Eliciting Preferences For Combination Vaccines Protecting Against Multiple Respiratory Viruses: A Cross-sectional Discrete Choice Experiment of Adults Aged 50+ in the US

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Disclosures

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CdC, **AR**, **DA**, **MB**, and **MT** are employees of Sanofi.

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Study Overview

Background

- Respiratory viruses (RV) include respiratory syncytial virus (RSV), influenza (flu), human metapneumovirus (HMPV), and parainfluenza virus type 3 (PIV3).
  - In many cases, symptoms are minor; however, they can cause serious complications such as bronchiolitis and pneumonia.
  - Older adults, including those with underlying medical conditions, are at an increased risk of severe illness.
- Older individuals face complex RV vaccination decisions, balancing which viruses a vaccine protects against with overall protection against different RV.
- Standalone vaccines exist for RSV and flu, and combination vaccines are in development; combination vaccines offer protection against multiple RV with fewer injections, while enhancing coverage and uptake, but may have higher reactogenicity than standalone counterparts.

Objectives

- To quantify the **relative importance** of RV vaccine attributes.
- To quantify **willingness to vaccinate** across defined profiles.

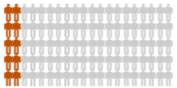
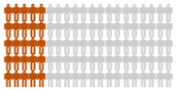
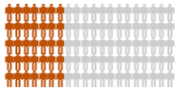
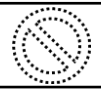
DCE Design

- A discrete choice experiment (DCE) was developed using insights from a targeted literature review and concept elicitation interviews.
- A D-efficient design with six blocks was generated; each participant saw eight experimental tasks each with three options: two vaccine profiles and a no-vaccine opt-out.
- The DCE was administered to older US adults (≥50 years) in an online survey in October 2024.

	Attributes	Levels
Benefits	Reduction in the risk of mild-to-moderate respiratory illness*	45%- 75%
	Reduction in the risk of hospitalization due to severe respiratory illness**	30% - 75%
Risks	Risk of local AEs	1%-50%
	Risk of systemic AEs	1%-50%
Administration	Viruses protected against	RSV, HMPV, and/or PIV3 + flu
	Number of shots	1 – 3 shots
	Duration of protection	1 – 3 years

Abbreviations: AE = adverse event; flu = influenza; HMPV = human metapneumovirus; PIV3 = parainfluenza virus type 3; RSV = respiratory syncytial virus

