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Moderna Investigational Influenza Vaccine mRNA-1010 in Adults ≥50 Years

Moderna, Inc.

June 18, 2026

Vaccines and Related Biological Products Advisory Committee

Introduction
Moderna Investigational Influenza Vaccine mRNA-1010 in Adults ≥50 Years

Rituparna Das, MD, PhD

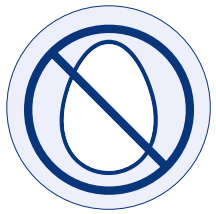
Senior Vice President, Clinical Development,
Infectious and Rare Diseases

Moderna, Inc.

mRNA-1010 Was Designed to Address Key Limitations of Current Seasonal Influenza Vaccines

1. Precise antigen match

Encodes membrane-bound HA of WHO-recommended seasonal influenza strains



2. No egg adaptation

Does not require egg-based propagation or other complex culture systems

3. Flexible production timeline

Allows for strain selection closer to start of influenza season, decreasing risk of mismatch

mRNA-1010

Designed to overcome limitations of current influenza vaccines and improve protection against influenza in a population that continues to experience substantial disease burden

Moderna is Seeking Approval of One Vaccine, One Dose, for Adults ≥50 Years

1 Indication

Prevention of influenza A and B in individuals ≥50 years of age

1 Dose

Single dose, 0.38 mL prefilled syringe, administered IM

2 Pathways

Traditional approval in adults 50-64 years

Accelerated approval in adults ≥65 years

TODAY'S FOCUS

Overall benefit-risk profile supporting approval of mRNA-1010 in adults ≥50 years

FDA Discussions Led to Two Regulatory Pathways

1 Initial Development Strategy
Program designed to support licensure in adults ≥50 years

2 FDA Review
Highlighted different ACIP recommendations for influenza vaccines by age group

3 Post Type A Meeting Regulatory Framework
Application structured into 2 pathways aligned to evidence and remaining post-marketing question

Traditional Approval
Adults 50 – 64 years

- Direct efficacy vs SD vaccine
- Supportive immunogenicity
- Acceptable safety profile
- mRNA platform benefits

Evidence Supports Traditional Approval

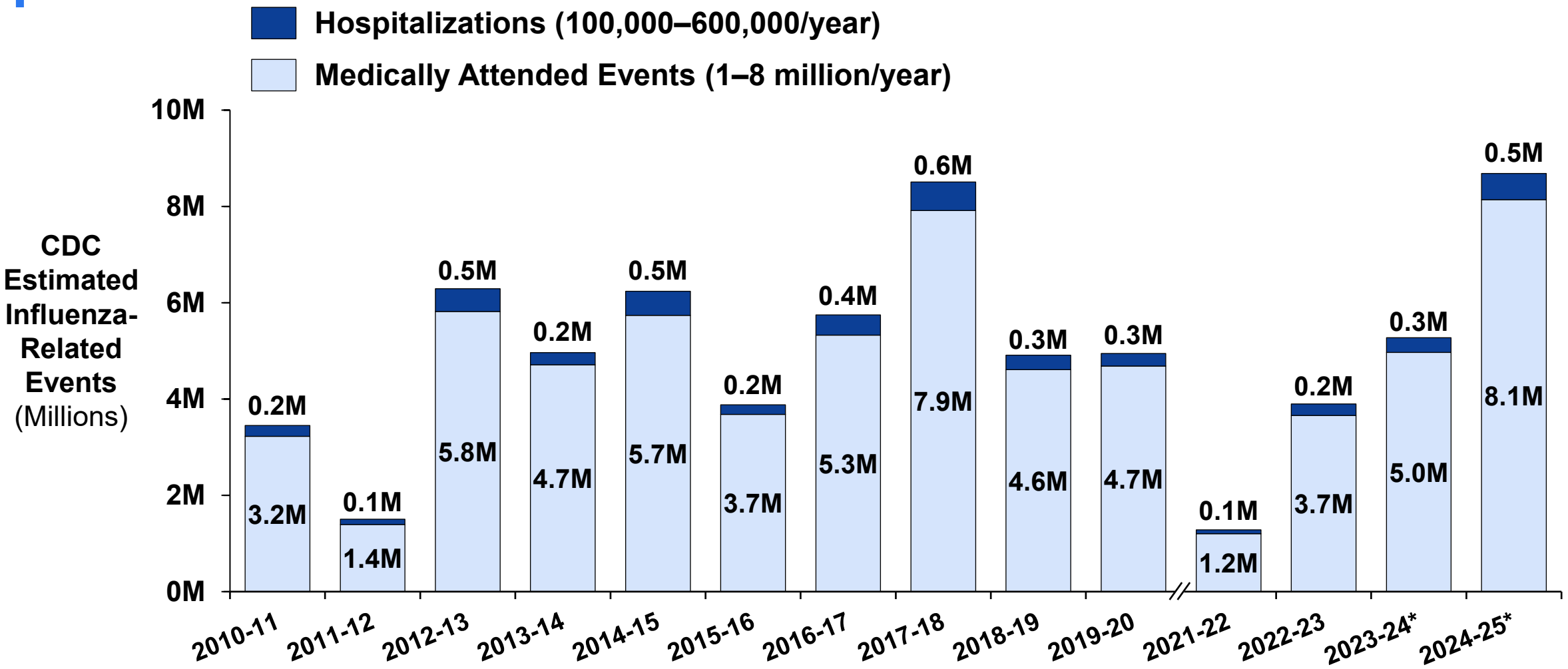
Accelerated Approval
Adults ≥65 years

- Superior immune responses vs HD vaccine
- Direct efficacy vs SD vaccine
- Acceptable safety profile
- **Confirmatory RWE study vs enhanced vaccines**
- mRNA platform benefits

Evidence Supports Accelerated Approval

SD - Standard Dose; HD - High Dose; RWE - Real World Evidence

Influenza Continues to Cause Substantial Disease Burden in Adults ≥50 Years



CDC. Seasonal Influenza Burden Estimates in US, Adults ≥50 Years. https://www.cdc.gov/flu-burden/php/data-vis/index.html. Accessed 10JUN2026.
No CDC estimates for 2020-2021.
*Estimates for 2023-2024 and 2024-2025 season are preliminary and may change

Older Adults Experience a Disproportionate Burden of Severe Influenza Outcomes

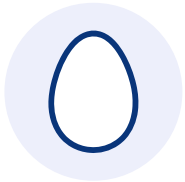
- **Adults ≥50 | CDC estimates from 2024–2025 influenza season in US[1]**
  - **>546,000** influenza hospitalizations
  - **>41,000** influenza deaths
- **Adults ≥65 | Account for majority of severe outcomes[1]**
  - **57%** of influenza hospitalizations
  - **71%** of influenza deaths
- **Increased burden reflects well-established vulnerability of older adults and high-risk individuals[2,3]**
  - Risk of severe influenza complications increases with age
  - Influenza exacerbates underlying medical conditions and comorbidities

1. CDC. Estimated US Flu Disease Burden. https://www.cdc.gov/flu-burden/php/data-vis/index.html. Accessed 10JUN2026.
2. CDC. Flu and People 65 Years and Older. https://www.cdc.gov/flu/highrisk/65over.htm. Accessed 10JUN2026.
3. CDC. People at Increased Risk for Flu Complications. https://www.cdc.gov/flu/highrisk/index.htm. Accessed 10JUN2026.

Current Influenza Vaccines Are Limited by Manufacturing Timelines and Strain-Match Challenges

Production Time

- Strain selection occurs months before vaccination season
- During that interval, circulating viruses can continue to evolve



Egg Adaptation

- Egg-based manufacturing can introduce egg-adaptive changes
- Egg-based vaccines: >95% of doses administered to US adults ≥65[1]

Strain Variability

- Naturally occurring antigenic drift and egg adaption can contribute to strain mismatch

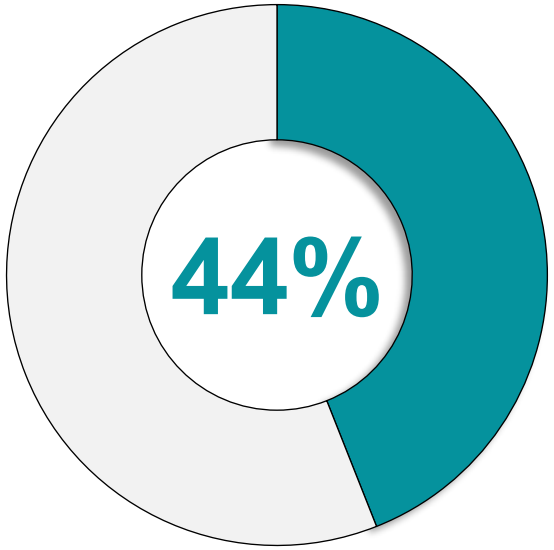
- **Diversifying influenza vaccine manufacturing is public health priority[2]**
- **Approval of mRNA-1010 would provide seasonal influenza vaccine platform to support influenza pandemic preparedness**

1. Unpublished data, IQVIA, 2026. Data covering 2024-25 influenza season (August 1, 2024 through July 31, 2025).
2. U.S. Department of Health and Human Services. National Influenza Vaccine Modernization Strategy 2020–2030. https://aspr.hhs.gov/legal/NIVMS/Documents/nivms-2020-2030.pdf. Accessed 10JUN2026.

Frequent Antigenic Mismatch Due to Drift or Egg-Adaptive Mutations

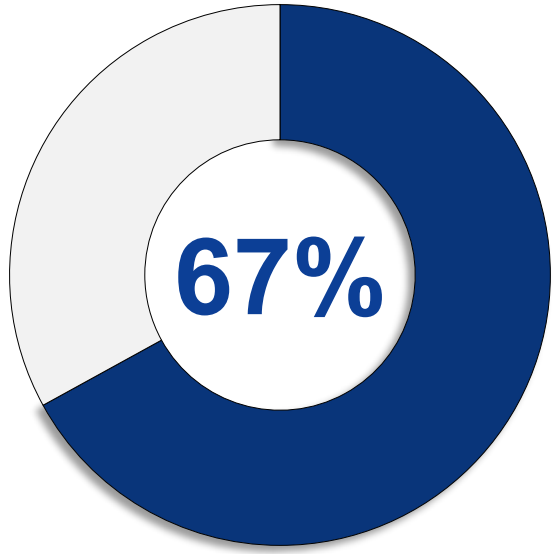
Antigenic Drift

4 of 9 influenza seasons



Egg-Adaptive Mutations

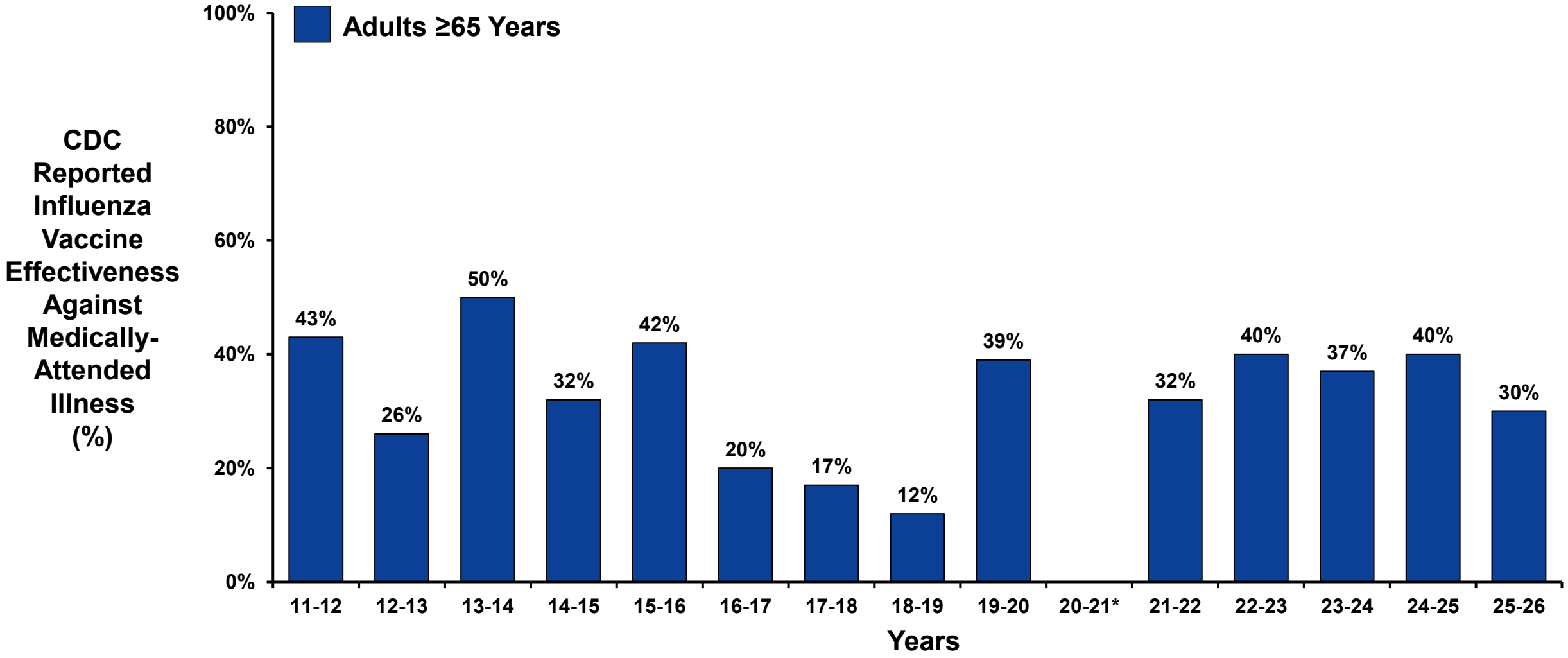
6 of 9 influenza seasons



2024 Review of Vaccine Mismatch | Northern Hemisphere

Russell CA, et al. Hum Vaccin Immunother. 2024

Variable Vaccine Effectiveness Against Medically-Attended Illness Highlights Need for Improved Influenza Prevention



* 2020-2021 VE not estimated due to COVID-19 pandemic; CDC. Flu Burden Prevented by Vaccination. https://www.cdc.gov/flu-burden/php/data-vis-vac/index.html Accessed 10JUN2026. Flannery B, et al. CID 2019. Maloney P, et al. MMWR 2026. 2025-26 preliminary VE data from VISION network.

Regulatory Filing for mRNA-1010 Supported by Efficacy, Immunogenicity, and Safety Data Across >71,000 Adults, ≥50 Years

Studies	Assessments	Comparator	Participants (N)*	Age (Years)
304	Efficacy, Immunogenicity and Safety	Standard-Dose (SD) Influenza Vaccine	40,703	≥50
303C	Immunogenicity and Safety	High-Dose (HD) Influenza Vaccine	2,992	≥65
301‡ 302‡ 303 304	Safety (Integrated Summary)	SD and HD Influenza Vaccines	71,916	≥50

* mRNA-1010 + comparator influenza vaccine; SD - Standard Dose; HD - High Dose

‡ Includes supportive safety data from Studies 301 & 302 using an earlier mRNA-10 candidate vaccine that was subsequently discontinued

Leroux Roels I, et al. New Engl J Med. 2026; Soens M, et al. Vaccine. 2025; Kandinov B, et al. Hum Vaccin Immunother. 2025

Adults ≥50 Years: Totality of Evidence Supports a Positive Benefit-Risk Profile for mRNA-1010

Efficacy	▪ Statistically superior efficacy vs standard dose (SD) influenza vaccine ▪ Consistent protection across strains, high-risk groups, and age
Immunogenicity	▪ Higher immune responses vs SD influenza vaccine ▪ Statistically superior responses vs HD influenza vaccine in adults ≥65
Safety	▪ Increased local & systemic reactions vs SD & HD influenza vaccine ▪ Reactions typically mild-moderate, short duration, and resolved without medical attention ▪ Acceptable safety profile; no safety concerns identified
Public Health Benefit	▪ Potential to reduce influenza burden beyond current licensed vaccines ▪ Leverages precision and adaptability of mRNA platform; potential to improve strain matching

mRNA-1010 Efficacy Consistent with Evidence Used to Support Licensure of Other Enhanced Influenza Vaccines

Vaccine	Standard Dose (SD) Comparator	N*	Age (Years)	rVE (95%) vs Protocol-Defined Influenza	Influenza Season
mRNA-1010[1]	**Fluarix**	**40,303**	**≥50**	**26.6%** (16.7, 35.4)	**2024–2025**
		19,260	≥65	**27.4%** (12.1, 40.0)	
Fluzone-HD High Dose[2]	**Fluzone**	**31,983**	**≥65**	**24.2%** (9.7, 36.5)	**2011–2012** **2012–2013**
Flublok Recombinant[3]	**Fluarix**	**8,604**	**≥50**	**30%** (10, 47)	**2014–2015**
		~3,486	≥65	**17%** (-20, 43)	

- **FLUAD** (Adjuvanted) was licensed using accelerated approval based on immunogenicity data without efficacy data[4]

Per-protocol sample size for rVE estimation

1. Leroux-Roels I et al. N Engl J Med, 2026; 2. DiazGranados CA et al. N Engl J Med, 2014; 3. Dunkle LM et al. N Engl J Med, 2017; 4. Frey SE et al. Vaccine, 2014

Agenda

Epidemiology of Influenza and Effectiveness of Current Vaccines	**Evan Anderson, MD, FIDSA, FPIDS** Vice President, Epidemiology Moderna, Inc.
Clinical Efficacy and Immunogenicity	**Rituparna Das, MD, PhD** Senior Vice President, Clinical Development Moderna, Inc.
Clinical Safety	**Eleanor Wilson, MD, MHS** Executive Director, Clinical Development Moderna, Inc.
Benefit-Risk and Summary	**Rituparna Das, MD, PhD**

Epidemiology of Seasonal Influenza in US Adults ≥50 Years and Effectiveness of Current Vaccines

Evan Anderson, MD, FIDSA, FPIDS

Vice President, Epidemiology

Moderna, Inc.

