Supplementary Material for:

Potential impact of nirsevimab on RSV transmission and medically attended lower respiratory tract illness caused by RSV: a disease transmission model

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Supplementary Methods

Model presentation

The model assumes 10 RSV disease states. Newborns benefit from a waning maternal protective immunity (M) during an average of ω^{-1} days after which they became susceptible to a first RSV infection (S_0). Throughout life, they may acquire consecutive infections I_1, I_2 and I_3 and be infectious for an average duration of γ_1^{-1}, γ_2^{-1} and γ_3^{-1}days respectively after which they acquire short-term waning immunity (P_1, P_2 and P_3) lasting on average p^{-1} days. Reduced susceptibility to infection (S_1, S_2) due to acquired partial immunity, is developed after consecutive infections, with decreasing infection duration (σ_1, σ_2) and decreasing infectiousness (ρ_1, ρ_2).

RSV-LRTI is assumed to occur among infected individuals with age-specific probabilities (d_1, d_2 and d_3) depending on the infection number, with a certain proportion (h) of those cases that have been coded in the Truven Health Marketscan® databases assumed to represent RSV-MALRTIs.

RSV transmission was assumed to be frequency-dependent and was based on the projected US contact matrix described elsewhere [1]. Seasonal patterns and amplitudes of RSV outbreaks were captured using a cosine forcing function. The model diagram is presented in supplementary material (**Figure S1**), as well as the US contact matrix (**Figure S2**).

Demographic data based on age-stratified US Census population estimates and projections from 2008 to 2015 [2] birth rates obtained from the 2014 US vital statistics [3] and death rates from the 2013 US vital statistics [4] were included in the model. Continuous ageing rates were included in the ordinary differential equations, with individuals assumed to age into the next age group with rate equal to 1/(width of the age class). Migration was not considered.

Model equations:

$$\frac{dM_a}{dt} = B_0 - (\omega + \mu_a)M_a - \kappa_a M_a + \kappa_{a-1} M_{a-1}$$

$$\frac{dS_{0,a}}{dt} = \omega M_a - \lambda_a S_{0,a} - \mu_a S_{0,a} - \kappa_a S_{0,a} + \kappa_{a-1} S_{0,a-1}$$

$$\frac{dI_{1,a}}{dt} = \lambda_a S_{0,a} - (\gamma_1 + \mu_a) I_{1,a} - \kappa_a I_{1,a} + \kappa_{a-1} I_{1,a-1}$$

$$\frac{dP_{1,a}}{dt} = \gamma_1 I_{1,a} - (p + \mu_a) P_{1,a} - \kappa_a P_{1,a} + \kappa_{a-1} P_{1,a-1}$$

$$\frac{dS_{1,a}}{dt} = p P_{1,a} - \sigma_1 \lambda_a S_{1,a} - \mu_a S_{1,a} - \kappa_a S_{1,a} + \kappa_{a-1} S_{1,a-1}$$

$$\frac{dI_{2,a}}{dt} = \sigma_1 \lambda_a S_{1,a} - (\gamma_2 + \mu_a) I_{2,a} - \kappa_a I_{2,a} + \kappa_{a-1} I_{2,a-1}$$

$$\frac{dP_{2,a}}{dt} = \gamma_2 I_{2,a} - (p + \mu_a) P_{2,a} - \kappa_a P_{2,a} + \kappa_{a-1} P_{2,a-1}$$

$$\frac{dS_{2,a}}{dt} = p(P_{2,a} + P_{3,a}) - \sigma_2 \lambda_a S_{2,a} - \mu_a S_{2,a} - \kappa_a S_{2,a} + \kappa_{a-1} S_{2,a-1}$$

$$\frac{dI_{3,a}}{dt} = \sigma_2 \lambda_a S_{2,a} - (\gamma_3 + \mu_a) I_{3,a} - \kappa_a I_{3,a} + \kappa_{a-1} I_{3,a-1}$$

$$\frac{dP_{3,a}}{dt} = \gamma_3 I_{3,a} - (p + \mu_a) P_{3,a} - \kappa_a P_{3,a} + \kappa_{a-1} P_{3,a-1}$$

With a = 1…32, corresponding to age groups "[0-1[months", "[1-2[months", "[2-3[months", "[3-4[months", "[4-5[months", "[5-6[months", "[6-7[months", "[7-8[months", "[8-9[months", "[9-10[months", "[10-11[months", "[11-12[months", [12-13[months", "[13-14[months", "[14-15[months", "[15-16[months", "[16-17[months", "[17-18[months", "[18-19[months", "[19-20[months", "[20-21[months", "[21-22[months", "[22-23[months", "[23-24[months", "[2-4[years", "[5-9[years", "[10-19[years", "[20-39[years", "[40-59[years", "[60-64[years", "[65-74[years" and “75-++[years".

$B_0 = 0$ if $a > 1$ and $\kappa_{a-1} = 0$ if $a = 1$

$$\lambda_a = \beta_0 \left(1 + b\cos(\frac{2\pi}{12}(t + \varphi)\right) \sum_{j=1}^{n} \frac{C_{a,j}}{N_j} \left(I_{1,j} + \rho_1 I_{2,j} + \rho_2 I_{3,j}\right)$$

$C_{a,j}$ is the US contact matrix, and N_a the total number of persons in group age a.

$$LRTIs_a = d_{1,a} I_{1,a} + d_{2,a} I_{2,a} + d_{3,a} I_{3,a}$$

$$MALRTIs_a = h \times LRTIs_a$$

Calibration

The model was calibrated, and the parameters estimated by maximum-likelihood assuming that the monthly age-specific MALRTIs count, $y_{m,a}$, follows a Poisson distribution with mean equal to the model-predicted count $\hat{y}_{m,a}$. The log-likelihood of the model is given by the following equation:

$$LL = \sum_{m} \sum_{a} (y_{m,a} \log(\hat{y}_{m,a}) - \hat{y}_{m,a} - \sum_{i=1}^{y_{m,a}} \log(i))$$

The model was fitted to the incidence of age-specific RSV-MALRTI by calendar month, and four parameters were estimated: seasonality amplitude (b) and phase (φ), per contact transmission probability ($\boldsymbol{\beta_0}$), and reporting fraction (i.e. proportion of individuals with LRTD who were coded as RSV-MALRTI in the Truven Health Marketscan® databases) (h). For each fit, the model was seeded with one infectious individual and a burn-in period of 50 years was used to ensure equilibrium was reached. Maximum likelihood parameters estimated were obtained using the Nelder-Mead algorithm [5]. The number of RSV-MALRTIs in each age group during each calendar month was assumed to follow a Poisson distribution, assuming the mean of RSV-MALRTIs for any single age group is equal to the model-predicted number of RSV episodes for that age group. Numerical goodness-of-fit was then determined by calculating the root mean square error (RMSE) and R-squared (R^2).

Potential impact of nirsevimab:

We modelled a universal immunization strategy whereby nirsevimab is given to all infants aged 0–7 months entering their first RSV epidemic season or born during the epidemic season (1 November–31 March). Coverage of single-dose nirsevimab was assumed to be 71% [6] and protection against severe RSV-LRTI was assumed immediate and season-long (5 months) with constant 70% efficacy over the window of protection. We ran our model according to two scenarios: in scenario 1, we assumed no impact of nirsevimab on RSV transmission; and in scenario 2, we assumed RSV viral shedding can be reduced and assumed an arbitrary 50% reduction in transmission.

Modifications of equations for the potential effect of nirsevimab on LRTIs is as follows:

$$LRTIs_a = (1 - \theta\psi)(d_{1,a}I_{1,a} + d_{2,a}I_{2,a} + d_{3,a}I_{3,a})$$

for t between October 1st and March 31th, with θ=nirsevimab coverage (71%) and ψ=nirsevimab constant efficacy (70%) during 5 months.