Example Choice Task

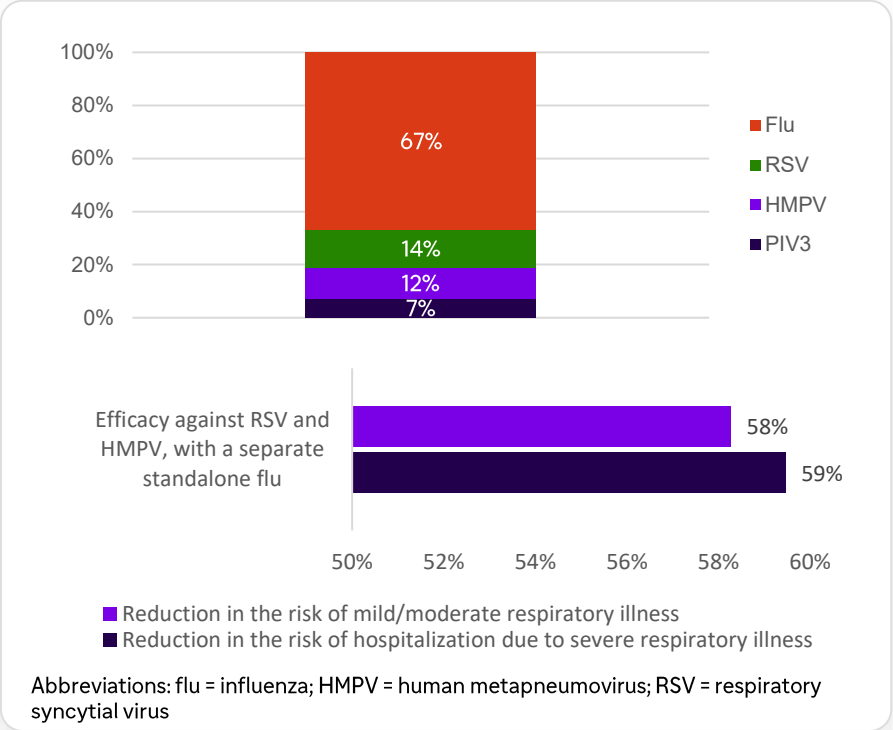
	OPTION A	OPTION B	NONE
Benefits	60% less likely to get **mild to moderate respiratory illness** 60%	50% less likely to get **mild to moderate respiratory illness** 50%	No change in likelihood of **mild to moderate respiratory illness** 0%
Benefits	45% less likely to be **hospitalized due to severe respiratory illness** 45%	45% less likely to be **hospitalized due to severe respiratory illness** 60%	No change in likelihood of **hospitalisation due to severe respiratory illness** 0%
Risks	10% (10 out of 100) will experience **side effects at injection site** 	50% (50 out of 100) will experience **side effects at injection site** 	No risk of side effects at injection site
Risks	25% (25 out of 100) will experience **side effects in whole body** 	35% (35 out of 100) will experience **side effects in whole body** 	No risk of side effects in whole body
Administration	Protected against RSV, HMPV, Flu 	Protected against RSV, Flu 	Not protected against any viruses 
Administration	1 shot **at 1 appointment** 	2 shots **at 1 or more appointments** 	No shots 
Administration	Protection against viruses 	Protection against viruses 	Not Protected 
	What is your preferred option		

Abbreviations: flu = influenza; HMPV = human metapneumovirus; RSV = respiratory syncytial virus

Identifying the Level Range for Benefit Attributes

- Burden-adjusted vaccine efficacy was calculated to account for multiple viruses in standalone or combination vaccines.
  - Allowed a common denominator of lower respiratory tract disease (LRTD) illness or hospitalization, across viruses
- Influenza and RSV data were taken from national surveillance data
  - Assumptions included constant vaccine efficacy and no indirect protection or between-strain competition.
  - Influenza burden adjusted for vaccination; no adjustments for HMPV and PIV3 due to lack of vaccines, or RSV due to low initial coverage.
- Ratios used to estimate burden of HMPV and PIV3 relative to RSV were based on hospital and community surveillance data.

Estimated Burden of Influenza, PIV3, HMPV, and RSV Among US Adults Aged 65 Years, Assuming the Absence of an Influenza Vaccine



Abbreviations: flu = influenza; HMPV = human metapneumovirus; RSV = respiratory syncytial virus

Analysis

- Descriptive statistics were used to summarize sociodemographic and clinical characteristics, data quality measures, and health literacy and numeracy responses.
- Choice data were analyzed using a mixed logit (MXL) model:
  - MXL accounts for heterogeneity in treatment choices.
  - The estimated parameters were assumed to follow a normal distribution.
  - After testing, a combination of dummy and linear coding was used:
    - *Linear attributes: Safety and efficacy attributes*
    - *Categorical attributes (dummy coded): Duration of protection, viruses protected against, number of shots*
- Marginal utilities were used to calculate relative attribute importance, attribute trade-offs, and predicted choice probabilities.