Influenza Infection Can Lead to Serious Complications Beyond Respiratory Illness

Acute Cardiovascular Events[1,2]

- **Heart attack** – ~ 6x more likely within 7 days of influenza infection[3]
- **Heart failure** – elevated risk of hospitalization within 7 days[4]
- **Stroke** – elevated risk within 28 days following infection[5]

Acute Pulmonary Events

- **Pneumonia** – may be complicated by bacterial superinfection[6,7]
  - May occur with or without respiratory failure
- Exacerbations of **chronic obstructive pulmonary disease**[8]

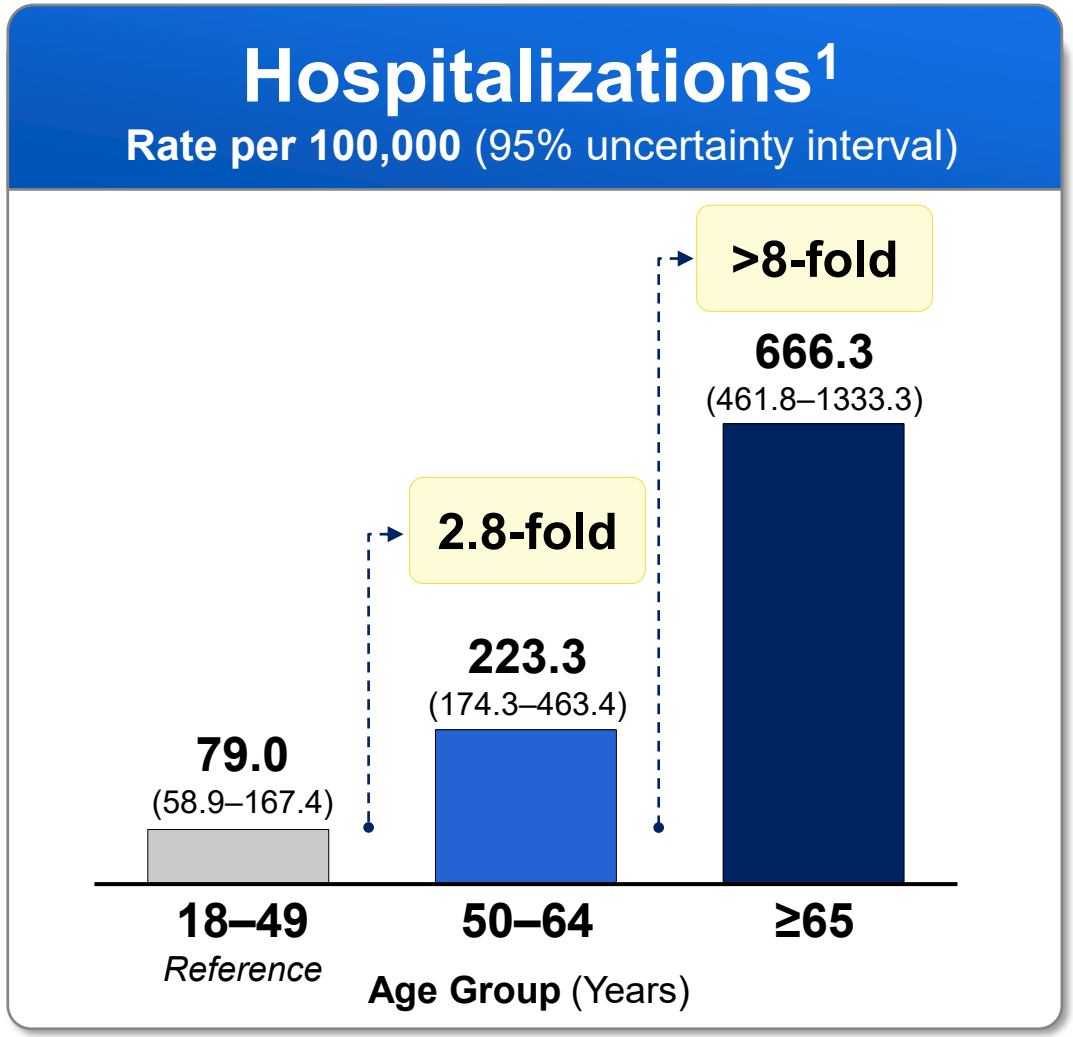
Other Complications[9,10]

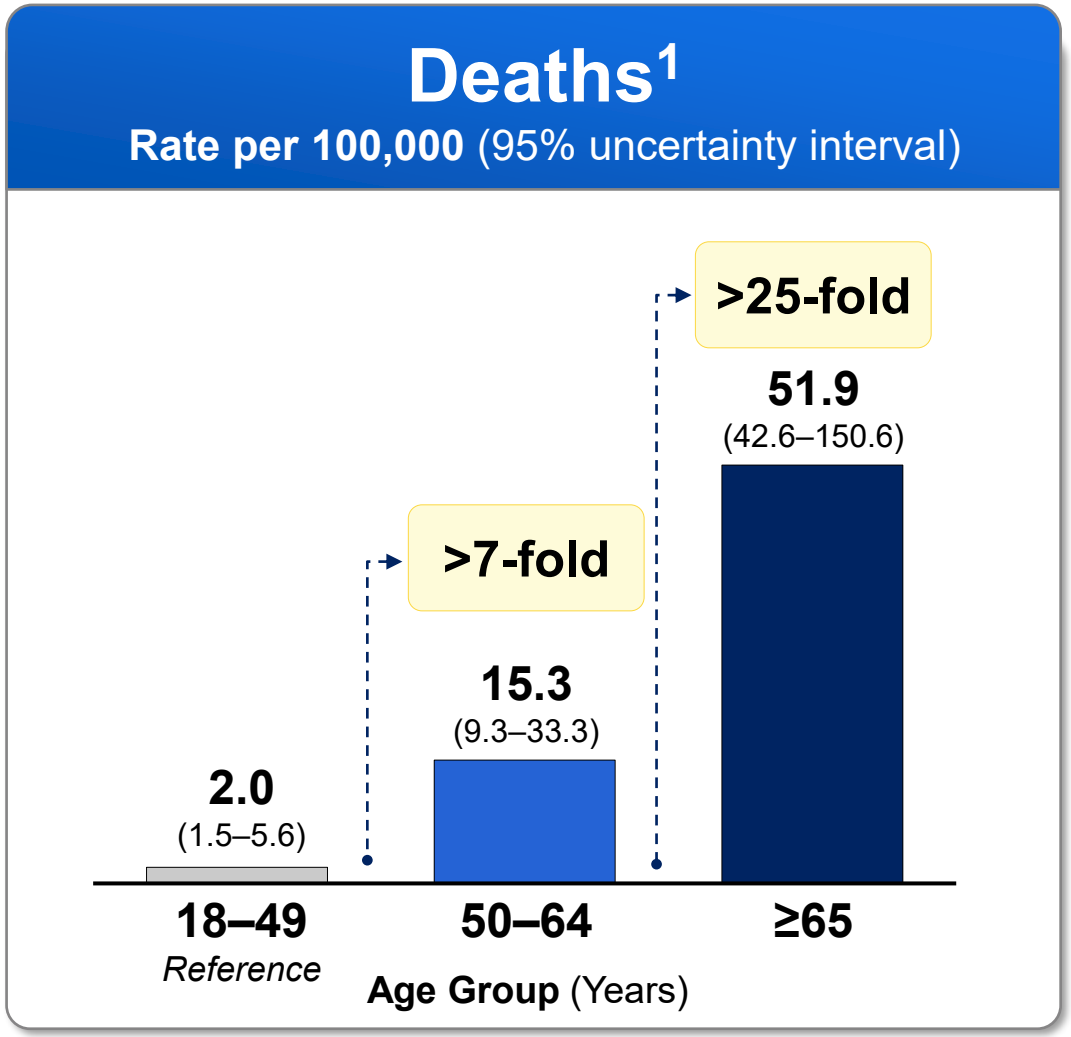
- **Neurologic**
- **Muscular**
- **Renal**

Complications beyond respiratory illness contribute significantly to the overall clinical burden of influenza in older adults

1. Johansen ND et al. JAMA Cardiology 2025; 2. Fröbert O et al. Circulation 2021; 3. Kwong JC et al. New Engl J Med 2018; 4. Sin P et al. Glob Heart 2022; 5. Nguyen TQ et al. Cardio Res 2025; 6. Jain S et al. New Engl J Med 2015; 7. Lei B et al. Front Microbiol 2025; 8. Wedzicha JA et al. Lancet 2007; 9. Rosero CI et al. Drugs and Aging 2025; 10. Sellers SA et al. IORV 2017

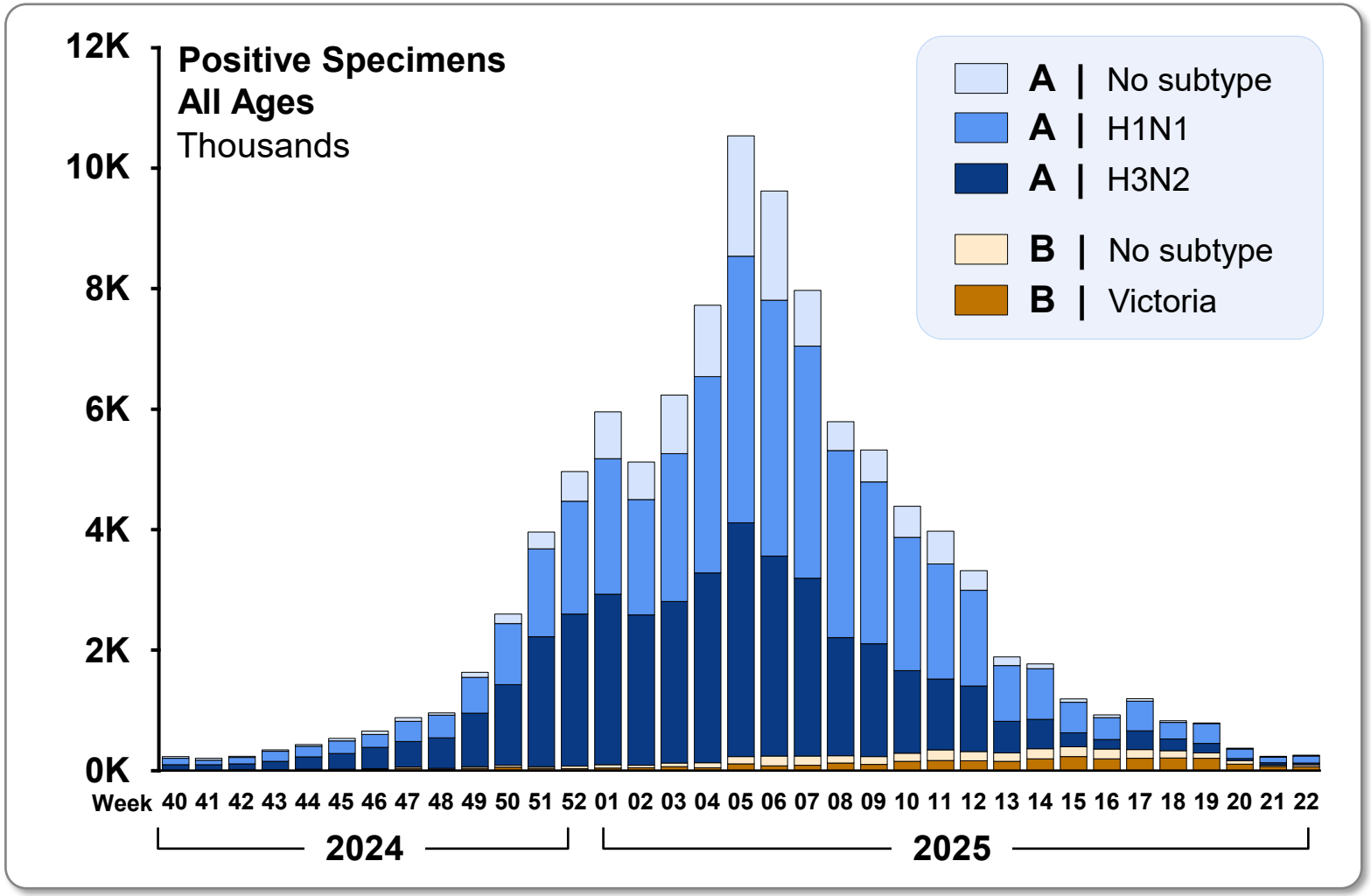
Risk of Influenza-Related Hospitalization and Death Increases Substantially with Age





1. CDC. Estimated US Flu Disease Burden. https://www.cdc.gov/flu-burden/php/data-vis/index.html; Accessed 11JUN2026. 2024-2025 CDC preliminary incidence rates

Influenza A Predominant During 2024–2025 Season, with Limited Influenza B Cases



Influenza A[1]

- **53% | H1N1**
- **47% | H3N2**
- January peak
- Influenza A historically predominant driver of influenza activity
- Over 9 seasons, **>83%** of hospitalizations in adults ≥50 years[2]

Influenza B

- **0.8%** of total cases in adults ≥65 years[3]
- March peak

1. CDC. FluView Interactive. National Level Outpatient Illness and Viral Surveillance. https://gis.cdc.gov/grasp/fluview/fluportaldashboard.html; Accessed 11JUN2026. 2. Sumner KM et al. Lancet Microbe 2023. 3. CDC. FluView Interactive. Age Group Distribution of Influenza Positive Specimens Reported by Public Health Laboratories, National Summary, 2024-25 Influenza Season. https://gis.cdc.gov/grasp/fluview/flu_by_age_virus.html; Accessed 11JUN2026.

Licensed Influenza Vaccines Use Multiple Technologies, but Remain Vulnerable to Strain Evolution

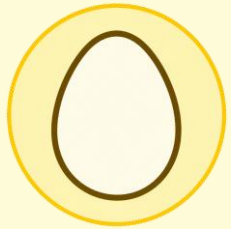
Current Vaccine Approaches

Egg-based inactive

Cell culture-based

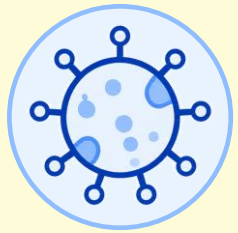
Enhanced for older adults
High-dose, adjuvanted, recombinant

ACIP Recommended for Adults ≥65 Years[1]



Egg-based adaptation

Changes that may occur when influenza virus is propagated in eggs, potentially producing a vaccine antigen that differs from the originally selected strain



Antigenic drift

Natural viral evolution that occurs over time after strain selection and before or during the influenza season

Both mechanisms contribute to mismatch between vaccine strains and circulating viruses

1. Grohskopf L et al. MMWR 2022.

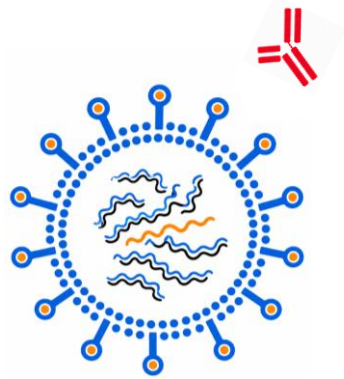
Long Manufacturing Timelines Create Opportunities for Strain Mismatch due to Egg Adaptation and Antigenic Drift

Influenza Strain Selection

US Approval; Vaccination Begins

~6 Months between strain selection and vaccination season

FEB → MAR → APR → MAY → JUN → JUL → AUG – SEPT



Long interval may allow circulating viruses to evolve

Weir J et al. Influenza Other Resp Viruses 2016

COVID-19 Experience Demonstrates the Speed of the mRNA Platform From Strain Selection to Vaccine Availability

Influenza Strain Selection

~6 Months between strain selection and vaccination season

US Approval; Vaccination Begins

FEB → MAR → APR → MAY → JUN → JUL → AUG – SEPT

2-3 Months

COVID-19 Annual Strain Selection

COVID-19 Precedent

https://www.fda.gov/vaccines-blood-biologics/industry-biologics/covid-19-vaccines-2025-2026-formula-use-united-states-beginning-fall-2025; Accessed 11JUN2026.
https://www.fda.gov/media/164807/download Accessed 14JUN2026.
Weir J et al. Influenza Other Resp Viruses 2016

2025–2026 Season Illustrates How Viral Evolution After Strain Selection Can Lead to Mismatch

