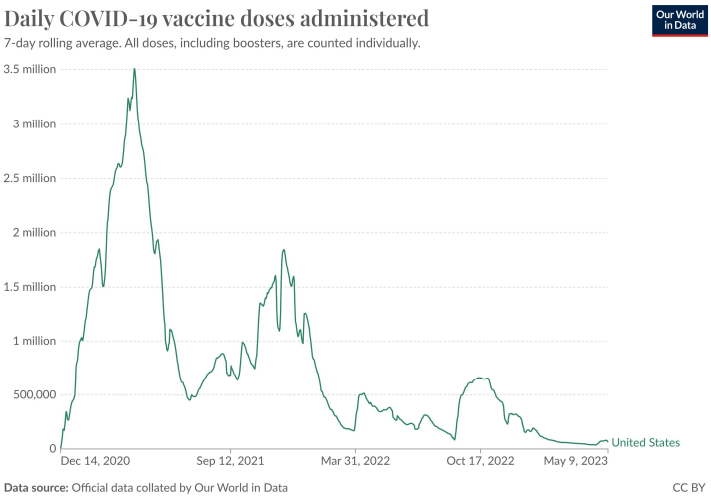
Financial Disclosures

- Nothing to disclose

COVID-19 Pandemic

Rapidly changing recommendations for treatment of disease	Community view that vaccine was developed rapidly – Operation Warp Speed	Robust public health efforts
Healthcare professionals combating misinformation in the media	Engaging in active learning strategies	Not just a challenge in the United States but across the world

COVID Vaccine Trends



https://ourworldindata.org/covid-vaccinations

COVID Vaccine Challenges

- Vaccine access challenges – initial sign ups online only which left out most vulnerable populations
- Grassroots efforts – taking vaccines to the people insuring vaccination centers were at community locations, on transportation routes (bus lines), convenient times
- Incentives for vaccinations
- Partnering with community leaders outside of healthcare such as elected officials and clergy

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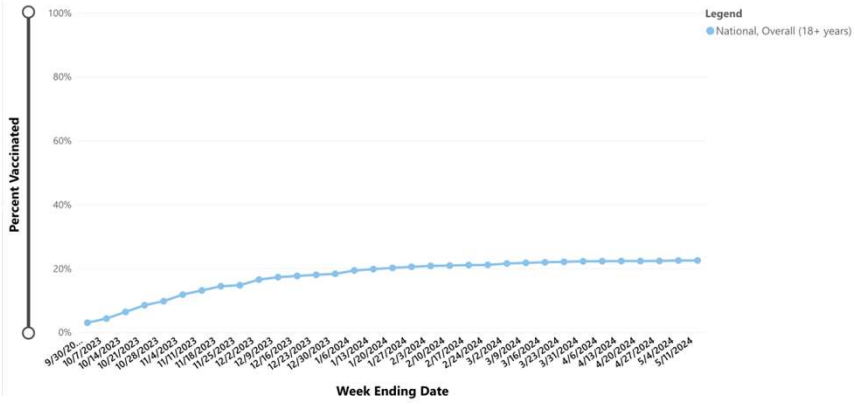
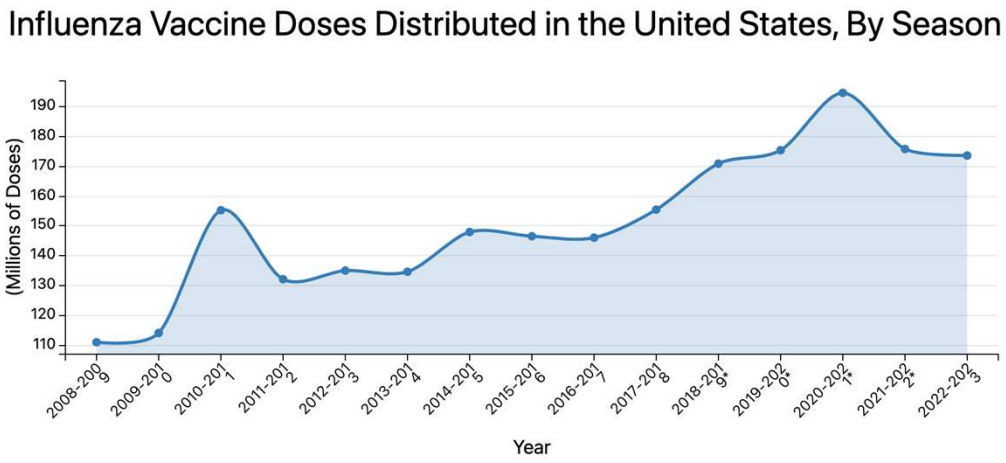
Recent Adult COVID-19 Vaccination Rates

Figure 3A. Cumulative Percentage of Adults 18 Years and Older Vaccinated with the Updated 2023-24 COVID-19 Vaccine*,†,‡,±
Data Source: National Immunization Survey–Adult COVID Module



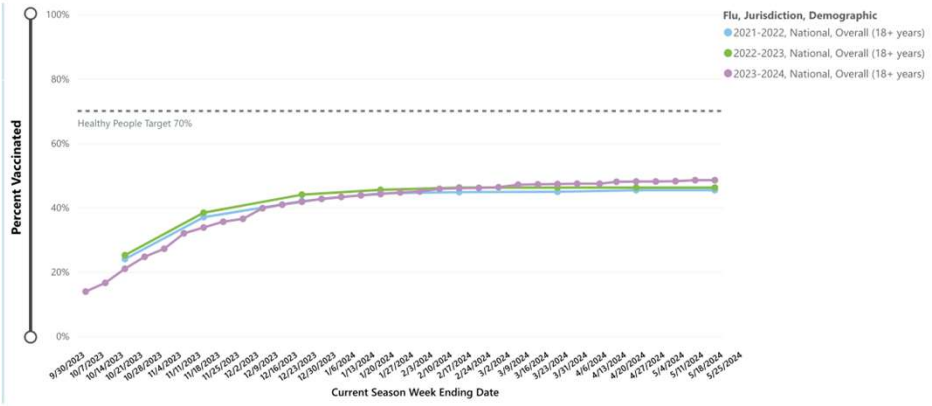
https://www.cdc.gov/vaccines/imz-managers/coverage/covidvaxview/interactive/adult-coverage-vaccination.html

