Potential Clinical Impact of Respiratory Syncytial Virus (RSV) Vaccination in Older Adults in the United States

Kelly Fust,[1] Michele Kohli,[1] Catherine A. Panozzo,[2] Milton C. Weinstein,[3] Philip O. Buck,[2] Parinaz Ghaswalla[2,*]

[1]Quadrant Health Economics Inc., Cambridge, ON, Canada; [2]Moderna, Inc., Cambridge, MA, USA; [3]Harvard T.H. Chan School of Public Health, Boston, MA, USA
*Presenting author

BACKGROUND

- Respiratory syncytial virus (RSV) is a common seasonal virus that is a major cause of respiratory infections worldwide[1,2]
- For certain individuals, such as older adults, RSV can cause acute respiratory disease (ARD) and severe lower respiratory tract disease (LRTD), which can lead to an exacerbation of chronic illnesses, hospitalization, and mortality[3]
  - In the United States, approximately 177,000 older adults become hospitalized due to RSV infection, leading to approximately 14,000 deaths annually[4]
- Despite this substantial burden, no vaccines are currently approved to prevent or reduce the severity of RSV disease.[3] However, efforts are ongoing to develop an RSV vaccine

OBJECTIVE

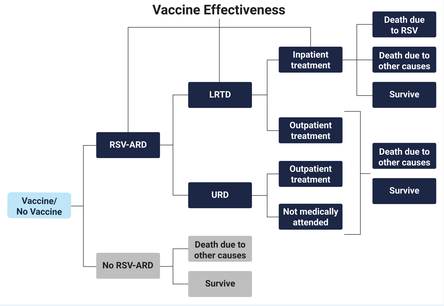
- To examine the clinical impact of a hypothetical RSV vaccine with 75% efficacy compared with no RSV vaccine over a 1-year time period in a target population of adults aged ≥60 years from the US healthcare sector perspective

METHODS

Study Design

- A decision-analytic model was developed (**Figure 1**) to estimate the following clinical outcomes: RSV-ARD and RSV-LRTD cases; numbers of hospitalizations and deaths due to RSV-LRTD; and number needed to vaccinate (NNV) to prevent 1 RSV-LRTD case, hospitalization, or death
- Two base-case scenarios exploring differences in RSV-LRTD hospitalization rates were examined (key inputs shown in **Table 1**)
  - Base-case scenario 1: hospitalization rates for RSV-LRTD that used RSV-specific claim codes for inpatient admissions with a principal diagnosis of an RSV-specific or attributable respiratory condition[9]
  - Base-case scenario 2: hospitalization rates increased by 96% to account for underreporting in claims[9]
- Sensitivity analyses were also performed to assess the impact of specific parameter estimates (key inputs shown in **Table 1**)

Figure 1. Model Diagram



ARD, acute respiratory disease; LRTD, lower respiratory tract disease; RSV, respiratory syncytial virus; URD, upper respiratory disease.
For both base-case scenarios, RSV-URD was assumed to be treated in an outpatient setting only, and the RSV-related mortality rate applied to hospitalized patients only.