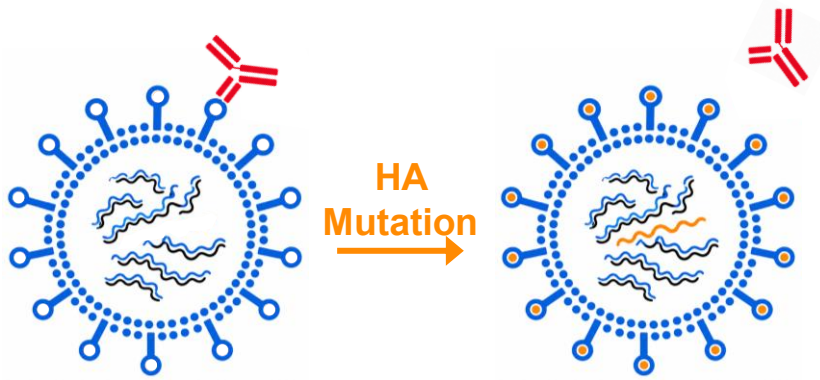
Influenza Strain Selection

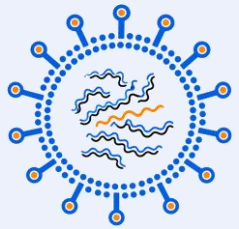
US Approval; Vaccination Begins

FEB | MAR | APR | MAY | JUN | JUL | AUG | SEP | OCT | NOV | DEC

2025–2026 Season (Subclade K Identified in June 2025)

- After WHO strain selection, circulating H3N2 viruses **drifted antigenically** (subclade K)
- HA receptor-binding domain substitutions may contribute to **reduced antibody recognition**

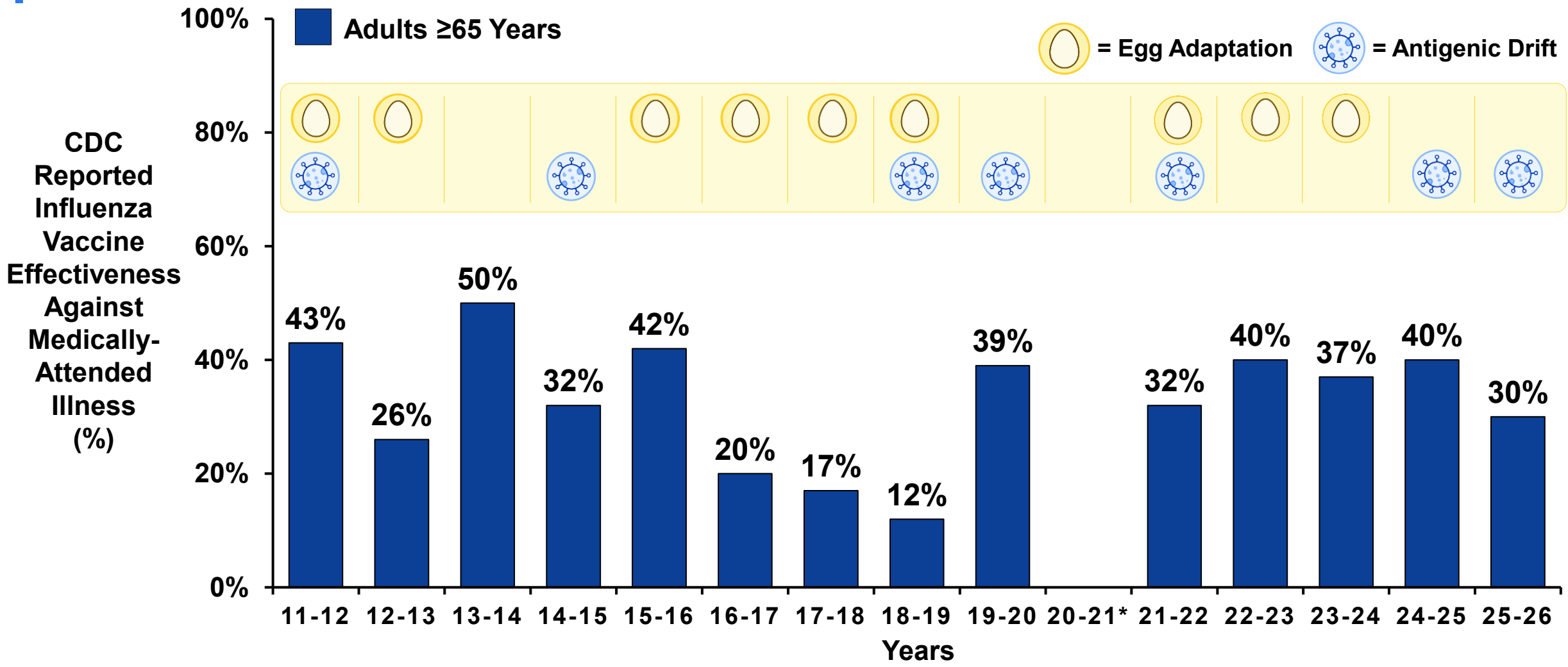




Subclade K
92.9% of circulating A (H3N2) viruses
characterized by CDC

Weir J et al. Influenza Other Resp Viruses 2016; Rasmussen SA et al. New Engl J Med 2026; CDC. Weekly US Influenza Surveillance Report: Key Updates for Week 20, ending May 23, 2026. https://www.cdc.gov/fluview/surveillance/2026-week-20.html. Accessed 11JUN2026.

Factors Including Egg Adaptation and Antigenic Drift May Contribute to Variable Vaccine Effectiveness



Russell CA, et al. Hum Vaccin Immunother 2024; Bolton MJ, et al. Cell Reports 2022; Stein AN, et al. IORV 2025; Stein AN, et al. Infect Dis Ther 2025; CDC. Influenza Activity in the United States during the 2024–25 Season. https://www.cdc.gov/flu/whats-new/2025-2026-influenza-activity.html Accessed 10JUN2026; Flannery B, et al. CID 2019. Maloney P, et al. MMWR 2026. 2025-26 preliminary VE data from VISION network; CDC. Flu Burden Prevented by Vaccination. https://www.cdc.gov/flu-burden/php/data-vis-vac/index.html Accessed 10JUN2026. * 2020-2021 vaccine effectiveness not estimated due to COVID-19 pandemic.

Risk of an Influenza Type B Mismatch in 2026-27 Season

Northern Hemisphere

Background

- In 2025-26 season, **B/Victoria subclade C.3.1 increased** in prevalence
- Clade had **multiple mutations resulting in antigenic escape** from 2025-26 vaccine

WHO 2026-27 Vaccine Strain Selection

- **B/Victoria subclade C.3.1 selected** for influenza vaccine

Egg-based vaccines (B/Tokyo)

- Egg-adaptive mutations remove N-glycosylation site at 197-199
- Potential mismatch to C.3.1/C.3.3 viruses

Cell, recombinant, mRNA vaccines (B/Penn)

- Retains N-linked glycan at site 197 present in circulating C.3/C.3.1/C.3.3 viruses

Potential Mismatch

~8-fold reduction in HAI titers

B/Tokyo vs B/Penn against circulating C.3.1 viruses based on early immunogenicity testing

Highlights potential value of mRNA-based vaccines for improving strain match

WHO. Recommended composition of influenza virus vaccines for use in the 2026-2027 northern hemisphere influenza season. https://cdn.who.int/media/docs/default-source/vcm-northern-hemisphere-recommendation-2026-2027/a.-27-feb-2026-recommended-composition-of-influenza-virus-vaccines-for-use-in-the-2026-2027-nouthern-hemisphere-influenza-season---full-report.pdf?download=true&sfvrsn=6a722e7d_9 Accessed 11JUN2026. WHO Meeting on the 2026-27 Northern Hemisphere Influenza Vaccine Composition. 27FEB2026. Accessed 11JUN2026. Available at https://youtu.be/JMMfQVf9rco?t=2921

Persistent Influenza Burden and Variable Vaccine Effectiveness Support the Need for Improved Prevention

Clinical Burden

- Influenza remains a serious and life-threatening illness in US adults ≥50 years; highest risk in adults ≥65 years
- Influenza contributes to cardiovascular, pulmonary, and other complications
- Influenza A is primary driver of severe influenza-related outcomes in older adults

Current Vaccines

- Currently licensed influenza vaccines remain important foundation of public health
- Effectiveness varies across seasons
- Strain mismatch can occur due to lengthy manufacturing timelines, antigenic drift, and egg adaptation

Why Improvement Matters

- Together, these challenges highlight the need for improved influenza vaccines
- An improved vaccine could help reduce morbidity and mortality in older adults
- May help address limitations of current seasonal influenza vaccine technologies

For adults ≥50 years there remains an unmet need for improved influenza vaccines

Clinical Data: Efficacy and Immunogenicity of mRNA-1010

Rituparna Das, MD, PhD

Senior Vice President, Clinical Development,
Infectious and Rare Diseases

Moderna, Inc.

Key mRNA-1010 Clinical Trials

Study 101
Phase 1/2

N = 678

Adults ≥18 Years

Safety, immunogenicity, and dose selection vs placebo / SD influenza vaccine

25, 50, 100, 200 µg QIV

Informed dose for Phase 3

Study 304
Phase 3

N = 40,703

Adults ≥50 Years

Efficacy, safety, immunogenicity vs SD influenza vaccine

37.5 µg TIV
12.5 µg per strain

Demonstrated superior vaccine efficacy vs SD influenza vaccine

Study 303C
Phase 3

N = 2,992

Adults ≥65 Years

Safety and immunogenicity vs HD influenza vaccine

50 µg QIV
12.5 µg per strain

Demonstrated superior immunogenicity vs HD influenza vaccine

N includes mRNA-1010 + comparator group; TIV – trivalent influenza vaccine; QIV – quadrivalent influenza vaccine

mRNA-1010 Composition Changed During Clinical Program; Dose per Strain Remained Constant

12.5 µg Dose per Influenza Strain

- A/H1N1 – 12.5 µg
- A/H3N2 – 12.5 µg
- B/Victoria – 12.5 µg
- B/Yamagata – 12.5 µg

- WHO and FDA Strain Recommendations Update 2024: B/Yamagata lineage no longer recommended for inclusion in influenza vaccines[1]
- mRNA-1010 transition from quadrivalent (QIV) to trivalent (TIV) reflected WHO update

1. World Health Organization. Recommended composition of influenza virus vaccines for use in 2024-2025 northern hemisphere influenza season. February 2024.

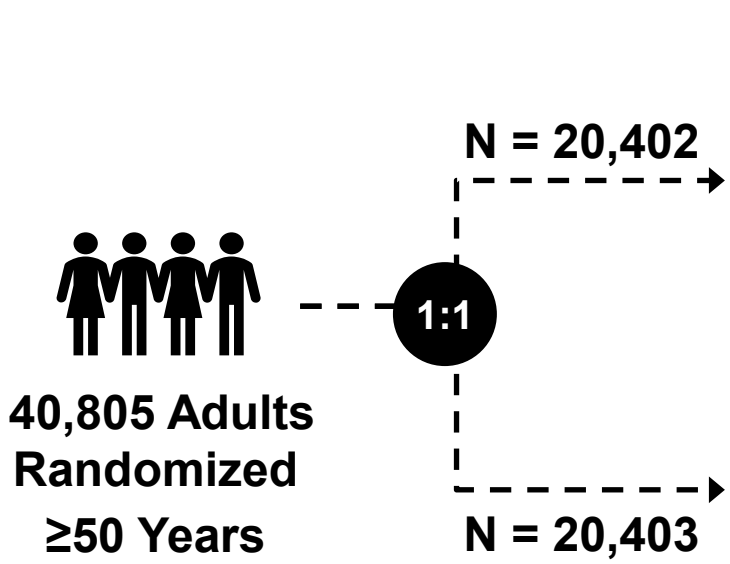
Pivotal Relative Vaccine Efficacy Trial

Study 304

Leroux-Roels et al. N. Engl. J. Med, 2026

Design of Pivotal Efficacy, Immunogenicity and Safety Trial

Study 304: Randomized, Double-blind, Active-controlled Phase 3 Trial



mRNA-1010 (37.5 µg TIV)

mRNA Seasonal Influenza Vaccine Candidate

Licensed SD Influenza Vaccine
(45 µg TIV or 60 µg QIV)

Licensed Inactivated Standard Dose Seasonal Influenza Vaccine

Stratified Randomization:

- Age groups: 50-64, ≥65 years
- Influenza vaccine status in previous influenza season (received/not received)

Follow up through 6 months (Day 181) or end of influenza season, whichever longer

TIV – trivalent influenza vaccine; QIV – quadrivalent influenza vaccine

Leroux-Roels et al. New Engl. J. Med, 2026

Standard-Dose (SD) Comparator Selection Supported by Multiple Considerations

Aligned with Regulatory Guidance* and Precedent

Licensed SD vaccines have historically served as the benchmark for demonstrating the added value of enhanced influenza vaccines

Appropriate for Multinational Enrollment

Enhanced-vaccine recommendations vary across countries; SD vaccines remain licensed and widely used globally

Supported by Phase 3 Immunogenicity Data

Study 303C directly compared mRNA-1010 with HD vaccine in adults ≥65 years

* 21 CFR 601.2 (a) and ICH E10; FDA influenza vaccine development guidance 2007

Study Objectives

Study 304

Primary Objectives

- Non-inferiority and superiority of relative vaccine efficacy (rVE) of mRNA-1010 vs licensed SD influenza vaccines against RT-PCR confirmed protocol-defined Influenza-Like Illness (ILI) by any influenza A or influenza B strains
- Safety and reactogenicity of mRNA-1010

Secondary Objectives

- Immunogenicity in a subset of participants

Exploratory Objective

- rVE of mRNA-1010 vs licensed SD influenza vaccine against medically-attended ILI

SD – standard dose

Demographics

Study 304

Adults ≥50 Years: Demographics and Baseline Characteristics Balanced Between Groups

Study 304 - Safety Set

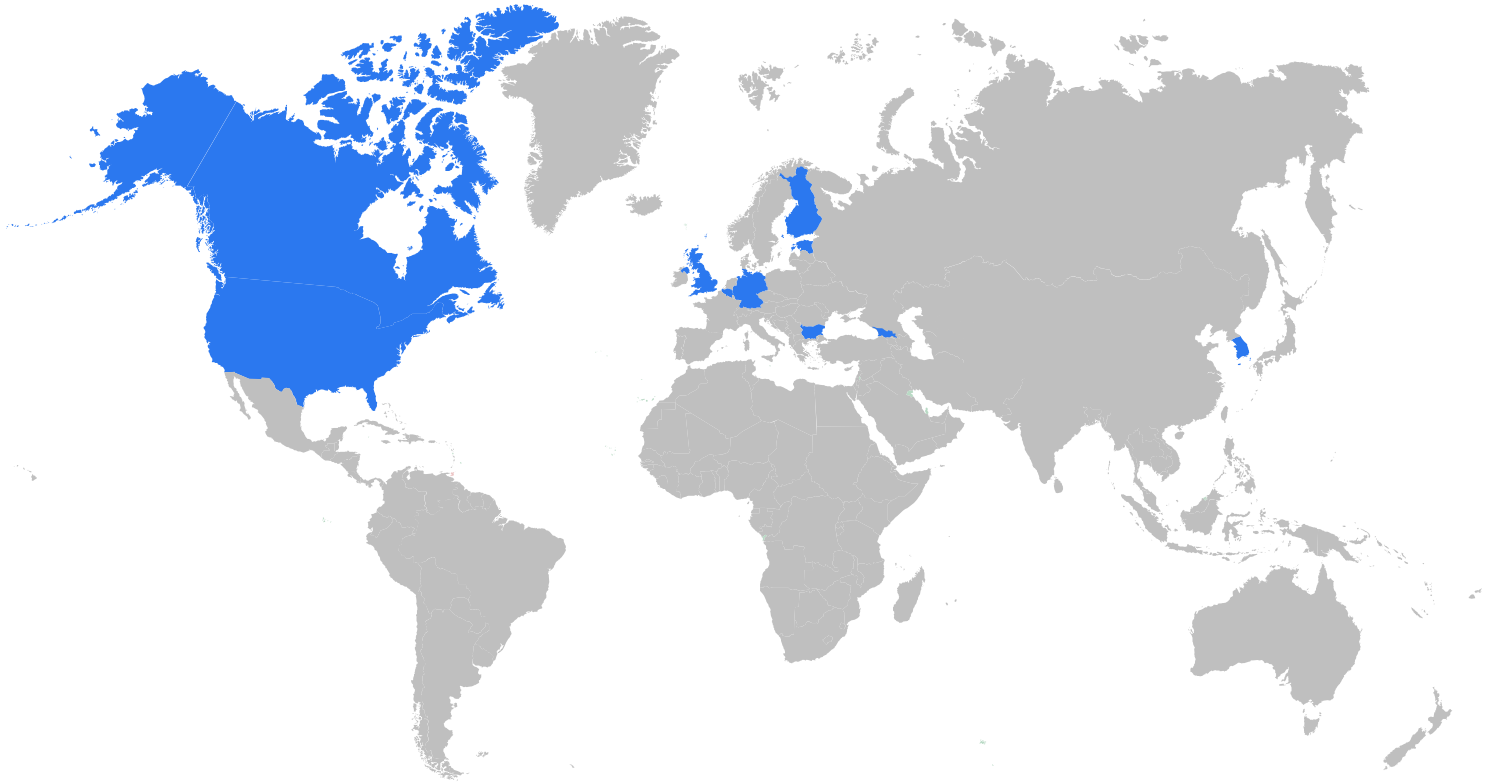
		mRNA-1010 (N = 20,350)		Licensed SD Influenza Vaccine (N = 20,353)	
Median Age, years		**64.0**		**64.0**	
Age Group	**50-64 Years**	**52.2%**	10,624	**52.2%**	10,615
	≥65 Years	**47.8%**	9,726	**47.8%**	9,738
	65-74 Years	**36.2%**	7,372	**36.2%**	7,375
	≥75 Years	**11.6%**	2,354	**11.6%**	2,363
Male		**43.4%**	8,834	**42.8%**	8,720
Vaccinated Previous Influenza Season		**47.0%**	9,569	**46.9%**	9,547
North American participants		**70.4%**	14,333	**70.5%**	14,340
Race/Ethnicity	**White**	**82.6%**	16,814	**82.6%**	16,811
	Black or African American	**13.2%**	2,687	**13.3%**	2,698
	Asian	**2.4%**	496	**2.4%**	483
	Hispanic / Latino Ethnicity	**10.6%**	2,147	**10.2%**	2,067
Frailty in ≥65 years (≥4 on Edmonton scale)[1]		**26.5%**	2,575	**26.6%**	2,583
Baseline High-risk Conditions*		**57.0%**	11,596	**57.1%**	11,620
Alternate High-risk Definition[2]		**82.0%**	16,676	**81.6%**	16,610

