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Effect of respiratory syncytial virus (RSV) vaccines on hospital admissions in Wales

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Contents

Summary

- Respiratory Syncytial Virus (RSV) exerts significant pressure on healthcare systems in Wales particularly during winter, making accurate forecasting of potential hospital admissions critical for healthcare resource planning.
- We developed a mathematical transmission model to estimate the impact of the RSV vaccination programme on hospital admissions that quantifies the number of admissions potentially averted in infants and adults aged 75-79 under varying levels of vaccine uptake.
- Model scenarios were compared against observed hospital admission data from Wales during the 2024/25 winter season and used to generate forward-looking scenarios for winter 2025/26.
- The model estimates that 9-30% of admissions among infants aged 1–6 months, 3-12% in infants aged 7–12 months, and 26-53% among adults aged 75-79 years could be prevented in the second year of vaccine rollout (winter 2025/26) with RSV vaccine uptake levels of 30-90%.
- These projections are intended to inform planning and preparedness within Wales.

Introduction

Respiratory Syncytial Virus (RSV) is a common respiratory virus that typically causes mild, cold-like symptoms.[1] RSV infects up to 90% of children within the first two years of life, with most hospitalisations occurring in this age group.[1] However, RSV can also reinfect vulnerable children and older adults (aged 65 and above) who accounted for 21% of the total RSV admissions in Wales during the 2023/24 winter.[2]

The UK became the first country to introduce RSV vaccines for pregnant women and adults aged 75-79 starting in September 2024.[3] The NHS adult vaccine campaign includes a routine program where older adults are offered the RSV vaccination within 12 weeks of their 75th birthday and a one-off catch-up campaign for those aged 75 to 79. The aim of this paper is to produce a modelled estimate of the number of hospital admissions averted in infants aged 0-6 months, 7-12 months, and adults aged 75-79 years as a result of RSV vaccination program targeted towards pregnant women and older adults (catch-up program).

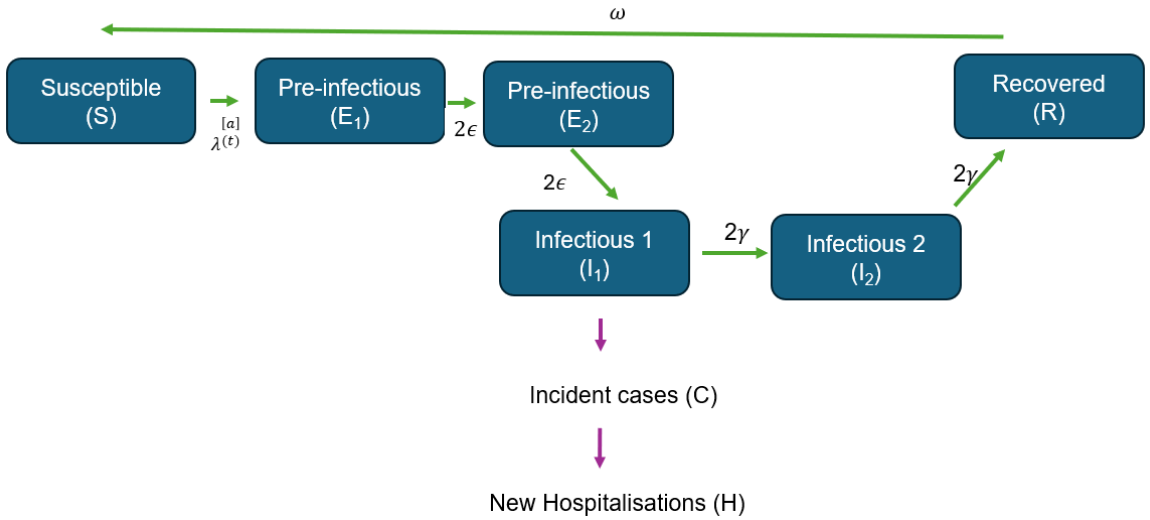
[1] Respiratory syncytial virus (RSV) immunisation programme for infants and older adults: JCVI full statement, 11 September 2023 - GOV.UK
[2] Science Evidence Advice: winter modelling 2024 to 2025
[3] National RSV vaccination programme announced - GOV.UK

Methods

The base model structure

A modified SEIRS compartment transmission model was employed (SE_2I_2RS), incorporating two compartments for the pre-infectious and infectious states **(Figure 1)**.[4]

Figure 1: Age-stratified transmission compartment model structure for modelling RSV hospital admissions



Source: Science, Research and Evidence team

The population was stratified by age and assumed to mix non-randomly, based on the contact matrix from the POLYMOD survey **(Figure 3 and 4)**.[5] The aging rates were adjusted to keep the demographic structure consistent i.e. the various compartments are aged but leaving the population size of each age group constant over time.

[4] fluEvidenceSynthesis: An R package for evidence synthesis based analysis of epidemiological outbreaks | PLOS Computational Biology
[5] Social contacts and mixing patterns relevant to the spread of infectious diseases - PubMed

Equations for the base model [6]

$$\frac{dS^{[a]}}{dt} = -\lambda^{[a]}(t)S^{[a]} + \omega R^{[a]} - \tau_{out}^{[a]}S^{[a]} + \tau_{in}^{[a]}S^{[a-1]} + \kappa$$

$$\frac{dE_1^{[a]}}{dt} = +\lambda^{[a]}(t)S^{[a]} - 2\epsilon E_1^{[a]} - \tau_{out}^{[a]}E_1^{[a]} + \tau_{in}^{[a]}E_1^{[a-1]}$$

$$\frac{dE_2^{[a]}}{dt} = 2\epsilon(E_1^{[a]} - E_2^{[a]}) - \tau_{out}^{[a]}E_2^{[a]} + \tau_{in}^{[a]}E_2^{[a-1]}$$

$$\frac{dI_1^{[a]}}{dt} = 2\epsilon E_2^{[a]} - 2\gamma I_1^{[a]} - \tau_{out}^{[a]}I_1^{[a]} + \tau_{in}^{[a]}I_1^{[a-1]}$$

$$\frac{dI_2^{[a]}}{dt} = 2\gamma\left(I_1^{[a]} - I_2^{[a]}\right) - \tau_{out}^{[a]}I_2^{[a]} + \tau_{in}^{[a]}I_2^{[a-1]}$$

$$\frac{dR^{[a]}}{dt} = 2\gamma\left(I_2^{[a]}\right) - \omega R^{[a]} - \tau_{out}^{[a]}R^{[a]} + \tau_{in}^{[a]}R^{[a-1]}$$

S denotes the susceptible compartment, E_1 and E_2 are the pre-infectious compartments, I_1 and I_2 represent the infectious compartments, and R is the recovered compartment. Parameters and compartments that vary by age are identified with superscripts [a-1] and [a], where [a-1] denotes the previous age group, and [a] represents the current age group.

ϵ, γ, ω and $\lambda^{[a]}(t)$ represent the overall rate of loss of latency, infectiousness and natural immunity and force of infection for age group a. $\tau_{in}^{[a]}$ and $\tau_{out}^{[a]}$ represent the aging rates for age group a and κ represents births. $\tau_{in}^{[a]}$ indicates the rate at which individuals from the previous age group enter the current age group while $\tau_{out}^{[a]}$ indicates the rate at which individuals leave the current age group. $\tau_{in}^{[a]}$ and $\tau_{out}^{[a]}$ depend on the size of the age bands used in the model and were calculated using the same methods in Giannini et al.[7] For the model structure and equations including the effects of vaccination, please refer to Figure 2 and the Appendix

[6] Please note that the model equations include aging which is not shown in **Figure 1**

[7] Modelling respiratory syncytial virus age-specific risk of hospitalisation in term and preterm infants - PubMed

The force of infection (the rate at which susceptible individuals become infected with the disease) was modelled as a product of age-specific contact rates, number of infected individuals within each age group with transmissibility that is a cosine function of time. The amplitude of the transmissibility function was determined by the constants b_0 and b_1 and the phase shift was determined by the age-specific constant ϕ^a to capture the seasonality in RSV admissions.

$$\lambda^{[a]}(t) = b_0(1 + b_1 \cos\left(2\pi \frac{t}{365} - \varphi^{[a]}\right) \sum_{b=1}^{b=29} C^{[a,b]} \frac{(I_1^{[b]}(t) + I_2^{[b]}(t))}{N^b}$$

$\lambda^{[a]}(t)$ is the force of infection for age group 'a', $C^{[a,b]}$ is relative contact rate between age group a and b, $I_1^{[b]}$ and $I_2^{[b]}$ are the number of infectious individuals within age group b, $N^{[b]}$ the total population size of the age group b.

The incident cases were derived from the new infectious individuals entering the initial infectious compartment (I_1, **Figure 1**) from the pre-infectious compartment (E_2, **Figure 1**). New hospital admissions were calculated as a proportion of the incident cases (defined by age-specific infection to hospitalisation ratios $h^{[a]}$).[8]

Equations for calculating incident cases and hospital admissions

$$\frac{dC^{[a]}}{dt} = 2\epsilon E_2^{[a]}$$

$$H^{[a]} = C^{[a]} * h^{[a]}$$

The ordinary differential equations were written using R package Odin and solved numerically using the Euler method.[9]

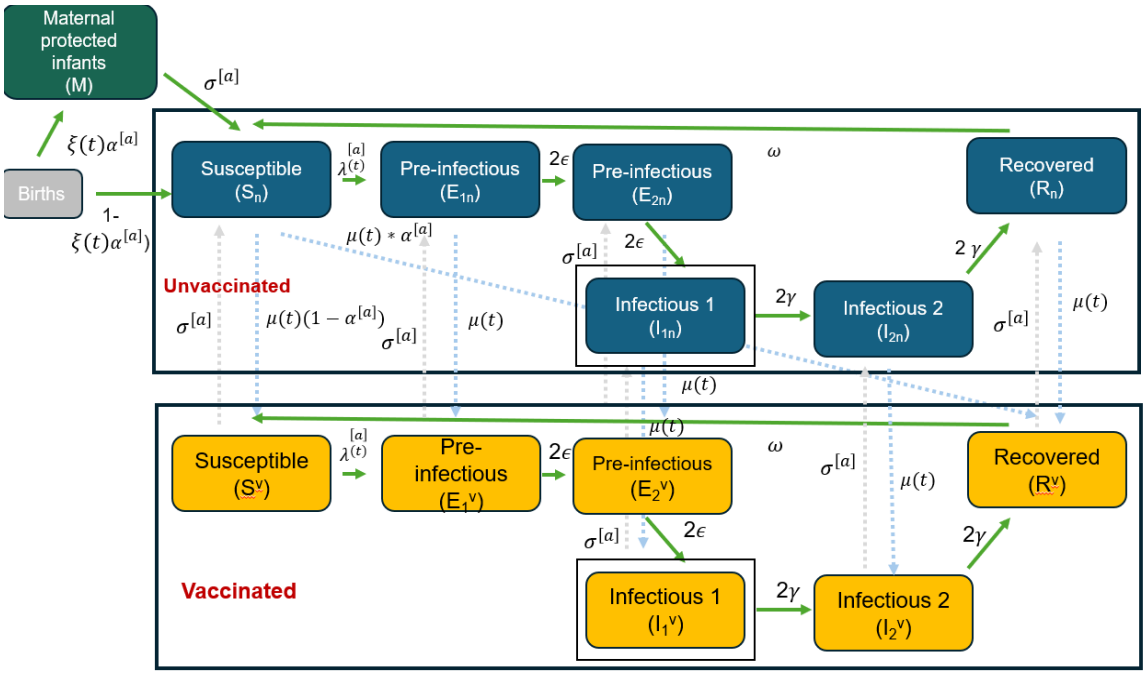
The vaccination model structure

To account for the effects of maternal vaccination on infant births, a new compartment (M, or maternally protected) was included in the model (**Figure 2**). Births protected by the vaccination (as a result of being born to pregnant women who

[8] Please note that the incident cases and admissions are not separate compartments themselves, but calculations based on the individuals entering the I_1 compartments.
[9] CRAN: Package odin

are vaccinated) enter the M compartment, whilst those not protected by the vaccine enter the susceptible compartment. The model however does not transfer pregnant women into another compartment, therefore doesn't include the direct and indirect effects of vaccinating pregnant women. The probability of infants entering the M compartment ($\xi(t)$) is determined by the product of vaccine uptake in pregnant mothers (%) and vaccine efficacy, with a 12-week delay to account for the time between vaccinating 28-week pregnant mothers and the birth of protected infants.

Figure 2: Age-stratified transmission compartment model structure for modelling RSV hospital admissions including the effects of vaccination



To account for the effects of vaccination in 75–79-year-olds, each of the epidemiological compartments (SE_2I_2R) in the model were further divided into vaccinated (yellow boxes in **Figure 2**) and unvaccinated groups (blue boxes in **Figure 2**) as done in Leeuwen et al.[10] The rate of transferring adults from unvaccinated compartments to vaccinated compartments was dictated by time-sensitive parameter ($\mu(t)$) - the slope of the logistic fit of flu vaccine uptake update extrapolated for the duration of vaccination (See **Figure 6**).

