Assessing the Potential Public Health Impact of the mRNA-Based Respiratory Syncytial Virus (RSV) Vaccine, mRNA-1345, With a Broad Vaccination Campaign Among Older Adults in the United Kingdom: Modelling Study

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BACKGROUND

- Respiratory syncytial virus (RSV) is one of the most common causes of respiratory infections in children and adults[1]
- In the United Kingdom, the RSV season typically begins in October, reaches its peak in December, and gradually subsides by March[2]
- RSV is associated with a significant clinical burden in older adults, leading to substantial morbidity, mortality, and economic disruption
  - In England, the reported incidence of RSV hospitalisation for the 2022/2023 season was 43 and 65 admissions per 100,000 individuals for people aged ≥65 years and ≥75 years, respectively;[3] however, it is recognised that the burden of disease is largely underestimated, likely because of variations in clinical specimens, suboptimal sensitivity of diagnostic tests, and a lack of testing performed in hospitals[4-6]
- Recommendations from the Joint Committee on Vaccination and Immunisation (JCVI) advised vaccination against RSV for adults aged 75-80 years as a one-off campaign, and then vaccinating those turning 75 years in subsequent years
- Few studies have evaluated the potential public health impact of a broader RSV vaccination campaign in older adults aged ≥60 years in the UK, including the indirect effects of vaccination using dynamic transmission models
  - It was shown that such broader campaigns are expected to have a greater impact on the burden of disease[2], highlighting the need for further evidence-generation efforts to inform public health decision-making

OBJECTIVE

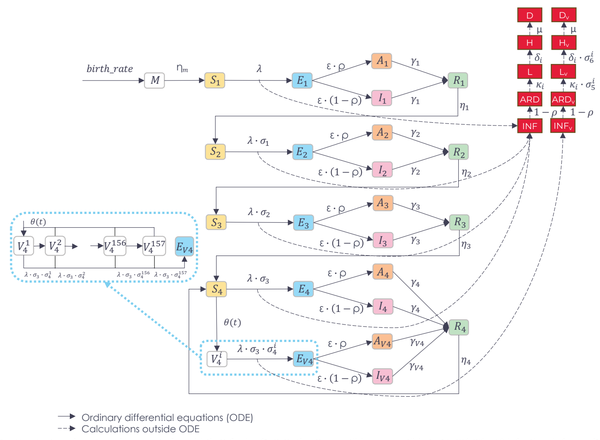
- The aim of this study was to estimate the public health impact of an RSV vaccination campaign with mRNA-1345 vaccine among adults aged ≥60 years over a 20-year time horizon

METHODS

Model Overview

- RSV epidemiology and the impact of vaccination in the total UK population was simulated using an age-stratified dynamic transmission model adapted from Hodgson et al.[7] and incorporating vaccination of older adults
  - The model accounts for RSV seasonality, changes in population size and age structure over time, and contact patterns by age, and estimates the number of incident RSV infections, RSV-associated acute respiratory disease (ARD), lower respiratory tract disease (LRTD), hospitalisations, and deaths by age
  - The model structure is presented in **Figure 1**

Figure 1. Dynamic Transmission Model Structure



Main compartments: M – Maternal: maternal immunity from birth, S_i for $i \in \{1, 2, 3, 4\}$ – Susceptible: susceptible to 1st, 2nd, 3rd, ≥4th infection, E_i for $i \in \{1, 2, 3, 4\}$ – Exposed: exposure to infection, A_i for $i \in \{1, 2, 3, 4\}$ – Asymptomatic and infectious, I_i for $i \in \{1, 2, 3, 4\}$ – Symptomatic and infectious (ARD), R_i for $i \in \{1, 2, 3, 4\}$ – Recovered: infection-induced immunity, V_4^j for $j \in \{1, ..., 157\}$ – Vaccinated after 3+ infections, i-th week since vaccination, E_{V4} – Exposed: after vaccination, A_{V4} – Asymptomatic and infectious: after vaccination, I_{V4} – Symptomatic and infectious (ARD): after vaccination.

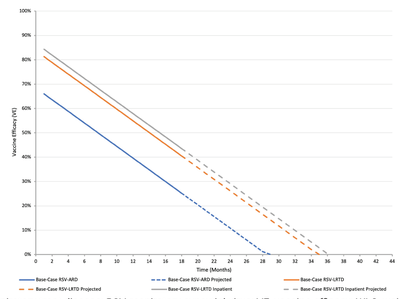
Observational compartments: INF/INF_v – Total number of RSV infections, ARD/ARD_v – Number of ARD cases, L/L_v – Number of LRTD cases, H/H_v – Number of hospitalised cases, D/D_v – Number of fatal cases.