Modification of equations for the potential effect of nirsevimab on transmission is as follows:

$$\lambda_a = \beta_0 \left(1 + b\cos(\frac{2\pi}{12}(t + \varphi)\right) \sum_{j=1}^{n} \frac{C_{a,j}}{N_j} (1 - \theta\psi\xi)\left(I_{1,j} + \rho_1 I_{2,j} + \rho_2 I_{3,j}\right)$$

for t between October 1st and March 31th, with θ=nirsevimab coverage (71%), ψ=nirsevimab constant efficacy (70%) during 5 months, ξ=nirsevimab reduction of transmission (50%).

Data source and definitions

Index MALRTI event due to RSV was defined as hospitalization, a visit to the emergency department/urgent care (UC), or outpatient visit attributable to RSV identified using the following International Classification of Diseases Clinical Modification (9th revision) (ICD-9-CM) codes: respiratory syncytial virus (079.6), acute bronchiolitis due to respiratory syncytial virus (466.11), or pneumonia due to respiratory syncytial virus (480.1). For inpatient admissions, RSV-MALRTI was defined by a principal RSV diagnosis code while for outpatient visits both first and secondary diagnosis codes were used. A new RSV-MALRTIs was considered to be attributable to a new RSV infection if it occurred more than 28 days following any previous RSV-MALRTI with the same diagnostic codes.

Age-specific incidence of MALRTI due to RSV was calculated by calendar month by dividing the number of RSV-associated cases occurring in a specific age group by the number of persons in that same age range covered by Truven Health insurance during the respective particular month. The numbers of RSV MALRTI were then calculated for the general US population by multiplying RSV incidence for specific age groups by the age-stratified US Census population estimates and projections from 2008 to 2015[2].

Epidemiological year was defined from August 1^{st} to July 31^{st} each year. We presented results according to two specific periods of RSV circulation intensity, from November 1^{st} to March 31^{st}, defined as the RSV epidemic season [6], and from April 1^{st} to October 30^{th} defined as the RSV inter-epidemic period.

Since date of birth was not available in the MarketScan database, we first assign the date of the first claim of birth to approximate the birth date, and then used the enrolment date as a proxy for birth date when year of first enrolment and birth year were equivalent [7]. As >75% claims with a newborn code occurred within 5 days of the first enrolment date, it seems to be a good approximation approach. Using this method, we retrieve half of patients with missing birth claim (currently 15-20% of missing birth date vs. 30-40% previously) and reduce the imbalance of incidence between patients with and without birth date, excepted for years of 2010-2011.

Supplementary Tables and Figures

Supplementary Table S1. Observed number of RSV-MALRTIs by season and age group in the US

Season	0-6 months	6-12 months	12-18 months	18-24 months	2-4 years	5-65 years	65+ years	Overall
2009-2010	165125 (23.9%)	142970 (20.7%)	91628 (13.3%)	56316 (8.2%)	95144 (13.8%)	111414 (16.1%)	27923 (4.0%)	690520 (100.0%)
2010-2011	170551 (25.2%)	149359 (22.1%)	86370 (12.8%)	54082 (8%)	89838 (13.3%)	97463 (14.4%)	28348 (4.2%)	676011 (100.0%)
2011-2012	152880 (24.4%)	143114 (22.8%)	83412 (13.3%)	49183 (7.8%)	87999 (14.0%)	81720 (13.0%)	29504 (4.7%)	627812 (100.0%)
2012-2013	171280 (26.0%)	147920 (22.4%)	83508 (12.7%)	54428 (8.3%)	92167 (14.0%)	78459 (11.9%)	31918 (4.8%)	659680 (100.0%)
2013-2014	144129 (26.3%)	128453 (23.5%)	69082 (12.6%)	44509 (8.1%)	77479 (14.2%)	57424 (10.5%)	26146 (4.8%)	547222 (100.0%)
2014-2015	146646 (25.3%)	135604 (23.4%)	80542 (13.9%)	47461 (8.2%)	86841 (15.0%)	58335 (10.1%)	23306 (4.0%)	578735 (100.0%)
Seasonal average	158435 (25.1%)	141237 (22.4%)	82424 (13.1%)	50997 (8.1%)	88245 (14%)	80803 (12.8%)	27858 (4.4%)	629997 (100.0%)

Supplementary Table S2. Observed incidence rates per 1,000 persons of RSV-MALRTIs by season and age group in the USA

Season	0-6 months	6-12 months	12-18 months	18-24 months	2-4 years	5-65 years	65+ years
2009-2010	69.4	70.7	41.6	28.3	7.8	0.4	0.7
2010-2011	74.5	73.8	39.9	27.0	7.4	0.4	0.7
2011-2012	70.3	72.3	38.5	24.6	7.3	0.3	0.7
2012-2013	79.7	76.2	40.4	28.6	7.8	0.3	0.7
2013-2014	67.3	65.8	33.0	22.6	6.4	0.2	0.6
2014-2015	67.2	66.8	37.9	23.7	7.2	0.2	0.5
Overall	71.6	71.1	38.4	25.7	7.3	0.3	0.7

Supplementary Table S3. Potential impact of nirsevimab on expected numbers of RSV-MALRTIs, by season, for scenario 1 (A) or scenario 2 (B)

Absolute variation in the number of RSV-MALRTIs with nirsevimab compared to without nirsevimab, by age group. assuming nirsevimab has no effect on RSV transmission (A) and assuming nirsevimab reduces RSV viral shedding by 50% (B)

A. Scenario 1

Period	Season	0-6 months	6-12 months	12-24 months	2-4 years	5-65 years	65+ years	Overall
RSV epidemic season	2008-2009	0	0	0	0	0	0	0
RSV epidemic season	2009-2010	-58177	-38191	0	0	0	0	-96368
RSV epidemic season	2010-2011	-58081	-38139	0	0	0	0	-96220
RSV epidemic season	2011-2012	-57991	-38090	0	0	0	0	-96082
RSV epidemic season	2012-2013	-57909	-38046	0	0	0	0	-95955
RSV epidemic season	2013-2014	-57836	-38006	0	0	0	0	-95842
RSV epidemic season	2014-2015	-57772	-37972	0	0	0	0	-95744
RSV epidemic season	Average	-57961	-38074	0	0	0	0	-96035
RSV inter-epidemic season	2008-2009	0	0	0	0	0	0	0
RSV inter-epidemic season	2009-2010	-7347	0	0	0	0	0	-7347
RSV inter-epidemic season	2010-2011	-7338	0	0	0	0	0	-7338
RSV inter-epidemic season	2011-2012	-7331	0	0	0	0	0	-7331

RSV inter-epidemic season	2012-2013	-7323	0	0	0	0	0	-7323
RSV inter-epidemic season	2013-2014	-7317	0	0	0	0	0	-7317
RSV inter-epidemic season	2014-2015	-7312	0	0	0	0	0	-7312
RSV inter-epidemic season	2015-2016	0	0	0	0	0	0	0
RSV inter-epidemics season	Average*	-7328	0	0	0	0	0	-7328
Overall	2008-2009	0	0	0	0	0	0	0
Overall	2009-2010	-65523	-38191	0	0	0	0	-103715
Overall	2010-2011	-65420	-38139	0	0	0	0	-103559
Overall	2011-2012	-65322	-38090	0	0	0	0	-103412
Overall	2012-2013	-65233	-38046	0	0	0	0	-103279
Overall	2013-2014	-65153	-38006	0	0	0	0	-103159
Overall	2014-2015	-65084	-37972	0	0	0	0	-103056
Overall	2015-2016	0	0	0	0	0	0	0
RSV season	Average*	-65289	-38074	0	0	0	0	-103363

The RSV epidemic season was defined as the period from November 1st to March 31st. The RSV inter-epidemic period lasted from April 1st to October 30th.

An RSV season was defined as the period from August 1st to July 31st. Nirsevimab was assumed to be introduced from the 1st November 2009.

*Average calculated from 2010 to 2014 since nirsevimab was assumed to be introduced 1st November 2009t.

**Average calculated from 2010–2011 to 2014–2015 seasons since nirsevimab was assumed to be introduced 1st November 2009.

