Assessing the Public Health Benefit of an mRNA-Based Respiratory Syncytial Virus Vaccine (mRNA-1345) Among Adults ≥65 Years in France

Nadia El Mouaddin,[1,*] Mathieu Uhart,[1] Laure Abily,[1] Parinaz Ghaswalla,[2] Keya Joshi,[2] Kelly Fust,[3] Michele Kohli,[3] Loic Biron,[4] Jérémy Carette[4]

[1]Moderna, Inc., Paris, France; [2]Moderna, Inc., Cambridge, MA, USA; [3]Quadrant Health Economics, Inc., Cambridge, Ontario, Canada; [4]Public Health Expertise, Paris, France
*Presenting author.

BACKGROUND

- Respiratory syncytial virus (RSV) is a major cause of lower respiratory tract disease (LRTD) and can result in significant morbidity and mortality in adults ≥60 years[1-3]
- An mRNA RSV vaccine, mRNA-1345 (mRESVIA; Moderna, Inc.), was approved in Europe in August 2024 for the prevention of RSV-LRTD in adults ≥60 years[3]
- This vaccine has demonstrated efficacy against RSV-LRTD and RSV-acute respiratory tract disease (ARD) in adults ≥60 years[4]
- Since October 2024, mRNA-1345 has been included in the recommendation from the Technical Committee for Vaccinations of the French Health Technology Assessment (HTA) agency (Haute Autorité de Santé; HAS), which recommends seasonal vaccination against RSV in adults aged ≥75 years and adults aged 65 to 74 years at increased risk of severe disease (i.e., with chronic cardiac or respiratory diseases)[5]

OBJECTIVE

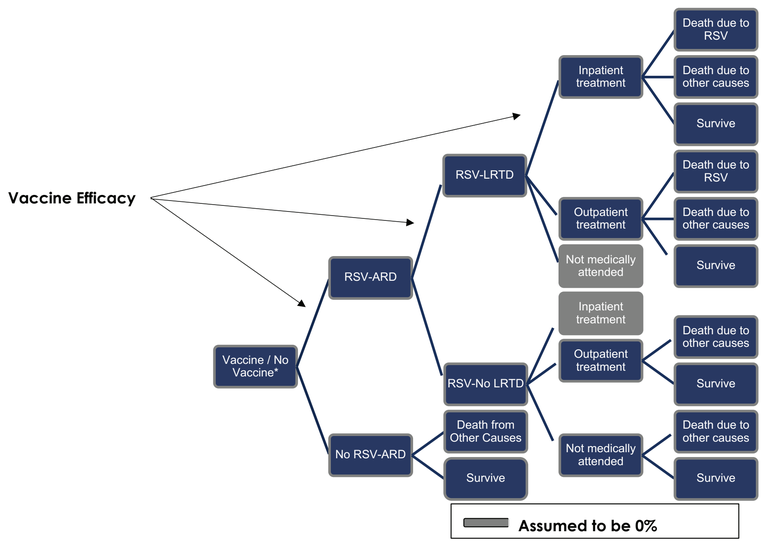
- The objective of the study was to estimate the potential public health impact of vaccination with mRNA-1345 in the French population targeted by the HAS recommendation over a 3-year time frame

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 with no vaccination
- Vaccine efficacy (VE) data, derived from clinical trials, was applied to three endpoints: RSV-ARD, RSV-LRTD, and RSV-LRTD hospitalizations[4]

Figure 1. Model Structure[a,b]



ARD, acute respiratory disease; 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.
[b]Following no vaccination or vaccination, participants may have developed RSV-ARD. Participants with RSV-ARD were split into those with RSV-LRTD (≥2 lower respiratory [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**)

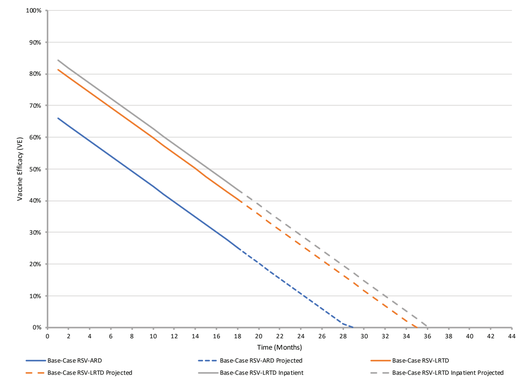
Table 1. Model Parameters

Model parameter	Value (DSA range)			Data source
Vaccine coverage				
65+ years	54.0%			Santé Publique France[6]
Annual incidence of RSV-ARD, unvaccinated				
% with symptomatic RSV-ARD	8.55 (95% CI, 7.98-11.40)[a]			Derived from Korsten et al. (2021)[7] and adjusted for underdetection using McLaughlin et al. (2022)[8]
Hospitalization rates per 100,000 (year 1)				
65-74 years	93			Predicted by model based on calibration targets from Fahfoufi et al. (2023)[9]
75+ years	256			
Outpatient visit rates per 100,000 (year 1)				
65+ years	2209			Predicted by model based on calibration targets from Santé Publique France Réseau Sentinelles and Reseau de Laboratoires de biologie médicale privés[10,11]
% LRTD with RSV-related death				
	Care setting			
	Inpatient[b]	Outpatient[b]	No treatment	
65-74 years	8.92	4.87	0	Inpatient mortality at 90 days from ESTIVARS – French PMSI study[12] Outpatient mortality predicted by a model based on the proportion of deaths in the hospital and outpatient settings for influenza cases as a calibration target[13,14]
75+ years	13.54	7.31	0	

ARD, acute respiratory disease; CI, confidence interval; DSA, deterministic sensitivity analysis; LRTD, lower respiratory tract disease; PMSI, Programme de Médicalisation des Systèmes d'Information; RSV, respiratory syncytial virus.
[a]CIs for use in sensitivity analyses were calculated using Mc Laughlin et al. (2022) range values for the RSV detection multiplier.
[b]DSA ranges were established using ± 20% value variation.