Table 1. Base-Case Model and Sensitivity Analysis Inputs

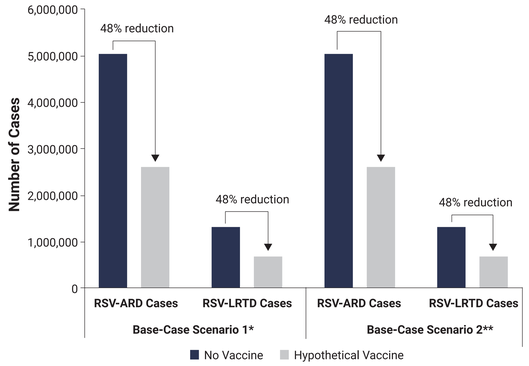
Parameter	Value	
Population size by age group, n		
60-64 years	20,984,053[5]	
65-74 years	31,575,561[5]	
75-84 years	16,140,238[5]	
≥85 years	6,358,229[5]	
Incidence of RSV without vaccination, %		
Symptomatic RSV-ARD	6.7[6]	
RSV-LRTD	26[7]	
RSV-URD	74[7]	
Base-case analyses: scenario 1[a] and scenario 2[a,b]		
	Scenario 1	**Scenario 2**
LRTD hospitalization rates by age group,[c] %		
60-64 years	3.4[9]	6.7[9]
65-74 years	9.0[9]	17.7[9]
75-84 years	15.1[9]	29.6[9]
≥85 years	18.4[9]	36.0[9]
LRTD outpatient rates by age group, %		
60-64 years	96.6[9]	93.3[9]
65-74 years	91.0[9]	82.3[9]
75-84 years	84.9[9]	70.4[9]
≥85 years	81.6[9]	64.0[9]
RSV-related mortality rate (applies to hospitalized patients with RSV-LRTD), %	7.6[6]	
Vaccine coverage, %	50.6 (60-64 years)[10] 69.8 (≥65 years)[10]	
Assumed vaccine efficacy against RSV-ARD, RSV-LRTD, RSV-LRTD requiring inpatient care, and RSV-URD requiring inpatient care	75%	
Individuals with RSV-URD requiring outpatient care	19.5[6]	
Sensitivity analyses, %		
Vaccine efficacy against RSV-ARD, RSV-LRTD, RSV-LRTD requiring inpatient care, and RSV-URD requiring inpatient care	65-80	
Individuals experiencing RSV-ARD (seasonal variation in RSV-ARD)[d]	1.5-7.1	
Individuals experiencing RSV-LRTD[e]	19.5-32.4	
RSV-related mortality (applies to hospitalized patients with RSV-LRTD)[f]	3.1-12.1	

ARD, acute respiratory disease; LRTD, lower respiratory tract disease; RSV, respiratory syncytial virus; URD, upper respiratory disease.
[a]Base-case scenario 1: hospitalization rates for RSV-LRTD that used RSV-specific claim codes for inpatient admissions with a principal diagnosis of an RSV-specific or attributable respiratory condition.[9]
[b]Base-case scenario 2: Due to underreporting of RSV hospitalization events (only 51% of events are reported[9]), hospitalization rates were increased by 96% ([100/51-1]=0.96) to correct for underestimation.[9]
[c]International Classification of Diseases, 9th revision, Clinical Modification (ICD-9-CM) code for all pneumonia (480-486, including RSV-specific 480.1), influenza with pneumonia (487.0), acute bronchiolitis (466.1, including RSV-specific 466.11), obstructive chronic bronchitis (491.2), or RSV (079.6).
[d]The range used for RSV-ARD incidence reflects seasonal variation, with 1.5% based on the 2002-2003 season and 7.1% based on the 2000-2001 season.[9]
[e]For % RSV-LRTD, the 95% confidence interval was calculated from Hall 2001.[7]
[f]For mortality, the 95% CI was calculated from Falsey 2005.[6]

RESULTS

In both base-case scenarios, an RSV vaccine would prevent 2.4 million RSV-ARD cases, of which 600,000 represent RSV-LRTD cases (**Figure 2**)

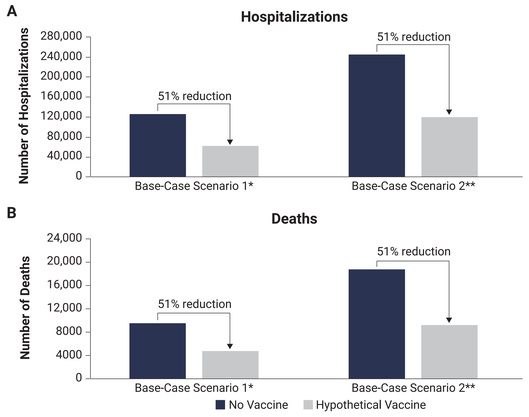
Figure 2. Potential Reduction in RSV-ARD and RSV-LRTD Cases Following Receipt of a Hypothetical RSV Vaccine



ARD, acute respiratory disease; LRTD, lower respiratory tract disease; RSV, respiratory syncytial virus.
*Base-case scenario 1: hospitalization rates that used RSV-specific claim codes.
**Base-case scenario 2: hospitalization rates increased by 96% to account for underreporting in claims. Note: varying the hospitalization rate in Base-Case Scenario 2 had no impact on ARD and LRTD cases.