B. Scenario 2

Period	Season	0-6 months	6-12 months	12-24 months	2-4 years	5-65 years	65+ years	Overall
RSV epidemic season	2008-2009	0	0	0	0	0	0	0
RSV epidemic season	2009-2010	-64170	-44625	-9725	-564	-8992	-1058	-129134
RSV epidemic season	2010-2011	-62592	-41854	-2558	-374	-6835	-819	-115033
RSV epidemic season	2011-2012	-58358	-37380	3097	104	-656	-154	-93347
RSV epidemic season	2012-2013	-60921	-40771	-3564	-160	-4476	-580	-110473
RSV epidemic season	2013-2014	-58737	-38050	1108	51	-1316	-243	-97187
RSV epidemic season	2014-2015	-58590	-38197	-43	53	-1125	-230	-98132
RSV epidemic season	Average	-60561	-40146	-1948	-148	-3900	-514	-107218
RSV inter-epidemic season	2008-2009	0	0	0	0	0	0	0
RSV inter-epidemic season	2009-2010	-10607	-3292	-2953	-211	-3230	-363	-20656
RSV inter-epidemic season	2010-2011	-10610	-2558	-1409	-162	-2734	-310	-17783
RSV inter-epidemic season	2011-2012	-8729	-1307	-435	-52	-1333	-160	-12015
RSV inter-epidemic season	2012-2013	-9574	-2142	-1664	-100	-2036	-239	-15755
RSV inter-epidemic season	2013-2014	-8789	-1356	-767	-52	-1299	-161	-12424
RSV inter-epidemic season	2014-2015	-8594	-1348	-985	-48	-1189	-151	-12315

RSV inter-epidemic season	2015-2016	-101	-60	-37	-1	-48	-7	-254
RSV inter-epidemics season	Average*	-9484	-2001	-1369	-104	-1970	-231	-15158
Overall	2008-2009	0	0	0	0	0	0	0
Overall	2009-2010	-74777	-47917	-12678	-776	-12222	-1421	-149791
Overall	2010-2011	-73202	-44412	-3966	-537	-9570	-1129	-132816
Overall	2011-2012	-67087	-38687	2662	52	-1989	-313	-105362
Overall	2012-2013	-70495	-42913	-5229	-260	-6512	-819	-126228
Overall	2013-2014	-67526	-39406	341	-1	-2615	-404	-109611
Overall	2014-2015	-67184	-39545	-1028	5	-2314	-381	-110448
Overall	2015-2016	-101	-60	-37	-1	-48	-7	-254
RSV season	Average*	-70045	-42147	-3317	-253	-5870	-745	-122376

The RSV epidemic season was defined as the period from November 1st to March 31st. The RSV inter-epidemic period lasted from April 1st to October 30th.

An RSV season was defined as the period from August 1st to July 31st. Nirsevimab was assumed to be introduced from the 1st November 2009.

*Average calculated from 2010 to 2014 since nirsevimab was assumed to be introduced 1st November 2009t.

**Average calculated from 2010–2011 to 2014–2015 seasons since nirsevimab was assumed to be introduced 1st November 2009.

Supplementary Table S4. Quantification of nirsevimab indirect effects by age groups and season.

		Potential change in number of RSV-MALRTIs due to indirect effects							Percentage of total change due to indirect effects						
Period	Season	0-6 months	6-12 months	12-24 months	2-4 years	5-65 years	65+ years	Overall	0-6 months	6-12 months	12-24 months	2-4 years	5-65 years	65+ years	Overall
RSV epidemic season	2008-2009	0	0	0	0	0	0	0							
RSV epidemic season	2009-2010	-5993	-6434	-9725	-564	-8992	-1058	-32766	9.3%	14.4%	100.0%	100.0%	100.0%	100.0%	25.4%
RSV epidemic season	2010-2011	-4511	-3715	-2558	-374	-6835	-819	-18813	7.2%	8.9%	100.0%	100.0%	100.0%	100.0%	16.4%
RSV epidemic season	2011-2012	-367	710	3097	104	-656	-154	2735	0.6%	-1.9%	100.0%	100.0%	100.0%	100.0%	-2.9%
RSV epidemic season	2012-2013	-3012	-2725	-3564	-160	-4476	-580	-14518	4.9%	6.7%	100.0%	100.0%	100.0%	100.0%	13.1%
RSV epidemic season	2013-2014	-901	-44	1108	51	-1316	-243	-1345	1.5%	0.1%	100.0%	100.0%	100.0%	100.0%	1.4%
RSV epidemic season	2014-2015	-818	-225	-43	53	-1125	-230	-2388	1.4%	0.6%	100.0%	100.0%	100.0%	100.0%	2.4%
RSV epidemic season	Average	-2600	-2072	-1948	-148	-3900	-514	-11183	4.3%	5.2%	100.0%	100.0%	100.0%	100.0%	10.4%
RSV inter-epidemic season	2008-2009	0	0	0	0	0	0	0							
RSV inter-epidemic season	2009-2010	-3260	-3292	-2953	-211	-3230	-363	-13309	30.7%	100.0%	100.0%	100.0%	100.0%	100.0%	64.4%
RSV inter-epidemic season	2010-2011	-3272	-2558	-1409	-162	-2734	-310	-10445	30.8%	100.0%	100.0%	100.0%	100.0%	100.0%	58.7%
RSV inter-epidemic season	2011-2012	-1398	-1307	-435	-52	-1333	-160	-4684	16.0%	100.0%	100.0%	100.0%	100.0%	100.0%	39.0%
RSV inter-epidemic season	2012-2013	-2251	-2142	-1664	-100	-2036	-239	-8432	23.5%	100.0%	100.0%	100.0%	100.0%	100.0%	53.5%
RSV inter-epidemic season	2013-2014	-1472	-1356	-767	-52	-1299	-161	-5107	16.7%	100.0%	100.0%	100.0%	100.0%	100.0%	41.1%
RSV inter-epidemic season	2014-2015	-1282	-1348	-985	-48	-1189	-151	-5003	14.9%	100.0%	100.0%	100.0%	100.0%	100.0%	40.6%
RSV inter-epidemic season	2015-2016	-101	-60	-37	-1	-48	-7	-254							
RSV inter-epidemics season	Average*	**-2156**	**-2001**	**-1369**	**-104**	**-1970**	**-231**	**-7830**	22.7%	100.0%	100.0%	100.0%	100.0%	100.0%	51.7%
Overall	2008-2009	0	0	0	0	0	0	0							
Overall	2009-2010	-9254	-9726	-12678	-776	-12222	-1421	-46076	12.4%	20.3%	100.0%	100.0%	100.0%	100.0%	30.8%

Overall	2010-2011	-7782	-6273	-3966	-537	-9570	-1129	-29257	10.6%	14.1%	100.0%	100.0%	100.0%	100.0%	22.0%
Overall	2011-2012	-1765	-597	2662	52	-1989	-313	-1950	2.6%	1.5%	100.0%	100.0%	100.0%	100.0%	1.9%
Overall	2012-2013	-5262	-4867	-5229	-260	-6512	-819	-22949	7.5%	11.3%	100.0%	100.0%	100.0%	100.0%	18.2%
Overall	2013-2014	-2373	-1400	341	-1	-2615	-404	-6452	3.5%	3.6%	100.0%	100.0%	100.0%	100.0%	5.9%
Overall	2014-2015	-2100	-1573	-1028	5	-2314	-381	-7392	3.1%	4.0%	100.0%	100.0%	100.0%	100.0%	6.7%
Overall	2015-2016	-101	-60	-37	-1	-48	-7	-254							
RSV season	Average*	**-4756**	**-4073**	**-3317**	**-253**	**-5870**	**-745**	**-19013**	**6.8%**	**9.7%**	**100.0%**	**100.0%**	**100.0%**	**100.0%**	**15.5%**

The RSV epidemic season was defined as the period from November 1st to March 31st. The RSV inter-epidemic period lasted from April 1st to October 30th. An RSV season was defined as the period from August 1st to July 31st. Nirsevimab was assumed to be introduced from the 1st November 2009.

*Average calculated from 2010 to 2014 since nirsevimab was assumed to be introduced 1st November 2009t.

**Average calculated from 2010–2011 to 2014–2015 seasons since nirsevimab was assumed to be introduced 1st November 2009.