Sample Characteristics

A total of 803 individuals participated in the study:

Experience with*:

- Flu: 485 (60.4%)
- COVID-19: 403 (50.2%)
- RSV: 39 (4.9%)
- PIV3: 27 (3.4%)
- HMPV: 21 (2.6%)

Vaccinated against:

- COVID-19: 682 (84.9%)
- Flu: 592 (73.7%)
- RSV: 226 (28.1%)

Fear of injections:

- Not at all: 529 (65.9%)
- A little: 179 (22.3%)
- Moderately: 57 (7.1%)

Medical conditions*:

- Diabetes: 159 (19.8%)
- Cardiovascular disease 74 (9.2%)
- COPD: 50 (6.2%)
- Other chronic illness: 114 (14.2%)
- None listed: 486 (60.5%)

Experience with vaccine side effects:

- Yes: 254 (31.6%)

Age:

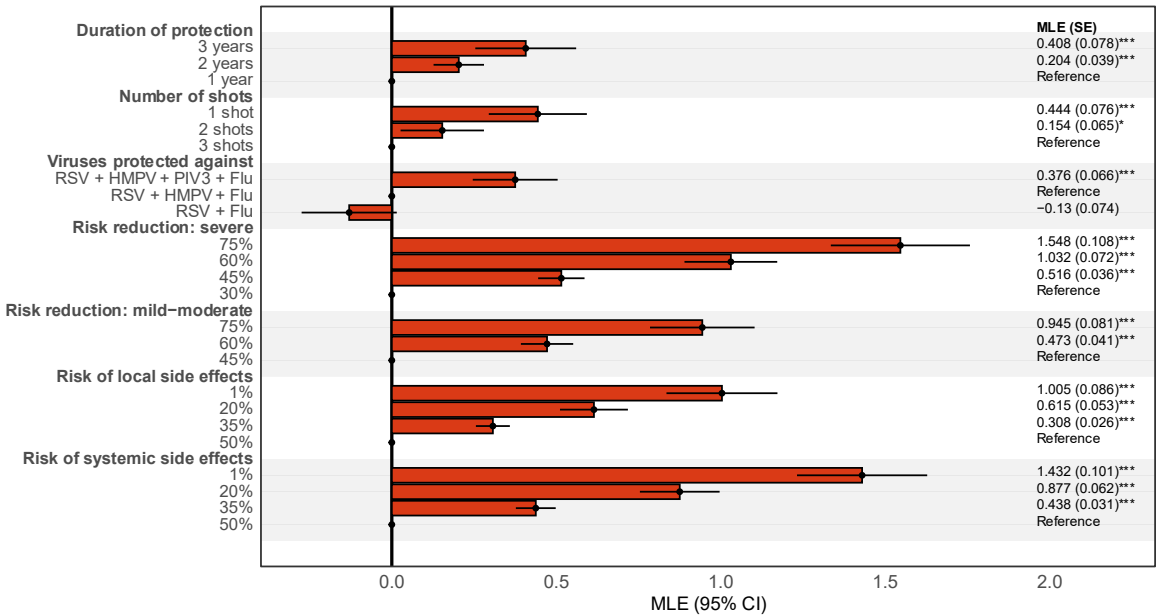
- Mean (SD): 63.8 years (8.0)

Gender:

- Male: 397 (49.4%)
- Female: 406 (50.6%)

*Not mutually exclusive
Abbreviations: COPD = chronic obstructive pulmonary disease; flu = influenza; HMPV = human metapneumovirus; PIV3 = parainfluenza virus type 3; RSV = respiratory syncytial virus