1. Edmonton scale only collected for participants ≥65 years. Percentages based on persons ≥65 years in Safety Set. 2. Watson KB, et al. Prev Chronic Dis. 2025.
*Most common high-risk conditions: obesity (BMI ≥30 kg/m²), diabetes mellitus, asthma, and chronic obstructive pulmonary disease

Pivotal Efficacy Study Conducted Across 301 Sites in 11 Countries with Independent Oversight

Study 304

Country	Sites
Belgium	4
Bulgaria	16
Canada	15
Estonia	5
Finland	5
Georgia	6
Germany	21
Republic of Korea	8
Taiwan	4
United Kingdom	28
United States	189



- Local ethics committees and national health agencies provided oversight and approval of study in each country
- Independent external Data Safety Monitoring Board (DSMB) reviewed all unblinded efficacy and safety data

Study Methods

Study 304

Active Influenza Surveillance Over Study Duration

Study 304

E-Diary used to report any respiratory symptoms

Participants prompted 2 times/week to report symptoms

If participant reported respiratory symptoms

- Site scheduled clinical assessment visit within 72 hours of symptom onset
- RT-PCR nasal swab or local results collected
- Study staff followed up with participants twice weekly to collect information on all current and new symptoms until resolution of the respiratory illness
- Protocol-defined ILI cases reviewed to determine if participant sought medical attention

Influenza-Like Illness (ILI) Case Definitions

Study 304

Protocol-Defined ILI	▪ ≥1 systemic symptom: Oral temperature >37.2°C (>99.0°F), chills, feverish, tiredness, headaches, or myalgia **AND** ▪ ≥1 respiratory symptom: Sore throat, cough, sputum production, wheezing, or difficulty breathing
Modified CDC-Defined ILI[1]	▪ Oral temperature >37.2°C (>99.0°F), a cough and/or a sore throat
CDC-Defined ILI[2]	▪ Oral temperature ≥37.8°C (≥100.0°F), a cough and/or a sore throat
WHO-Defined ILI[3]	▪ An acute respiratory infection with measured fever ≥38.0°C (≥100.4°F) and cough, with onset within the last 10 days

All cases required RT-PCR confirmation within 7 days of illness onset

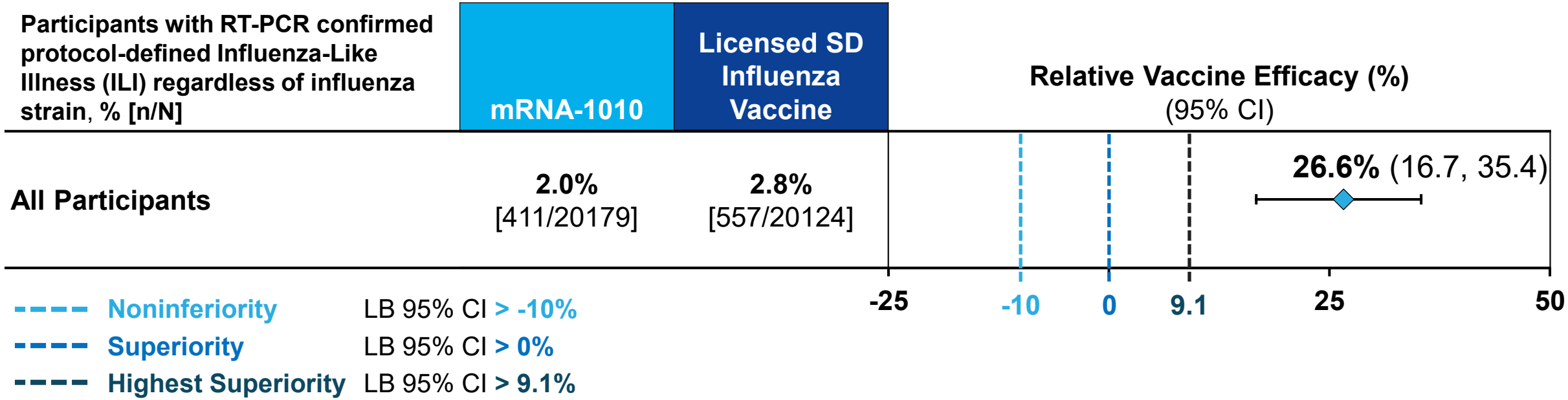
1. DiazGranados et al. N Engl J Med 2014; 2. CDC Glossary of influenza (Flu) Terms. link: https://www.cdc.gov/flu/glossary/index.html ; 3. WHO surveillance case definitions for ILI and SARI https://www.who.int/teams/global-influenza-programme/surveillance-and-monitoring/case-definitions-for-ili-and-sari

Relative Vaccine Efficacy Results

Study 304

Adults ≥50 Years: Prespecified Success Criteria Met for Relative Vaccine Efficacy of mRNA-1010 vs Licensed SD Influenza Vaccines

Study 304 – Primary Endpoint – Per-Protocol Set (Median 6 months of follow up)



- **Highest superiority success criterion met**
- **LB of 95% CI > 9.1%; 1-sided p-value = 0.0005**

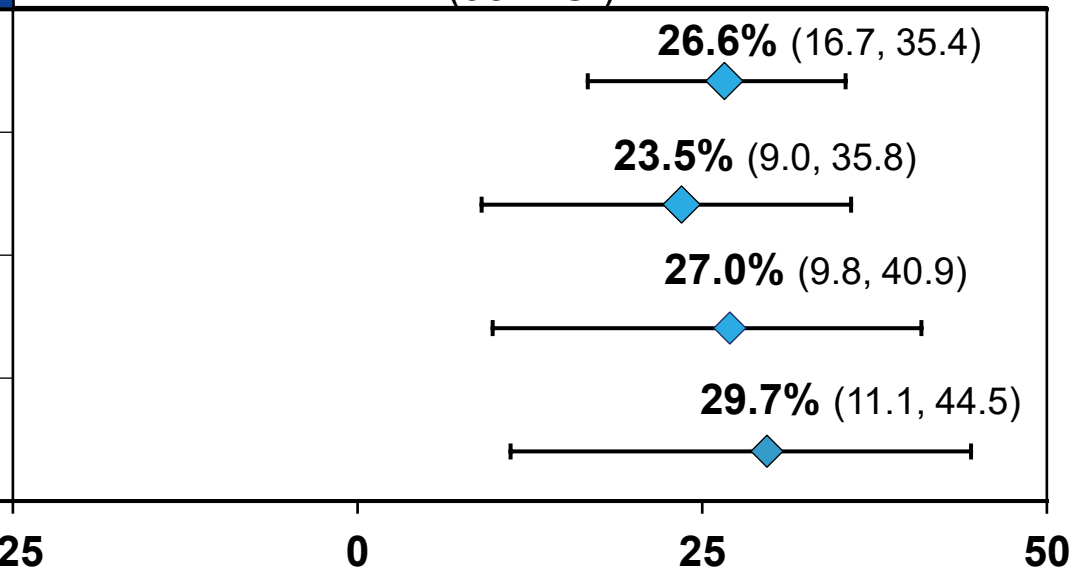
CI, confidence interval; LB, lower bound; RT-PCR, reverse transcription polymerase chain reaction; SD, standard dose

Leroux-Roels I et al. N Engl. J. Med, 2026

Adults ≥50 Years: Relative Vaccine Efficacy Favorable for mRNA-1010 vs Licensed SD Influenza Vaccine Regardless of Influenza-like Illness (ILI) Definition

Study 304 - Per-Protocol Set

Adults with ILI by Definition, N [%]	mRNA-1010 N = 20,179	Licensed SD Influenza Vaccine N = 20,124	Relative Vaccine Efficacy (%) (95% CI)
Protocol-defined ILI	**411** [2.0%]	**557** [2.8%]	**26.6%** (16.7, 35.4)
Modified CDC-defined ILI	**223** [1.1%]	**290** [1.4%]	**23.5%** (9.0, 35.8)
CDC-defined ILI	**149** [0.7%]	**203** [1.0%]	**27.0%** (9.8, 40.9)
WHO-defined ILI	**118** [0.6%]	**167** [0.8%]	**29.7%** (11.1, 44.5)

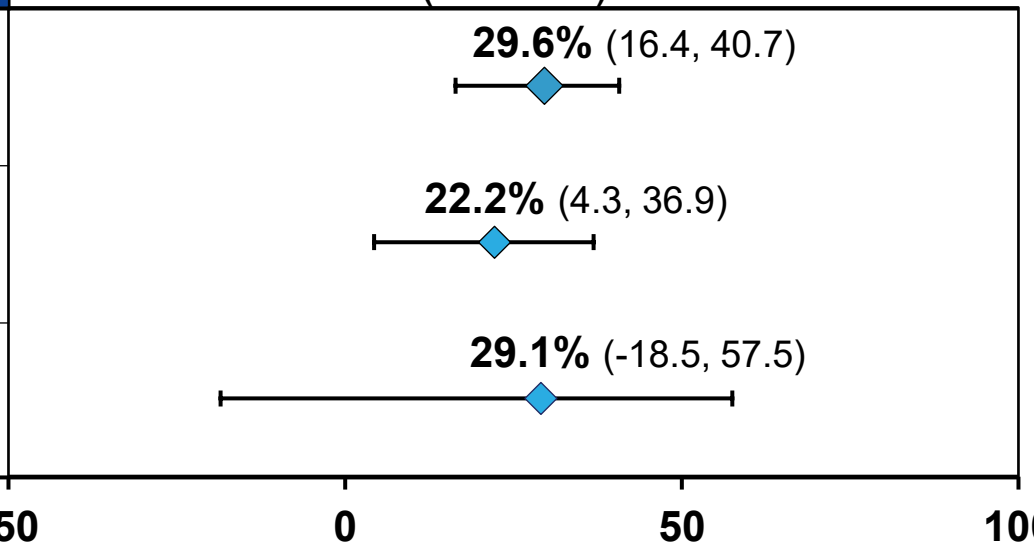


All cases of ILI required RT-PCR confirmation within 7 days of illness onset.

Adults ≥50 Years: Relative Vaccine Efficacy Favorable for mRNA-1010 vs Licensed SD Influenza Vaccine Across Influenza Strains

Study 304 - Influenza-Like Illness (ILI) Events - Per-Protocol Set

Adults with ILI[1] by influenza strain, N [%]	mRNA-1010 N = 20,179	Licensed SD Influenza Vaccine N = 20,124	Relative Vaccine Efficacy (%) (95% CI)
Influenza A H1N1	223 [1.1%]	315 [1.6%]	**29.6%** (16.4, 40.7)
Influenza A H3N2	158 [0.8%]	202 [1.0%]	**22.2%** (4.3, 36.9)
Influenza B Victoria	25 [0.1%]	35 [0.2%]	**29.1%** (-18.5, 57.5)



1. Based on RT-PCR-confirmed protocol-defined ILI

Influenza B Relative Vaccine Efficacy (rVE) for mRNA-1010 Consistent with rVE for Enhanced Vaccines in Clinical Trials

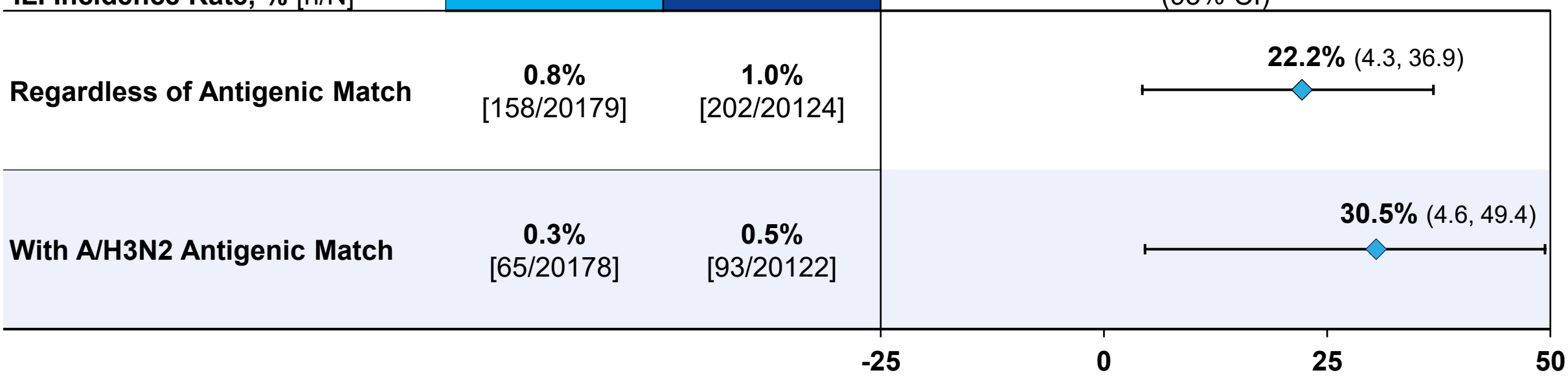
Investigational Influenza Vaccine	Licensed Standard Dose (SD) Vaccine Comparator	Number of Influenza B Cases	rVE (95% CI)	Age of Study Population
mRNA-1010[1]	**Fluarix SD**	**60**	**29.1%** (-18.5, 57.5)	**≥50**
Fluzone HD[2] High dose	**Fluzone SD**	**89**	**25.5%** (-15.7, 52.4)	**≥65**
FluBlok[3] Recombinant	**Fluarix SD**	**47**	**4%** (-72, 46)	**≥50**

1. Leroux-Roels I, et al. N Engl J Med, 2026; 2. DiazGranados CA et al, New Engl J Med, 2014; 3. Dunkle LM et al. New Engl J Med, 2017.

Adults ≥50 Years: Relative Vaccine Efficacy of mRNA-1010 vs Licensed SD Influenza Vaccine With Antigenic Match for A/H3N2

Study 304 - Influenza-like-illness (ILI) events – Per-Protocol Set

ILI Incidence Rate, % [n/N]	mRNA-1010	Licensed SD Influenza Vaccine	Relative Vaccine Efficacy (%) (95% CI)
Regardless of Antigenic Match	**0.8%** [158/20179]	**1.0%** [202/20124]	**22.2%** (4.3, 36.9)
With A/H3N2 Antigenic Match	**0.3%** [65/20178]	**0.5%** [93/20122]	**30.5%** (4.6, 49.4)



All cases of ILI required RT-PCR confirmation within 7 days of illness onset.