Supplementary Table S5. Sensitivity analyses. Impact of the contact matrix assumptions on the results.

While preserving the initial structure of the contact matrix, and instead of assuming a homogeneity of contact rates for children <5 years old, we assumed an increase of contact rates with age until <5 years old (see Adapted Contact Matrix, Supplementary Figure S2). The analysis was re-run without (A) and with (B) calibration and assessed whether the results and their interpretations were changed.

A. Results with adapted contact matrix assuming increase of contacts within age groups <5 years old, without re-calibration of the model

Assuming nirsevimab has no effect on RSV transmission

Period	Season	0-6 months	6-12 months	12-24 months	2-4 years	5-65 years	65+ years	Overall
RSV epidemic season	2008-2009	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
RSV epidemic season	2009-2010	-49.7%	-34.9%	0.0%	0.0%	0.0%	0.0%	-23.1%
RSV epidemic season	2010-2011	-49.7%	-34.9%	0.0%	0.0%	0.0%	0.0%	-23.1%
RSV epidemic season	2011-2012	-49.7%	-34.9%	0.0%	0.0%	0.0%	0.0%	-23.1%
RSV epidemic season	2012-2013	-49.7%	-34.9%	0.0%	0.0%	0.0%	0.0%	-23.1%
RSV epidemic season	2013-2014	-49.7%	-34.9%	0.0%	0.0%	0.0%	0.0%	-23.1%
RSV epidemic season	2014-2015	-49.7%	-34.9%	0.0%	0.0%	0.0%	0.0%	-23.1%
RSV epidemic season	Average	-49.7%	-34.9%	0.0%	0.0%	0.0%	0.0%	-23.1%
RSV inter-epidemic season	2008-2009	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
RSV inter-epidemic season	2009-2010	-17.6%	0.0%	0.0%	0.0%	0.0%	0.0%	-5.1%
RSV inter-epidemic season	2010-2011	-17.6%	0.0%	0.0%	0.0%	0.0%	0.0%	-5.1%
RSV inter-epidemic season	2011-2012	-17.6%	0.0%	0.0%	0.0%	0.0%	0.0%	-5.1%
RSV inter-epidemic season	2012-2013	-17.6%	0.0%	0.0%	0.0%	0.0%	0.0%	-5.1%
RSV inter-epidemic season	2013-2014	-17.6%	0.0%	0.0%	0.0%	0.0%	0.0%	-5.1%
RSV inter-epidemic season	2014-2015	-17.6%	0.0%	0.0%	0.0%	0.0%	0.0%	-5.1%
RSV inter-epidemic season	2015-2016	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
RSV inter-epidemics season	Average*	-17.6%	0.0%	0.0%	0.0%	0.0%	0.0%	-5.1%

Overall	2008-2009	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Overall	2009-2010	-41.2%	-26.2%	0.0%	0.0%	0.0%	0.0%	-18.5%
Overall	2010-2011	-41.2%	-26.2%	0.0%	0.0%	0.0%	0.0%	-18.5%
Overall	2011-2012	-41.2%	-26.2%	0.0%	0.0%	0.0%	0.0%	-18.5%
Overall	2012-2013	-41.2%	-26.2%	0.0%	0.0%	0.0%	0.0%	-18.5%
Overall	2013-2014	-41.2%	-26.2%	0.0%	0.0%	0.0%	0.0%	-18.5%
Overall	2014-2015	-41.2%	-26.2%	0.0%	0.0%	0.0%	0.0%	-18.5%
Overall	2015-2016	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
RSV season	Average**	-41.2%	-26.2%	0.0%	0.0%	0.0%	0.0%	-18.5%

The RSV epidemic season was defined as the period from November 1st to March 31st. The RSV inter-epidemic period lasted from April 1st to October 30th.

An RSV season was defined as the period from August 1st to July 31st. Nirsevimab was assumed to be introduced from the 1st November 2009.

*Average calculated from 2010 to 2014 since nirsevimab was assumed to be introduced 1st November 2009t.

**Average calculated from 2010–2011 to 2014–2015 seasons since nirsevimab was assumed to be introduced 1st November 2009.

Assuming nirsevimab reduces RSV viral shedding by 50%

Period	Season	0-6 months	6-12 months	12-24 months	2-4 years	5-65 years	65+ years	Overall
RSV epidemic season	2008-2009	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
RSV epidemic season	2009-2010	-54.5%	-40.4%	-9.3%	-11.4%	-11.9%	-12.5%	-30.7%
RSV epidemic season	2010-2011	-53.3%	-38.1%	-2.5%	-7.6%	-9.1%	-9.8%	-27.5%
RSV epidemic season	2011-2012	-49.8%	-34.1%	3.0%	2.1%	-0.9%	-1.9%	-22.3%
RSV epidemic season	2012-2013	-52.1%	-37.2%	-3.6%	-3.5%	-6.1%	-7.2%	-26.5%
RSV epidemic season	2013-2014	-50.2%	-34.7%	1.1%	1.0%	-1.7%	-3.0%	-23.3%
RSV epidemic season	2014-2015	-50.2%	-35.0%	-0.2%	0.8%	-1.6%	-2.9%	-23.6%
RSV epidemic season	Average	-51.7%	-36.6%	-1.9%	-3.1%	-5.3%	-6.2%	-25.7%
RSV inter-epidemic season	2008-2009	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
RSV inter-epidemic season	2009-2010	-25.2%	-8.9%	-8.6%	-12.4%	-12.4%	-12.5%	-14.3%

RSV inter-epidemic season	2010-2011	-25.2%	-7.0%	-4.2%	-9.4%	-10.6%	-10.8%	-12.4%
RSV inter-epidemic season	2011-2012	-20.9%	-3.7%	-1.4%	-3.1%	-5.2%	-5.6%	-8.5%
RSV inter-epidemic season	2012-2013	-22.9%	-6.0%	-5.0%	-6.0%	-8.0%	-8.5%	-11.1%
RSV inter-epidemic season	2013-2014	-21.0%	-3.8%	-2.3%	-3.1%	-5.1%	-5.7%	-8.7%
RSV inter-epidemic season	2014-2015	-20.6%	-3.8%	-3.1%	-3.0%	-4.7%	-5.5%	-8.7%
RSV inter-epidemic season	2015-2016	-3.1%	-2.3%	-1.6%	-1.1%	-2.7%	-3.3%	-2.4%
RSV inter-epidemics season	Average*	-22.6%	-5.5%	-4.1%	-6.1%	-7.7%	-8.1%	-10.6%
Overall	2008-2009	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Overall	2009-2010	-46.7%	-32.6%	-9.1%	-11.7%	-12.1%	-12.5%	-26.5%
Overall	2010-2011	-45.9%	-30.3%	-2.9%	-8.0%	-9.5%	-10.1%	-23.6%
Overall	2011-2012	-42.2%	-26.5%	1.9%	0.7%	-2.0%	-2.8%	-18.8%
Overall	2012-2013	-44.4%	-29.4%	-3.9%	-4.1%	-6.6%	-7.5%	-22.6%
Overall	2013-2014	-42.5%	-27.0%	0.3%	-0.1%	-2.6%	-3.7%	-19.6%
Overall	2014-2015	-42.4%	-27.2%	-0.9%	-0.1%	-2.4%	-3.6%	-19.8%
Overall	2015-2016	-3.1%	-2.3%	-1.6%	-1.1%	-2.7%	-3.3%	-2.4%
RSV season	Average**	-44.0%	-28.9%	-2.5%	-3.9%	-5.9%	-6.7%	-21.8%