- The analysis assumed a vaccination coverage of 54.0%, similar to the influenza vaccination coverage rate observed in 2023-2024 in adults aged ≥65 years in France[6]
- The age-specific proportions of patients with RSV-LRTD were estimated via a calibration process using targets from Fahfoufi et al. (2023)[9]
- Monthly VE was estimated using the following approach:
  - Initial VE estimates were 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,4,15]



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.

Model Analyses

- Clinical outcomes included the number of cases of RSV-ARD, RSV-LRTD, RSV-related outpatient visits, RSV-related hospitalizations, and deaths over the 3-year time frame
- Deterministic sensitivity analyses were performed to assess the impact of varying RSV-ARD incidence (**Table 1**), mRNA-1345 VE, percentage of patients with RSV-LRTD (**Supplemental Table 1**), percentage of RSV-LRTD requiring inpatient treatment (**Supplemental Table 1**), and RSV-related mortality (**Table 1**) on RSV-LRTD hospitalizations and deaths prevented by mRNA-1345

RESULTS

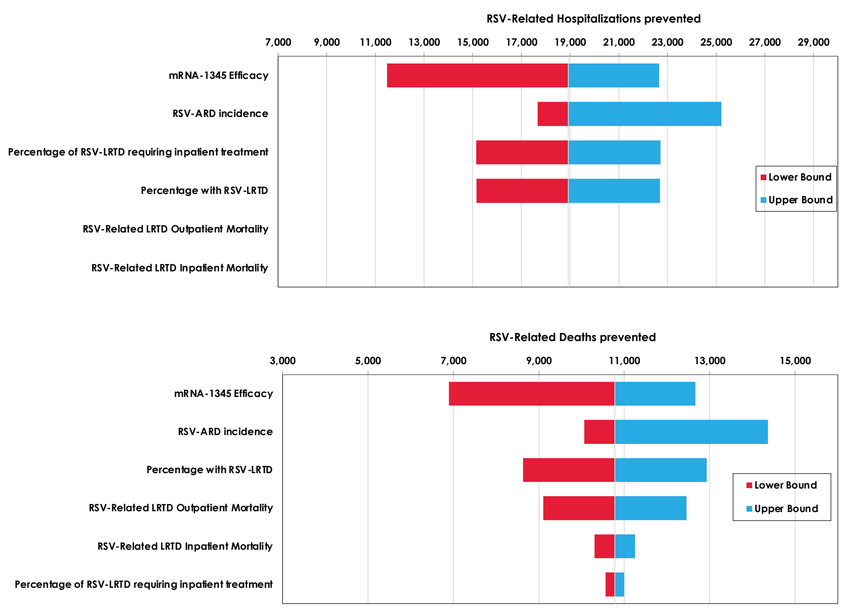
- Vaccination with mRNA-1345 could prevent 455,000 RSV-ARD cases (18% reduction), 159,000 RSV-related outpatient visits (23% reduction), 19,000 RSV-LRTD hospitalizations (28% reduction), and 11,000 deaths attributable to RSV (27% reduction) over the 3-year time frame compared with no RSV vaccination (**Table 2**)
- The number needed to vaccinate (NNV) to prevent one RSV-ARD case, one RSV-related outpatient visit, one LRTD case, one LRTD hospitalization, and one death were estimated at 12, 34, 38, 286, and 503, respectively (**Table 2**)
- Model results are most sensitive to mRNA-1345 VE and RSV-ARD incidence, which causes all downstream effects, such as hospitalizations and deaths, to also vary (**Figure 3**)

Table 2. Clinical Results Over a 3-Year Time Frame

Model parameter	No vaccine	mRNA-1345	Difference[a]	% Change	NNV[b]
RSV-ARD cases	2,480,380	2,025,806	−454,574	−18%	12
RSV-related outpatient visits	689,945	530,526	−159,419	−23%	34
RSV-LRTD cases	537,791	394,740	-143,051	-27%	38
RSV-LRTD hospitalizations	67,056	48,132	−18,924	−28%	286
Deaths	40,261	29,481	−10,779	−27%	503

ARD, acute respiratory disease; LRTD, lower respiratory tract disease; NNV, number needed to vaccinate; RSV, respiratory syncytial virus.
[a]mRNA-1345 minus no vaccine.
[b]NNV: Number needed to vaccinate with mRNA-1345 to prevent one case, outpatient visit, hospitalization, or death.

Figure 3. 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[16,17]
- 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[5]

CONCLUSIONS

- There could be a substantial reduction in the burden of RSV disease among older adults in France under the current HAS recommendation, when assuming vaccination coverage rates for RSV are equivalent to influenza
  - mRNA-1345 could prevent nearly 159,419 RSV outpatient visits (23% reduction), 18,924 RSV-LRTD hospitalizations (28% reduction), and 10,779 deaths (27% reduction) compared with no vaccination

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Disclosures

MK is a shareholder in Quadrant Health Economics, Inc., which was contracted by Moderna, Inc., to develop the model. KF is a consultant at Quadrant Health Economics, Inc. NEM, MU, LA, PG, and KJ are employed by Moderna, Inc., and hold stock/stock options in the company. JC and LB are consultants at Public Health Expertise.

ADDITIONAL INFORMATION

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For additional information, please contact Nadia El Mouaddin (nadia.elmouaddin@modernatx.com).

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