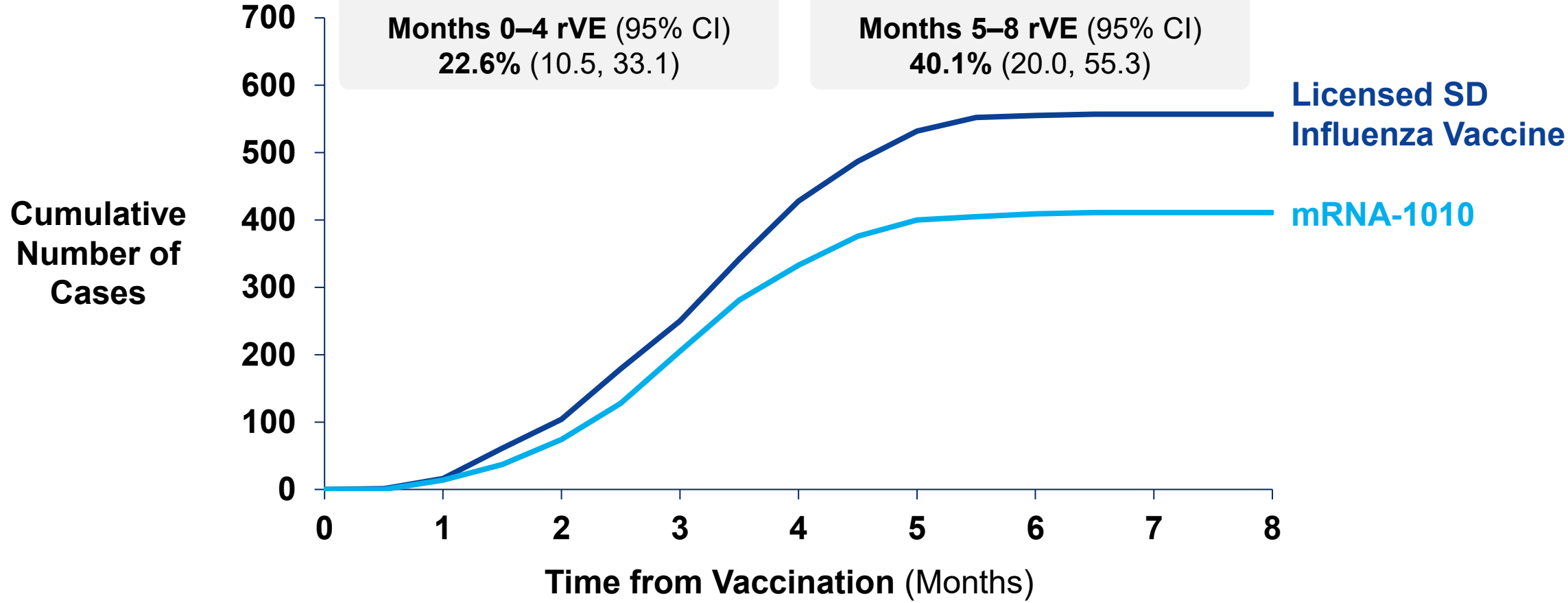
Adults ≥50 Years: mRNA-1010 Demonstrates Sustained Relative Vaccine Efficacy (rVE) Throughout 2024-2025 Influenza Season

Study 304

Overall rVE (95% CI) = **26.6%** (16.7, 35.4)

Months 0–4 rVE (95% CI)
22.6% (10.5, 33.1)

Months 5–8 rVE (95% CI)
40.1% (20.0, 55.3)



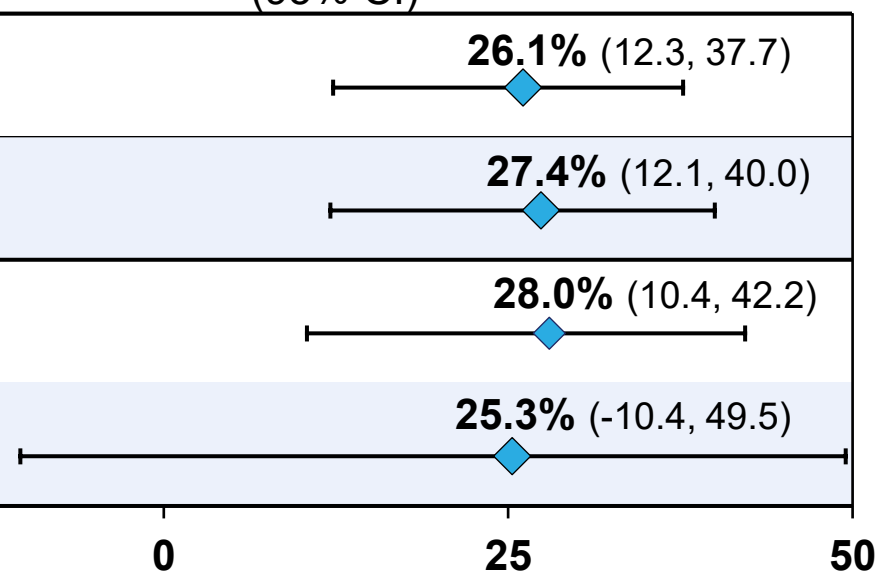
Licensed Influenza Vaccine	At Risk	20124	19871	19663	19383	19027	18774	10098	1932	0
	Events	0	16	104	250	428	532	555	557	557
mRNA-1010	At Risk	20179	19930	19765	19506	19151	18925	10180	1962	0
	Events	0	14	74	205	333	400	409	411	411

*Per Protocol-defined Influenza-like illness (ILI): all cases required RT-PCR confirmation within 7 days of illness onset

Relative Vaccine Efficacy Favorable for mRNA-1010 vs Licensed SD Influenza Vaccine Regardless of Age

Study 304 - Influenza Like Illness (ILI) Events - Per-Protocol Set

Participants with ILI[1] by age, % [n/N]	mRNA-1010	Licensed SD Influenza Vaccine	Relative Vaccine Efficacy (%) (95% CI)
50-64 Years	**2.2%** [229/10542]	**2.9%** [307/10501]	**26.1%** (12.3, 37.7)
≥65 Years	**1.9%** [182/9637]	**2.6%** [250/9623]	**27.4%** (12.1, 40.0)
65-74 Years	**1.9%** [138/7307]	**2.6%** [191/7289]	**28.0%** (10.4, 42.2)
≥75 Years	**1.9%** [44/2330]	**2.5%** [59/2334]	**25.3%** (-10.4, 49.5)



1. Based on RT-PCR-confirmed protocol-defined ILI regardless of influenza strain

Adults ≥50 Years: Similar Relative Vaccine Efficacy Demonstrated Regardless of Receipt of Influenza Vaccine in Previous Influenza Season

Study 304 – Influenza-like-illness (ILI) Events – Per-Protocol Set

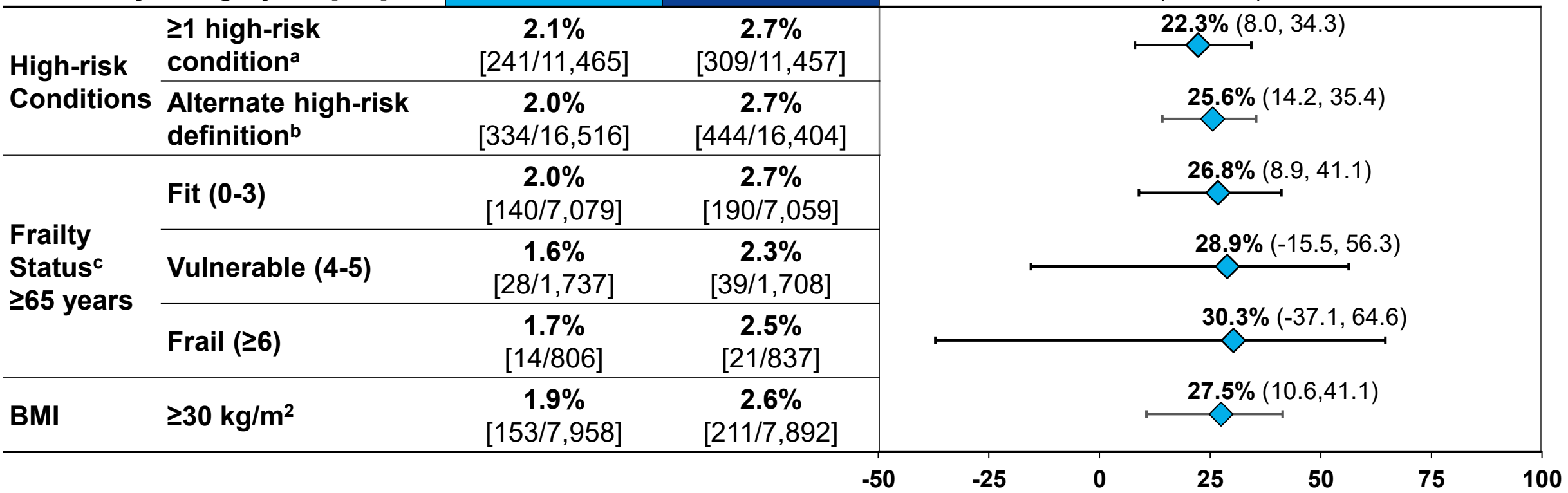
Participants with ILI[1] by category, % [n/N]	mRNA-1010	Licensed SD Influenza Vaccine	Relative Vaccine Efficacy (%) (95% CI)
Overall	**2.0%** [411/20179]	**2.8%** [557/20124]	**26.6%** (16.7, 35.4)
Influenza Vaccine in Prior Season			
Received	**2.5%** [238/9456]	**3.4%** [316/9421]	**25.2%** (11.5, 36.8)
Did Not Receive	**1.6%** [173/10723]	**2.3%** [241/10703]	**28.6%** (13.2, 41.3)

1.Based on RT-PCR-confirmed protocol-defined ILI regardless of influenza strain

Adults ≥50 Years: Relative Vaccine Efficacy Favorable for mRNA-1010 in Individuals with High-Risk Conditions and Frailty

Study 304 – Influenza-like illness (ILI) events – Per-Protocol Set

Adults with ILI by Category, % [n/N]		mRNA-1010	Licensed SD Influenza Vaccine	Relative Vaccine Efficacy, (%) (95% CI)
High-risk Conditions	≥1 high-risk condition[a]	**2.1%** [241/11,465]	**2.7%** [309/11,457]	**22.3%** (8.0, 34.3)
	Alternate high-risk definition[b]	**2.0%** [334/16,516]	**2.7%** [444/16,404]	**25.6%** (14.2, 35.4)
Frailty Status[c] ≥65 years	Fit (0-3)	**2.0%** [140/7,079]	**2.7%** [190/7,059]	**26.8%** (8.9, 41.1)
	Vulnerable (4-5)	**1.6%** [28/1,737]	**2.3%** [39/1,708]	**28.9%** (-15.5, 56.3)
	Frail (≥6)	**1.7%** [14/806]	**2.5%** [21/837]	**30.3%** (-37.1, 64.6)
BMI	≥30 kg/m²	**1.9%** [153/7,958]	**2.6%** [211/7,892]	**27.5%** (10.6,41.1)

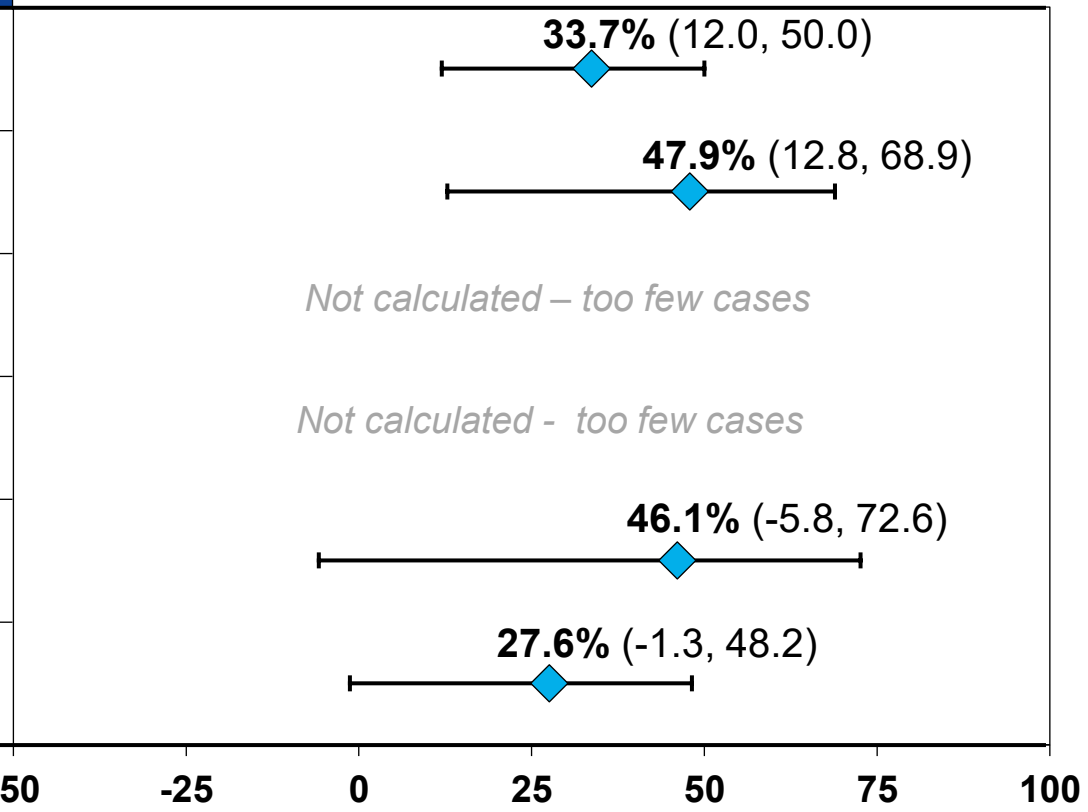


a. High-risk conditions: BMI ≥30 kg/m², diabetes, pulmonary disorders, cardiac disorders, nervous systems disorders and other CDC defined risk factors.
b. Alternate high-risk definition also includes arthritis, non-skin cancers, depression, hypertension, hyperlipidemia (Watson KG et al. Prev Chronic Dis, 2025)
c. Frailty based on Edmonton Frail Scale; score only available for participants ≥65 years

Adults ≥50 Years: Exploratory Analysis Suggests mRNA-1010 Prevented More Medically-Attended Illness

Study 304 – Influenza-like illness (ILI) events – Per-Protocol Set

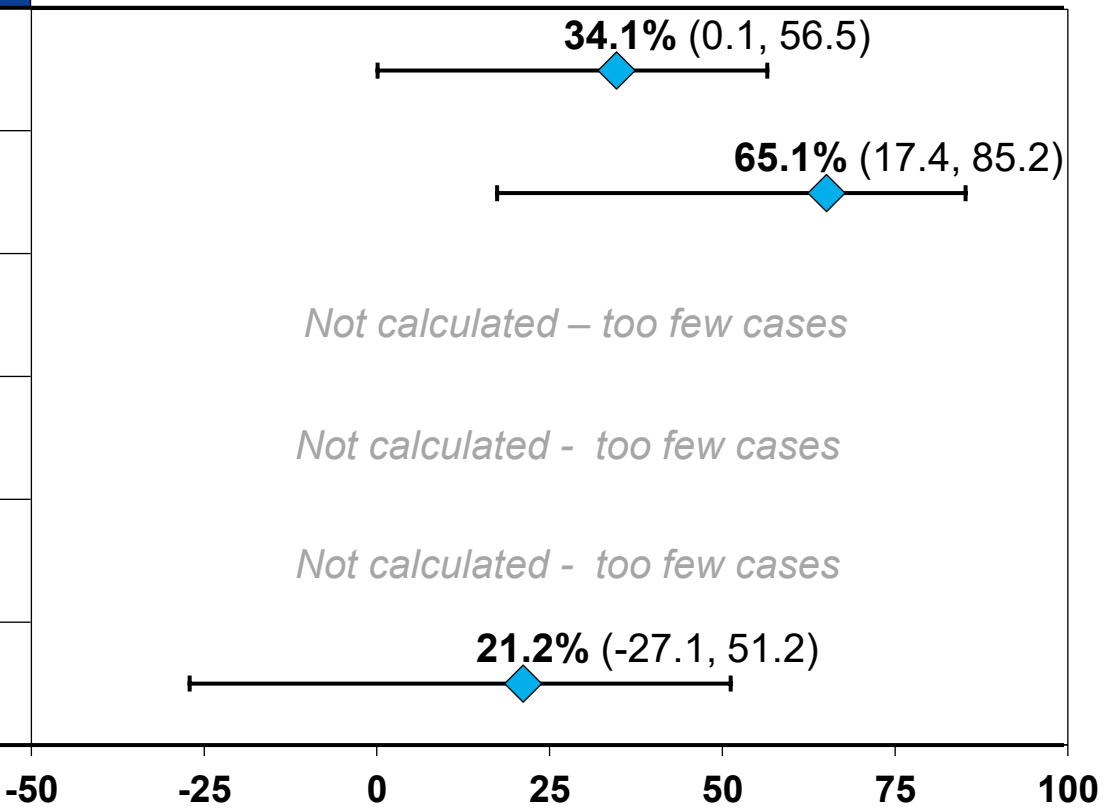
Healthcare encounters associated w/ RT-PCR confirmed protocol-defined ILI, N [%]		mRNA-1010 N = 20,179	Licensed SD Influenza Vaccine N = 20,214	Relative Vaccine Efficacy (%) (95% CI)
Any healthcare encounter Attributable to laboratory-confirmed influenza		**80** [0.4%]	**120** [0.6%]	**33.7%** (12.0, 50.0)
Seeking a Higher Level of Care	**Any Higher-Level Encounter**	**22** [0.11%]	**42** [0.21%]	**47.9%** (12.8, 68.9)
	Hospitalization	**4** [0.02%]	**8** [0.04%]	*Not calculated – too few cases*
	ER visit	**6** [0.03%]	**12** [0.06%]	*Not calculated - too few cases*
	Urgent care visit	**13** [0.06%]	**24** [0.12%]	**46.1%** (-5.8, 72.6)
Outpatient Clinic Visit		**59** [0.29%]	**81** [0.40%]	**27.6%** (-1.3, 48.2)



Adults ≥65 Years: Exploratory Analysis Suggests mRNA-1010 Prevented More Medically-Attended Illness

Study 304 - Influenza-like illness (ILI) events - Per-Protocol Set

Healthcare encounters associated w/ RT-PCR confirmed protocol-defined ILI, N [%]		mRNA-1010 N = 9,637	Licensed SD Influenza Vaccine N = 9,623	Relative Vaccine Efficacy (%) (95% CI)
Any healthcare encounter Attributable to laboratory-confirmed influenza		**37** [0.38%]	**56** [0.58%]	**34.1%** (0.1, 56.5)
Seeking a Higher Level of Care	**Any Higher-Level Encounter**	**7** [0.07%]	**20** [0.21%]	**65.1%** (17.4, 85.2)
	Hospitalization	**1** [0.01%]	**4** [0.04%]	*Not calculated – too few cases*
	ER visit	**1** [0.01%]	**5** [0.05%]	*Not calculated - too few cases*
	Urgent care visit	**5** [0.05%]	**12** [0.12%]	*Not calculated - too few cases*
Outpatient Clinic Visit		**30** [0.31%]	**38** [0.39%]	**21.2%** (-27.1, 51.2)