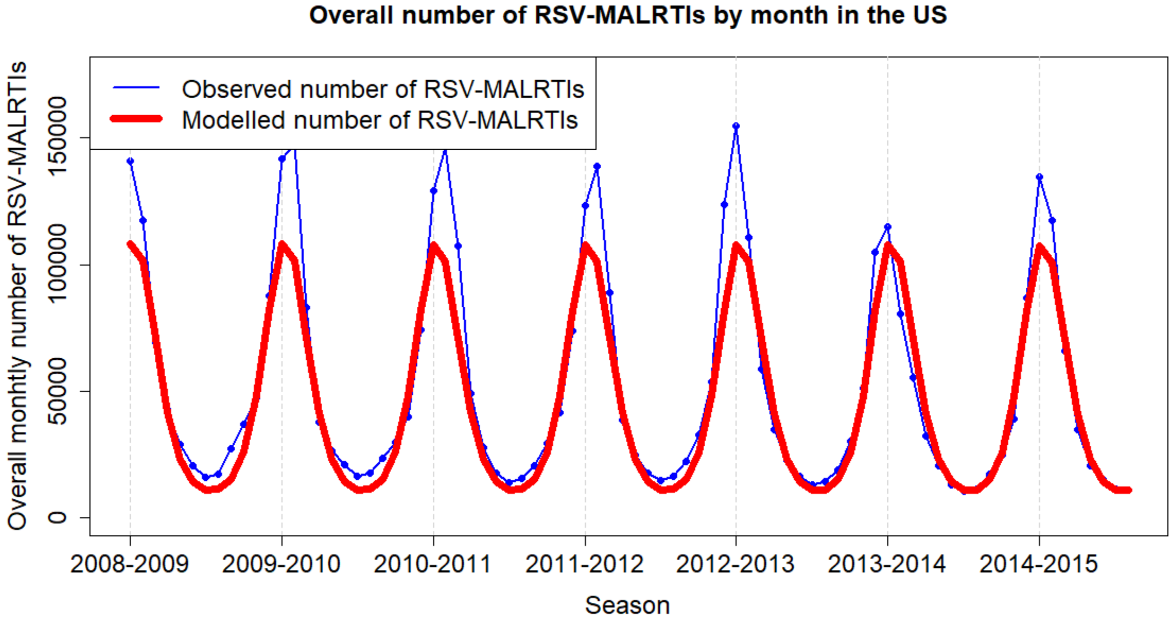
The RSV epidemic season was defined as the period from November 1st to March 31st. The RSV inter-epidemic period lasted from April 1st to October 30th.

An RSV season was defined as the period from August 1st to July 31st. Nirsevimab was assumed to be introduced from the 1st November 2009.

*Average calculated from 2010 to 2014 since nirsevimab was assumed to be introduced 1st November 2009t.

**Average calculated from 2010–2011 to 2014–2015 seasons since nirsevimab was assumed to be introduced 1st November 2009.

B. Results with adapted contact matrix assuming increase of contacts within age groups <5 years old, with re-calibration of the model



Assuming nirsevimab has no effect on RSV transmission

Period	Season	0-6 months	6-12 months	12-24 months	2-4 years	5-65 years	65+ years	Overall
RSV epidemic season	2008-2009	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
RSV epidemic season	2009-2010	-49.7%	-34.9%	0.0%	0.0%	0.0%	0.0%	-23.8%
RSV epidemic season	2010-2011	-49.7%	-34.9%	0.0%	0.0%	0.0%	0.0%	-23.8%
RSV epidemic season	2011-2012	-49.7%	-34.9%	0.0%	0.0%	0.0%	0.0%	-23.8%
RSV epidemic season	2012-2013	-49.7%	-34.9%	0.0%	0.0%	0.0%	0.0%	-23.8%
RSV epidemic season	2013-2014	-49.7%	-34.9%	0.0%	0.0%	0.0%	0.0%	-23.8%
RSV epidemic season	2014-2015	-49.7%	-34.9%	0.0%	0.0%	0.0%	0.0%	-23.8%
RSV epidemic season	Average	-49.7%	-34.9%	0.0%	0.0%	0.0%	0.0%	-23.8%

RSV inter-epidemic season	2008-2009	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
RSV inter-epidemic season	2009-2010	-17.5%	0.0%	0.0%	0.0%	0.0%	0.0%	-5.3%
RSV inter-epidemic season	2010-2011	-17.5%	0.0%	0.0%	0.0%	0.0%	0.0%	-5.3%
RSV inter-epidemic season	2011-2012	-17.5%	0.0%	0.0%	0.0%	0.0%	0.0%	-5.3%
RSV inter-epidemic season	2012-2013	-17.5%	0.0%	0.0%	0.0%	0.0%	0.0%	-5.3%
RSV inter-epidemic season	2013-2014	-17.5%	0.0%	0.0%	0.0%	0.0%	0.0%	-5.3%
RSV inter-epidemic season	2014-2015	-17.5%	0.0%	0.0%	0.0%	0.0%	0.0%	-5.3%
RSV inter-epidemic season	2015-2016	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
RSV inter-epidemics season	Average*	-17.5%	0.0%	0.0%	0.0%	0.0%	0.0%	-5.3%
Overall	2008-2009	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Overall	2009-2010	-41.1%	-26.2%	0.0%	0.0%	0.0%	0.0%	-19.0%
Overall	2010-2011	-41.1%	-26.2%	0.0%	0.0%	0.0%	0.0%	-19.0%
Overall	2011-2012	-41.1%	-26.2%	0.0%	0.0%	0.0%	0.0%	-19.0%
Overall	2012-2013	-41.1%	-26.2%	0.0%	0.0%	0.0%	0.0%	-19.0%
Overall	2013-2014	-41.1%	-26.1%	0.0%	0.0%	0.0%	0.0%	-19.0%
Overall	2014-2015	-41.1%	-26.1%	0.0%	0.0%	0.0%	0.0%	-19.0%
Overall	2015-2016	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
RSV season	Average**	-41.1%	-26.2%	0.0%	0.0%	0.0%	0.0%	-19.0%

The RSV epidemic season was defined as the period from November 1st to March 31st. The RSV inter-epidemic period lasted from April 1st to October 30th.

An RSV season was defined as the period from August 1st to July 31st. Nirsevimab was assumed to be introduced from the 1st November 2009.

*Average calculated from 2010 to 2014 since nirsevimab was assumed to be introduced 1st November 2009t.

**Average calculated from 2010–2011 to 2014–2015 seasons since nirsevimab was assumed to be introduced 1st November 2009.

Assuming nirsevimab reduces RSV viral shedding by 50%

Period	Season	0-6 months	6-12 months	12-24 months	2-4 years	5-65 years	65+ years	Overall
RSV epidemic season	2008-2009	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
RSV epidemic season	2009-2010	-54.9%	-40.8%	-10.0%	-12.7%	-13.2%	-13.8%	-31.9%
RSV epidemic season	2010-2011	-51.9%	-36.1%	0.6%	-4.4%	-6.2%	-6.9%	-25.8%
RSV epidemic season	2011-2012	-50.9%	-35.4%	0.2%	-0.8%	-3.6%	-4.5%	-24.9%
RSV epidemic season	2012-2013	-51.7%	-36.6%	-2.1%	-2.8%	-5.6%	-6.7%	-26.4%
RSV epidemic season	2013-2014	-50.0%	-34.5%	1.3%	1.6%	-1.4%	-2.7%	-23.7%
RSV epidemic season	2014-2015	-50.7%	-35.5%	-1.0%	-0.3%	-2.9%	-4.3%	-25.0%
RSV epidemic season	Average	-51.7%	-36.5%	-1.8%	-3.2%	-5.5%	-6.5%	-26.3%
RSV inter-epidemic season	2008-2009	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
RSV inter-epidemic season	2009-2010	-25.1%	-8.5%	-8.1%	-12.8%	-12.9%	-12.9%	-14.3%
RSV inter-epidemic season	2010-2011	-23.8%	-5.5%	-2.7%	-7.9%	-9.1%	-9.3%	-11.1%
RSV inter-epidemic season	2011-2012	-21.9%	-4.8%	-3.0%	-5.2%	-7.3%	-7.7%	-10.1%
RSV inter-epidemic season	2012-2013	-22.6%	-5.3%	-4.0%	-5.8%	-7.9%	-8.4%	-10.8%
RSV inter-epidemic season	2013-2014	-20.9%	-3.8%	-2.4%	-3.2%	-5.4%	-6.1%	-8.9%
RSV inter-epidemic season	2014-2015	-21.2%	-4.2%	-3.5%	-3.9%	-5.8%	-6.6%	-9.5%
RSV inter-epidemic season	2015-2016	-2.5%	-1.2%	-0.2%	-0.3%	-2.1%	-2.8%	-1.5%
RSV inter-epidemics season	Average*	-22.6%	-5.3%	-3.9%	-6.5%	-8.1%	-8.5%	-10.8%
Overall	2008-2009	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Overall	2009-2010	-46.9%	-32.7%	-9.5%	-12.7%	-13.1%	-13.6%	-27.4%
Overall	2010-2011	-44.4%	-28.5%	-0.2%	-5.3%	-6.9%	-7.6%	-22.0%
Overall	2011-2012	-43.1%	-27.8%	-0.6%	-1.9%	-4.5%	-5.4%	-21.1%
Overall	2012-2013	-44.0%	-28.7%	-2.6%	-3.6%	-6.2%	-7.1%	-22.4%
Overall	2013-2014	-42.2%	-26.8%	0.4%	0.4%	-2.4%	-3.6%	-19.9%
Overall	2014-2015	-42.8%	-27.6%	-1.6%	-1.2%	-3.6%	-4.9%	-21.0%
Overall	2015-2016	-2.5%	-1.2%	-0.2%	-0.3%	-2.1%	-2.8%	-1.5%
RSV season	Average**	-43.9%	-28.7%	-2.4%	-4.0%	-6.1%	-7.0%	-22.3%