- An RSV vaccination strategy would reduce the total number of RSV-LRTD hospitalizations and deaths by 63,600 and 4800, respectively, in scenario 1, and 124,700 and 9500 in scenario 2 (**Figure 3**)

Figure 3. Potential Reduction of (A) RSV-LRTD Hospitalizations and (B) Deaths Following Receipt of a Hypothetical RSV Vaccine



LRTD, lower respiratory tract disease; RSV, respiratory syncytial virus.
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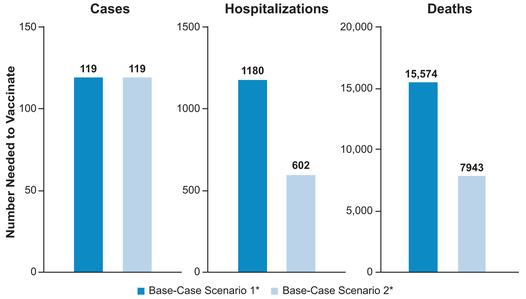
- The NNVs to prevent 1 RSV-LRTD case, hospitalization, or death are presented in **Figure 4**

Figure 4. NNV to Prevent 1 RSV-LRTD Case, Hospitalization, or Death

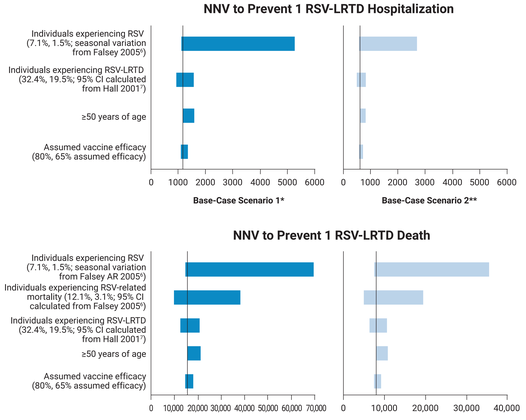


Number needed to vaccinate = $1/(Rate_{NoVaccine}-Rate_{HypotheticalVaccine})$.
LRTD, lower respiratory tract disease; NNV, number needed to vaccinate; RSV, respiratory syncytial virus.
*Base-case scenario 1: hospitalization rates that used RSV-specific claim codes.
**Base-case scenario 2: hospitalization rates increased by 96% to account for underreporting in claims.

Sensitivity Analyses

- For both scenarios, the NNVs to prevent 1 RSV-LRTD hospitalization or death were most sensitive to seasonal variation in RSV incidence (**Figure 5**)
- After seasonal variation, results were most sensitive to the proportion of patients experiencing RSV-LRTD and the mortality rate applied to patients hospitalized with RSV-LRTD

Figure 5. NNV to Prevent 1 RSV-LRTD Hospitalization or Death



CI, confidence interval; LRTD, lower respiratory tract disease; NNV, number needed to vaccinate; RSV, respiratory syncytial virus.
*Base-case scenario 1: hospitalization rates that used RSV-specific claim codes.
**Base-case scenario 2: hospitalization rates increased by 96% to account for underreporting in claims.

CONCLUSIONS

- Results suggest that an effective RSV vaccine (75% efficacy) would substantially reduce RSV-ARD and RSV-LRTD cases, as well as RSV-LRTD hospitalizations and deaths, in adults aged ≥60 years
- Although results varied with RSV-LRTD hospitalization rates, the sensitivity analyses revealed that results were most sensitive to the incidence of RSV-ARD, which is not only variable by season, but also highly uncertain
  - Falsey 2005 was a landmark prospective study that identified symptomatic RSV cases in the community and among hospitalized cases, but had a limited sample size (5-20 cases per year)
- Additional studies that estimate the incidence of RSV-ARD and RSV-LRTD by location of care are warranted, as the magnitude of impact depends on RSV epidemiology in older adults, which is still being defined

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For additional information, please contact Parinaz Ghaswalla, PhD (Parinaz.Ghaswalla@modernatx.com).

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MK is a shareholder in Quadrant Health Economics Inc., which was contracted by Moderna, Inc., to conduct this study. KF and MCW are consultants at Quadrant Health Economics Inc. CAP, POB, and PG are employees of Moderna, Inc., and hold stock/stock options in the company.