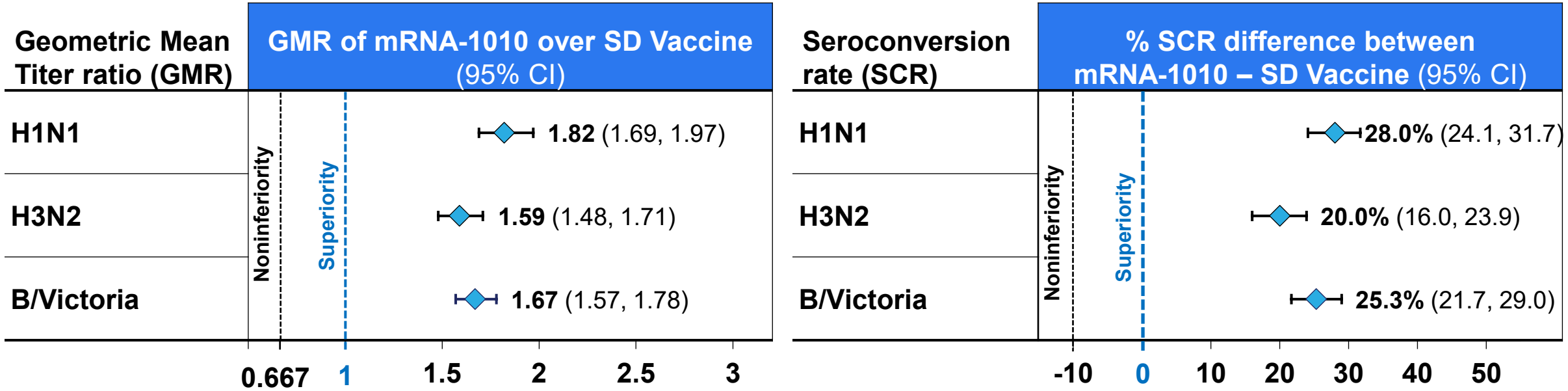


Immunogenicity Data – Phase 3 Efficacy Trial

Study 304

Adults ≥50 Years: mRNA-1010 Elicited Higher Day 29 HAI Levels Compared to Licensed SD Influenza Vaccine (GMR and SCR Difference)

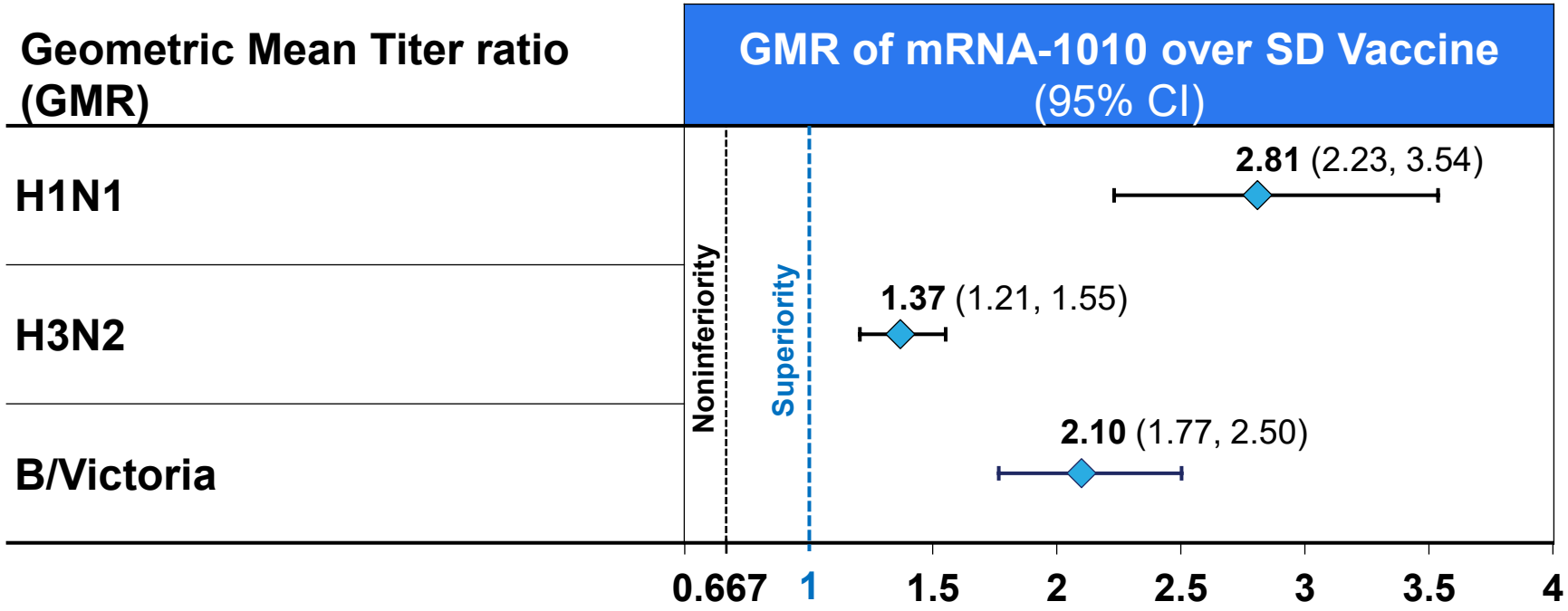
Study 304 – Per-Protocol Immunogenicity Subset (N = 2,342)



GMR – Ratio of mean titer of mRNA-1010 over mean titer for SD vaccine; SCR defined as either baseline HAI titer < 1:10 and post-baseline titer ≥ 1:40 or baseline HAI titer ≥ 1:10 and minimum 4-fold rise in post-baseline HAI antibody titer.
SD – standard dose licensed influenza vaccine; mRNA-1010, n = 1167; licensed SD vaccine, n = 1175.
GMR and corresponding 95% CI obtained by transforming least square mean estimate and CI back to original scale for presentation
Malkin E et al., IDWeek 2025

Adults ≥50 Years: mRNA-1010 Elicited Higher Day 29 Microneutralization (MN) GMT at Day 29 Compared to Licensed SD Influenza Vaccine

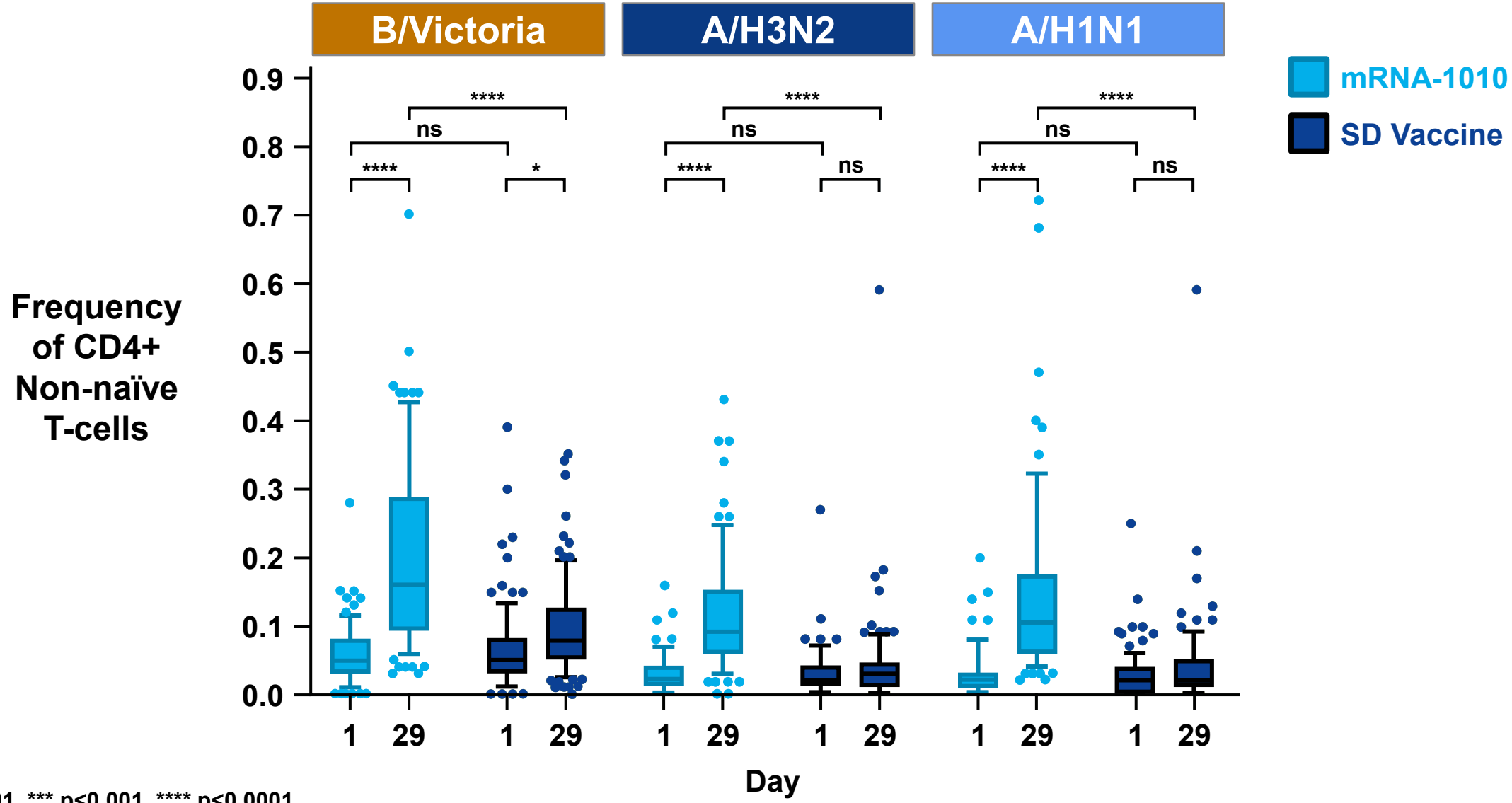
Study 304 – Per-Protocol Immunogenicity Subset – MN Subset (N = 500)



GMR – Ratio of mean titer of mRNA-1010 over mean titer for SD vaccine
SD – standard dose licensed influenza vaccine; mRNA-1010, n = 247; licensed SD vaccine, n = 253.
GMT, GMR, and corresponding 95% CI obtained by transforming least square mean estimate and CI back to original scale for presentation

Adults ≥50 Years: mRNA-1010 Induced Robust Polyfunctional, Antigen-Specific CD4+ T-cell Responses

Study 304



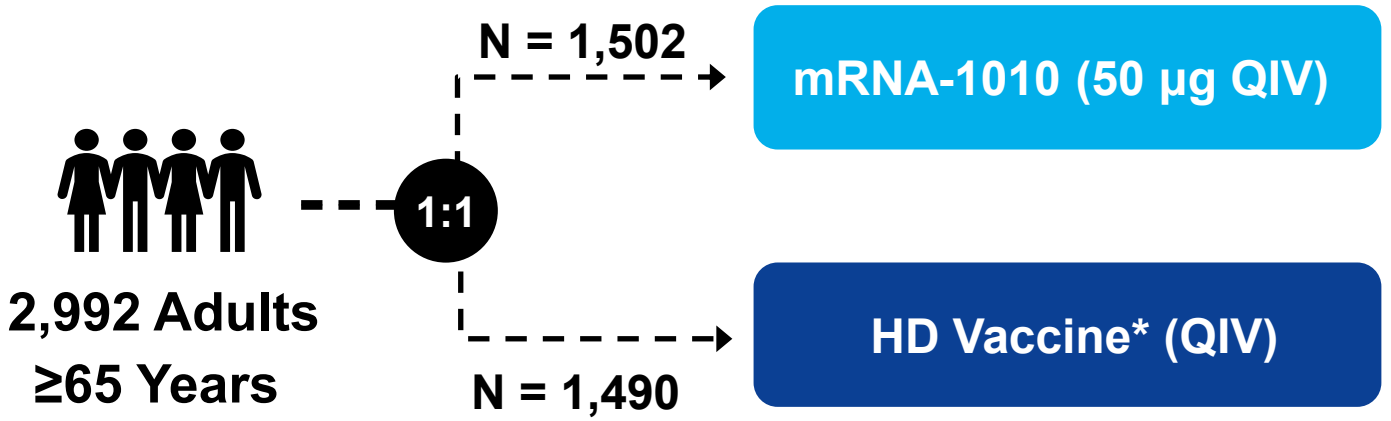
* p<0.05, **p<0.01, *** p<0.001, **** p<0.0001

Immunogenicity and Persistence of Antibody of mRNA-1010 vs High Dose Influenza Vaccine in Adults ≥65 Years

Study 303, Part C

Adults ≥65 Years: Study Design – Safety and Immunogenicity of mRNA-1010 vs Fluzone High Dose (HD)

Study 303, Part C: Randomized, Double-blind, Active-controlled Phase 3 Trial in US



- Non-inferiority and superiority assessed
- Follow up through 6 months (median 171 days)

Clinicaltrials.gov/study/NCT05827978
*HD Vaccine - Fluzone HD, licensed high dose influenza vaccine (4x antigen of standard dose influenza vaccine)
QIV - Quadrivalent influenza vaccine

Study Objectives

Study 303, Part C

Primary Objectives

- Non-inferiority of mRNA-1010 immune response vs HD QIV against 4 vaccine-matched influenza virus A and B strains at Day 29
- Safety and reactogenicity of mRNA-1010

Key Secondary Objective

- Superiority of mRNA-1010 immune response vs HD QIV against vaccine-matched influenza A and B strains at Day 29

HD = High dose influenza vaccine; QIV = Quadrivalent influenza vaccine

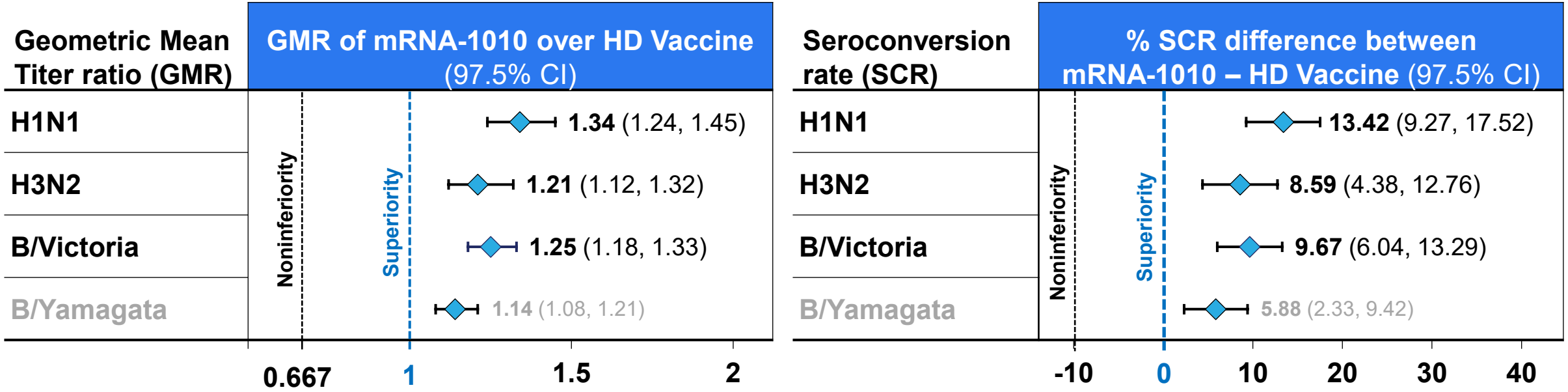
Adults ≥65 Years: Demographics and Baseline Characteristics Balanced Between Groups

Study 303, Part C – Safety Set

		mRNA-1010 (N = 1,502)		Licensed HD Influenza Vaccine (N = 1,490)	
Median Age, years		**70.0**		**70.0**	
Age Group, % (n)	**50 - 64 Years**	0	0	**<0.1%**	1
	65 - 74 Years	**78.3%**	1,176	**77.4%**	1,154
	≥75 Years	**21.7%**	326	**22.5%**	335
Male, % (n)		**41.5%**	624	**42.8%**	638
Vaccinated Previous Influenza Season, % (n)		**52.4%**	787	**52.8%**	787
North American participants, % (n)		**100%**	1,502	**100%**	1,490
Race/Ethnicity, % (n)	**White**	**83.6%**	1,255	**81.9%**	1,220
	Black or African American	**14.9%**	234	**15.8%**	235
	Asian	**0.7%**	10	**0.7%**	10
	Hispanic / Latino Ethnicity	**30.0%**	450	**30.5%**	454
Baseline Frail/High-risk Conditions, % (n)		**37.7%**	567	**40.7%**	607

Adults ≥65 Years: mRNA-1010 Demonstrated Superior HAI Immunogenicity Over HD Influenza Vaccine in (Day 29)

