The Potential Benefit of Respiratory Syncytial Virus (RSV) Vaccination in Older Adults: A Comparison of the United States (US) and United Kingdom (UK)

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BACKGROUND

- Respiratory syncytial virus (RSV) is a major cause of severe respiratory disease in older adults and adults with underlying conditions such as chronic heart or lung disease[1]
  - However, RSV burden in older adults is likely underestimated due to a lack of routine testing[2,3]
- Globally, there are approximately 1.5 million annual episodes of RSV-associated acute respiratory infections in adults aged 65 years or older,[4] leading to an estimated 336,000 hospitalisations and 14,000 in-hospital deaths
- Despite the substantial burden of RSV, no vaccines are currently approved to prevent or reduce the severity of RSV disease.[1] However, several efforts are ongoing to develop RSV vaccines, including a novel mRNA-based vaccine, mRNA-1345, that is currently being investigated in older adults in a phase 2/3 trial

OBJECTIVE

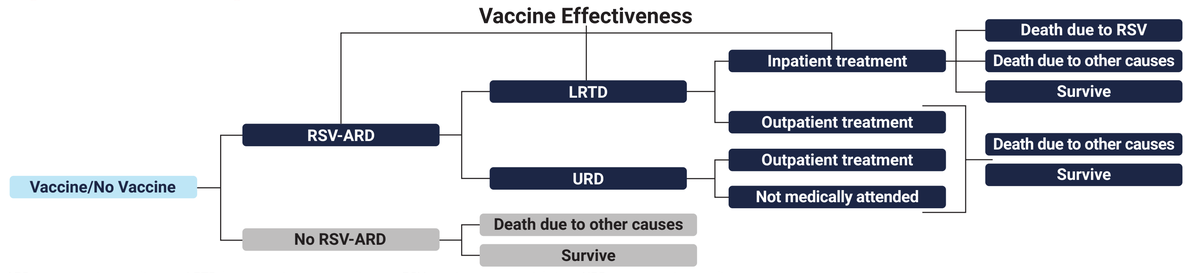
- To compare the potential benefit of a hypothetical RSV vaccine with 75% efficacy compared with no vaccine in 1 million older adults aged ≥60 years in the United States (US) and United Kingdom (UK) over a 1-year time horizon

METHODS

Study Design

- A decision-analytic model was developed (**Figure 1**) to estimate the following clinical outcomes: RSV-acute respiratory disease (ARD) cases, RSV-lower respiratory tract disease (LRTD) cases, RSV-LRTD hospitalisations, RSV-LRTD mortality, and the number needed to vaccinate (NNV) to prevent these outcomes
  - NNV was calculated as the reciprocal of the absolute value of the difference of the event rate in the vaccinated and unvaccinated cohorts
- Model inputs (**Table 1 and Supplemental Table 1; accessible through the QR code**) were estimated from published literature and other publicly available sources[2,5-11]
  - UK estimates included hospital- and community-associated RSV deaths, whereas US estimates were based on in-hospital deaths only
- Sensitivity analyses for the UK were performed to assess the impact of varying hospitalisation rates and vaccine efficacy on the NNVs
  - Hospitalisation rates: in a US retrospective electronic medical record review, Datta et al found that RSV infection was documented in discharge coding in only 51% of cases[12]; assuming the Fleming study may have some of the same challenges, the UK base-case hospitalisation rates were inflated by 96% ([100/51-1]=0.96) to correct for underestimation[5]
  - Vaccine efficacy against all endpoints was varied using a targeted range of 65% to 80%