Influenza Vaccines 2008-2023



Recent Influenza Vaccination Rates

Figure 4A. Influenza Vaccination Coverage, by Selected Demographics, 2023-24 and Jurisdiction
Adults 18 years and Older, United States,*‡†±
Data Source: National Immunization Survey-Adult COVID Module



https://www.cdc.gov/flu/fluvaxview/dashboard/vaccination-adult-coverage.html

Barriers to vaccination

- Adult limited access to healthcare services
- Lack of physician/provider recommendations for vaccination
- Misconceptions about vaccination needs
- Lack of insurance coverage
- Incomplete use of evidence based strategies such as standing orders and recall systems
- Lack of regulatory or legal requirements

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SDoH Barriers to Vaccination

Distrust of Healthcare system

History of discrimination in medical research in communities of color

Limited access to healthcare services

Low health literacy rates – decreased desire to engage in preventive measures

Lack of publicly funded vaccines and reimbursements to providers

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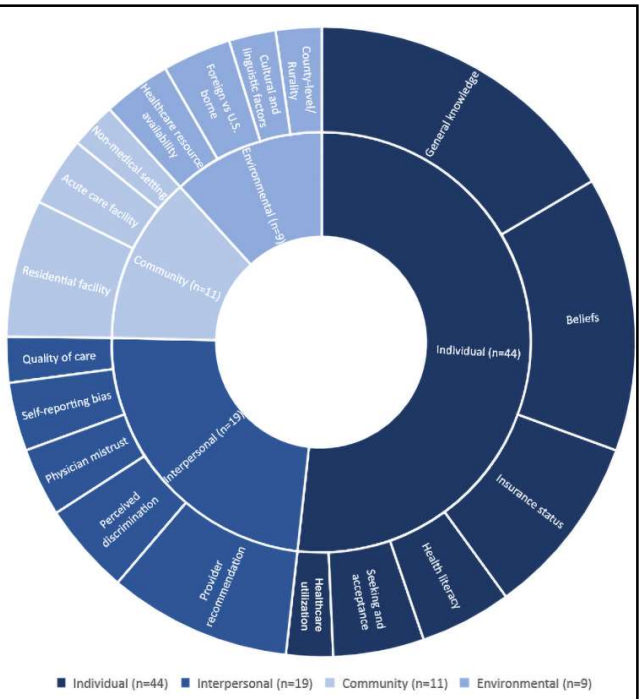
Reasons and associations for disparities in adult vaccination by social ecological model

Granade CJ, Lindley MC, Jatlaoui T, Asif AF, Jones-Jack N. Racial and Ethnic Disparities in Adult Vaccination: A Review of the State of Evidence. Health Equity. 2022 Mar 7;6(1):206-223. doi: 10.1089/heq.2021.0177. PMID: 35402775; PMCID: PMC8985539.



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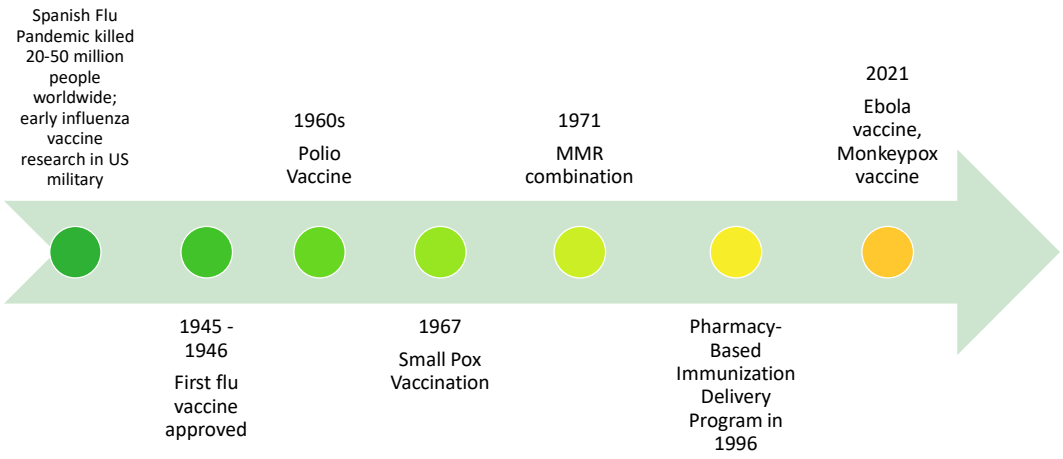
Reasons and Associations

Individual	• Low health literacy and awareness/understanding of need for vaccination
Interpersonal	• Differences in receipt of provider recommendation for vaccination • Lack of healthcare provider knowledge about adult immunization recommendations
Community	• Demographic driven focusing on community education efforts
Environmental	• Cultural and linguistic factors with need for social supports

Other Historical Considerations



Summary

Overall, more robust community education efforts are needed to assist with increasing adult immunization uptake

Physicians and other healthcare provider education is needed to reinforce adult vaccination recommendations

Further considerations of the impact of SDoH on communities must be explored with barriers to vaccination

Healthcare professionals should continue to foster relationships with community leaders and influencers to assist with education and vaccine administration

Questions?

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