Study 303, Part C

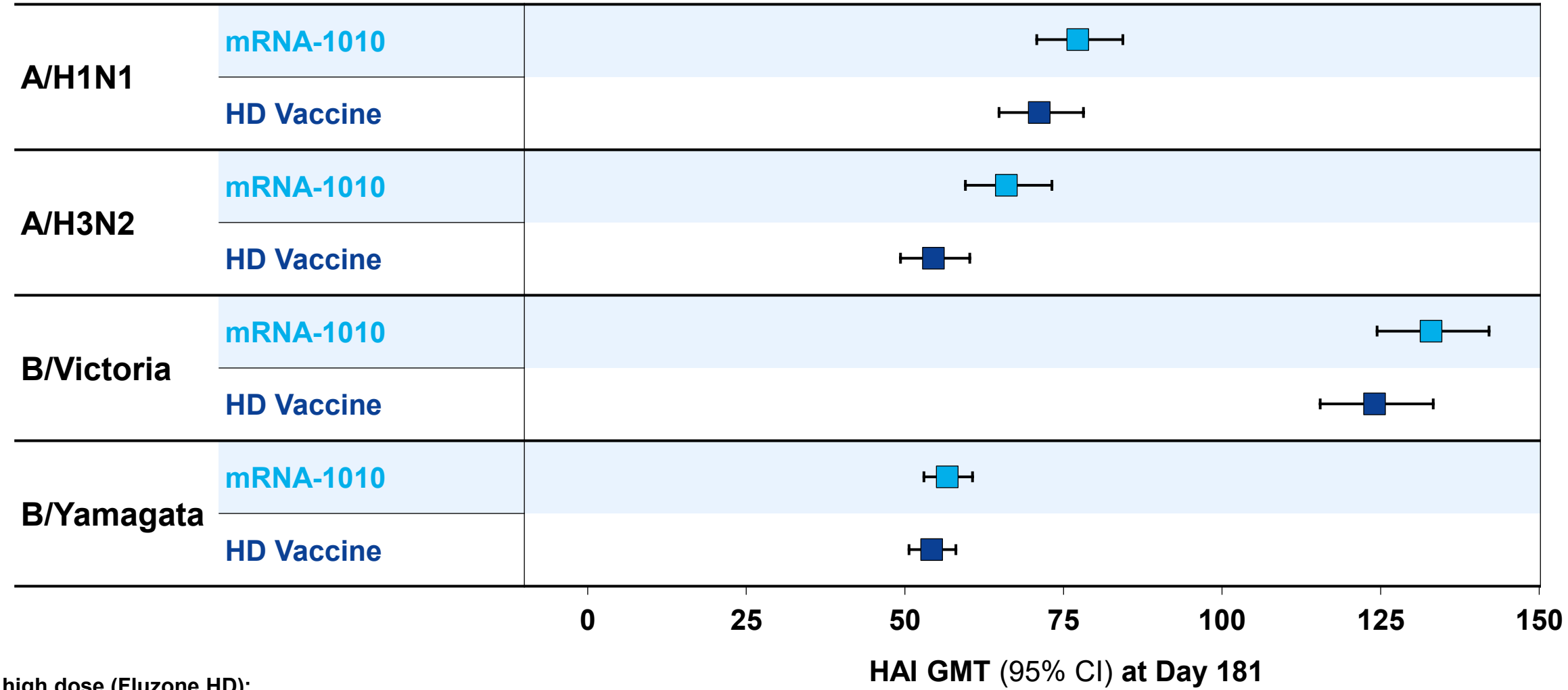


- Superiority was demonstrated for all 8 HAI immunogenicity endpoints (secondary objective)
  - GMR: Lower bound of 97.5% CI > 1 for all 4 strains
  - SCR difference: Lower bound of 97.5% CI > 0 for all 4 strains

GMR – Ratio of mean titer of mRNA-1010 over mean titer for SD vaccine; Seroconversion is defined as either a baseline HAI titer < 1:10 and a post-baseline titer ≥ 1:40 or a baseline HAI titer ≥ 1:10 and a minimum 4-fold rise in post-baseline HAI antibody titer.
mRNA-1010 (N=1425) & high dose (HD) vaccine (Fluzone) (N=1409) were both quadrivalent Influenza Vaccine (QIV)
GMR and corresponding 95% CI obtained by transforming least square mean estimate and CI back to original scale for presentation

Adults ≥65 Years: mRNA-1010 Elicited Persistent HAI Antibody Response Consistent with HD Influenza Vaccine Over 6 Months

Study 303, Part C - Day 181 Per-protocol Immunogenicity Set (N ~450 per Group)



HD – high dose (Fluzone HD);
HAI - hemagglutination inhibition

Adults ≥50 Years: Summary of Efficacy and Immunogenicity of mRNA-1010 Influenza Vaccine

Relative Vaccine Efficacy (rVE)

- rVE of 26.6% (95% CI: 16.7, 35.4) vs licensed SD influenza vaccine
- Met most stringent prespecified efficacy success criterion (p=0.0005)
- Consistent rVE by strain, age, vaccination history, high-risk conditions, ILI definition, and frailty status
- Durable protection through end of Northern Hemisphere influenza season
- Prevented more influenza-associated medically-attended illness (47.9% rVE [95% CI: 12.8, 68.9])
- Efficacy consistent with that of enhanced influenza vaccines

Immunogenicity

- Higher immunogenicity vs SD and HD influenza vaccines across influenza A and B strains
- HAI and microneutralization strongly associated with efficacy at group level, CMI responses also observed
- HAI titers sustained over time and remained higher with mRNA-1010 than with HD comparator

HAI – hemagglutination inhibition
ILI – influenza-like illness; rVE – relative vaccine efficacy; SD – standard dose; HD – high dose; CMI – cell-mediated immunity

Clinical Safety

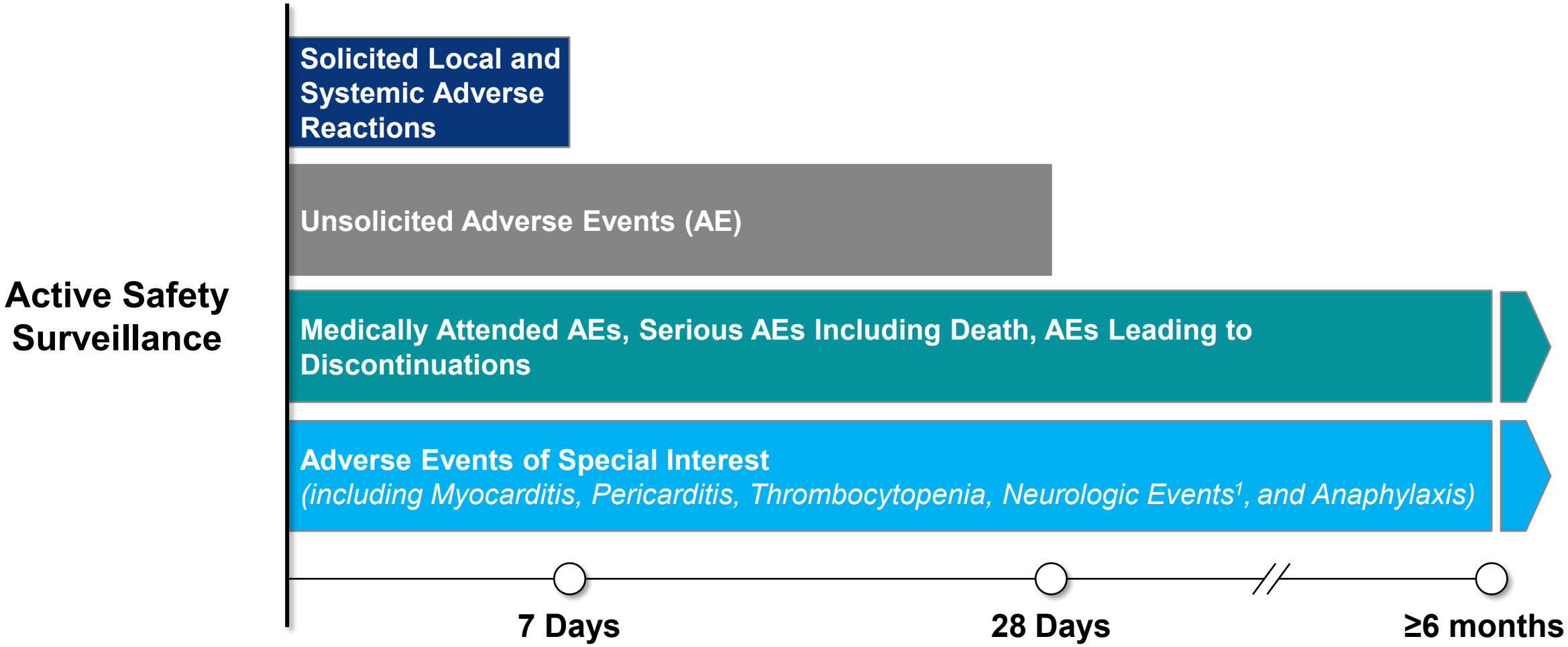
Eleanor Wilson, MD, MHS

Executive Director, Clinical Development

Moderna, Inc.

Primary Safety Endpoints and Duration of Follow-Up

mRNA-1010



1. Includes Guillain-Barre syndrome, acute disseminated encephalomyelitis, Bell's palsy, and seizures

Safety Data – Phase 3 Efficacy Trial

Study 304

Safety Set

~6 months follow-up (Day 184)

Safety Assessments

Study 304

Electronic Diary (eDiary)

Subset of 6012 participants

- **Solicited adverse reactions**
  - Day 1 to Day 7

Safety Follow-up at Subsequent Visits / Phone Contacts

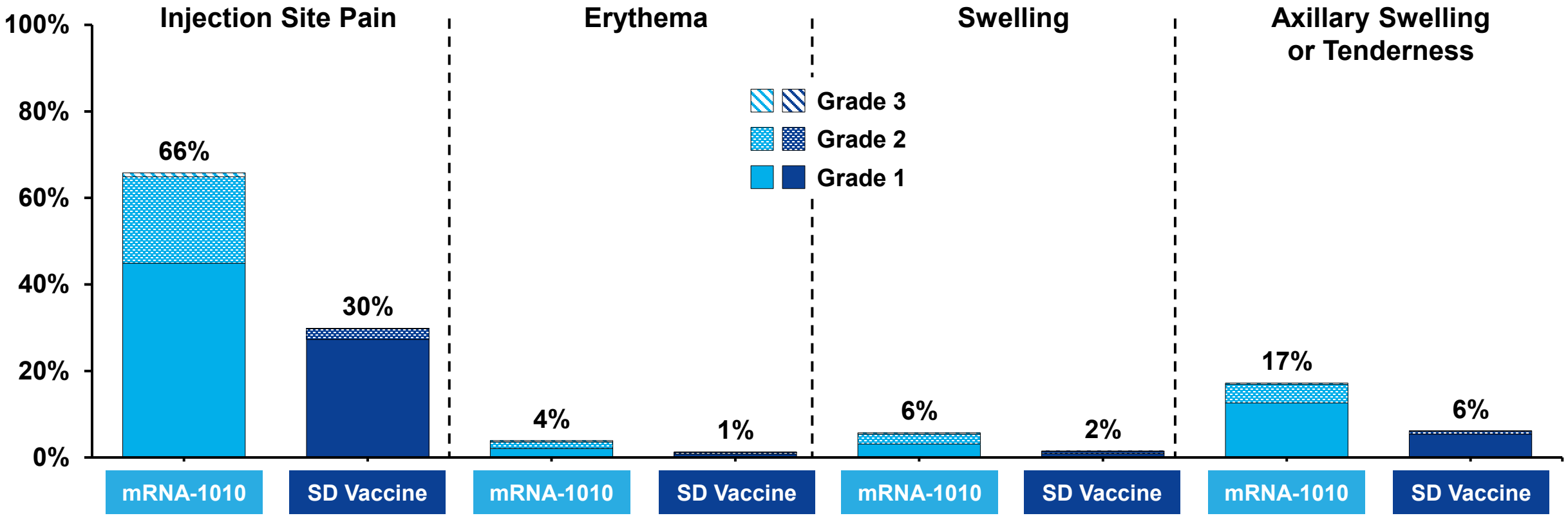
All 40,703 study participants

- **Unsolicited adverse events**
  - Day 1 to Day 28
- **Medically Attended AEs, AESI, SAEs**
  - Through Day 181

AE – adverse event; AESI – adverse event of special interest; SAE – serious adverse event

Adults ≥50 Years: Solicited Local Reactions More Frequent with mRNA-1010; Most Grade 1 or 2, Median Duration 2 Days

Study 304 – mRNA-1010 TIV – Solicited Safety Set

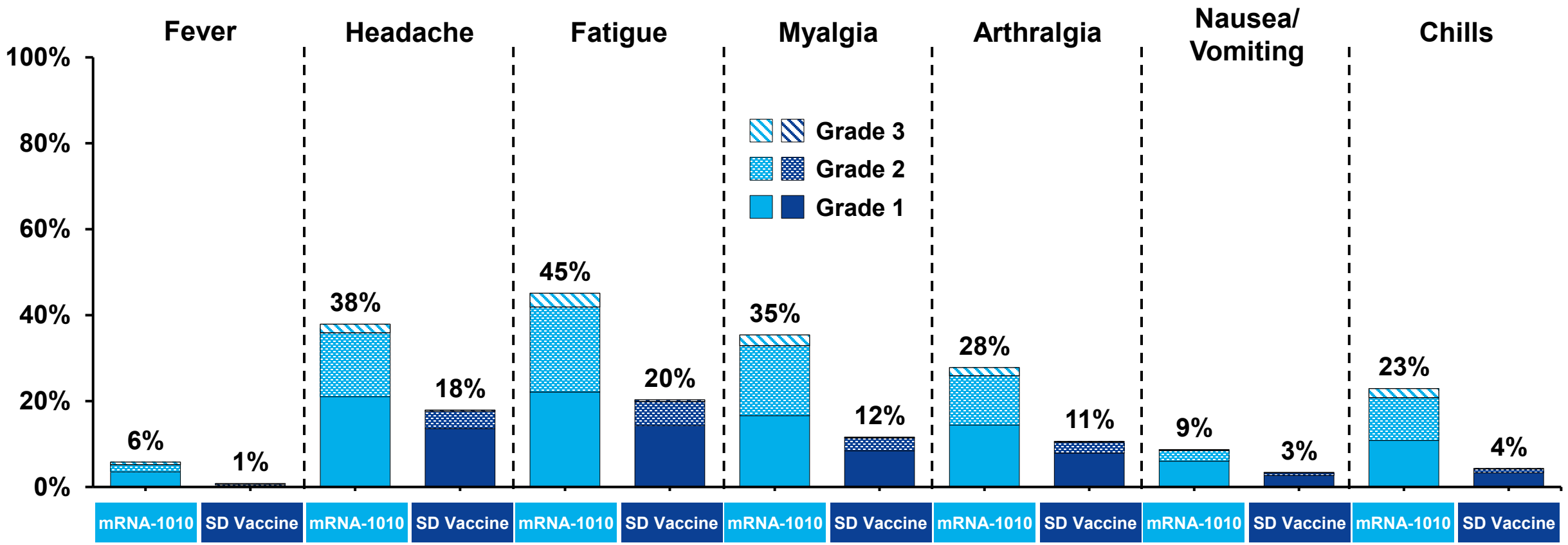


- No Grade 4 reactions; Grade 3 reactions transient and did not require medical attention
- Fewer reactions reported by participants ≥65 years in both groups, pattern remained similar

mRNA-1010, N = 3015; Licensed SD influenza vaccine N = 2997

Adults ≥50 Years: Solicited Systemic Reactions More Frequent with mRNA-1010; Most Grade 1 or 2, Median Duration 2 Days

Study 304 – mRNA-1010 TIV – Solicited Safety Set



- No Grade 4 reactions; Grade 3 reactions transient and did not require medical attention
- Fewer reactions reported by participants ≥65 years in both groups, pattern remained similar

mRNA-1010, N = 3015; Licensed SD influenza vaccine N = 2997

Adults ≥50 Years: Unsolicited Adverse Events Through 28 Days After Injection, Regardless of Relationship, Were Balanced Between Groups

Study 304 – mRNA-1010 TIV – Safety Set

	mRNA-1010 (N = 20,350)		Licensed SD Influenza Vaccine (N = 20,353)	
All Unsolicited AEs, % (n)	**5.9%**	1,204	**5.7%**	1,167
Serious	**0.5%**	92	**0.5%**	92
Fatal	**<0.1%**	7	**<0.1%**	9
Medically attended	**3.8%**	775	**3.8%**	782
Leading to study discontinuation	**<0.1%**	1	**0**	0
Any AE of Special Interest (AESI)	**<0.1%**	4	**<0.1%**	3

Frequency of unsolicited AEs remains balanced through Day 181

SD - standard dose

Safety Data – Phase 3 Trial of mRNA-1010 vs High Dose Influenza Vaccine in Adults ≥65 Years