[10] fluEvidenceSynthesis: An R package for evidence synthesis based analysis of epidemiological outbreaks | PLOS Computational Biology

Equations for the vaccination model [11]

The differential equations below incorporate the effects of vaccination in the SE_2I_2R model.

$$\frac{dM_v^{[a]}}{dt} = -\sigma^{[a]}M_v^{[a]} + births * \xi(t) * \alpha^{[a]} - \tau_{out}^{[a]} * M_v^{[a]} + \tau_{in}^{[a]} * M_v^{[a-1]}$$

$$\frac{dS_n^{[a]}}{dt} - \lambda^{[a]}(t)S_n{}^{[a]} + \omega R_n{}^{[a]} - \tau_{out}^{[a]}S_n{}^{[a]} + \tau_{in}^{[a]}S_n{}^{[a-1]} - \mu(t)S_n{}^{[a]} + \sigma^{[a]}S_v{}^{[a]} + \sigma^{[a]}M_v^{[a]} + births(1 - \xi(t)\alpha^{[a]})$$

$$\frac{dE_{1n}^{[a]}}{dt} = +\lambda^{[a]}(t)S_n{}^{[a]} - 2\epsilon E_{1n}{}^{[a]} - \tau_{out}^{[a]}E_{1n}^{[a]} + \tau_{in}^{[a]}E_{1n}^{[a-1]} - \mu(t)E_{1n}{}^{[a]} + \sigma^{[a]}E_{1v}{}^{[a]}$$

$$\frac{dE_{2n}^{[a]}}{dt} = 2\epsilon(E_{1n}^{[a]} - E_{2n}^{[a]}) - \tau_{out}^{[a]}E_{2n}^{[a]} + \tau_{in}^{[a]}E_{2n}^{[a-1]} - \mu(t)E_{2n}{}^{[a]} + \sigma^{[a]}E_{2v}{}^{[a]}$$

$$\frac{dI_{1n}^{[a]}}{dt} = 2\epsilon E_{2n}^{[a]} - 2\gamma I_{1n}^{[a]} - \tau_{out}^{[a]}I_{1n}^{[a]} + \tau_{in}^{[a]}I_{1n}^{[a-1]} - \mu(t)I_{1n}{}^{[a]} + \sigma^{[a]}I_{1v}{}^{[a]}$$

$$\frac{dI_{2n}^{[a]}}{dt} = 2\gamma\left(I_{1n}^{[a]} - I_{2n}^{[a]}\right) - \tau_{out}^{[a]}I_{2n}^{[a]} + \tau_{in}^{[a]}I_{2n}^{[a-1]} - \mu(t)I_{2n}{}^{[a]} + \sigma^{[a]}I_{2v}{}^{[a]}$$

$$\frac{dR_n{}^{[a]}}{dt} = 2\gamma\left(I_{2n}^{[a]}\right) - \omega R_n{}^{[a]} - \tau_{out}^{[a]}R_n{}^{[a]} + \tau_{in}^{[a]}R_n{}^{[a-1]} - \mu(t)R_n{}^{[a]} + \sigma^{[a]}R_v{}^{[a]}$$

$$\frac{dS_v^{[a]}}{dt} = -\lambda^{[a]}(t)S_v{}^{[a]} + \omega R_v{}^{[a]} - \tau_{out}^{[a]}S_v{}^{[a]} + \tau_{in}^{[a]}S_v{}^{[a-1]} + \mu(t)(1 - \alpha^{[a]})S_n{}^{[a]} - \sigma^{[a]}S_v{}^{[a]}$$

$$\frac{dE_{1v}^{[a]}}{dt} = +\lambda^{[a]}(t)S_v{}^{[a]} - \epsilon E_{1n}{}^{[a]} - \tau_{out}^{[a]}E_{1n}^{[a]} + \tau_{in}^{[a]} + \mu(t)E_{1n}{}^{[a]} - \sigma^{[a]}E_{1v}{}^{[a]}$$

$$\frac{dE_{2v}^{[a]}}{dt} = 2\epsilon(E_{1v}^{[a]} - E_{2v}^{[a]}) - \tau_{out}^{[a]}E_{2v}^{[a]} + \tau_{in}^{[a]}E_{2v}^{[a-1]} + \mu(t)E_{2n}{}^{[a]} - \sigma^{[a]}E_{2v}{}^{[a]}$$

$$\frac{dI_{1v}^{[a]}}{dt} = 2\epsilon E_{2v}^{[a]} - 2\gamma I_{1v}^{[a]} - \tau_{out}^{[a]}I_{1v}^{[a]} + \tau_{in}^{[a]}I_{1v}^{[a-1]} + \mu(t)I_{1n}{}^{[a]} - \sigma^{[a]}I_{1v}{}^{[a]}$$

$$\frac{dI_{2v}^{[a]}}{dt} = 2\gamma\left(I_{1v}^{[a]} - I_{2v}^{[a]}\right) - \tau_{out}^{[a]}I_{2v}^{[a]} + \tau_{in}^{[a]}I_{2v}^{[a-1]} + \mu(t)I_{2n}{}^{[a]} - \sigma^{[a]}I_{2v}{}^{[a]}$$

$$\frac{dR_v{}^{[a]}}{dt} = 2\gamma\left(I_{2v}^{[a]}\right) - \omega R_v{}^{[a]} - \tau_{out}^{[a]}R_v{}^{[a]} + \tau_{in}^{[a]}R_v{}^{[a-1]} + \mu(t)R_n{}^{[a]} - \sigma^{[a]}R_v{}^{[a]} + \mu(t)\,\alpha^{[a]}S_n{}^{[a]}$$

[11] Please note that the model equations include aging which is not shown in **Figure 2**

ϵ, γ and ω represent the overall rate of loss of latency, infectiousness and natural immunity, $\lambda(t)$ represents the force of infection, τ_{in} and τ_{out} represent the aging rates.

Compartment M_v represents births that are protected due to vaccination. $\mu(t)$ represents the vaccination rate in adults (calculated as slope of the uptake graph), $\xi(t)$ represents % of births from pregnant women that are vaccinated (calculated as % of deliveries from vaccinated mothers), $\alpha^{[a]}$ represents the vaccine efficacy against infection in adults and infants, and $\sigma^{[a]}$ represents loss of immunity from vaccination. Vaccinated individuals who are infected are assumed to equally infectious as unvaccinated individuals.

Equations for calculating hospital admissions

$$\frac{dC^{[a]}}{dt} = 2\epsilon E_{2n}^{[a]} + 2\epsilon E_{2v}^{[a]}(1 - \alpha_H^a)$$

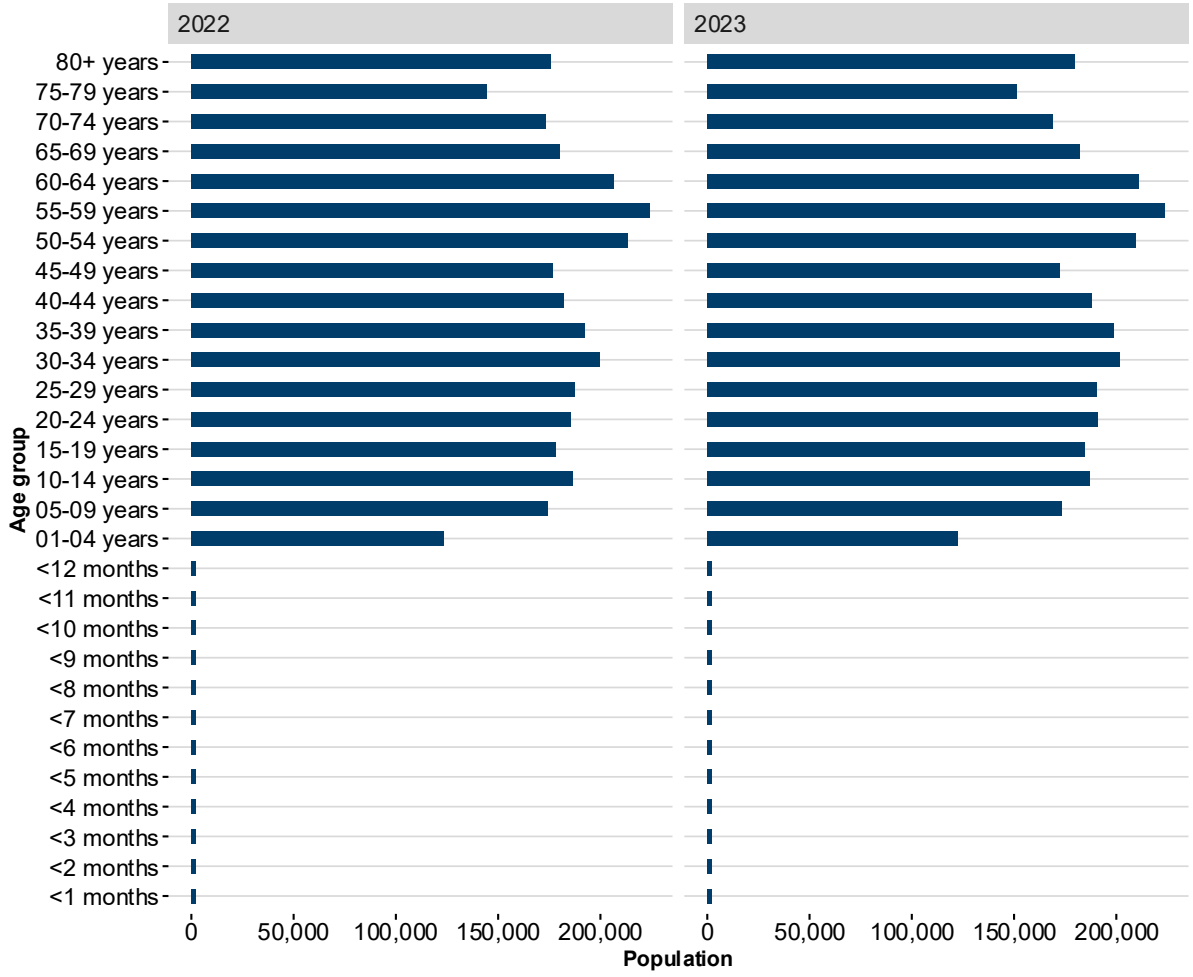
$$H^{[a]} = C^{[a]} * h^{[a]}$$

$h^{[a]}$ indicates age-specific infection hospitalisation ratios (proportion of infected cases that become hospitalised) and α_H^a represents age specific vaccine efficacy against hospitalisation.

Data Sources

Population data: The population data for Wales was obtained from Stats Wales (based on the ONS 2022 and 2023 mid-year estimates).[12] Given the implementation of a maternal vaccination program, our model places significant emphasis on the first year of life. The 0-1 year age band was divided into 12 one-month compartments (**Figure 3**). For older age bands, 5-year age bands were used, except for the 1-4 year and 80+ group.

Figure 3: Demographic structure used to model RSV admissions in Wales



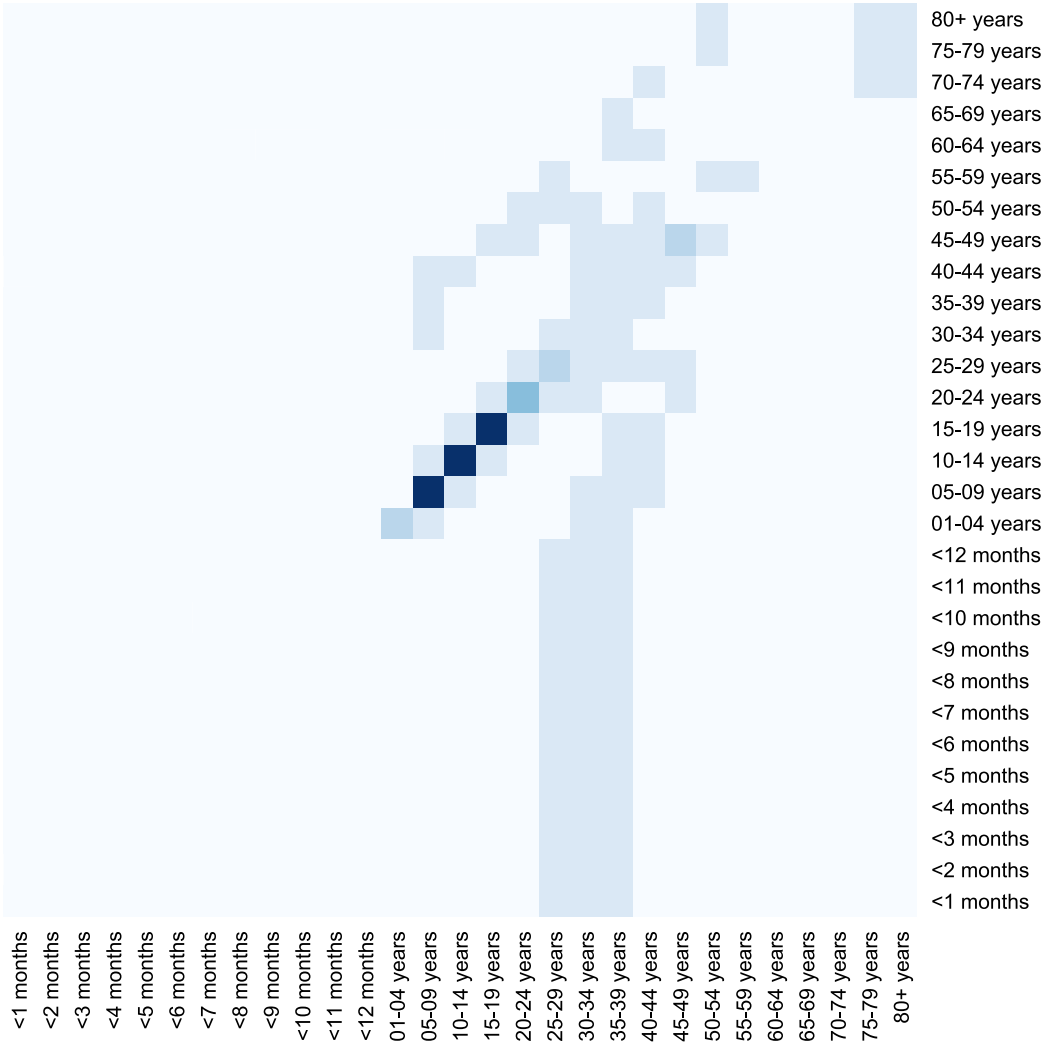
Source: National level population estimates by year, and age (Stats Wales)

Contact matrix: To incorporate non-random mixing within the population of Wales, the contact matrix from the POLYMOD survey was imported using the R package

[12] National level population estimates by year, age and UK country

socialmixr. [13] [14] This is widely used in epidemiology to estimate transmission rates and predict the spread of diseases between different demographic age groups in Great Britain, as seen in the heat map below (**Figure 4**). Since the age groups under 1 year were categorised by months, these groups were assigned the same contact rate as the 0-1 year age group. The age groups 75-79 and 80 years and above were assigned the same contact rates as those aged 75 and older (**Figure 4**).

Figure 4: Contact matrix showing relative contact rates between age groups in Great Britain



Source: Social contacts and mixing patterns relevant to the spread of infectious diseases

[13] Social Mixing Matrices for Infectious Disease Modelling • socialmixr
[14] Social contacts and mixing patterns relevant to the spread of infectious diseases - PubMed

Hospitalisation data: The hospitalisation admissions data was obtained from Digital Health Care for Wales (DHCW).[15] Admissions due to RSV were deduced using the following ICD-10 codes: B97.4 (Respiratory syncytial virus causing diseases classed elsewhere), J12.1 (Respiratory syncytial virus pneumonia), J20.5 (Acute bronchitis due to respiratory syncytial virus) and J21.0 (Acute bronchiolitis due to respiratory syncytial virus). Admissions were classified into the following age groups to align with the vaccination target groups: 1-6 months, 7-12 months, 1-4 years, 5-74 years, 75-79 years, and 80+ years.[16] It is important to note that relying solely on these ICD-10 codes may underestimate admissions, as they only account for patients who were tested for the pathogen. There may have been additional patients with RSV who were not tested for the virus or have not been clinically coded yet (The ICD-10 coding process may experience delays of several months, resulting in incomplete coding at the time the data is received).

Parameters and model fitting

The epidemiological model was fitted to the hospital admissions data using adaptive Markov Chain Monte Carlo (MCMC) methods.[17] This approach allows us to derive the posterior distribution of parameter values of the model without knowing all of the distribution's mathematical properties by randomly sampling values from the distribution.[18]

3 Markov chains were run for 5,000 steps, where the first 1,000 steps were the burn-in and the final 4,000 steps were used as the empirical samples for the posterior distributions for each of the parameters. As some of the parameters showed correlations, parallel tempering with 5 rungs was used to ensure that there is enough mixing. To generate posterior samples, three chains were randomly sampled 1,000 times. Using this method, the force of infection parameters, infection to hospitalisation ratios, incubation, infectious, and immunity periods were estimated. Uniform and normal distributions were used as priors for parameters.

