EE466

# The Potential Public Health and Economic Benefit of an mRNA-Based Respiratory Syncytial Virus Vaccine Among Adults ≥60 Years in the United States (US)

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## BACKGROUND

- In older adults, respiratory syncytial virus (RSV) is an important cause of lower respiratory tract disease (LRTD), which can result in hospitalization and death[1, 2]
- An mRNA RSV vaccine, mRNA-1345 (mRESVIA, Moderna, Inc.), was approved in the US in May 2024 for the prevention of RSV-LRTD in adults aged ≥60 years[3, 4]
- Given that the RSV vaccination program has only been available for one season (2023/2024), coverage is low;[5] however, there is the potential to reduce RSV disease burden more substantially if coverage levels are increased to those of influenza vaccines

## OBJECTIVE

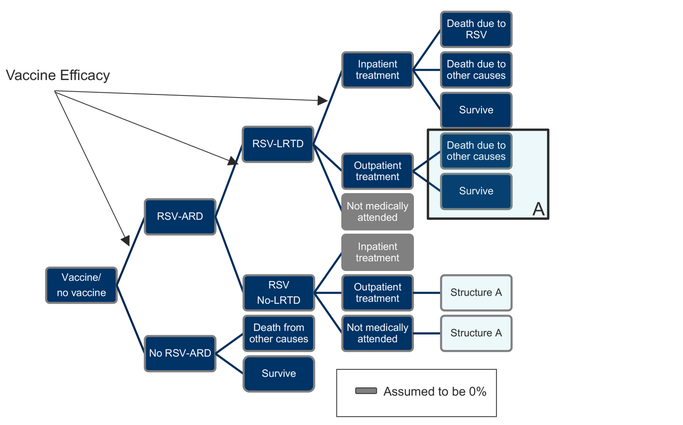
- To estimate the potential public health and economic impact of vaccination with mRNA-1345 in adults aged ≥60 years over a 3-year time frame in the US

## METHODS

### Study Design

- A static decision-analytic model (**Figure 1**) was developed to compare vaccination with a single dose of mRNA-1345 administered before the RSV season to no vaccination
- The vaccine was assumed to be effective against three endpoints, RSV- associated acute respiratory disease (ARD), RSV-LRTD, and RSV-LRTD hospitalizations, based on clinical trial data[6]

**Figure 1. Model Structure[a,b]**




ARD, acute respiratory disease; LR, lower respiratory; LRTD, lower respiratory tract disease; RSV, respiratory syncytial virus.

[a]Diagram represents a simplified version of the decision tree to compare vaccination with no vaccination. Patients in the vaccine arm were eligible for vaccination, but receipt of the vaccine depended on coverage rates.

[b]Following no vaccination or vaccination, participants may have developed RSV-ARD. Participants with RSV-ARD were split into those with RSV-LRTD (≥2 LR signs or symptoms) and those with RSV No-LRTD (RSV-ARD with <2 LR signs or symptoms).

### Model Inputs

- Model inputs were estimated from published literature and other publicly available sources (**Table 1; Supplemental Table 1**)