Main parameters: birth_rate – Birth rate, η_m – Waning rate of maternal immunity, λ – Force of infection, ε – Rate of becoming infectious, σ_i for $i \in \{1, 2, 3\}$ – Relative risk of re-infection, ρ – Proportion of infections that are asymptomatic, γ_i for $i \in \{1, 2, 3, 4\}$ – Recovery rate from infection, η_i for $i \in \{1, 2, 3, 4\}$ – Waning rate of post-infection immunity, κ_i for $i \in \{1, 2, 3, 4\}$ – Proportion of ARD that are LRTD, δ_i for $i \in \{1, 2, 3, 4\}$ – Proportion of hospitalisations due to LRTDs, μ – Proportion of deaths due to hospitalised LRTD, θ – Vaccination coverage, γ_{V4} – Recovery rate from infection in vaccinated, σ_4^i – Relative risk of RSV infection in vaccinated vs not vaccinated, in i-th week since vaccination, σ_5^i – Relative risk of LRTD given ARD in vaccinated vs not vaccinated, in i-th week since vaccination, σ_6^i – Relative risk of hospitalisation given LRTD in vaccinated vs not vaccinated, in i-th week since vaccination.

Model Inputs

- The model was calibrated to reproduce the expected number of RSV-related hospitalisations in the UK, informed by surveillance reports for 2023/2024 season[8]
- To account for underreporting, an adjustment factor of 1.5 was applied,[5] ensuring a more accurate estimate of RSV hospitalisations
- Other input parameters were based on UK-specific data, when available, and other relevant literature
- Vaccine efficacy inputs for mRNA-1345 were informed by a pivotal phase 2/3 ConquerRSV trial (median follow-up of ~1.5 years; data cutoff: March 8, 2024), which considered RSV ARD, RSV LRTD, and hospitalisation due to RSV LRTD as main endpoints
- Vaccine efficacy was projected linearly for up to 3 years post-vaccination, with an estimated monthly waning rate of 2.4% for all types of efficacy (**Figure 2**)
- Two vaccination strategies were assessed, targeting individuals aged ≥60 years or ≥65 years, with 80% coverage, similar to influenza coverage, and biennial vaccination starting from September 2024
- Vaccination strategy in the ≥60-year age group aligns with the clinical trial population, and the strategy in the ≥65-year age group was selected in line with JCVI's review of cost-effectiveness of the immunisation programme against RSV in this population

Figure 2. Base-Case Vaccine Efficacy[a,9,10]



ARD, acute respiratory disease; 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.

RESULTS

Public Health Impact in the Total Population

- Compared with no RSV vaccination, vaccinating adults aged ≥60 years over a 20-year time horizon could prevent more than 45,000,000 RSV infections (symptomatic and asymptomatic), 190,000 RSV hospitalisations (21% reduction), and 95,000 deaths (52% reduction) across all age groups in the total UK population (**Table 1; Figure 3**)
- Vaccination in adults aged ≥65 years would also have a considerable impact, preventing more than 34,000,000 RSV infections, 170,000 hospitalisations (19% reduction), and 90,000 deaths (49% reduction) across all age groups in the total UK population (**Table 1; Figure 3**)

Table1. Public Health Impact in the Total Population, mRNA-1345 vs. No Vaccination

Outcome	No vaccination	Vaccination in the ≥60-year age group		Vaccination in the ≥65-year age group	
	Number of cases in the total population	Number of cases	Number of cases avoided (%)	Number of cases	Number of cases avoided (%)
RSV infections	433,654,682	388,113,000	45,541,682 (11)	399,142,254	34,512,429 (8)
RSV ARD	139,687,377	127,955,439	11,731,937 (8)	130,808,355	8,879,021 (6)
RSV LRTD	14,612,633	12,374,450	2,238,183 (15)	12,763,704	1,848,929 (13)
RSV hospitalisations	903,970	713,494	190,477 (21)	733,199	170,771 (19)
RSV deaths	184,305	88,932	95,374 (52)	93,905	90,400 (49)

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

Note: The number of vaccine doses administered was 153,588,857 for the vaccination campaign in adults aged ≥60 years old and 119,716,348 for the vaccination campaign in adults aged ≥65 years old.