[15] Hospital Admissions Annual Tables - Digital Health and Care Wales
[16] These age groups are different from the ones used in model structures.
[17] fluEvidenceSynthesis: An R package for evidence synthesis based analysis of epidemiological outbreaks | PLOS Computational Biology
[18] A simple introduction to Markov Chain Monte–Carlo sampling - PMC

To test if the chains have converged, Gelman-Rubin convergence diagnostic was calculated. [19]

Likelihood function: Due to the high level of noise in the admissions data, rolling averages rather than admission counts were used to calculate the likelihood function. Assuming that the rolling average of admissions for an age group a is a random variable from a normal distribution, the likelihood function for Data *D* and parameters θ is given as

$$L(D/\theta) = \prod_{a=1}^{a=6} \prod_{t=1}^{t=365} Normal(y_{a,t}|\mu,\sigma)$$

where $y_{a,t}$ is the rolling average of admissions for age group a at time t, while μ and σ represent the mean and standard deviation (SD) of the predicted model fit respectively.

Details about the priors are described below (**Table 1**) and the posterior samples are shown in the Appendix (**Table S1**).

Table 1: Priors and the biological description of the fitted parameters used in the model

Parameter name in the equation	Age-specific	Biological description	Priors
b_0	No	Amplitude of the cosine function used in modelling force of infection	*U(0.01, 1)*[20]
b_1	No	Amplitude of the cosine function used in modelling force of infection	*U(0.2, 1)*
$\varphi^{0-1\text{years}}$	Yes	Phase shift of the cosine function used in	*U(-1,pi)*

[19] Convergence tests for MCMC
[20] Modelling respiratory syncytial virus age-specific risk of hospitalisation in term and preterm infants - PMC

		modelling force of infection for ages 0-1 year	
$\varphi^{1-74\ \text{years}}$	Yes	Phase shift of the cosine function used in modelling force of infection for ages 1-74 years	*U(-1, pi)*
$\varphi^{74-79\text{years}}$	Yes	Phase shift of the cosine function used in modelling force of infection for ages 75-79 years	*U(-1,2*pi)*
$\varphi^{80\ \text{years and above}}$	Yes	Phase shift of the cosine function used in modelling force of infection for ages 80 years and above	*U(-1, 2*pi)*
$1/\epsilon$	No	Incubation period	*N(4.4, 1.24)*[21]
$1/\gamma$	No	Infectious period	*N(10, 1)* [22]
$1/\omega$	No	Natural immunity	*U(182, 304)*[23]
$\mathrm{h}^{1-6\text{months}}$	Yes	Infection to hospitalisation ratio for 1-6 months	*U(0.001,0.1)*
$\mathrm{h}^{7-12\text{months}}$	Yes	Infection to hospitalisation ratio for 7-12 months	*U(0.001,0.1)*
$\mathrm{h}^{1-4\ \text{years}}$	Yes	Infection to hospitalisation ratio for 1-4 years	*U(0.0001,0.1)*

[21] Incubation periods of acute respiratory viral infections: a systematic review - The Lancet Infectious Diseases
[22] Modelling the Seasonal Epidemics of Respiratory Syncytial Virus in Young Children | PLOS One
[23] Exploring the dynamics of respiratory syncytial virus (RSV) transmission in children - ScienceDirect

$h^{5-74\ years}$	Yes	Infection to hospitalisation ratio for age groups 5-74 years	*U(0.00001,0.1)*
$h^{75-79\ years}$	Yes	Infection to hospitalisation ratio for adults aged 75-79 years	*U(0.00001,0.1)*
$h^{80\ years\ and\ above}$	Yes	Infection to hospitalisation ratio for adults aged 80 years and above	*U(0.00001,0.1)*
p^{sus}	No	Proportion of population that is susceptible	*U(0.1, 1)*

U(x,y) describes a uniform distribution between x and y and *N(x,y) represents a normal distribution with mean x and standard deviation y*.

Modelling the effects of the RSV vaccination program

To model the year-round vaccination program, the vaccination was assumed to be given to pregnant women and adults aged 75-79 between 1st September in year 1 and 30th August in year 2. Historical influenza vaccine uptake was fit using a logistic curve, which was then extrapolated by one year to serve as a proxy for RSV vaccine uptake. The asymptote of the logistic function was adjusted to reflect the target uptake level specified for each scenario.[24]

The vaccine efficacy against hospitalisation in infants was assumed to be 57% (95% CI 26.5-74.8) and 82.3% (95% CI, 70.6 to 90) in adults based on clinical data.[25] [26] Vaccine efficacy against infection was assumed to equal that against hospitalisation. The immunity from vaccination was assumed to last for 180 days after birth in infants

[24] SSlogis function - RDocumentation
[25] Vaccine effectiveness of a bivalent respiratory syncytial virus (RSV) pre-F vaccine against RSV-associated hospitalisation among adults aged 75-79 years in England | medRxiv
[26] Efficacy and safety of vaccines to prevent respiratory syncytial virus infection in infants and older adults: A systematic review and meta-analysis - ScienceDirect

and for two years in older adults (aged 75-79 years).[27] [28] Using the 2022/23 winter and the 2023/24 season as the reference seasons, and varying the final vaccine uptake value from 0 to 90%, a total of eight distinct scenarios were developed.

Table 2: Definition of scenarios created

Scenario	Final vaccine uptake (%) in pregnant women/adults at the end of the season	Reference season
Scenario 1a	0%	2022/23 winter
Scenario 2a	30%	2022/23 winter
Scenario 3a	60%	2022/23 winter
Scenario 4a	90%	2022/23 winter
Scenario 1b	0%	2023/24 winter
Scenario 2b	30%	2023/24 winter
Scenario 3b	60%	2023/24 winter
Scenario 4b	90%	2023/24 winter

Model Evaluation Measures

The model best fit was compared against the actual admissions data using the following evaluation measures [29]:

- **Absolute error of the median**: The absolute difference between the median of the predictive distribution and the observed value. The lower the absolute error, the better the model fit.
- **Weighted Interval Scores:** This measure combines overprediction and underprediction, along with sharpness, a measure of the model's concentration of the predictive distributions (ie. how wide its intervals are). It is bounded between 0 and 1; lower scores indicate a better fit to observed data.

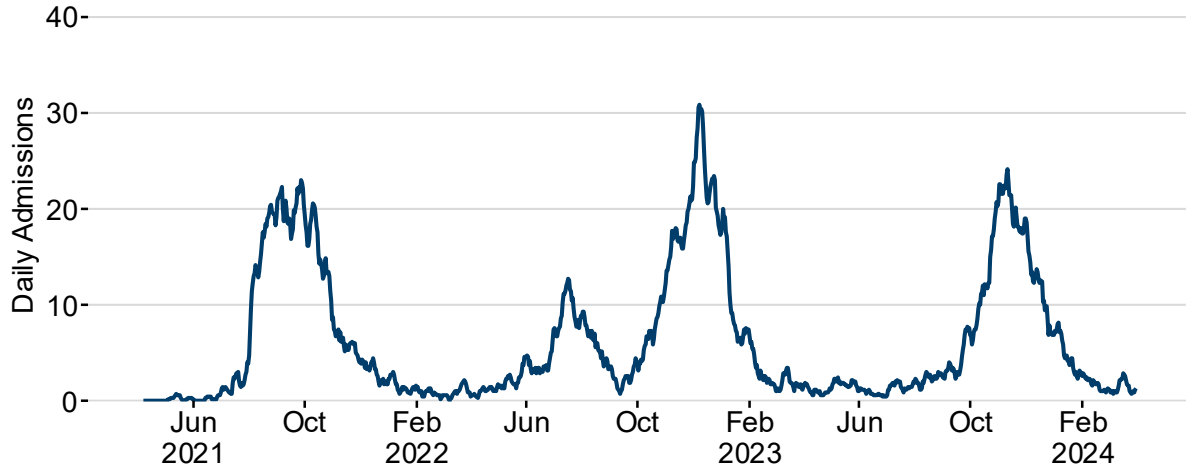
[27] GitHub - midas-network/rsv-scenario-modeling-hub: RSV Scenario Modeling Hub
[28] Respiratory syncytial virus (RSV) immunisation programme for infants and older adults: JCVI full statement, 11 September 2023 - GOV.UK
[29] Scoring rules in `scoringutils` • scoringutils

- **Bias:** This refers to the relative tendency of a model to over- or under-predict, representing an aspect of calibration. It is bounded between -1 and 1, where negative values reflect underprediction and positive values reflect overprediction. Values closer to zero indicate a better model fit.

Results

Estimating the burden of RSV admissions before the implementation of the RSV program

Figure 5: 7-day rolling averages of RSV daily admissions (all ages) in Wales between April 2021 and March 2024



Source: SRE analysis of Digital Health and Care Wales (DHCW) data

Using a narrow set of ICD-10 codes for RSV admissions (B97.4, J12.1, J20.5 and J21.0) resulted in fewer admissions each winter, ranging from 1,415 to 2,014, compared to the broader set of ICD-10 codes used in the winter modelling report.[30] The narrower set of ICD-10 codes for RSV admissions will be used in this report.

Table 3: Summary of RSV admissions for all ages between the winters of 2021/22 and 2023/24 [Note 1]

Winter	Total admissions	Total admissions per 100,000 population	Daily peak value of 7-day rolling average of admissions	Peak date
2021/22	1,415	46	23	27 September 2021
2022/23	2,014	64	31	08 December 2022
2023/24	1,715	54	24	11 November 2023

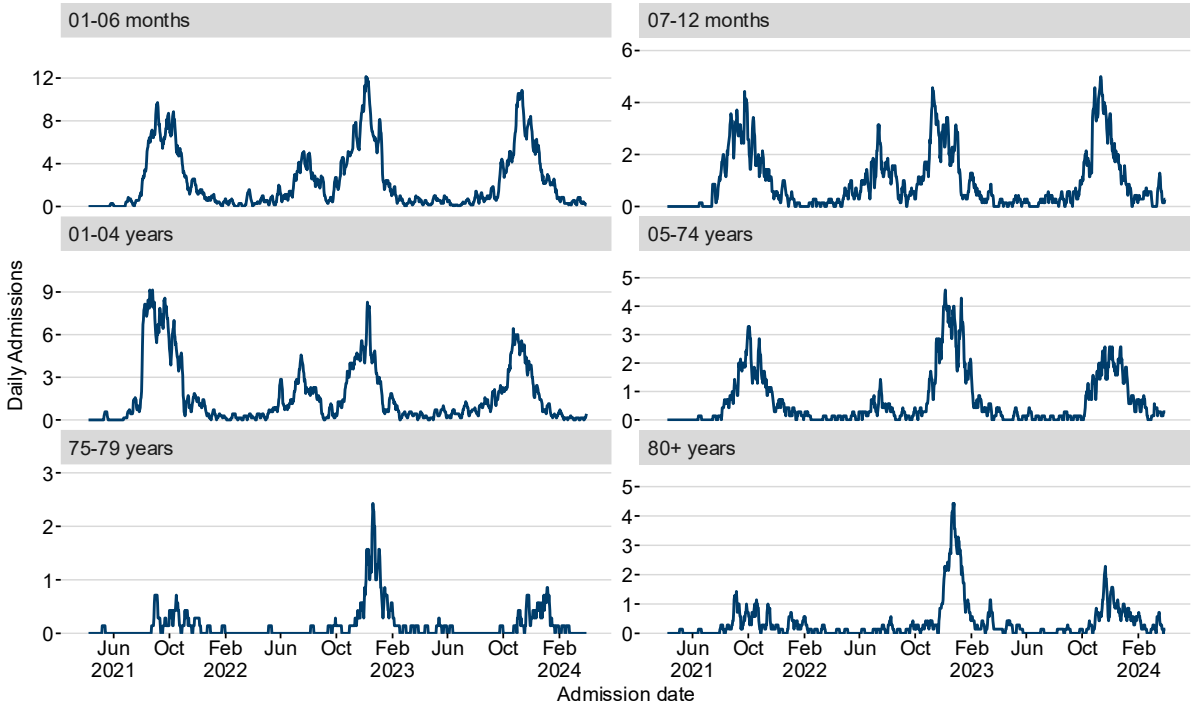
[30] Science Evidence Advice: winter modelling 2024 to 2025

Source: Digital Health and Care Wales (DHCW)

[Note 1]: Winter is defined as the period between 1 September and 31 March (inclusive) every financial year.

The daily admissions peaked in late September for the 2021/22 winter, [31] in the first week of December in 2022/23 and in November for the 2023/24 winter (**Figure 5, Table 3**).