**Table1. Model Parameters**

| Model Parameter | Value (DSA Range) | | | Data Source |
|---|---|---|---|---|
| **Vaccine coverage** | | | | |
| 60-64 years | 50.6% | | | US CDC Flu Vaccination Coverage, United States, 2019-2020 Influenza Season[7] |
| 65+ years | 69.8% | | | |
| **Annual incidence of RSV-ARD, unvaccinated** | | | | |
| % with symptomatic RSV-ARD | 5.73 (95% CI: 3.69, 8.17)[a] | | | Derived from Falsey et al. (2005)[8] and data on file at Moderna[9] |
| **Hospitalization rates per 100,000 (year 1)** | | | | |
| 60-64[b] years | 23.4 | | | Predicted by model based on calibration targets from McLaughlin et al. (2022)[10] (adjusted for underdetection) and CDC RSV-NET hospitalization data[11] |
| 65-69 years | 88.0 | | | |
| 70-74 years | 111.8 | | | |
| 75-79 years | 475.4 | | | |
| 80-84 years | 475.4 | | | |
| 85+ years | 578.3 | | | |
| **Outpatient visit rates per 100,000 (year 1)** | | | | |
| 60-64[b] years | 1832.6 | | | Predicted by model based on calibration targets from McLaughlin et al. (2022)[10] (adjusted for underdetection) |
| 65-69 years | 1845.4 | | | |
| 70-74 years | 2041.4 | | | |
| 75-79 years | 3272.9 | | | |
| 80-84 years | 3272.9 | | | |
| 85+ years | 3169.9 | | | |
| **% with RSV-related death** | | | | |
| | Care setting | | | |
| | Inpatient | Outpatient | No treatment | |
| All ages | 7.6[c] | 0 | 0 | Falsey et al. (2005)[8] |
| **RSV-related healthcare costs[d]** | | | | |
| | Care setting | | | |
| | Inpatient | Outpatient | No treatment | |
| All ages | $11,876 ($8407 - $47,512)[12, 13] | $2273[c] | $0 | Wyffels et al. (2020)[14] |
| **RSV-related work days lost[e]** | | | | |
| | Care setting | | | |
| | Inpatient | Outpatient | No treatment | |
| 60-74 years | 7.5 | 2.3 | 2.3 | Ackerson et al. (2020);[15] Falsey et al. (2005);[8] Chit et al. (2015)[16] |
| 75-84 years | 7.9 | 2.3 | 2.3 | |
| 85+ years | 7.0 | 2.3 | 2.3 | |

ARD, acute respiratory disease; CDC, Centers for Disease Control and Prevention; CI, confidence interval; DSA, deterministic sensitivity analysis; LRTD, lower respiratory tract disease; RSV, respiratory syncytial virus; RSV-NET, Respiratory Syncytial Virus Hospitalization Surveillance Network; SE, standard error; US, United States.

[a]CI for use in sensitivity analyses was calculated using a SE equal to 20% of the mean (SE = 1.15%) using a beta distribution.

[b]Estimates calculated based on the RSV-NET ratio.

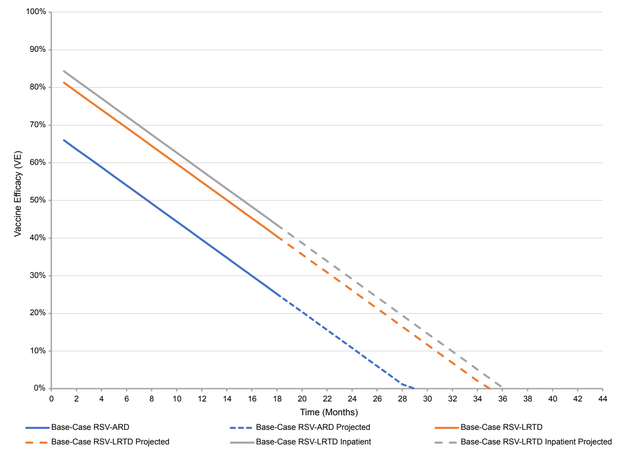
[c]DSA performed using age-specific estimates from Hutton et al. (mortality: 60-64 years: 3.9%; 65-74 years: 4.3%; ≥75 years: 5.7%; outpatient costs: $117.58 for 60-64 years and $100.86 for ≥65 years).[11]

[d]RSV-related costs were estimated from Wyffels et al. (2020),[14] who present mean costs for patients 180 days pre- and post-RSV diagnosis, increasing the likelihood that the cost estimates reflect RSV-attributable costs and include any longer-term costs associated with RSV infection.

[e]The cost of lost productivity is calculated by multiplying the mean hourly income for the total population[17] accounting for the employment rate[18] by the average number of hours worked per day obtained from the Bureau of Labor Statistics,[19] further multiplied by the days expected to be lost from work due to RSV infection.