Marginal Utilities

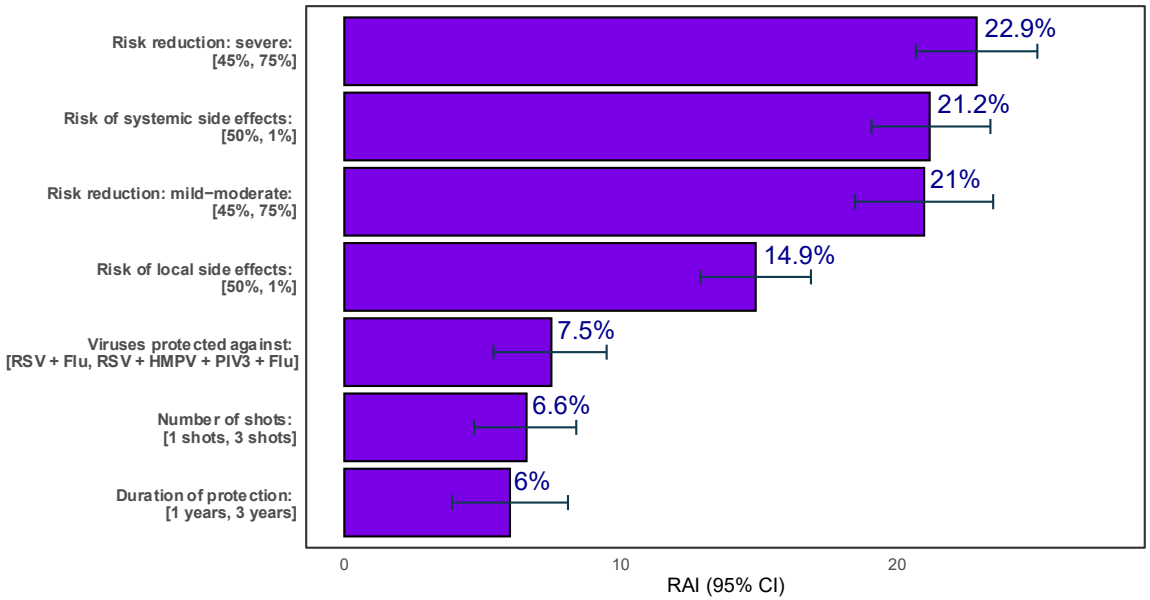


Significance: ***P-value <0.1%; ** P-value <1%; *P-value <5%

Abbreviations: flu = influenza; HMPV = human metapneumovirus; MLE = maximum likelihood estimator; PIV3 = parainfluenza virus type 3; RSV = respiratory syncytial virus

- Individuals were more likely to select vaccines that:
  - Provided **additional duration of protection.**
  - Required **fewer shots**
  - Provided **protection against more viruses** (P-value <0.1%); adding protection against HMPV to an RSV+flu vaccine did not significantly impact preferences
  - Provided **greater protection** against **mild-to-moderate** and **severe** illness
  - Had lower risks of **local** and **systemic side effects**

Preference Insight 1: Relative Attribute Importance



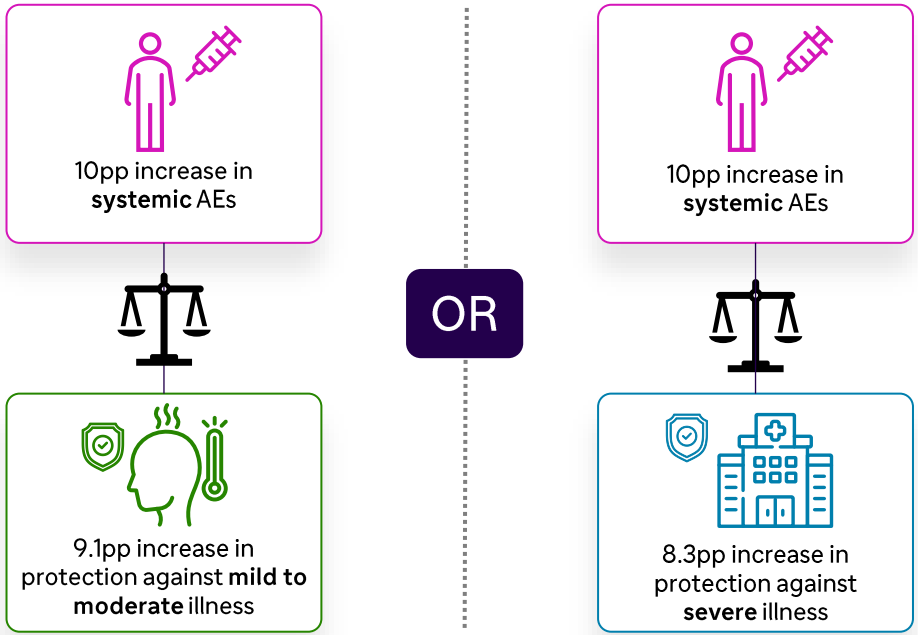
RAI scores capture the percentage contribution of each attribute to a vaccine preference.
RAI scores are conditional on the range of attribute levels and sum to 100%.