Figure 6: 7-day rolling averages of RSV daily admissions in Wales between April 2021 and March 2024, by age group

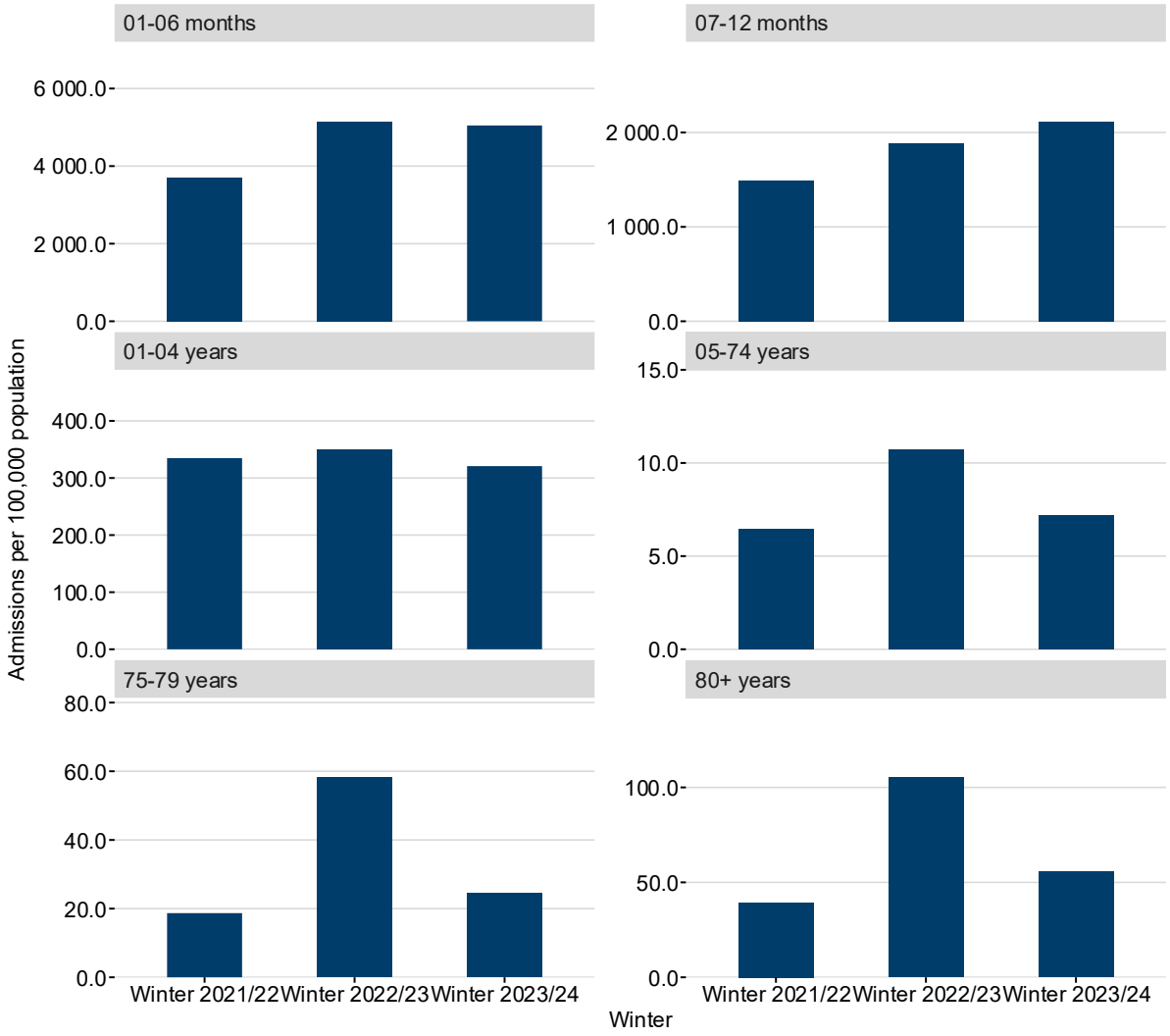


Source: SRE analysis of Digital Health and Care Wales (DHCW) data

From the winter of 2021/22 to the winter of 2023/24, RSV admissions rates for all ages were around 46-64 per 100,000 population in Wales (**Table 3)**. Infants aged 1-6 months had the highest admission rates (3,707-5,147 per 100,000 population, **Figure 7**), followed by those aged 7-12 months (1,494-2,115 per 100,000 population, **Figure 7).**

[31] Winter in this context (and throughout this report) refers to the period between September and March every financial year.

Figure 7: Cumulative RSV admissions per 100,000 population across age groups in Wales between winter of 2021/22 and 2023/24



Source: SRE analysis of Digital Health and Care Wales (DHCW) data

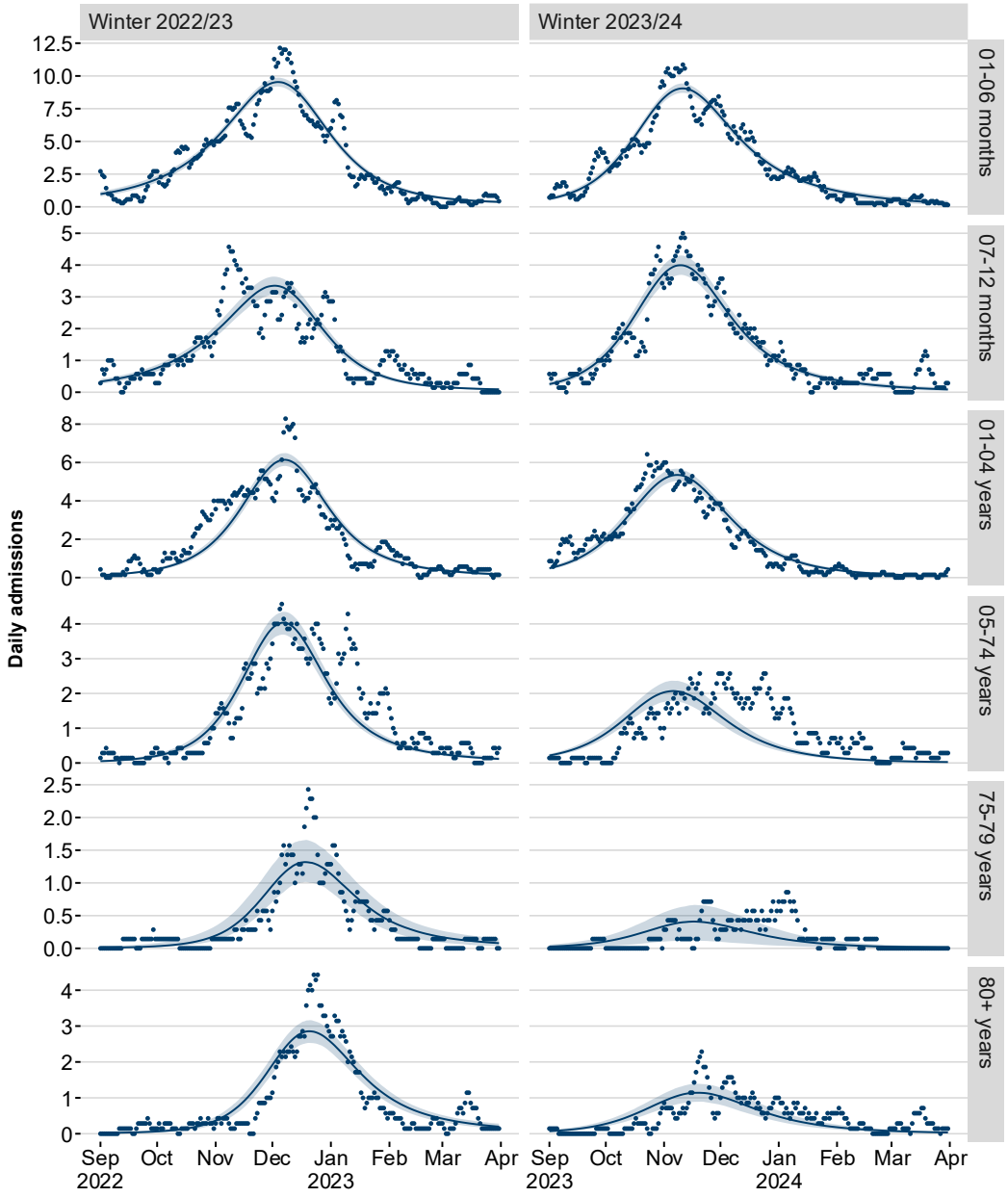
[Note 1]: Winter is defined as the period between 1 September and 31 March (inclusive) every financial year.

Older adults aged 75-79 and 80+ in Wales had lower rates compared to the younger age groups, with 19-58 and 39-105 admissions per 100,000 population respectively (Figure 6). These rates were comparable with what is observed in England where adults aged 75-79 had admission rates of around 33 admissions per 100,000 population in the financial year of 2023/24.[32]

[32] Estimating the disease burden of respiratory syncytial virus (RSV) in older adults in England during the 2023/24 season: a new national hospital-based surveillance system

Model fitting

Figure 8: Comparison of model fit versus actual RSV admissions data from Winter 2022/23 and Winter 2023/24 data, Wales, by age group [Note 1]



Source: SRE analysis

[Note 1]: The blue shading represents the 95% credible interval of the model [33]

Our modelling process consisted of two stages: fitting and projection. In the fitting stage, the SE_2I_2R model was fitted to RSV admissions data by age group (7-day rolling averages) in Wales separately for the winter of 2022/23 and 2023/24 using MCMC methods (**Figure 8**, the MCMC traces and posterior samples are shown in

[33] Understanding and interpreting confidence and credible intervals around effect estimates - PMC

the Appendix **Figure S1** and **Figure S2**). Overall, the model fit for the winter 2023/24 was slightly better than 2022/23 winter (as evidenced by the lower weight interval scores WIS= 0.28 for 2023/24 versus 0.35 for 2022/23) and lower absolute mean error of the median (0.37 for 2023/24 versus 0.45 for 2022/23). The model showed positive bias (Bias= 0.09 and 0.01 for 2022/23 and 2023/24 respectively) suggesting that it had a slight tendency to over-predict throughout the winter. However, the model showed a negative bias for certain age groups like 5-74 (bias -0.19) and 80+ years during the winter 2023/24 (Bias= -0.13). The model fit for older age groups: 75-79 and 80+ years were better than the younger age groups.

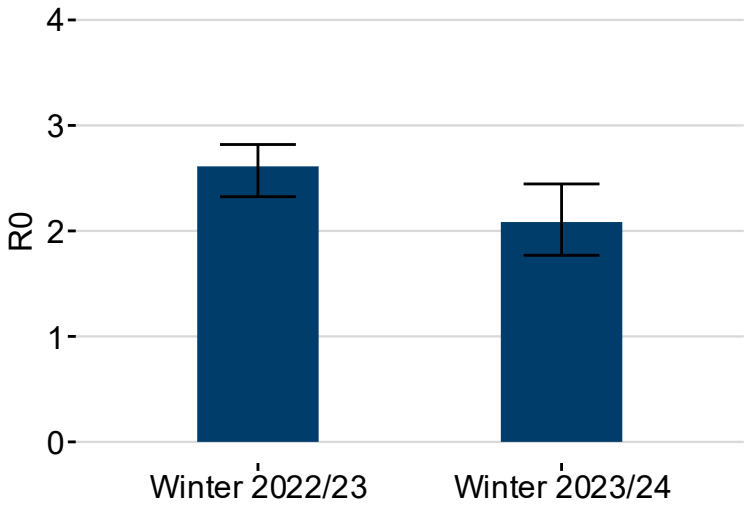
Table 4: Scoring metrics of the model best fit, by age group and year.

Winter	Age group	Absolute error of the median	WIS	Bias
Winter 2022/23	1-06 months	0.75	0.60	0.28
Winter 2022/23	7-12 months	0.42	0.35	0.02
Winter 2022/23	1-04 years	0.60	0.50	-0.11
Winter 2022/23	5-74 years	0.42	0.34	-0.19
Winter 2022/23	75-79 years	0.16	0.09	0.33
Winter 2022/23	80+ years	0.33	0.25	0.20
Winter 2022/23	**All ages**	**0.45**	**0.35**	**0.09**
Winter 2023/24	1-06 months	0.61	0.47	0.12
Winter 2023/24	7-12 months	0.31	0.22	-0.04
Winter 2023/24	1-04 years	0.38	0.28	0.10
Winter 2023/24	5-74 years	0.53	0.46	-0.19
Winter 2023/24	75-79 years	0.13	0.08	0.19
Winter 2023/24	80+ years	0.26	0.19	-0.13
Winter 2023/24	**All ages**	**0.37**	**0.28**	**0.01**

Source: SRE analysis

Basic reproduction number

Figure 9: R_0 values estimated by the model during the winter of 2022/23 and 2023/24 in Wales



Source: SRE analysis

[Note 1]: the height of the bar represents the median while the error bars represent the 95% credible interval.

Using the transmissibility, contact matrices and infectious period, the basic reproduction number was calculated as done in Leeuwen et al.[34] Our analysis showed a R_0 of 2.61 (95%CrI: 2.32, 2.82) and 2.08 (95%CrI:1.77, 2.45) during the winters of 2022/23 and 2023/24 respectively (**Figure 9**).

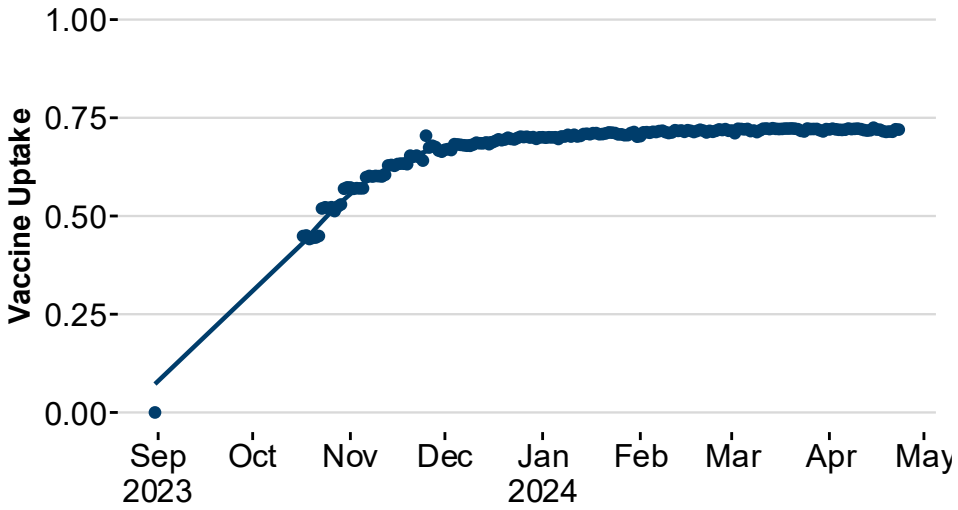
Projections and Scenario creation

The projection stage involved taking the results from the fitting stage and creating a range of scenarios. This also included estimating the vaccination calendar using historical seasonal influenza vaccine uptake data in adults aged 65 and above in

[34] fluEvidenceSynthesis: An R package for evidence synthesis based analysis of epidemiological outbreaks | PLOS Computational Biology

Wales which was fitted using a logistic curve (**Figure 10)**. To model year-round vaccination, the logistic curve was extrapolated beyond March (where the data ends) and assumed the uptake values plateaued until September. The final vaccine uptake value was varied between 30% and 90% and a total of 8 of scenarios were generated.