Figure 1. Model Diagram



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

Table 1. Base-Case Model Key Inputs

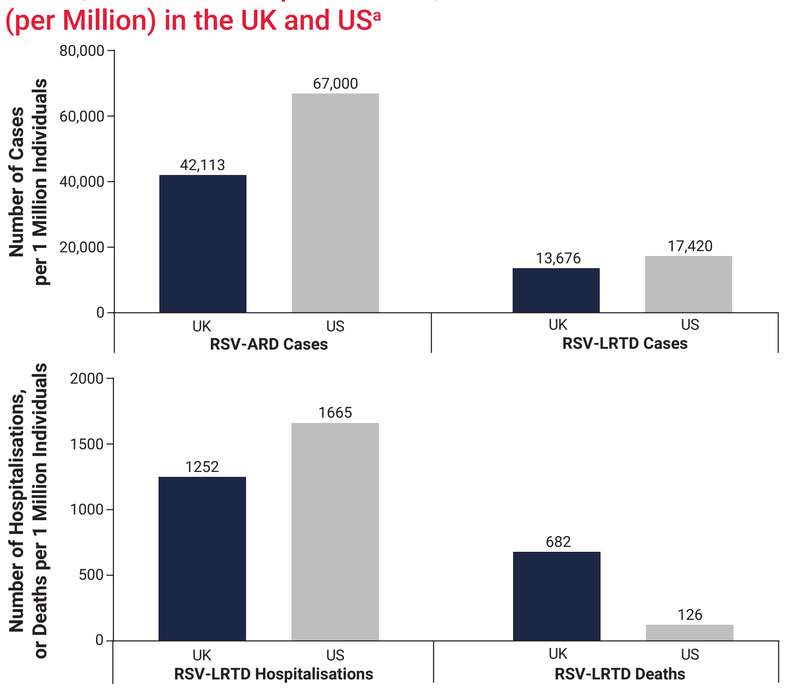
Parameter	Value	
	UK N = 1,000,000	US N = 1,000,000
Assumed vaccine efficacy against RSV-ARD, RSV-LRTD, RSV-LRTD requiring inpatient care, and RSV-URD requiring inpatient care, %	75.0	
RSV-URD requiring inpatient treatment, %	0[5]	0[2,a]
RSV-LRTD requiring inpatient treatment, %	60-64 years: 3.9[5] 65-74 years: 6.8[5] ≥75 years: 12.4[5]	50-64 years: 3.4[11] 65-74 years: 9.0[11] 75-84 years: 15.1[11] ≥85 years: 18.4[11]
Death due to RSV-LRTD requiring inpatient treatment, %		
60-64 years	20.0[5]	7.6[2]
65-74 years	33.7[5]	7.6[2]
≥75 years	66.2[5]	7.6[2]

ARD, acute respiratory disease; LRTD, lower respiratory tract disease; RSV, respiratory syncytial virus; UK, United Kingdom; URD, upper respiratory disease; US, United States.
[a]Falsey does not distinguish between URD and LRTD.

RESULTS

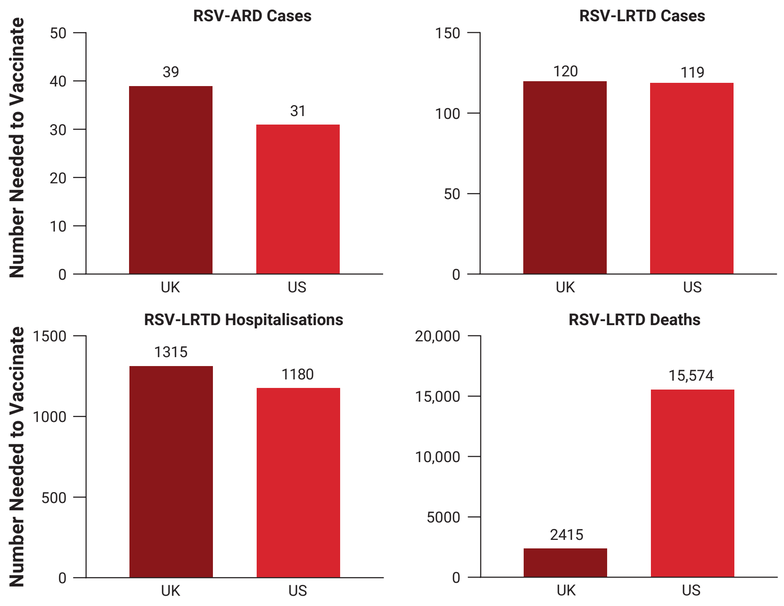
- In the absence of an RSV vaccine, the estimated number of RSV-ARD and RSV-LRTD cases per million were estimated to be lower in the UK than the US. Similarly, the estimated number of RSV-LRTD hospitalisations per million were lower in the UK compared with the US; however, the number of RSV-LRTD attributable deaths per million were higher in the UK than the US (**Figure 2**)
- The NNV to prevent 1 RSV-LRTD death was substantially higher in the US than the UK (**Figure 3**)

Figure 2. Estimated Number of RSV-ARD Cases, RSV-LRTD Cases, RSV-LRTD Hospitalisations, and RSV-LRTD Deaths (per Million) in the UK and US[a]



ARD, acute respiratory disease; LRTD, lower respiratory tract disease; RSV, respiratory syncytial virus; UK, United Kingdom; US, United States.
[a]UK mortality data include hospital- and community-associated deaths; US estimates were based on in-hospital deaths only.