Public Health Impact in Targeted Populations

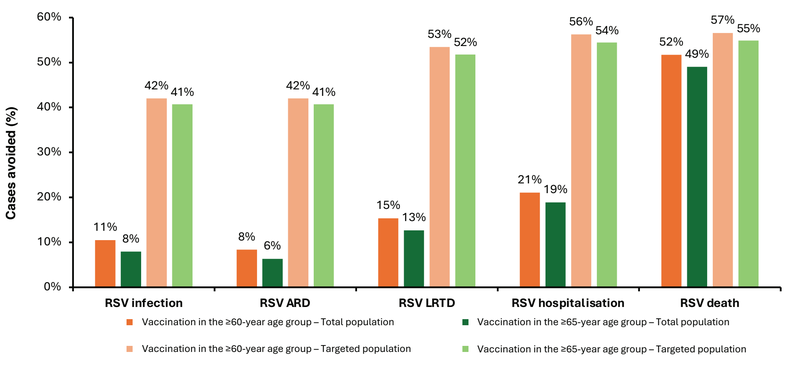
- Within the targeted population of adults aged ≥60 years, vaccination with mRNA-1345 is expected to prevent more than 25,000,000 RSV infections (symptomatic and asymptomatic), 169,000 hospitalisations (56% reduction), and 93,000 deaths (57% reductions) over 20 years, in comparison to no vaccination (**Table 2; Figure 4a**)
- For a targeted population of adults aged ≥65 years, the expected impact of vaccination would be also considerable, averting more than 17,000,000 RSV infections, 153,000 hospitalisations (54% reduction), and 89,000 of deaths (55% reduction) (**Table 2; Figure 4b**)

Table 2. Public Health impact in the Targeted Populations, mRNA-1345 vs. No Vaccination

Outcome	No vaccination		Vaccination in the ≥60-year age group		Vaccination in the ≥65-year age group	
	Number of cases, ≥60 years	Number of cases, ≥65 years	Number of cases	Number of cases avoided (%)	Number of cases	Number of cases avoided (%)
RSV infections	60,163,471	44,194,957	34,878,439	25,285,032 (42)	26,209,513	17,985,444 (41)
RSV ARD	14,138,416	10,385,815	8,196,433	5,941,983 (42)	6,159,236	4,226,579 (41)
RSV LRTD	3,266,372	2,784,682	1,520,689	1,745,684 (53)	1,343,011	1,441,671 (52)
RSV hospitalisations	301,338	282,448	131,853	169,485 (56)	128,652	153,796 (54)
RSV deaths	166,062	162,284	72,076	93,986 (57)	73,241	89,043 (55)

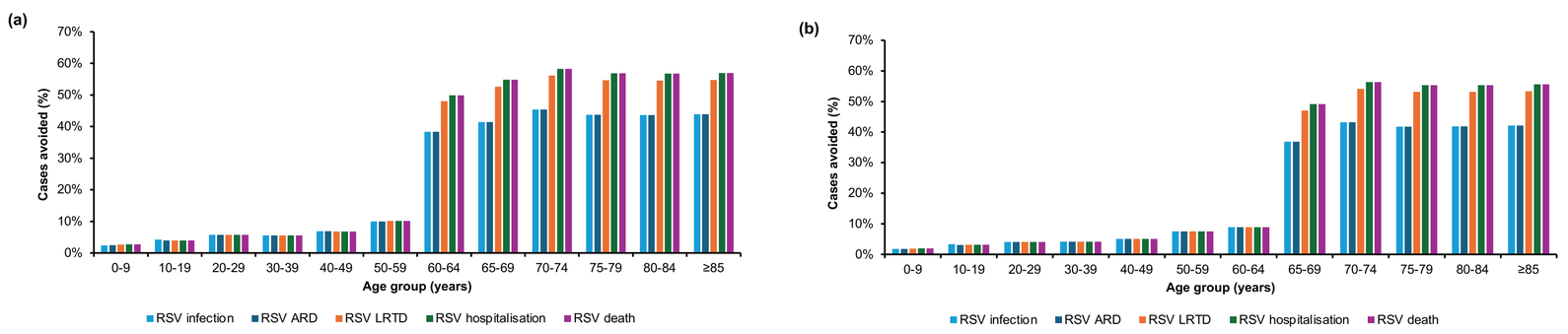
ARD, acute respiratory disease; LRTD, lower respiratory tract disease; RSV, respiratory syncytial virus.

Figure 3. Percentage of Cases Avoided in the Total and Targeted Populations, mRNA-1345 vs. No Vaccination



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

Figure 4. Percentage of Cases Avoided by Age Group, mRNA-1345 vs. No Vaccination, (a) Vaccination in Those Aged ≥60 Years, and (b) Vaccination in Those Aged ≥65 Years



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

CONCLUSIONS

- A broad mRNA-1345 vaccination campaign against RSV targeting older adults aged ≥60 years in the UK could substantially reduce the number of RSV infections, associated hospitalisations, and deaths, alleviating the winter pressure on NHS services and improving patient outcomes
- Further efforts to improve vaccine access and uptake in vulnerable populations, such as older adults, are essential to ensure a substantial long-term decrease in the burden of RSV disease on individuals and the healthcare system

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P Ghaswalla, O Balogh, and K Joshi are employees of Moderna, Inc., and may hold stock/stock options in the company.

ADDITIONAL INFORMATION

Please scan the QR code for a PDF copy of the poster.

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