Figure 10: Model fit of flu vaccine uptake among adults aged 65 and above in the 2023/24 season in Wales using a logistic curve. [Note 1]

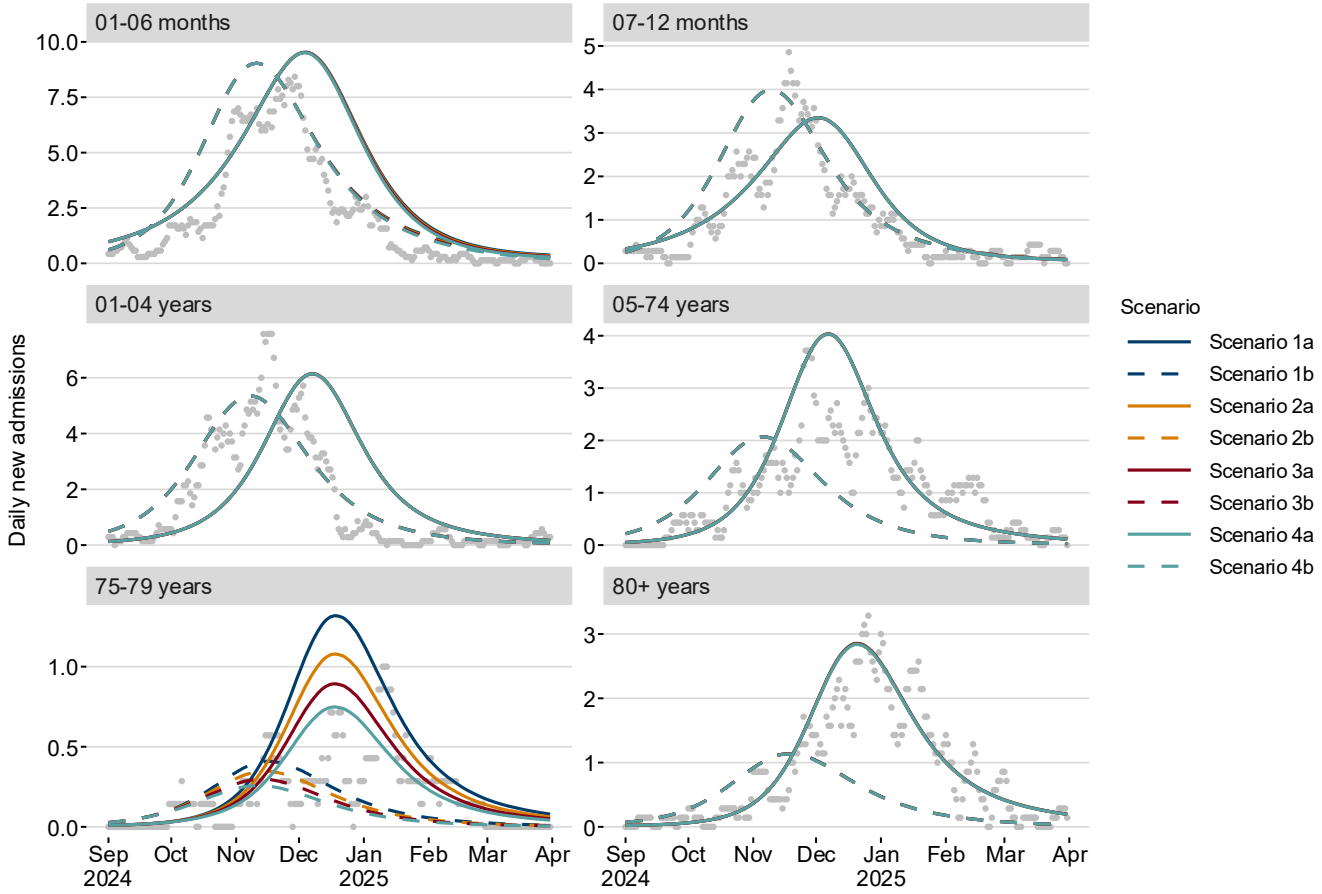


Source: Public Health Wales

[Note 1]: Dots represent the actual data while the line represents the best fit from logistic regression.

Scenarios for 2024/25 Winter

Figure 11: Comparing the 2024/25 model scenarios with the actual RSV admissions [Note 1] [Note 2] [Note 3]



Source: SRE analysis and DHCW for actuals admissions data

[Note 1]: Scenarios 1a and 1b are the baseline scenarios without vaccination (0% uptake).

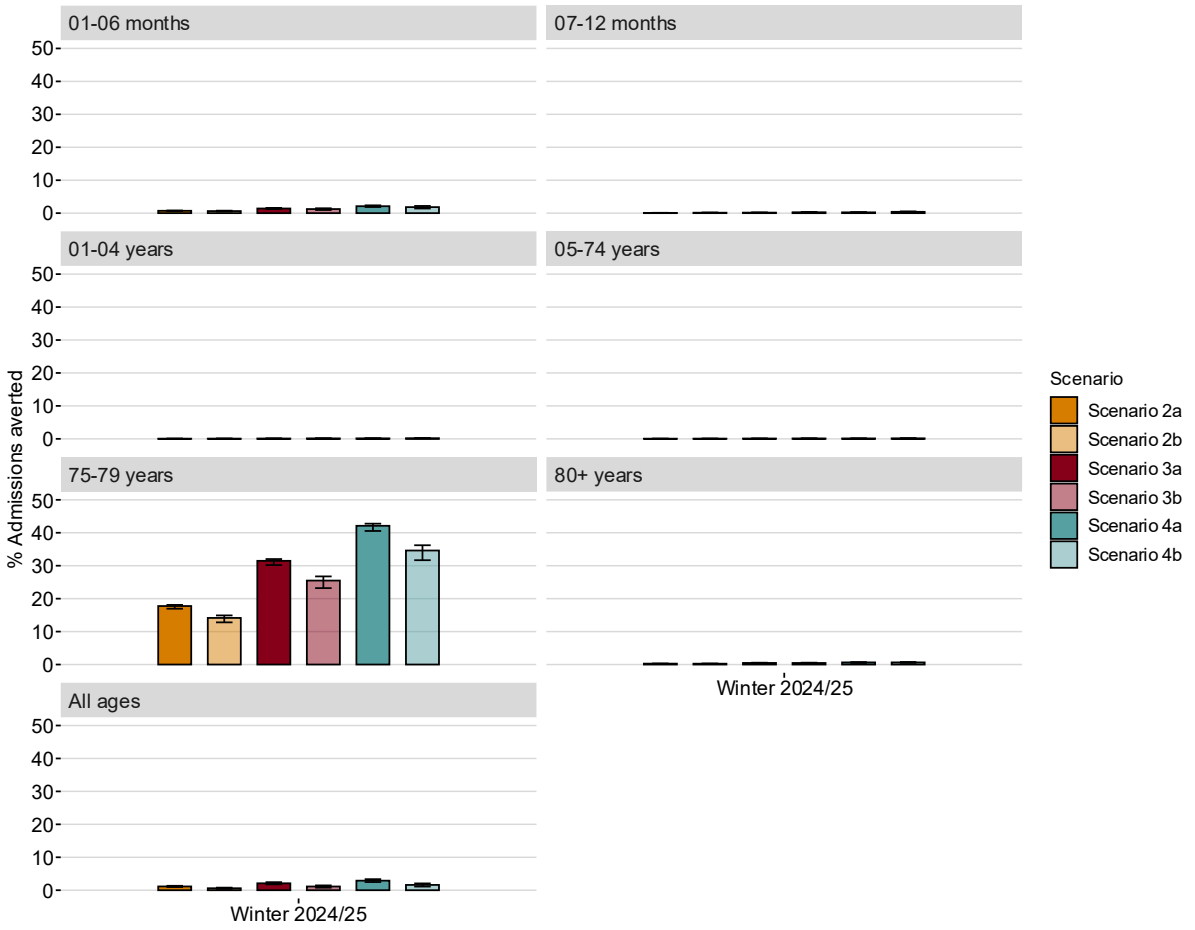
[Note 2]: Grey dots show the actuals admissions data.

[Note 3]: For the scenario names, 1,2,3 and 4 represent 0%, 30%, 60% and 90% vaccine uptake rate respectively and a and b represent the reference years 2022/23 and 2023/24 respectively

The initial modelling exercise examined how a year-long RSV vaccination program, running from September 2024 to September 2025, would affect hospital admissions across different age groups. For adults aged 75-79 during winter 2024/2025, scenarios based on the 2022/23 data (Scenarios 2a,3a,4a) predicted an 18% to 42% decrease in hospitalisations, while scenarios using the 2023/24 baseline (Scenarios

2b,3b,4b) projected reductions between 14% and 35% **(Figure 12)**. As expected, unvaccinated age groups saw minimal in admissions **(Figure 11 and 12)**.

Figure 12: % of RSV admissions averted in Wales during Winter 2024/25 as estimated by the model scenarios [Note 1] [Note 2]



Source: SRE analysis

[Note 1]: the height of the bar represents the median while the error bars represent the 95% prediction interval.

[Note 2]: For the scenario names, 1,2,3 and 4 represent 0%, 30%, 60% and 90% vaccine uptake rate respectively and a and b represent the reference years 2022/23 and 2023/24 respectively

As the vaccination season begins in September 2024, pregnant women receive the vaccine starting from that month. The infants who benefit from maternal vaccination are born approximately 12 weeks later, after the peak period for RSV admissions. This delay implies that the impact of maternal vaccination will not be evident during the 2024/2025 winter as the reduction in the number of susceptible infants (aged 1–6 months) occurs after the epidemic's growth phase. In line with this, the model

predicts a limited reduction in hospital admissions (1-2 % in 1–6-month-olds, **Figure 12**)

Comparing 2024/25 winter scenarios with actual admissions data
There were 1,461 admissions in the 2024/25 winter across all ages, representing a 15% decrease compared to the 2023/24 winter and a 27% decrease compared to the 2022/23 winter. There were 466 and 217 admissions in 1-6 month and 7–12-month age groups. This represents a decrease of 33% and 38% in 1–6-month-old and 26% and 21% in 7–12-month-old compared to the 2023/24 and 2022/23 winters, respectively. Overall, age groups 1-6 months and 7-12 months observed larger decrease in admissions averted than the model predicted.

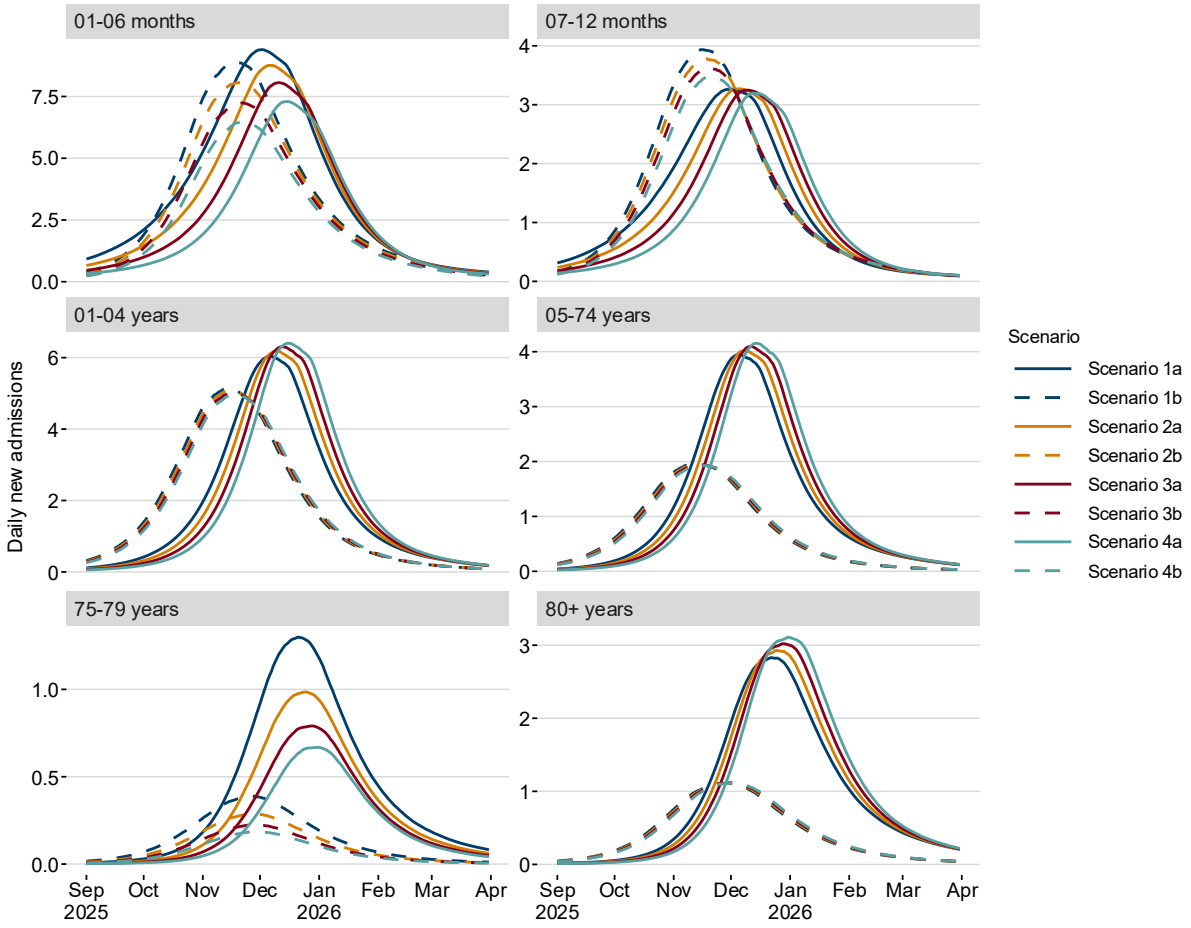
In contrast, the 75-79 years age group had a 48% decrease compared to the 2022/23 winter, but a 19% increase compared to the 2023/24 winter. Compared to the three-year average (2021/22 – 2023/24 winters), 75-79 years age group showed a decrease of 10% of admissions. It should be noted that hospital admissions for adults aged 75 -79 years are very low (fewer than 100 admissions each winter), which may result in greater variability in the data.

For the 1–6 ,7–12-month and 1-4 years age groups, admissions data closely tracked the projections from scenarios 1b-4b (based on data from the 2023/24 winter period). Similarly, admissions among the 5–74 years and 80+ years age groups were consistent with the scenarios 1a-4a (based on data from the 2022/23 winter period). In contrast, admissions for the 75–79 years age group showed different temporal dynamics than what the scenarios estimated. While the scenarios anticipated a peak between 10th November-18th December, the actual data showed a peak occurring later, between 10th and 12th January 2026. The peak admission value was comparable to that observed with a 30% vaccination uptake (Scenario 2b) (**Figure 12)**.

Scenarios for the 2025-26 Winter
This section considers the impact of running the RSV vaccine program for two years and examining its impact on the RSV hospital admissions during the winter of 2025/26. The scenarios generated here will be used as a part of 2025/26 winter modelling report.

If the vaccination program is prolonged for another year, ending in September 2026, projections from scenarios 2a-4a (base season 2022/23) suggest that during the winter of 2025/26, hospital admissions could be decreased by 11-31 % among infants aged 1–6 months, 4-12 % in infants aged 7–12 months, and 25-51% among adults aged 75-79 years (**Figure 14)**. According to scenarios 1b-4b (base season 2023/24), these reductions are estimated at 9-27 %, 3-10%, and 26-52 % in the same age groups (**Figure 14)**. In 2025-26, peak admissions are expected to occur later for all age groups: 18th November-15th December for ages 1–6 months, 16th November-13th December for ages 7–12 months, and 27th November – 1st January for those aged 75-79 years **(Figure 13)**.