Figure 3. Number Needed to Vaccinate[a] to Prevent 1 RSV-ARD Case, RSV-LRTD Case, RSV-LRTD Hospitalisation, or RSV-LRTD Death[b]

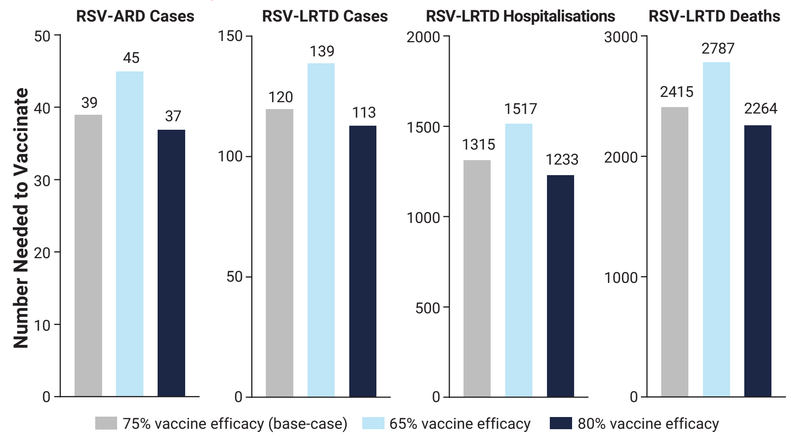


ARD, acute respiratory disease; LRTD, lower respiratory tract disease; RSV, respiratory syncytial virus; UK, United Kingdom; URD, upper respiratory disease; US, United States.
[a]Number needed to vaccinate = $1/(Rate_{NoVaccine}\text{-}Rate_{HypotheticalVaccine})$.
[b]Vaccine efficacy was assumed to be 75% against RSV-ARD, RSV-LRTD, RSV-LRTD requiring inpatient care, and RSV-URD requiring inpatient care.

Sensitivity Analyses (UK Only)

- Inflating hospitalisation rates by 96% to account for underreporting would cause the NNV to prevent 1 RSV-LRTD hospitalisation to fall from 1315 to 671
- Reducing vaccine efficacy from 75% to 65% would cause the NNVs to prevent 1 RSV-LRTD hospitalisation and RSV-LRTD death to increase to 1517 and 2787 in the UK, respectively, while an increase to 80% efficacy would cause the NNVs to prevent 1 RSV-LRTD hospitalisation and RSV-LRTD death to fall to 1233 and 2264, respectively (**Figure 4**)

Figure 4. Number Needed to Vaccinate[a] to Prevent 1 RSV-ARD Case, RSV-LRTD Case, RSV-LRTD Hospitalisation, or RSV-LRTD Death for the Base-Case Scenario With a Vaccine With 65% and 80% Efficacy in the UK



ARD, acute respiratory disease; LRTD, lower respiratory tract disease; RSV, respiratory syncytial virus; UK, United Kingdom.
[a]Number needed to vaccinate = $1/(Rate_{NoVaccine}\text{-}Rate_{HypotheticalVaccine})$.

CONCLUSIONS

- Results suggest there are higher rates of RSV-attributable death in the UK despite a lower hospitalisation rate; this is likely because the UK mortality data include hospital- and community-associated deaths
  - UK mortality data may also reflect longer-term follow-up and exacerbations triggered by RSV, whereas US mortality rates are based on the acute infection period only
- Despite limitations on US mortality data and differences in healthcare systems, in both countries, an effective RSV vaccine (75% efficacy) appears to prevent significant morbidity and mortality in adults aged ≥60 years
- Sensitivity analyses for the UK revealed that variations in vaccine efficacy would have a significant impact on the NNV to prevent 1 RSV-associated hospitalisation and death
- In the US, mortality data outside of the hospital are needed to characterise the full burden of severe RSV disease and for policy decision-makers to assess the value and cost-effectiveness of RSV vaccines under development

ABSTRACT PLAIN LANGUAGE SUMMARY

Please scan the QR code for a PDF of the poster, supplementary material, and an infographic plain language summary of the submitted abstract. Copies of the poster, supplementary material and summary obtained through the QR code are for personal use only and may not be reproduced without written permission of the authors.

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Disclosures

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.

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