The RSV epidemic season was defined as the period from November 1st to March 31st. The RSV inter-epidemic period lasted from April 1st to October 30th.

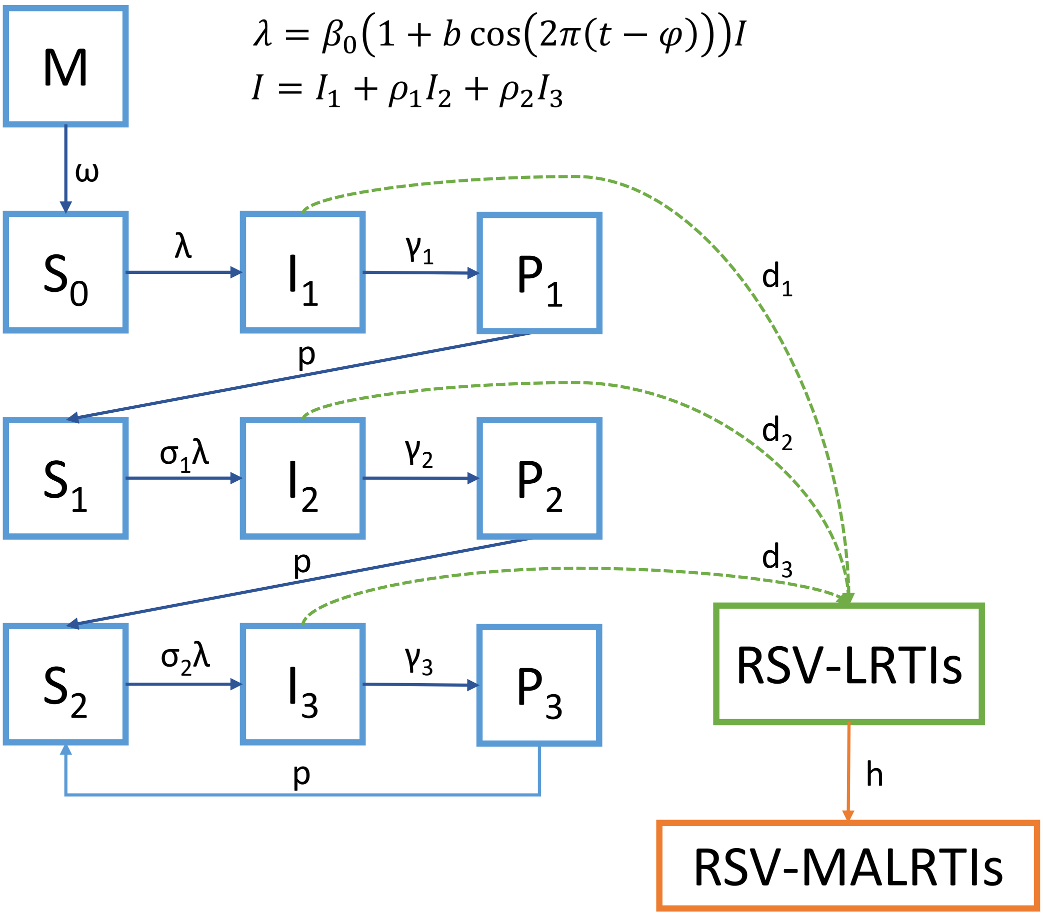
An RSV season was defined as the period from August 1st to July 31st. Nirsevimab was assumed to be introduced from the 1st November 2009.

*Average calculated from 2010 to 2014 since nirsevimab was assumed to be introduced 1st November 2009t.

**Average calculated from 2010–2011 to 2014–2015 seasons since nirsevimab was assumed to be introduced 1st November 2009.

Supplementary Figure S1. Model diagram

Footnote: Newborns benefit from maternal antibody protection (M), after which they become susceptible (S_0) to primary RSV infection. After each infection (I_1, I_2 and I_3), individuals recover and acquire short-term waning immunity (P_1, P_2, P_3), before becoming susceptible again (S_1, S_2). The model outcome is the number of RSV-MALTRIs.



Supplementary Figure S2. US contact matrix (number of contacts per day)

Original US contact matrix

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
1	2,60	1,05	0,40	0,24	0,34	0,65	0,87	0,83	0,42	0,35	0,32	0,40	0,31	0,21	0,09	0,12
2	1,05	5,39	1,56	0,39	0,20	0,43	0,91	1,08	0,79	0,45	0,46	0,47	0,30	0,28	0,19	0,16
3	0,40	1,56	8,28	2,02	0,34	0,26	0,62	0,89	1,03	0,66	0,68	0,46	0,22	0,23	0,19	0,24
4	0,24	0,39	2,02	11,11	2,12	0,83	0,57	0,83	1,15	1,33	0,98	0,62	0,30	0,15	0,19	0,18
5	0,34	0,20	0,34	2,12	4,26	1,88	1,07	0,88	0,89	0,99	0,88	0,59	0,27	0,17	0,10	0,09
6	0,65	0,43	0,26	0,83	1,88	3,41	1,69	1,31	1,13	0,95	1,10	0,86	0,39	0,20	0,13	0,09
7	0,87	0,91	0,62	0,57	1,07	1,69	2,72	1,63	1,38	1,09	0,98	0,88	0,47	0,29	0,14	0,14
8	0,83	1,08	0,89	0,83	0,88	1,31	1,63	2,78	1,75	1,26	1,01	0,72	0,52	0,34	0,23	0,16
9	0,42	0,79	1,03	1,15	0,89	1,13	1,38	1,75	2,52	1,44	1,28	0,74	0,42	0,33	0,31	0,19
10	0,35	0,45	0,66	1,33	0,99	0,95	1,09	1,26	1,44	2,03	1,39	0,73	0,37	0,21	0,24	0,25
11	0,32	0,46	0,68	0,98	0,88	1,10	0,98	1,01	1,28	1,39	1,93	1,05	0,43	0,24	0,20	0,23
12	0,40	0,47	0,46	0,62	0,59	0,86	0,88	0,72	0,74	0,73	1,05	1,60	0,63	0,33	0,19	0,14
13	0,31	0,30	0,22	0,30	0,27	0,39	0,47	0,52	0,42	0,37	0,43	0,63	1,07	0,43	0,33	0,12
14	0,21	0,28	0,23	0,15	0,17	0,20	0,29	0,34	0,33	0,21	0,24	0,33	0,43	0,90	0,35	0,17
15	0,09	0,19	0,19	0,19	0,10	0,13	0,14	0,23	0,31	0,24	0,20	0,19	0,33	0,35	0,68	0,23
16	0,12	0,16	0,24	0,18	0,09	0,09	0,14	0,16	0,19	0,25	0,23	0,14	0,12	0,17	0,23	0,40

The US contact matrix from Prem *et al.* has been rendered symmetric, and then extended and rearranged to fit the model age structure, assuming homogeneity of contacts within age groups.