Figure 13: RSV admissions scenarios for 2025/26 winter, by age. [Note 1]

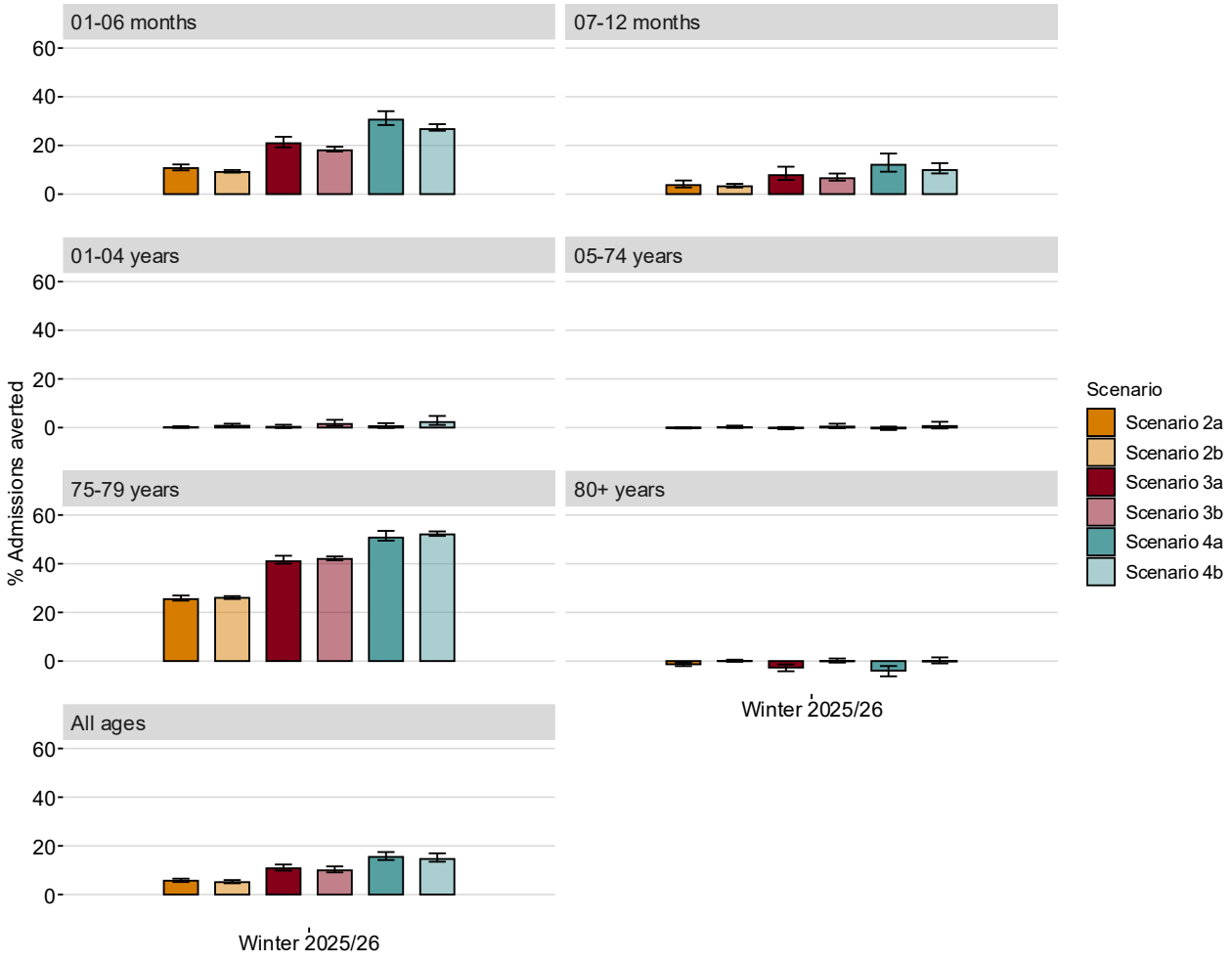


Source: SRE analysis

[Note 1]: For the scenario names, 1,2,3 and 4 represent 0%, 30%, 60% and 90% vaccine uptake rate respectively and a and b represent the reference years 2022/23 and 2023/24 respectively.

Older age groups 5-74 and 80+ showed a small increase in admissions, but negligible compared to the decrease observed in the vaccinated age groups. Overall, the model estimates that approximately 5-15% of admissions are prevented during the winter of 2025/26 respectively across all age groups.

Figure 14: % of RSV admissions averted in Wales during Winter 2025/26 as estimated by the model scenarios [Note 1] [Note 2]



Source: SRE analysis

[Note 1]: the height of the bar represents the median while the error bars represent the 95% prediction interval

[Note 2]: For the scenario names, 1,2,3 and 4 represent 0%, 30%, 60% and 90% vaccine uptake rate respectively and a and b represent the reference years 2022/23 and 2023/24 respectively

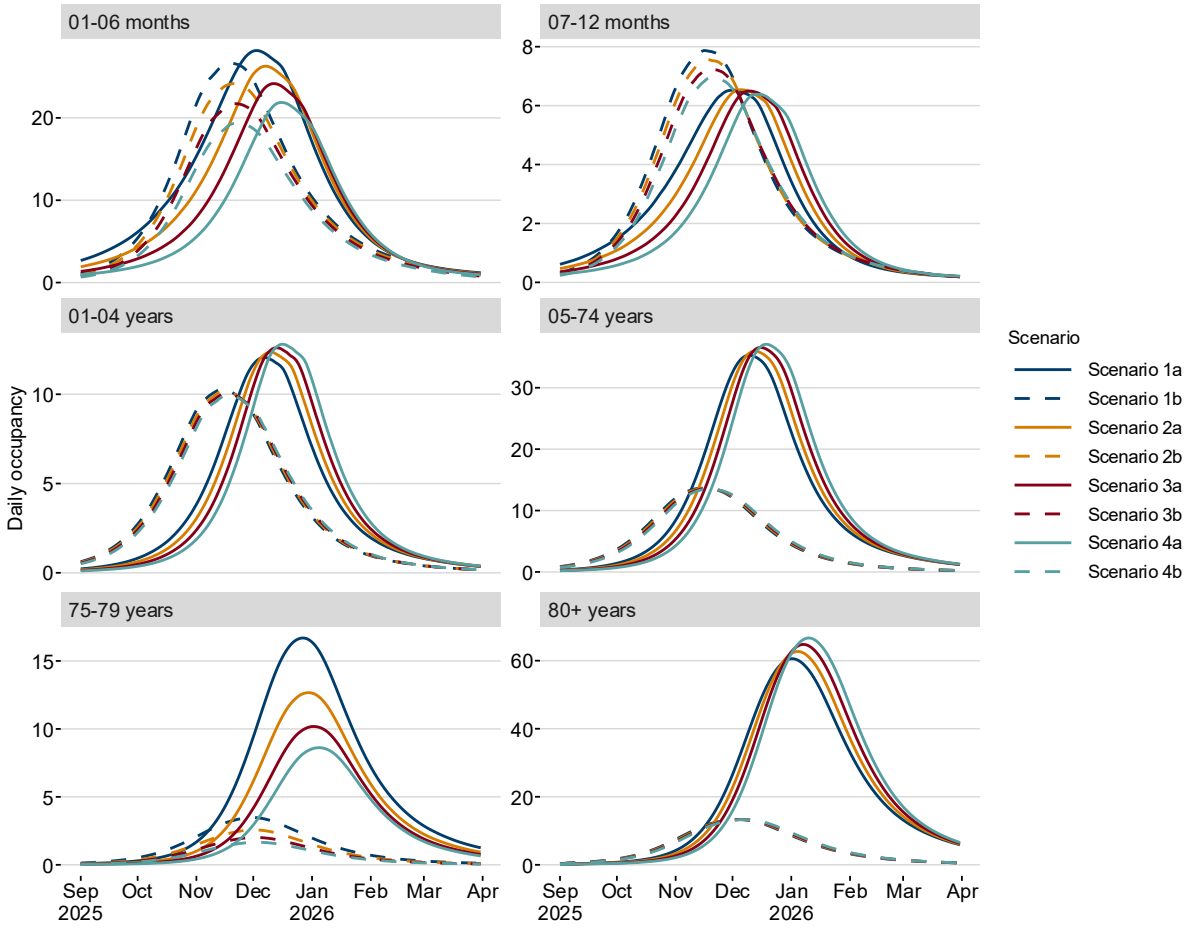
Using the length of stay data from the 2023/24 and 2024/25 winters, the hospital bed occupancy scenarios are created.

Table 5: Length of stay (in days) due to the RSV, by age

Age group	Season	Length of Stay (days)
01-06 months	Winter 2022/23	2.22
01-06 months	Winter 2023/24	2.18
07-12 months	Winter 2022/23	1.46
07-12 months	Winter 2023/24	1.56
01-04 years	Winter 2022/23	1.39
01-04 years	Winter 2023/24	1.31
05-74 years	Winter 2022/23	8.72
05-74 years	Winter 2023/24	6.58
75-79 years	Winter 2022/23	12.51
75-79 years	Winter 2023/24	8.22
80+ years	Winter 2022/23	21.30
80+ years	Winter 2023/24	11.34

Source: SRE calculations based on DHCW data

Figure 15: RSV occupancy scenarios for 2025/26 winter, by age [Note 1]



Source: SRE calculations

[Note 1]: For the scenario names, 1,2,3 and 4 represent 0%, 30%, 60% and 90% vaccine uptake rate respectively and a and b represent the reference years 2022/23 and 2023/24 respectively

Our modelling estimates indicate that occupancy is projected to reach its maximum value between 19th November- 16th December for the 1-6 months age group, 16th November- 13th December for the 7-12 months age group, and 30th November-5th January for the 75-79 years age group **(Figure 15)**. The expected peak values are 19-28 beds, 6-8 beds, and 2-17 beds, respectively, for these age groups **(Figure 15)**. The 80 and above age group is estimated to have reached the highest occupancy levels among all age groups, peaking between 13 and 67 beds from 4th December to 10th January.

Discussion

In this paper, a mechanistic compartment model was used to estimate the impact of RSV vaccination on hospital admissions across different age groups in Wales. The model assumed a SE_2I_2R structure with two compartments for pre-infectious and infectious states, similar to the approaches previously used to model influenza and RSV admissions.[35] [36] Using MCMC methods, the model was fitted to two seasons of RSV admissions data after which a range of scenarios was created.

Comparison of our model results with previous studies

Our model yielded R_0 values of 2.61 (95%CrI: 2.32, 2.82) and 2.08 (95%CrI: 1.77, 2.45) for Wales during the winters of 2022/23 and 2023/24 respectively. A review by Kaler et al. found that reported R_0 values for RSV range from one to five, with a typical estimate of three.[37] Similarly, a U.S. study over ten RSV seasons reported an average R_0 of 3.0 (SD 0.6) across all seasons and locations.[38] The authors observed some geographic variability in R_0 -The South Atlantic Division (Census Division 5) in

[35] fluEvidenceSynthesis: An R package for evidence synthesis based analysis of epidemiological outbreaks | PLOS Computational Biology
[36] Investigating the Impact of Non-Pharmaceutical Interventions (Npis) on Post-Pandemic Respiratory Syncytial Virus (Rsv) Seasonality and Susceptibility in Wales, UK by Gabriella Santiago, Biagio Lucini, Carla White, Mike B. Gravenor :: SSRN
[37] Respiratory Syncytial Virus: A Comprehensive Review of Transmission, Pathophysiology, and Manifestation - PMC
[38] Retrospective Parameter Estimation and Forecast of Respiratory Syncytial Virus in the United States - PMC

the USA, which stretches from Florida to Maryland, showed a mean R_0 of 2.5. Our R_0 estimates are consistent with the range reported in previous studies, but it is important to note that variability in R_0 can be due to a variety of environmental, behavioural factors and biological factors such as antigenicity of circulating strains.

The model produced eight scenarios, using two winter periods as base cases and varying vaccine uptake rates of 0%, 30%, 60%, and 90%. The scenarios (2a-4a and 2b-4b) for the 2024/25 winter suggest significant reduction in admissions only in adults aged 75-79 years after the first year of implementation (14-42%). The % of admissions averted is higher in older adults compared to infants possibly due higher vaccine efficacy and higher duration of protection. The model estimates small increase in admissions for age groups (5-74 years and 80+ years), though this increase is minor, and the overall effect is a reduction in hospital admissions due to RSV across all ages. This trend may be attributed to a shift in the average age of infection and the temporary protection conferred by vaccination. Other modelling studies have similar increases in older age groups. [39]

However, due to the delay in vaccinating pregnant mothers and subsequently giving birth to protected infants, the model estimated significant reductions in infants aged 1-6 months, and 7-12 months only in the second year of implementation (9-31% and 3-12% respectively in the 2025/26 winter). Hodgson et al found that with a vaccine uptake of 60% in pregnant women, year-round maternal RSV vaccination program is estimated to prevent 42.7%, 27.5% and 8.8% of hospital cases for those aged 0–2 months, 3-5 months and 6-11 months.[39] A review by Bicego et al. found that with the implementation of a maternal vaccination program with vaccine coverage of 50-95%, there were median reductions of 20% (range 10–53%) and 11% (range 3–40%) in children aged younger than 3 months and children aged between 3 to 5 months respectively.[40] It should be noted that age stratification in our analysis differs from the referenced studies; however, the findings are within a comparable range.

[39] Protecting infants against RSV disease: an impact and cost-effectiveness comparison of long-acting monoclonal antibodies and maternal vaccination - The Lancet Regional Health – Europe
[40] Effectiveness of maternal vaccines and long-acting monoclonal antibodies against respiratory syncytial virus hospitalisations in early life: a scoping review of dynamic modelling studies

Comparing the model estimations against actual data and policy implications
The observed admissions data (actuals) indicated that infants aged 1–6 months and 7–12 months experienced substantial reductions in admissions in the 2024/25 Winter—33% and 26% fewer than in 2023/24, and 38% and 21% fewer than in 2022/23, respectively. These decreases were higher than what the model estimated. One explanation could be the indirect effects of vaccinating pregnant women which the model doesn't account for (Vaccinating pregnant women will make them less infectious and thus reduces the force of infection). The 75-79 years age group experienced a 48% decrease in admissions compared to the 2022/23 winter, but a 19% increase compared to the 2023/24 winter. Compared to the three-year average (2021/22 – 2023/24 winters), there was a reduction in admissions of 7% during the 2024/25 winter season. However, interpretation of these results is challenging due to the low number of RSV admissions recorded in Wales. However, we expect more benefits to be observed in the following years if the year-long vaccination programme continues.

The effectiveness of the RSV vaccination program may depend on its start date. For example, in Scotland, where the RSV vaccination program began in August, admissions decreased by 62% in adults aged 75-79.[41] In contrast, England, which started the program in September, observed a 32% decrease in admissions in the same age group. Both studies employ regression discontinuity design which uses a predefined cutoff—an age-based eligibility for the vaccine—to estimate effects by comparing outcomes among individuals above and below the threshold. They compare the hospitalisation rate for those aged 75–79 in this season with a modelled expected hospitalisation rate for the 2024–25 season in the absence of a vaccine programme. However, neither study compares how the current RSV admission rates (from 2024/25 winter) to previous winters prior to the introduction of the vaccination programme.