- Coverage rates for the influenza vaccine were used as a proxy to estimate potential RSV vaccine coverage rates[7]
- The age-specific proportions of patients with RSV-LRTD were estimated via a calibration process using targets from McLaughlin et al. (2022),[10] who report hospitalization rates adjusted for under-detection based on a multiplier of 1.5, which reflects the increase observed when adding either serology or sputum to nasopharyngeal or nasal reverse transcription-polymerase chain reaction (RT-PCR) alone
- Monthly vaccine efficacy (VE) was estimated using the following approach:
  - Initial VE estimates are based on data from the phase 2/3 clinical trial primary analysis,[4] and were used to estimate VE at 0 months
  - Data from an extended analysis, with a median of 18.8 months follow-up, were used to linearly project the duration of vaccine protection over time (**Figure 2**)

**Figure 2. Base-Case Vaccine Efficacy[a,4,20]**




ARD, acute respiratory disease; CI, confidence interval; LRTD, lower respiratory tract disease; RSV, respiratory syncytial virus; VE, vaccine efficacy; WLS, weighted least square.

[a]VE duration of protection over time was calculated by estimating the VE for RSV-LRTD with ≥2 symptoms every 2 months through 18 months as an ad hoc analysis. A WLS regression was performed on the estimated VE for every 2 months. The weights were determined by the relative case numbers in the placebo arm. The estimated slope of 2.4% was used as the monthly waning rate for mRNA-1345 for RSV-ARD, RSV-LRTD, and RSV-LRTD requiring inpatient care. In sensitivity analyses, 95% CIs around the VE estimate from the primary analysis were used to vary the VE estimate at time 0 for all endpoints, while a monthly waning rate of 2.4% per month was maintained (**Supplemental Figure 1**).

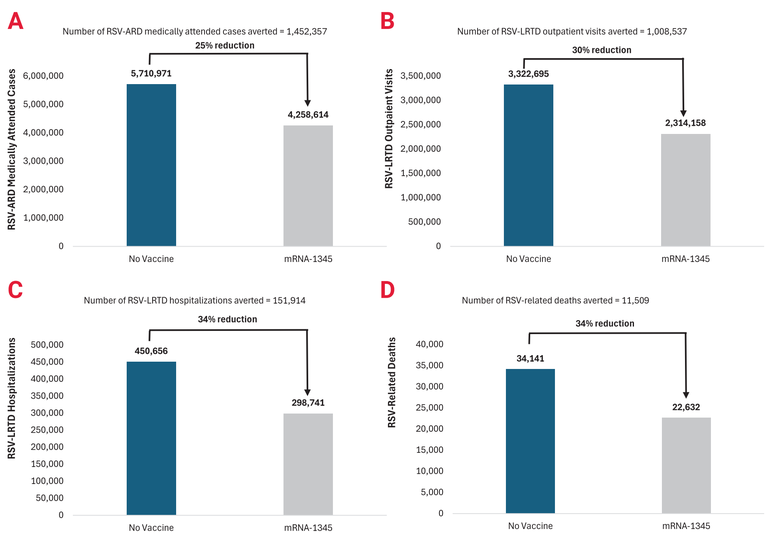
### Model Analyses

- Clinical outcomes include number of cases of RSV-ARD, RSV-LRTD, medically attended RSV, RSV-related hospitalizations, and deaths over the 3-year time frame (**Supplemental Table 2**)
- Economic outcomes include RSV-related costs, including direct healthcare-related costs and indirect costs due to lost productivity (**Table 2**)
- A scenario analysis was performed using a 2-year time frame (**Supplemental Tables 3 and 4**)
- Deterministic sensitivity analyses (DSAs) were performed to assess the impact of varying RSV-ARD incidence (Table 1), mRNA-1345 VE (**Supplemental Figure 1**), percentage of patients with RSV-LRTD (**Supplemental Table 1**), and RSV-related mortality (Table 1) on RSV-LRTD hospitalizations and deaths prevented by mRNA-1345; an additional DSA was performed on RSV-related costs prevented (including lost productivity) (**Supplemental Figure 2**)