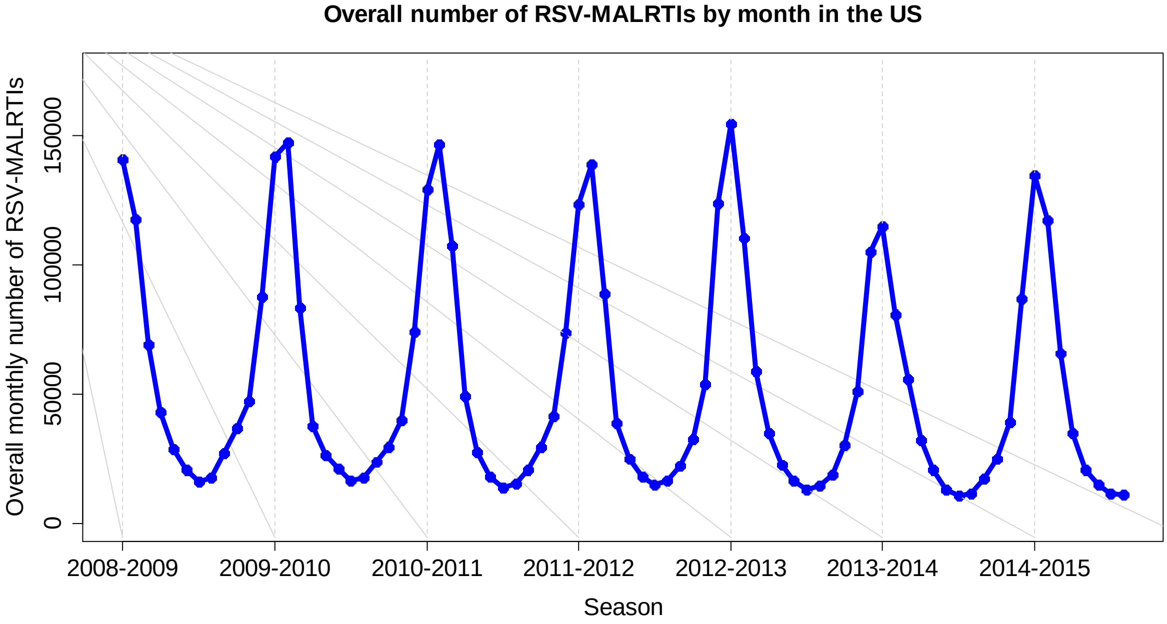
Adapted US contact matrix

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32
1	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	1,05	0,65	2,69	1,49	0,31	0,30	0,12
2	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	1,05	0,65	2,69	1,49	0,31	0,30	0,12
3	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	1,05	0,65	2,69	1,49	0,31	0,30	0,12
4	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	1,05	0,65	2,69	1,49	0,31	0,30	0,12
5	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	1,05	0,65	2,69	1,49	0,31	0,30	0,12
6	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	1,05	0,65	2,69	1,49	0,31	0,30	0,12
7	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	1,05	0,65	2,69	1,49	0,31	0,30	0,12
8	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	1,05	0,65	2,69	1,49	0,31	0,30	0,12
9	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	1,05	0,65	2,69	1,49	0,31	0,30	0,12
10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	1,05	0,65	2,69	1,49	0,31	0,30	0,12
11	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	1,05	0,65	2,69	1,49	0,31	0,30	0,12
12	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	1,05	0,65	2,69	1,49	0,31	0,30	0,12
13	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	1,05	0,65	2,69	1,49	0,31	0,30	0,12
14	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	1,05	0,65	2,69	1,49	0,31	0,30	0,12
15	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	1,05	0,65	2,69	1,49	0,31	0,30	0,12
16	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	1,05	0,65	2,69	1,49	0,31	0,30	0,12
17	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	1,05	0,65	2,69	1,49	0,31	0,30	0,12
18	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	1,05	0,65	2,69	1,49	0,31	0,30	0,12
19	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	1,05	0,65	2,69	1,49	0,31	0,30	0,12
20	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	1,05	0,65	2,69	1,49	0,31	0,30	0,12
21	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	1,05	0,65	2,69	1,49	0,31	0,30	0,12
22	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	1,05	0,65	2,69	1,49	0,31	0,30	0,12
23	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	1,05	0,65	2,69	1,49	0,31	0,30	0,12
24	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	1,05	0,65	2,69	1,49	0,31	0,30	0,12
25	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	0,10	1,05	0,65	2,69	1,49	0,31	0,30	0,12
26	1,05	1,05	1,05	1,05	1,05	1,05	1,05	1,05	1,05	1,05	1,05	1,05	1,05	1,05	1,05	1,05	1,05	1,05	1,05	1,05	1,05	1,05	1,05	1,05	1,05	5,39	1,95	2,62	2,18	0,30	0,46	0,16
27	0,65	0,65	0,65	0,65	0,65	0,65	0,65	0,65	0,65	0,65	0,65	0,65	0,65	0,65	0,65	0,65	0,65	0,65	0,65	0,65	0,65	0,65	0,65	0,65	0,65	1,95	23,43	6,46	6,91	0,52	0,76	0,41
28	2,69	2,69	2,69	2,69	2,69	2,69	2,69	2,69	2,69	2,69	2,69	2,69	2,69	2,69	2,69	2,69	2,69	2,69	2,69	2,69	2,69	2,69	2,69	2,69	2,69	2,62	6,46	30,10	16,46	1,65	1,60	0,47
29	1,49	1,49	1,49	1,49	1,49	1,49	1,49	1,49	1,49	1,49	1,49	1,49	1,49	1,49	1,49	1,49	1,49	1,49	1,49	1,49	1,49	1,49	1,49	1,49	1,49	2,18	6,91	16,46	21,35	1,85	2,05	0,81
30	0,31	0,31	0,31	0,31	0,31	0,31	0,31	0,31	0,31	0,31	0,31	0,31	0,31	0,31	0,31	0,31	0,31	0,31	0,31	0,31	0,31	0,31	0,31	0,31	0,31	0,30	0,52	1,65	1,85	1,07	0,76	0,12
31	0,30	0,30	0,30	0,30	0,30	0,30	0,30	0,30	0,30	0,30	0,30	0,30	0,30	0,30	0,30	0,30	0,30	0,30	0,30	0,30	0,30	0,30	0,30	0,30	0,30	0,46	0,76	1,60	2,05	0,76	2,29	0,40
32	0,12	0,12	0,12	0,12	0,12	0,12	0,12	0,12	0,12	0,12	0,12	0,12	0,12	0,12	0,12	0,12	0,12	0,12	0,12	0,12	0,12	0,12	0,12	0,12	0,12	0,16	0,41	0,47	0,81	0,12	0,40	0,40