Abbreviations: flu = influenza; HMPV = human metapneumovirus; PIV3 = parainfluenza virus type 3; RAI = relative attribute importance; RSV = respiratory syncytial virus

- The **viruses the vaccine protects against** is **less important** (ranked fifth) than the magnitude of protection the vaccine provides against **severe** (ranked first) and **mild to moderate** (ranked third) respiratory illness.
  - The viruses protected against, independent of the magnitude of protection against LRTD or vaccine risk, accounted for just 7.5% of participants' vaccine decision-making.

Preference Insight 2: Attribute Trade-offs [Systemic AEs]

To accept a vaccine with a **10-**percentage-point higher risk of **systemic AEs,** an individual would need a **9.1** percentage-point increase in protection against **mild to moderate illness**.



To accept a vaccine with a **10-**percentage-point higher risk of **systemic AEs,** an individual would need an **8.3** percentage-point increase in protection against **severe illness**.

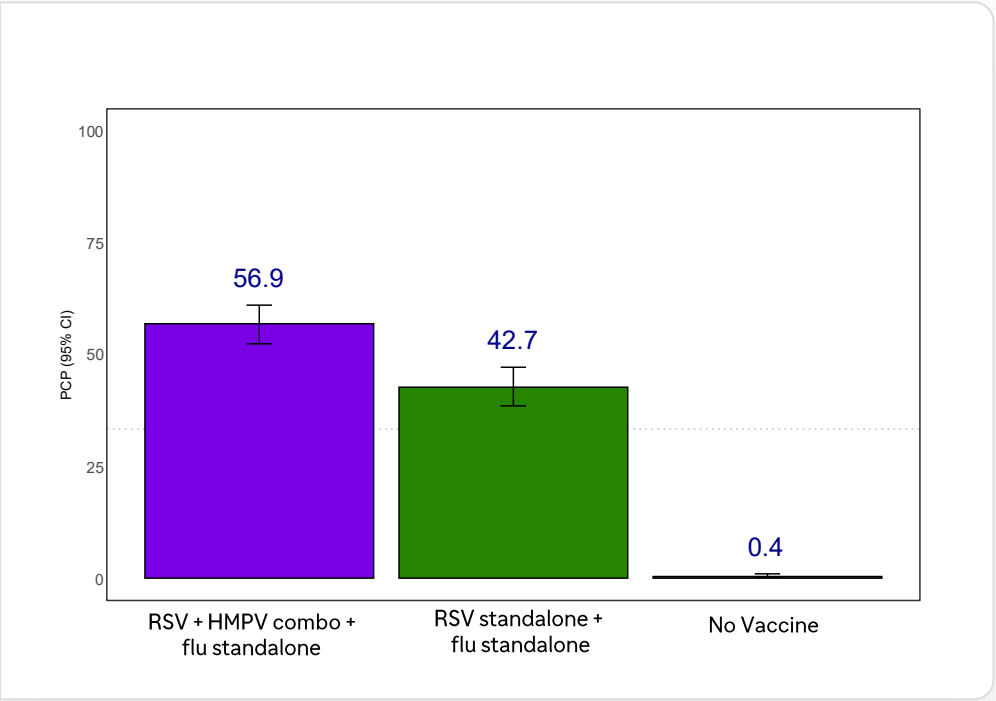
Abbreviation: AE = adverse event; pp = percentage point