Although age groups 75–79 and 80 years and above represent a smaller proportion of admissions compared to younger age groups, they have longer lengths of stay. Our modelling indicates that administering vaccines to individuals aged 75–79 years can substantially reduce bed occupancy due to RSV, with daily peak occupancy

[41] UK-wide report highlights success of Scotland's RSV vaccination programme - News - Public Health Scotland

declining by half. In contrast, patients aged 80 years and above experience longer hospital stays, and their peak occupancy is four times higher than that of the 75–79 years age group. However, patients aged 80 years and above are currently not eligible for vaccination in Wales. Vaccinating adults 80 years and above may result in a greater reduction in bed occupancy, provided that the risks of vaccination have been appropriately assessed.

Model Limitations

Similar to many mechanistic models, our approach relies heavily on several key parameters including the incubation period, the duration of the infectious period, contact rates, and the efficacy of the vaccine etc. Any uncertainty under this parametrisation might impact the results of the model. The model relies on contact rates from the UK POLYMOD survey, but does not spatially (home, school or work etc) or temporally filter these contact rates. The POLYMOD data is around twenty years old, so current patterns of social contact may be different than those captured in the model. Also, it's crucial to note that our model does not account for various biological, sociological, and environmental factors that might influence the size and timing of the epidemic peak.

Additionally, we used hospital admissions data with specific ICD-10 codes, which require testing for confirmation. This might lead to an underestimation of RSV admissions if testing is not widely available. The coding levels of the data may also not be complete leading to further underestimation of RSV admissions.

The model assumes that the vaccination program targets the 75-79 years age group during winter 2024/25 and 2025/26. If such a program will not be available for this age-group in winter 2025-26, the results may differ.

The model assumes that vaccine efficacy against infection is the same as vaccine efficacy against hospitalisation. However, efficacy against infection—and thus transmission—can sometimes be lower (i.e. vaccinated individuals might not require hospitalisation but still be infectious). In the absence of the data, we think this a pragmatic approach.

Finally, our model does not differentiate between admissions to general hospital wards or critical care units which require more resources. The RSV vaccine demonstrates a higher efficacy rate against medically attended severe lower respiratory tract infections (LRTI) compared to all medically attended LRTI. Therefore, the benefits of the vaccination program in terms of reduced need for beds, would free up these resources for other patients and further aid management of patient pathways in secondary care; however, these are outside the scope of the model.

In conclusion, a mechanistic mathematical model was employed to estimate the impact of RSV vaccination on hospital admissions in Wales. The model indicated that the greatest benefits were observed in adults aged 75–79, with delayed effects in infants due to maternal vaccination timing. As with all modelling studies, the results are contingent on several assumptions, including contact patterns, vaccine efficacy, and completeness of hospital coding. These assumptions introduce uncertainty and should be considered when interpreting the findings. Therefore, the model outputs should be viewed as indicative rather than definitive and as an estimation of what might happen rather than a prediction of what will happen.

Appendix

Figure S1: MCMC trace plot during the sampling phase (burn-in not included)

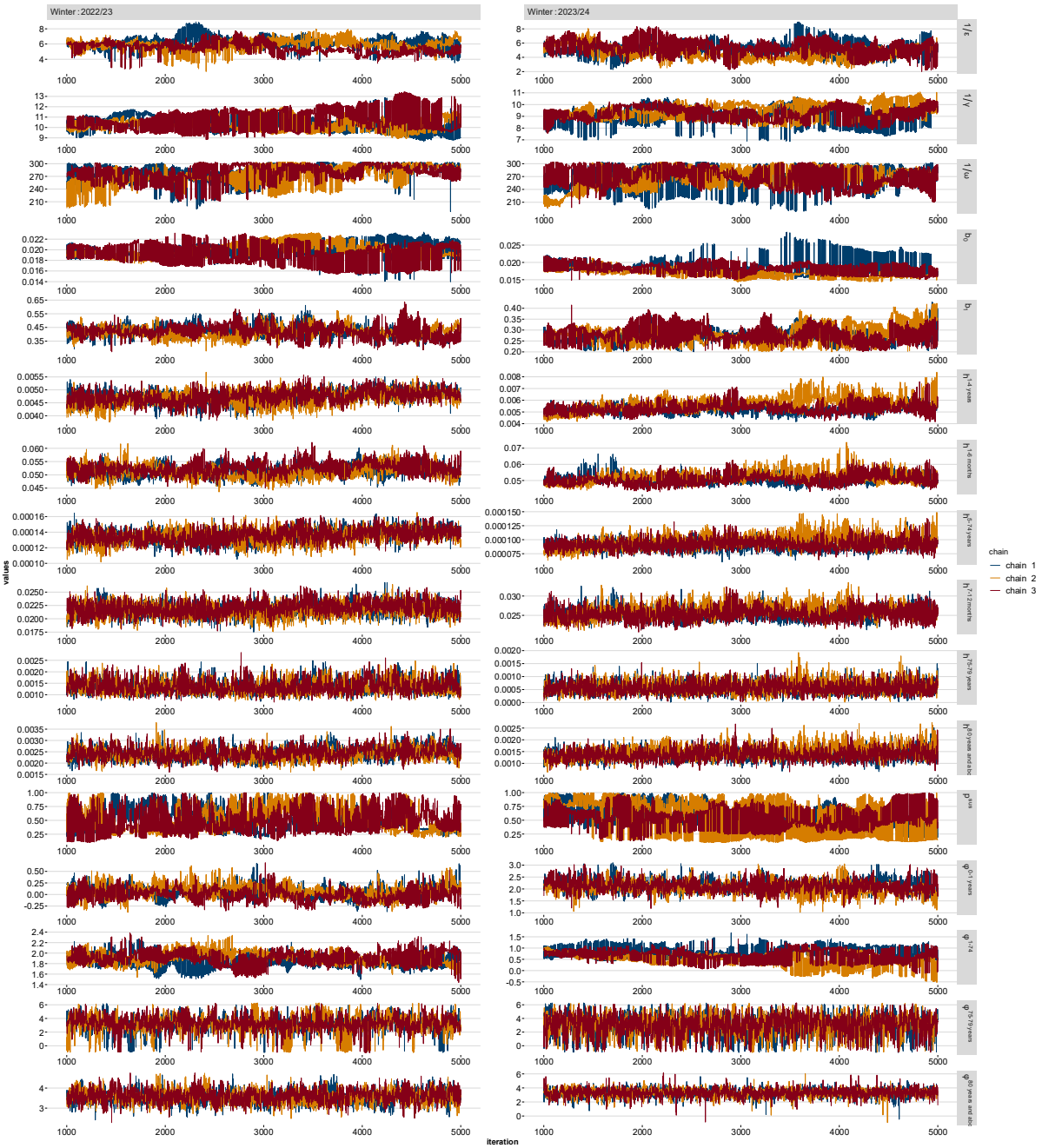


Figure S2: Posterior samples of the RSV model, by winter

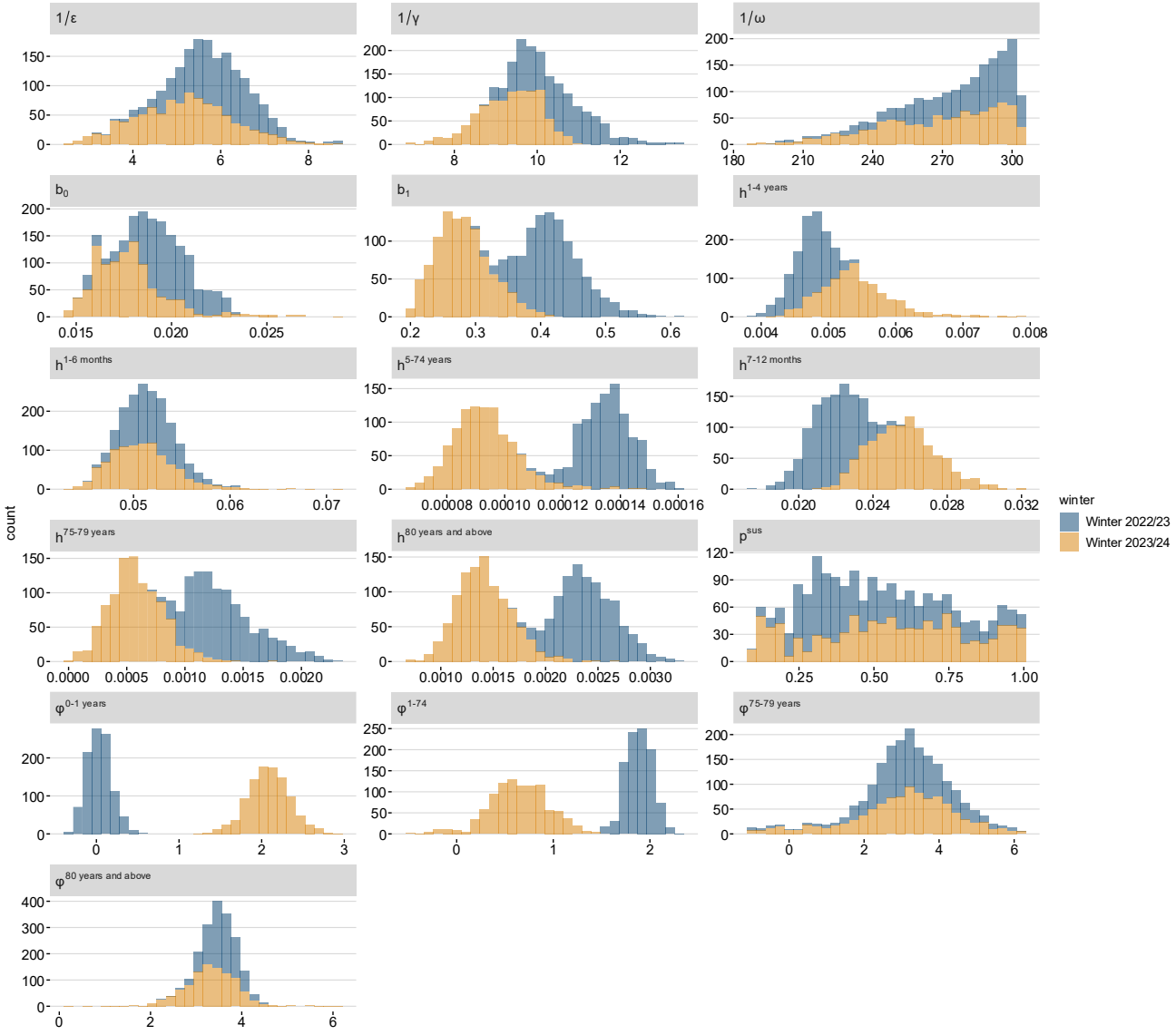


Table S1: Summary statistics of the posterior samples obtained through model fitting [Note 1]

Parameter	Winter 2022/23 estimates (median+ 95%CrI)	Winter 2023/24 estimates (median+ 95%CrI)
b_0	0.01967 [0.01574,0.02278]	0.01758 [0.01504,0.02317]
b_1	0.41735 [0.33774,0.52245]	0.27793 [0.21256,0.37033]
$h^{1-6\ \text{months}}$	0.05162 [0.04724,0.05684]	0.05067 [0.04551,0.05873]
$h^{7-12\ \text{months}}$	0.0218 [0.01942,0.02411]	0.02561 [0.02254,0.02959]
$h^{1-4\ \text{years}}$	0.00473 [0.00414,0.0052]	0.00535 [0.0045,0.00679]
$h^{5-74\ \text{years}}$	0.00014 [0.00012,0.00015]	0.00009 [0.00007,0.00012]
$h^{75-79\ \text{years}}$	0.00128 [0.00089,0.00204]	0.00056 [0.00016,0.00108]
$h^{80\ \text{years and above}}$	0.00237 [0.00191,0.00295]	0.00139 [0.00095,0.00197]
$1/\epsilon$	5.86904 [4.18858,7.35612]	5.19501 [3.1064,7.38347]
$1/\gamma$	10.42 [9.03459,12.29148]	9.38828 [7.6921,10.58426]
$1/\omega$	283.9756 [227.83023,302.88264]	272.92753 [211.49884,302.55354]
$\varphi^{0-1\text{years}}$	0.03238 [-0.24119,0.3459]	2.08616 [1.56178,2.61805]
$\varphi^{1-74\ \text{years}}$	1.88827 [1.61582,2.11732]	0.63785 [-0.07633,1.21835]
$\varphi^{74-79\text{years}}$	3.1961 [0.57937,5.286]	3.1902 [-0.38884,5.5267]
$\varphi^{80\ \text{years and above}}$	3.54454 [2.89449,4.18867]	3.32977 [2.15276,4.35834]
p^{sus}	0.43634 [0.1758,0.9534]	0.56124 [0.11462,0.98009]

[Note 1]: CrI indicates credible interval

Table S2: Gelman-Rubin convergence diagnostic for the model fit (2022/23 winter and 2023/24 winter) [Note1]

Parameter	Winter 2022/23 estimates	Winter 2023/24 estimates
b_0	1.0433	1.1249
b_1	1.0127	1.0022
$h^{1-6\ \text{months}}$	1.0379	1.037
$h^{7-12\ \text{months}}$	1.0202	1.0472
$h^{1-4\ \text{years}}$	1.0071	1.1074
$h^{5-74\ \text{years}}$	1.0041	1.067
$h^{75-79\ \text{years}}$	1.0033	1.0063
$h^{80\ \text{years and above}}$	1.0049	1.0431

$1/\epsilon$	1.1065	1.0641
$1/\gamma$	1.0477	1.0743
$1/\omega$	1.0293	1.0007
$\varphi^{0-1\text{years}}$	1.0346	1.0397
$\varphi^{1-74\text{ years}}$	1.0564	1.1758
$\varphi^{74-79\text{years}}$	1.0048	1.0006
$\varphi^{80\text{ years and above}}$	1.0066	1.0003
p^{sus}	1.0016	1.0035

Source: SRE calculations

[Note 1]: Values close to 1 indicate convergence.

Table S3: Summary of admissions averted (%) during the winter of 2024/25 as estimated by the model scenarios [Note 1].