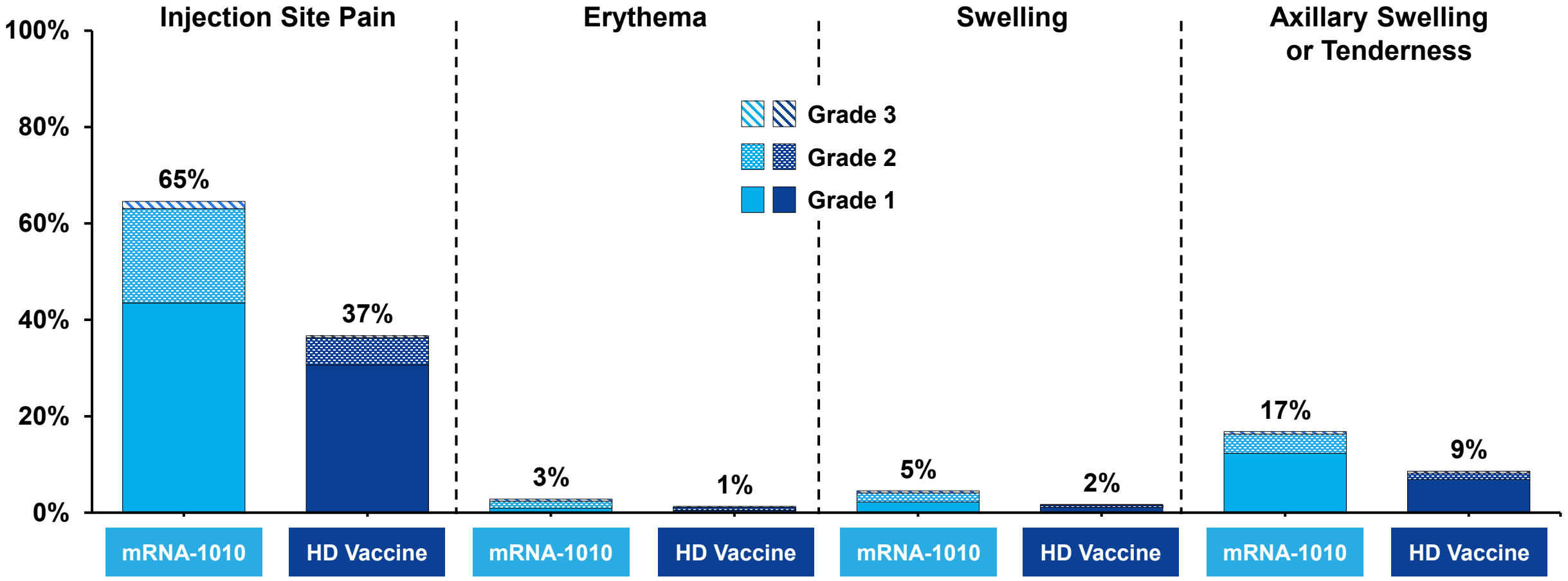
Study 303, Part C

Safety Set

Median ~6 months (171 days) follow-up

Adults ≥65 Years: Solicited Local Reactions More Frequent with mRNA-1010; Most Grade 1 or 2, Median Duration 2 Days

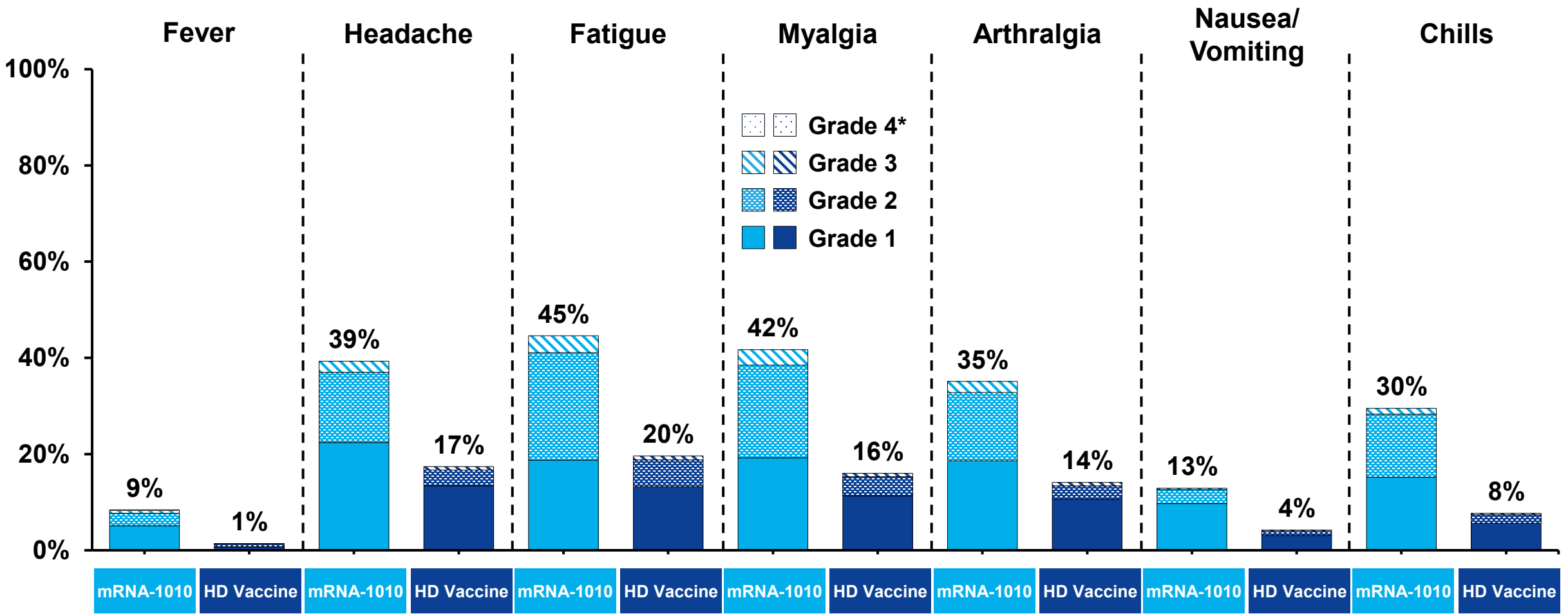
Study 303, Part C – mRNA-1010 QIV – Solicited Safety Set



mRNA-1010: N=1502 and HD vaccine: N=1490; HD = high-dose influenza vaccine, quadrivalent (Fluzone);

Adults ≥65 Years: Solicited Systemic Reactions More Frequent with mRNA-1010; Most Grade 1 or 2, Median Duration 2 Days

Study 303, Part C – mRNA-1010 QIV – Solicited Safety Set



mRNA-1010: N=1502 and HD vaccine: N=1490

*2 recipients of QIV mRNA-1010 reported Grade 4 fever on Day 2 or 3; 1 day duration; no medical attention sought

HD = high-dose influenza vaccine, quadrivalent (Fluzone);

Adults ≥65 Years: Incidence of Unsolicited AEs Through 28 Days After Injection, Regardless of Relationship, Balanced Between Groups

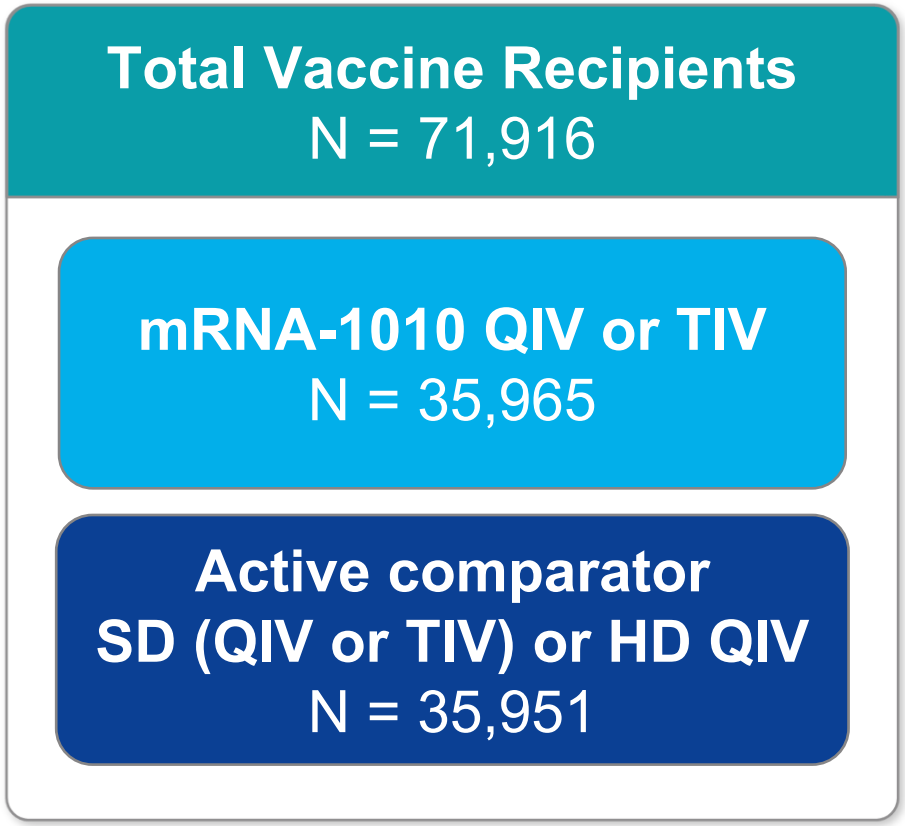
Study 303, Part C

	mRNA-1010 (N = 1,502)		Licensed HD Influenza Vaccine (N = 1,490)	
All unsolicited AEs	**10.3%**	155	**9.2%**	137
Serious	**0.6%**	9	**0.5%**	7
Fatal	**<0.1%**	1*	0	0
Medically attended	**5.9%**	89	**5.6%**	84
Leading to study discontinuation	0	0	0	0
AE of Special Interest	**<0.1%**	1	0	0

*** Assessed as unrelated to study injection by study investigator**
HD – High dose influenza vaccine; quadrivalent (Fluzone)

Adults ≥50 Years: Integrated Summary of Safety >71,000 Participants Across 4 Phase 3 Trials

Studies 301, 302, 303, and 304



Safety Data Pooled

- Analyzed throughout the study
  - Deaths
  - Serious adverse events (SAEs)
  - Adverse events of special interest (AESI)

QIV – quadrivalent influenza vaccine; TIV – trivalent influenza vaccine; HD – high dose vaccine; SD – standard dose vaccine

Adults ≥50 Years: No Safety Concerns Identified in Integrated Safety Analysis of >71,000 Vaccine Recipients – Through Day 28

Studies 301, 302, 303, and 304

	mRNA-1010 (N = 35,965)		Licensed SD or Licensed HD Influenza Vaccine (N = 35,951)	
Serious adverse events (SAEs)	**0.5%**	180	**0.5%**	163
Fatal SAEs	**<0.1%**	13	**<0.1%**	14
AE of Special Interest (AESI)	**<0.1%**	7	**<0.1%**	4

- **Frequency of SAEs, Fatal SAEs, and AESIs were balanced**
- **Results similar through Day 181 (6 months)**
- **Subgroup analysis by age (50-64 years, ≥65 years) did not suggest any patterns or concerns**

HD – high dose; SD – standard dose

Adults ≥50 Years: mRNA-1010 Demonstrated Acceptable Safety Profile Relative to SD and HD Influenza Vaccines

- **Higher rates of solicited local and systemic adverse reactions than SD or HD influenza vaccines**
  - Most grade 1 or 2 in severity
  - Resolved within 2 days without medical attention
  - Injection site pain, fatigue, and headache most common
- **Similar incidence of MAAEs, SAEs, Fatal SAEs, and AESIs between mRNA-1010 and SD/HD influenza vaccines**
- **Acceptable safety profile for adults 50-64 and ≥65 years**

SD – standard dose; HD – high dose
SAE – serious adverse event; MAAE – medically attended adverse event
Adverse Event of Special Interest (AESI) includes myocarditis, pericarditis, thrombocytopenia, neurologic events, and anaphylaxis

Benefit-Risk and Summary

Rituparna Das, MD, PhD

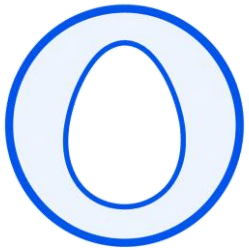
Senior Vice President, Clinical Development,
Infectious and Rare Diseases

Moderna, Inc.

mRNA-1010 Was Designed to Address Persistent Challenges in Influenza Prevention

Manufacturing Timelines

Antigenic Drift



Egg Adaptation

Strain Mismatch

Vulnerabilities of Licensed Influenza Vaccines

mRNA-1010

- Encodes selected HA antigens
- Avoids egg-based manufacturing
- Provides flexibility of mRNA platform

Potential to improve protection against influenza and its significant morbidity and mortality

HA – hemagglutination inhibition

Moderna is Seeking Approval of One Vaccine, One Dose, for Adults ≥50 Years

1 Indication

Prevention of influenza A and B in individuals ≥50 years of age

1 Dose

Single dose, 0.38 mL prefilled syringe, administered IM

2 Pathways

Traditional approval in adults 50-64 years

Accelerated approval in adults ≥65 years

Overall benefit-risk profile supports approval of mRNA-1010 in adults ≥50 years

Totality of Evidence Supports a Positive Benefit-Risk Profile for mRNA-1010 in Adults ≥50 Years

26.6%

Relative Vaccine Efficacy vs SD in Adults ≥50

Primary Endpoint: PCR-confirmed ILI

EFFICACY	▪ Statistically superior efficacy vs SD vaccine ▪ Consistent across strains, age, and high-risk groups
IMMUNO-GENICITY	▪ Higher immune response vs SD vaccine ▪ Statistically superior immune responses vs HD vaccine in adults ≥65
SAFETY	▪ Acceptable safety profile; no safety concerns identified ▪ Reactogenicity transient; did not require medical attention
PUBLIC HEALTH	▪ Potential to reduce influenza burden beyond current licensed vaccines

ILI – influenza-like illness; SD – standard dose

mRNA-1010 Could Reduce Influenza Burden Through Improved Vaccine Efficacy and Platform Advantages

Clinical Evidence

1 Adults 50–64 years

- 26.1% rVE vs SD vaccine (Study 304)

2 Adults ≥65 years

- 27.4% rVE vs SD vaccine (Study 304)
- Supported by superior immune responses vs HD vaccine (Study 303C)

Platform Advantages

3 Potential for later strain selection

- Strain selection ~3 months later could improve vaccine match in 22% of seasons[1]
- Modeling study estimated this could avert ~5,000-65,000 US hospitalizations in a mismatch season[2]

4 Non-egg-based manufacturing

- Cell-based vaccines have a 7.7–19.8% higher relative vaccine effectiveness than egg based vaccines[3-5]

1. de Rooij, AJH et al. npj Vaccines, 2025; 2. Lee K, et al. J Infect Dis 2024; 3. Stein AN et al. IORV 2025; 4. Stein AN et al. Infect Dis Ther 2025; 5. Stein AN, et al. OFID, 2024; rVE- relative vaccine efficacy; SD – standard dose; HD – high dose

Planned US Real-World Effectiveness Study of mRNA-1010 will Generate Direct Comparative Data vs Enhanced Influenza Vaccines

Adults ≥65 years

Planned enrollment ~400,000 per season

R 1:1 RANDOMIZATION

mRNA-1010
N ~ 200,000 per season

Enhanced Licensed Vaccine*
N ~ 200,000 per season

- **Clinical follow-up:** Healthcare encounters, vaccinations, and relevant outcomes
- **Laboratory confirmation of influenza illness:** PCR
- **Study design:** Pragmatic, cluster-randomized, non-inferiority study within US-based integrated healthcare system across 2 seasons**

Primary Endpoint

- rVE against lab-confirmed **medically attended** influenza

Key Secondary Endpoints

- rVE in preventing lab-confirmed influenza associated with:
  - Urgent care, emergency department, and/or hospitalization (composite)
  - Hospitalization
- Assess primary and secondary objectives by lab-confirmed Influenza A and B (separately)

- **Moderna is committed to confirming the clinical benefit of mRNA-1010 versus enhanced influenza vaccines in adults ≥65 years**
- **Finalizing design in order to initiate study prior to licensure**

rVE – relative vaccine efficacy; *High dose, recombinant, or other enhanced vaccine; **An interim analysis after Season 1 will assess adequacy of endpoint accrual; if sufficient, the study may conclude after one season.

mRNA-1010 Benefit-Risk is Positive Across Both Regulatory Pathways

Traditional Approval
Adults 50 – 64 years

- **Medical need remains**
  Especially among high-risk individuals
- **Direct efficacy**
  vs licensed SD vaccine
- **Higher immune response**
  vs SD vaccine; supports clinical response
- **Acceptable safety profile**
  More reactogenicity, generally short-lived
- **mRNA platform benefits**
  Potential for improved strain match

Positive Benefit-Risk Profile

Accelerated Approval
Adults ≥65 years

- **Highest burden**
  Medical need remains despite enhanced vaccines
- **Superior immune response**
  vs HD vaccine comparator
- **Direct efficacy vs SD vaccine**
  In range of licensed enhanced vaccines
- **Acceptable safety profile**
  More reactogenicity, generally short-lived
- **Confirmatory RWE Study**
  vs enhanced vaccine
- **mRNA platform benefits**
  Potential for improved strain match

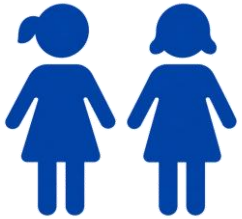
Positive Benefit-Risk Profile

SD – standard dose ; HD – high dose; RWE – real world effectiveness

Moderna is Committed to Generating Additional Clinical and Safety Data for mRNA-1010

Studies in Adults 18-49 Years

Data evaluating immune response and safety already generated[1-3]



Trials Planned to Fulfill Pediatric Study Plan

Dose-ranging study has started in children and adolescents 9–17 years

Pharmacovigilance

Ongoing safety assessment following licensure

1. Choi IT et al. Nature Communications, 2023; 2. Ananworanich J et al. J Infect Dis, 2025; 3. Soens M et al. Vaccine, 2025

Data Support Approval of mRNA-1010 for the Proposed Indication

mRNA-1010

Active immunization for the prevention of disease caused by influenza virus subtypes A and type B represented in the vaccine, in persons 50 years of age and older

Thank You

- Study investigators
- Study site personnel
- Data Safety Monitoring Board
- Most importantly, the study participants

Moderna Investigational Influenza Vaccine mRNA-1010 in Adults ≥50 Years

Moderna, Inc.

June 18, 2026

Vaccines and Related Biological Products Advisory Committee