Vaccine Profiles

Combination mRNA RSV + HMPV Standalone Flu	Standalone protein subunit RSV Standalone Flu	No Vaccine
58% less likely to get mild to moderate respiratory illness	52% less likely to get mild to moderate respiratory illness	0% No change in likelihood of mild to moderate respiratory illness
59% less likely to be hospitalized due to severe respiratory illness	54% less likely to be hospitalized due to severe respiratory illness	0% No change in likelihood of hospitalization due to severe respiratory illness
60.9% risk of local AEs	60.9% risk of local AEs	No risk of local AEs
33.6% risk of systemic AEs	33.6% risk of systemic AEs	No risk of systemic AEs
Protected against RSV, HMPV, influenza	Protected against RSV, influenza	Not protected against any viruses
Two shots at one or more appointments	Two shots at one or more appointments	No shots
Protection against viruses 2 Years	Protection against viruses 3 Years	Not Protected

Abbreviations: AE = adverse event; flu = influenza; HMPV = human metapneumovirus; RSV = respiratory syncytial virus

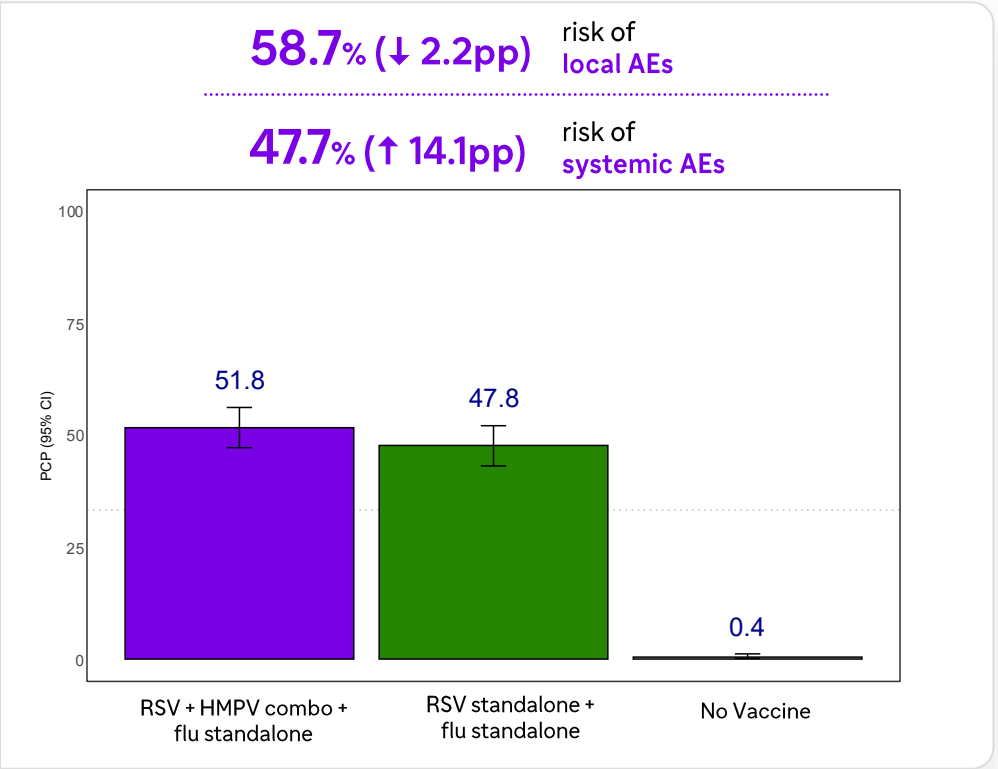
Preference Insight 3: Predicted Choice Probability



- A **combination vaccine** providing protection against HMPV in addition to RSV was **statistically significantly preferred** over a standalone RSV vaccine.
  - An **RSV + HMPV** combination vaccine co-administered with a standalone influenza vaccine had a **56.9%** likelihood of being preferred.
  - An **RSV standalone** vaccine co-administered with a standalone influenza vaccine had a **42.7%** likelihood of being preferred.
  - Fewer than 1% would prefer not to be vaccinated.