## RESULTS

- The vaccine would reduce RSV-ARD cases by 3.5 million (27% reduction) and RSV-LRTD cases by approximately 1.2 million (31% reduction) over the 3-year time frame, including 1.5 million (25% reduction) medically attended RSV cases (**Figure 3; Supplemental Table 2**)

**Figure 3. Projected Clinical Results Over 3-Year Time Frame**




ARD, acute respiratory disease; LRTD, lower respiratory tract disease; RSV, respiratory syncytial virus.

- Given the reduction in the RSV clinical burden associated with mRNA-1345, the vaccine would prevent $5110 million in costs for RSV-related healthcare and lost productivity (27% reduction) (**Table 2**)
  - This includes a reduction of $1770 million in RSV-related hospitalization costs (34% reduction)

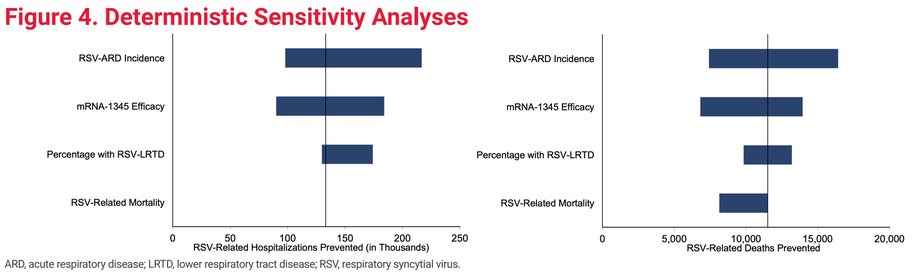
**Table 2. Economic Results (millions)**

| | No Vaccine | mRNA-1345 | Difference[a] | % Change |
|---|---|---|---|---|
| **Total costs** | $19,083 | $13,973 | -$5110 | -27% |
| Healthcare | $16,822 | $12,133 | -$4690 | -28% |
| Lost productivity | $2261 | $1,840 | -$420 | -19% |

[a]mRNA-1345 minus no vaccine.

- Model results are most sensitive to RSV-ARD incidence, which causes all downstream effects, such as hospitalizations and deaths, to also vary (**Figure 4**)

**Figure 4. Deterministic Sensitivity Analyses**




ARD, acute respiratory disease; LRTD, lower respiratory tract disease; RSV, respiratory syncytial virus.

## LIMITATIONS

- The value of vaccination with mRNA-1345 may be underestimated, as the burden of RSV extends beyond the acute phase of illness; for example, RSV can exacerbate underlying cardiac and lung conditions, which may increase healthcare utilization and mortality post-hospitalization[14, 21]
- The model was developed as a static cohort model, and therefore, secondary prevention of transmitted cases ("herd immunity") was not considered
- Long-term durability of RSV vaccines needs to be confirmed in real-world settings and the optimal timing and frequency of revaccination is still to be defined[22]

## CONCLUSIONS

- If RSV vaccination coverage rates are increased to influenza vaccination levels, there will be a substantial reduction of the public health and economic burden of RSV infections among older adults in the US
  - mRNA-1345 could prevent nearly 1.5 million cases of medically attended RSV-ARD (25% reduction), 151,900 RSV-LRTD hospitalizations (34% reduction), and 11,500 deaths (34% reduction) compared with no vaccination
  - mRNA-1345 could reduce RSV-related healthcare costs and lost productivity costs by $4690 million (28% reduction) and $420 million (19%), respectively

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### Disclosures

M Kohli is a shareholder in Quadrant Health Economics, Inc., which was contracted by Moderna, Inc., to conduct this study. K Fust is a consultant at Quadrant Health Economics, Inc. P Ghaswalla, K Joshi, and N Van de Velde are employed by Moderna, Inc., and hold stock/stock options in the company.

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