Age group	Scenarios	% of Admissions averted (median and 95% PI)
01-06 months	Scenario 2a	0.71(0.63,0.8)
01-06 months	Scenario 3a	1.42(1.25,1.59)
01-06 months	Scenario 4a	2.11(1.86,2.37)
01-06 months	Scenario 2b	0.63(0.49,0.76)
01-06 months	Scenario 3b	1.24(0.96,1.48)
01-06 months	Scenario 4b	1.83(1.41,2.18)
07-12 months	Scenario 2a	0.08(0.07,0.1)
07-12 months	Scenario 3a	0.16(0.13,0.21)
07-12 months	Scenario 4a	0.24(0.19,0.3)
07-12 months	Scenario 2b	0.14(0.1,0.18)
07-12 months	Scenario 3b	0.27(0.2,0.36)
07-12 months	Scenario 4b	0.4(0.29,0.53)
01-04 years	Scenario 2a	0.05(0.04,0.06)
01-04 years	Scenario 3a	0.1(0.07,0.12)
01-04 years	Scenario 4a	0.14(0.1,0.18)
01-04 years	Scenario 2b	0.06(0.05,0.08)
01-04 years	Scenario 3b	0.12(0.1,0.16)
01-04 years	Scenario 4b	0.18(0.14,0.24)
05-74 years	Scenario 2a	0.05(0.03,0.06)
05-74 years	Scenario 3a	0.08(0.06,0.1)
05-74 years	Scenario 4a	0.12(0.09,0.14)
05-74 years	Scenario 2b	0.06(0.04,0.08)
05-74 years	Scenario 3b	0.11(0.08,0.14)
05-74 years	Scenario 4b	0.15(0.12,0.2)
75-79 years	Scenario 2a	17.76(16.94,18.1)
75-79 years	Scenario 3a	31.48(30.19,32.02)
75-79 years	Scenario 4a	42.12(40.54,42.76)

75-79 years	Scenario 2b	14.15(12.8,14.91)
75-79 years	Scenario 3b	25.49(23.19,26.75)
75-79 years	Scenario 4b	34.61(31.67,36.21)
80+ years	Scenario 2a	0.27(0.2,0.31)
80+ years	Scenario 3a	0.48(0.35,0.56)
80+ years	Scenario 4a	0.65(0.48,0.75)
80+ years	Scenario 2b	0.26(0.2,0.31)
80+ years	Scenario 3b	0.47(0.37,0.57)
80+ years	Scenario 4b	0.64(0.5,0.77)
All ages	Scenario 2a	1.15(0.97,1.34)
All ages	Scenario 3a	2.1(1.78,2.44)
All ages	Scenario 4a	2.9(2.47,3.35)
All ages	Scenario 2b	0.6(0.4,0.78)
All ages	Scenario 3b	1.13(0.77,1.46)
All ages	Scenario 4b	1.61(1.11,2.06)

[Note 1]: PI indicates for prediction interval

Table S4: Peak admissions and timing during the winter of 2024/25 as estimated by the model scenarios. [Note 1]

Age group	Scenarios	Peak admission	Peak date
01-06 months	Scenario 1a	9.54	04 December 2024
01-06 months	Scenario 1b	9.03	11 November 2024
01-06 months	Scenario 2a	9.53	04 December 2024
01-06 months	Scenario 2b	9.03	11 November 2024
01-06 months	Scenario 3a	9.52	04 December 2024
01-06 months	Scenario 3b	9.03	11 November 2024
01-06 months	Scenario 4a	9.51	04 December 2024
01-06 months	Scenario 4b	9.03	11 November 2024
07-12 months	Scenario 1a	3.35	02 December 2024
07-12 months	Scenario 1b	3.99	09 November 2024
07-12 months	Scenario 2a	3.35	02 December 2024
07-12 months	Scenario 2b	3.99	09 November 2024
07-12 months	Scenario 3a	3.35	02 December 2024
07-12 months	Scenario 3b	3.99	09 November 2024
07-12 months	Scenario 4a	3.35	02 December 2024
07-12 months	Scenario 4b	3.99	09 November 2024
01-04 years	Scenario 1a	6.14	08 December 2024
01-04 years	Scenario 1b	5.35	08 November 2024
01-04 years	Scenario 2a	6.14	08 December 2024
01-04 years	Scenario 2b	5.35	08 November 2024

01-04 years	Scenario 3a	6.14	08 December 2024
01-04 years	Scenario 3b	5.35	08 November 2024
01-04 years	Scenario 4a	6.14	08 December 2024
01-04 years	Scenario 4b	5.35	08 November 2024
05-74 years	Scenario 1a	4.03	07 December 2024
05-74 years	Scenario 1b	2.07	06 November 2024
05-74 years	Scenario 2a	4.03	07 December 2024
05-74 years	Scenario 2b	2.07	06 November 2024
05-74 years	Scenario 3a	4.03	07 December 2024
05-74 years	Scenario 3b	2.07	06 November 2024
05-74 years	Scenario 4a	4.03	07 December 2024
05-74 years	Scenario 4b	2.07	06 November 2024
75-79 years	Scenario 1a	1.32	18 December 2024
75-79 years	Scenario 1b	0.41	17 November 2024
75-79 years	Scenario 2a	1.08	18 December 2024
75-79 years	Scenario 2b	0.35	15 November 2024
75-79 years	Scenario 3a	0.89	18 December 2024
75-79 years	Scenario 3b	0.30	15 November 2024
75-79 years	Scenario 4a	0.75	18 December 2024
75-79 years	Scenario 4b	0.26	10 November 2024
80+ years	Scenario 1a	2.86	20 December 2024
80+ years	Scenario 1b	1.14	19 November 2024
80+ years	Scenario 2a	2.85	21 December 2024
80+ years	Scenario 2b	1.14	19 November 2024
80+ years	Scenario 3a	2.84	20 December 2024
80+ years	Scenario 3b	1.14	19 November 2024
80+ years	Scenario 4a	2.84	20 December 2024
80+ years	Scenario 4b	1.13	19 November 2024

[Note 1]: Peaks were defined as the maximum value of admission observed in the winter. No thresholds were used in determining peaks.

Table S5: Summary of admissions averted (%) during the winter of 2025/26 as estimated by the model scenarios. [Note 1]

Age group	Scenarios	% of Admissions averted (median and 95% PI)
01-06 months	Scenario 2a	10.69(9.75,12.19)
01-06 months	Scenario 3a	20.91(19.21,23.55)
01-06 months	Scenario 4a	30.6(28.39,34.06)
01-06 months	Scenario 2b	9.1(8.82,9.89)
01-06 months	Scenario 3b	18(17.5,19.48)
01-06 months	Scenario 4b	26.71(26.04,28.73)
07-12 months	Scenario 2a	3.71(2.73,5.59)

07-12 months	Scenario 3a	7.79(5.82,11.25)
07-12 months	Scenario 4a	12.05(9.2,16.68)
07-12 months	Scenario 2b	3.22(2.7,4.2)
07-12 months	Scenario 3b	6.52(5.53,8.45)
07-12 months	Scenario 4b	9.89(8.49,12.73)
01-04 years	Scenario 2a	0.13(-0.12,0.55)
01-04 years	Scenario 3a	0.33(-0.17,1.17)
01-04 years	Scenario 4a	0.57(-0.15,1.82)
01-04 years	Scenario 2b	0.73(0.32,1.59)
01-04 years	Scenario 3b	1.49(0.69,3.19)
01-04 years	Scenario 4b	2.27(1.09,4.78)
05-74 years	Scenario 2a	-0.16(-0.37,0.09)
05-74 years	Scenario 3a	-0.28(-0.7,0.23)
05-74 years	Scenario 4a	-0.36(-0.99,0.43)
05-74 years	Scenario 2b	0.2(-0.16,0.81)
05-74 years	Scenario 3b	0.42(-0.28,1.6)
05-74 years	Scenario 4b	0.64(-0.37,2.39)
75-79 years	Scenario 2a	25.46(24.84,26.94)
75-79 years	Scenario 3a	41.01(40,43.27)
75-79 years	Scenario 4a	50.73(49.46,53.48)
75-79 years	Scenario 2b	25.98(25.51,26.69)
75-79 years	Scenario 3b	41.97(41.38,43)
75-79 years	Scenario 4b	52.05(51.43,53.27)
80+ years	Scenario 2a	-1.32(-2.07,-0.69)
80+ years	Scenario 3a	-2.67(-4.18,-1.39)
80+ years	Scenario 4a	-3.94(-6.26,-2.04)
80+ years	Scenario 2b	0(-0.29,0.58)
80+ years	Scenario 3b	-0.07(-0.62,1.06)
80+ years	Scenario 4b	-0.16(-0.97,1.51)
All ages	Scenario 2a	5.69(5.16,6.55)
All ages	Scenario 3a	10.79(9.84,12.35)
All ages	Scenario 4a	15.47(14.18,17.46)
All ages	Scenario 2b	5.11(4.64,5.96)
All ages	Scenario 3b	9.96(9.13,11.57)
All ages	Scenario 4b	14.62(13.49,16.93)

[Note 1]: PI indicates for prediction interval

Table S6: Peak admissions and timing during the winter of 2025/26 as estimated by the model scenarios.

Age group	Scenarios	Peak admission	Peak date
01-06 months	Scenario 1a	9.40	02 December 2025
01-06 months	Scenario 1b	8.88	18 November 2025
01-06 months	Scenario 2a	8.76	07 December 2025
01-06 months	Scenario 2b	8.06	20 November 2025
01-06 months	Scenario 3a	8.06	11 December 2025
01-06 months	Scenario 3b	7.24	20 November 2025
01-06 months	Scenario 4a	7.29	15 December 2025
01-06 months	Scenario 4b	6.46	22 November 2025
07-12 months	Scenario 1a	3.26	02 December 2025
07-12 months	Scenario 1b	3.94	16 November 2025
07-12 months	Scenario 2a	3.27	05 December 2025
07-12 months	Scenario 2b	3.78	18 November 2025
07-12 months	Scenario 3a	3.25	10 December 2025
07-12 months	Scenario 3b	3.64	19 November 2025
07-12 months	Scenario 4a	3.20	13 December 2025
07-12 months	Scenario 4b	3.48	19 November 2025
01-04 years	Scenario 1a	6.04	06 December 2025
01-04 years	Scenario 1b	5.15	14 November 2025
01-04 years	Scenario 2a	6.19	10 December 2025
01-04 years	Scenario 2b	5.10	15 November 2025
01-04 years	Scenario 3a	6.30	13 December 2025
01-04 years	Scenario 3b	5.04	16 November 2025
01-04 years	Scenario 4a	6.40	16 December 2025
01-04 years	Scenario 4b	4.99	17 November 2025
05-74 years	Scenario 1a	3.95	05 December 2025
05-74 years	Scenario 1b	1.95	11 November 2025
05-74 years	Scenario 2a	4.03	09 December 2025
05-74 years	Scenario 2b	1.95	12 November 2025
05-74 years	Scenario 3a	4.10	11 December 2025
05-74 years	Scenario 3b	1.94	14 November 2025
05-74 years	Scenario 4a	4.15	15 December 2025
05-74 years	Scenario 4b	1.93	15 November 2025
75-79 years	Scenario 1a	1.30	21 December 2025
75-79 years	Scenario 1b	0.39	26 November 2025
75-79 years	Scenario 2a	0.99	25 December 2025
75-79 years	Scenario 2b	0.29	27 November 2025
75-79 years	Scenario 3a	0.79	28 December 2025
75-79 years	Scenario 3b	0.23	26 November 2025
75-79 years	Scenario 4a	0.67	01 January 2026

75-79 years	Scenario 4b	0.19	27 November 2025
80+ years	Scenario 1a	2.83	22 December 2025
80+ years	Scenario 1b	1.12	01 December 2025
80+ years	Scenario 2a	2.93	25 December 2025
80+ years	Scenario 2b	1.12	30 November 2025
80+ years	Scenario 3a	3.02	28 December 2025
80+ years	Scenario 3b	1.11	01 December 2025
80+ years	Scenario 4a	3.11	31 December 2025
80+ years	Scenario 4b	1.11	02 December 2025

Table S7: Peak occupancy and timing during the winter of 2025/26 as estimated by the model scenarios.

Age group	Scenario	Peak occupancy	Peak date
01-06 months	Scenario 1a	28.18	03 December 2025
01-06 months	Scenario 1b	26.62	19 November 2025
01-06 months	Scenario 2a	26.27	07 December 2025
01-06 months	Scenario 2b	24.16	20 November 2025
01-06 months	Scenario 3a	24.16	12 December 2025
01-06 months	Scenario 3b	21.72	22 November 2025
01-06 months	Scenario 4a	21.87	16 December 2025
01-06 months	Scenario 4b	19.36	23 November 2025
07-12 months	Scenario 1a	6.53	02 December 2025
07-12 months	Scenario 1b	7.87	16 November 2025
07-12 months	Scenario 2a	6.54	05 December 2025
07-12 months	Scenario 2b	7.57	18 November 2025
07-12 months	Scenario 3a	6.49	11 December 2025
07-12 months	Scenario 3b	7.27	19 November 2025
07-12 months	Scenario 4a	6.39	13 December 2025
01-04 years	Scenario 1a	12.07	07 December 2025
01-04 years	Scenario 1b	10.28	14 November 2025
01-04 years	Scenario 2a	12.37	10 December 2025
01-04 years	Scenario 2b	10.19	15 November 2025
01-04 years	Scenario 3a	12.60	13 December 2025
01-04 years	Scenario 3b	10.08	17 November 2025
01-04 years	Scenario 4a	12.80	16 December 2025
01-04 years	Scenario 4b	9.97	18 November 2025
05-74 years	Scenario 1a	35.28	10 December 2025
05-74 years	Scenario 1b	13.65	15 November 2025
05-74 years	Scenario 2a	35.96	13 December 2025
05-74 years	Scenario 2b	13.60	17 November 2025
05-74 years	Scenario 3a	36.57	16 December 2025
05-74 years	Scenario 3b	13.55	18 November 2025
05-74 years	Scenario 4a	37.08	19 December 2025
05-74 years	Scenario 4b	13.49	19 November 2025
75-79 years	Scenario 1a	16.69	27 December 2025

75-79 years	Scenario 1b	3.48	30 November 2025
75-79 years	Scenario 2a	12.67	30 December 2025
75-79 years	Scenario 2b	2.57	01 December 2025
75-79 years	Scenario 3a	10.18	02 January 2026
75-79 years	Scenario 3b	2.01	02 December 2025
75-79 years	Scenario 4a	8.62	05 January 2026
75-79 years	Scenario 4b	1.66	03 December 2025
80+ years	Scenario 1a	60.58	01 January 2026
80+ years	Scenario 1b	13.30	04 December 2025
80+ years	Scenario 2a	62.71	04 January 2026
80+ years	Scenario 2b	13.30	05 December 2025
80+ years	Scenario 3a	64.78	07 January 2026
80+ years	Scenario 3b	13.30	06 December 2025
80+ years	Scenario 4a	66.67	10 January 2026
80+ years	Scenario 4b	13.30	07 December 2025

Initial conditions for the vaccination model

$$S_n^{[0]} = N * p^{sus} - inf$$

$$E_{1n}^{[0]} = 0$$

$$E_{2n}^{[0]} = 0$$

$$I_{1n}^{[0]} = inf$$

$$I_{2n}^{[0]} = 0$$

$$R_n^{[0]} = N * p^{sus}$$

$$S_v^{[0]} = 0$$

$$E_{1v}^{[0]} = 0$$

$$E_{2v}^{[0]} = 0$$

$$I_{1v}^{[0]} = 0$$

$$I_{2v}^{[0]} = 0$$

$$R_v^{[0]} = 0$$

$$M_v^{[0]} = 0$$

p^{sus} indicates proportion susceptible, N the total population and inf the infected individuals at the start of the model.

p^{sus} were obtained through model fitting.