Abbreviation: PCP = predicted choice probability

Preference Insight 3: Predicted Choice Probability
Sensitivity Analysis



- The **cumulative efficacy associated with a combination vaccines continues to outweigh their burdens**. When changing the risk of local and systemic AEs in line with a hypothetical 'worse case' mRNA combination profile:
  - An **RSV + HMPV** combination vaccine co-administered with a standalone influenza vaccine had a **51.8%** likelihood of being preferred.
  - An **RSV standalone** vaccine co-administered with a standalone influenza vaccine had a **47.8%** likelihood of being preferred.
  - Fewer than 1% would prefer not to be vaccinated.

Abbreviations: AE = adverse event; PCP = predicted choice probability

Key Preference Insights

1. Overall vaccine efficacy was more important than which viruses (i.e., RSV, HMPV, flu) they protect against.

2. Individuals were willing to bear systemic adverse event (AE) risks in return for greater efficacy.

3. Given the higher cumulative efficacy associated with combination vaccines, a larger number of individuals would prefer an RSV+HMPV combination vaccine over an RSV standalone vaccine, even when assuming higher risks of systemic AEs.

Thank *you*

[Copies of this slide deck obtained through Quick Response (QR) Code are for personal use only].

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Appendix

DATA SOURCES

Vaccine Option A

Combination RSV/HMPV Vaccine

- Protects against RSV and HMPV
- Provides 70% protection against mild to moderate LRTD from RSV
- Provides 75% protection against severe LRTD from RSV
- Provides 70% protection against mild to moderate LRTD from HMPV
- Provides 75% protection against severe LRTD from HMPV

+

Standalone Influenza Vaccine

- Protects against influenza
- Provides 58.7% protection against mild to moderate LRTD from influenza
- Provides 47.7% protection against severe LRTD from influenza

Vaccine Option A

- An RSV/HMPV combination vaccine co-administered with a standalone influenza vaccine provides:
- Aggregated protection of:
  - 58% against mild to moderate LRTD from RSV, HMPV, and influenza
  - 59% against severe LRTD from RSV, HMPV, and influenza*
- Associated risks:
  - 58.7% risk of local side effects
  - 47.7% risk of systemic side effects
- Requires two shots.
- Has a 2-year duration of protection.

Definitions: Mild to moderate LRTD = LRTD with two or fewer symptoms; Severe LRTD = LRTD with three or more symptoms
Abbreviations: HMPV = human metapneumovirus; LRTD = lower respiratory tract infection; RSV = respiratory syncytial virus

Vaccine Option B

Vaccine Option B

- A standalone RSV vaccine co-administered with a standalone influenza vaccine provides:
- Aggregated protection of:
  - 52% against mild to moderate LRTD from RSV, HMPV, and influenza
  - 54% against severe LRTD from RSV, HMPV, and influenza*
- Associated risks:
  - 60.9% risk of local side effects
  - 33.6% risk of systemic side effects
- Requires two shots.
- Has a 3-year duration of protection.

Standalone RSV Vaccine

- Protects against RSV
- Provides 83% protection against mild to moderate LRTD from RSV
- Provides 92% protection against severe LRTD from RSV
- Provides 0% protection against mild to moderate LRTD from HMPV
- Provides 0% protection against severe LRTD from HMPV

+

Standalone Influenza Vaccine

- Protects against influenza
- Provides 60% protection against mild to moderate LRTD from influenza
- Provides 60% protection against severe LRTD from influenza

Definitions: Mild to moderate LRTD = LRTD with two or fewer symptoms; Severe LRTD = LRTD with three or more symptoms
Abbreviations: HMPV = human metapneumovirus; LRTD = lower respiratory tract infection; RSV = respiratory syncytial virus