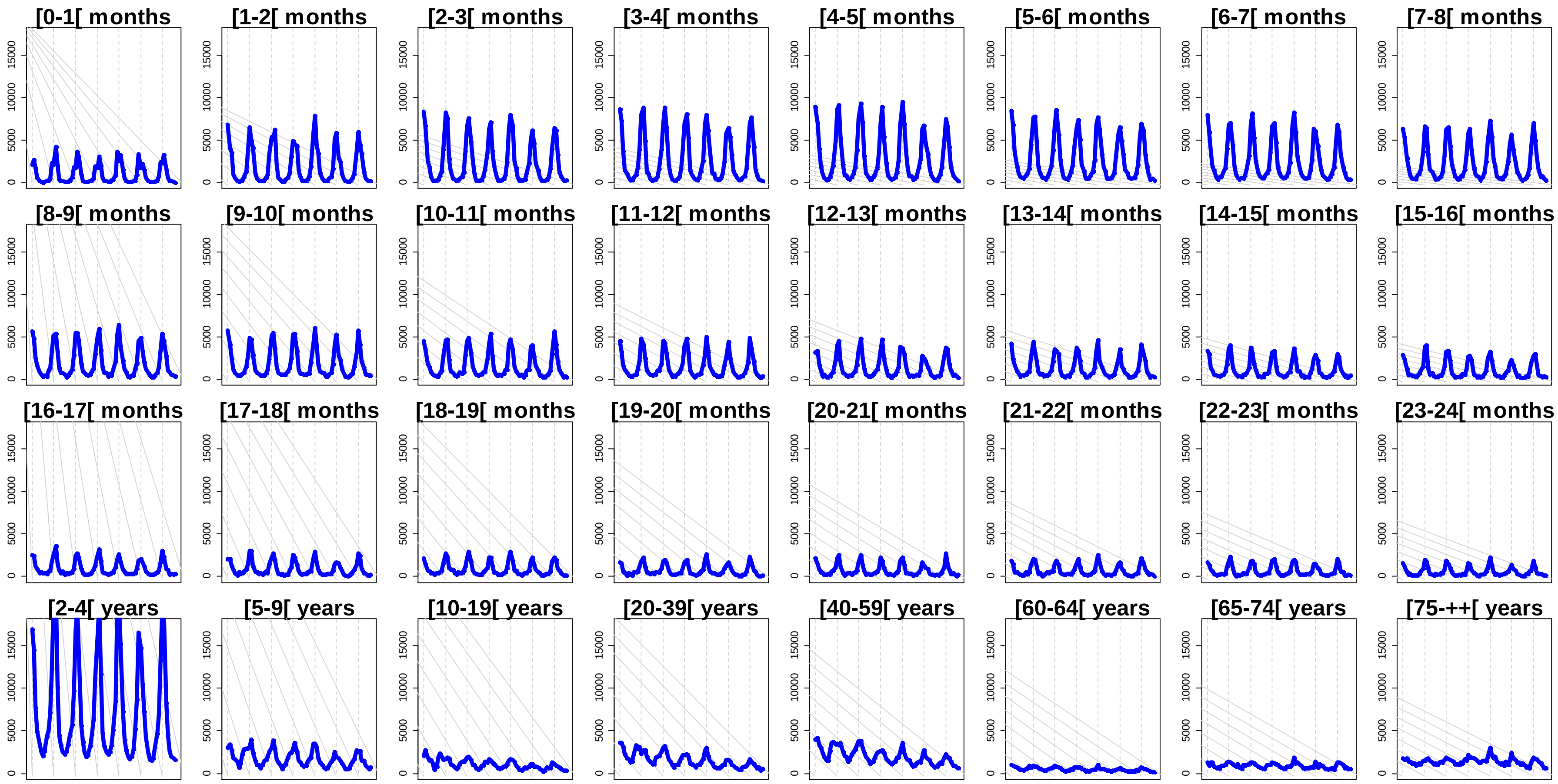
Supplementary Figure S3 Observed number of RSV-MALRTIs by season in the US

Footnote: Observed data were based on RSV-MALRTIs reported between 1 January 2008 and 31 December 2015 and were obtained from the Truven Health Marketscan® Commercial Claims and Encounters, and Medicare Supplemental and Coordination of Benefits databases (Truven Health Analytics, Michigan, USA). The numbers of RSV-MALRTIs were calculated for the general US population the age-stratified US Census population estimates and projections from 2008 to 2015.

A. Overall population

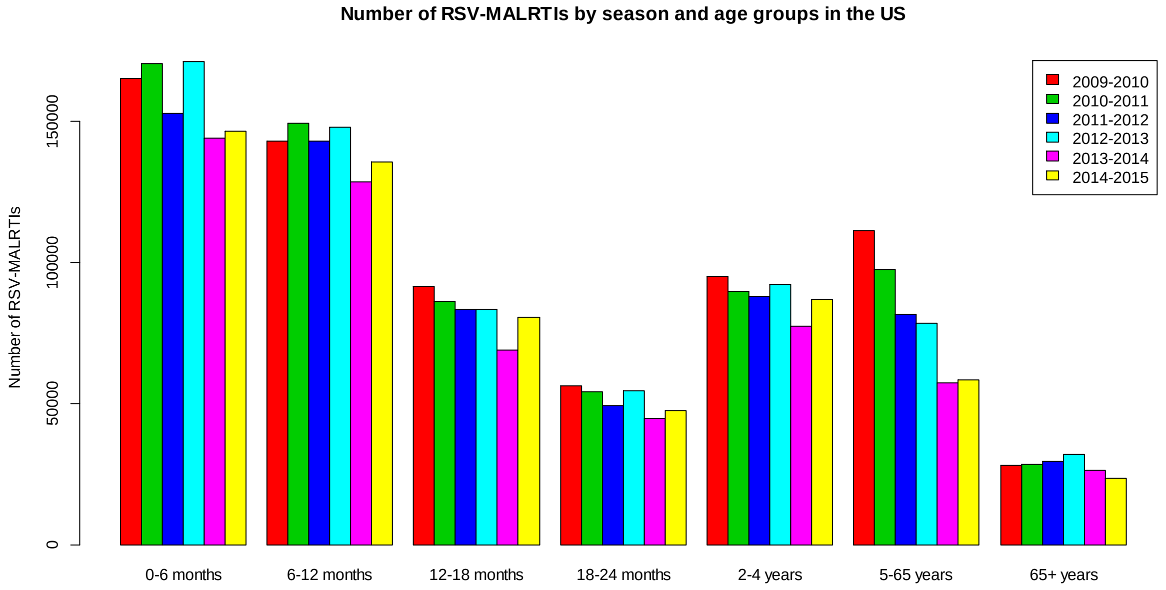


B. By 1-month interval age groups up to 24 months



Y-axes represent the same scale for each age group (0 to 15000 RSV-MALRTIs); months are plotted on the x-axis, representing 7 seasons from 2009 to 2015.

Supplementary Figure S4. Observed number of RSV-MALRTIs by season and age group in the US

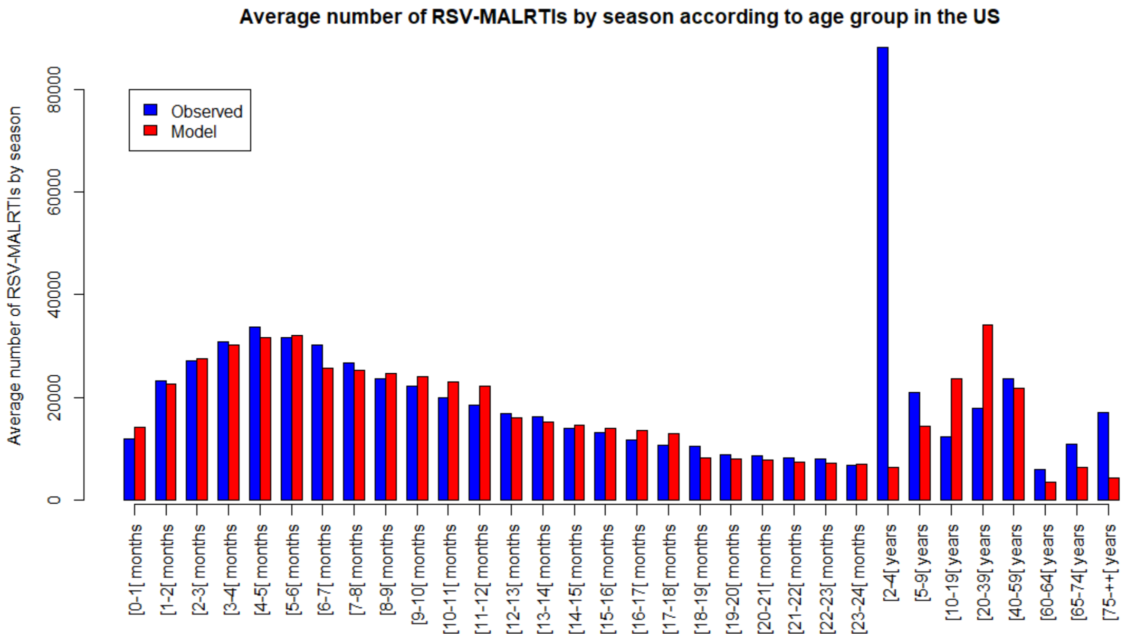


Supplementary Figures S5 and S6. Model calibration.

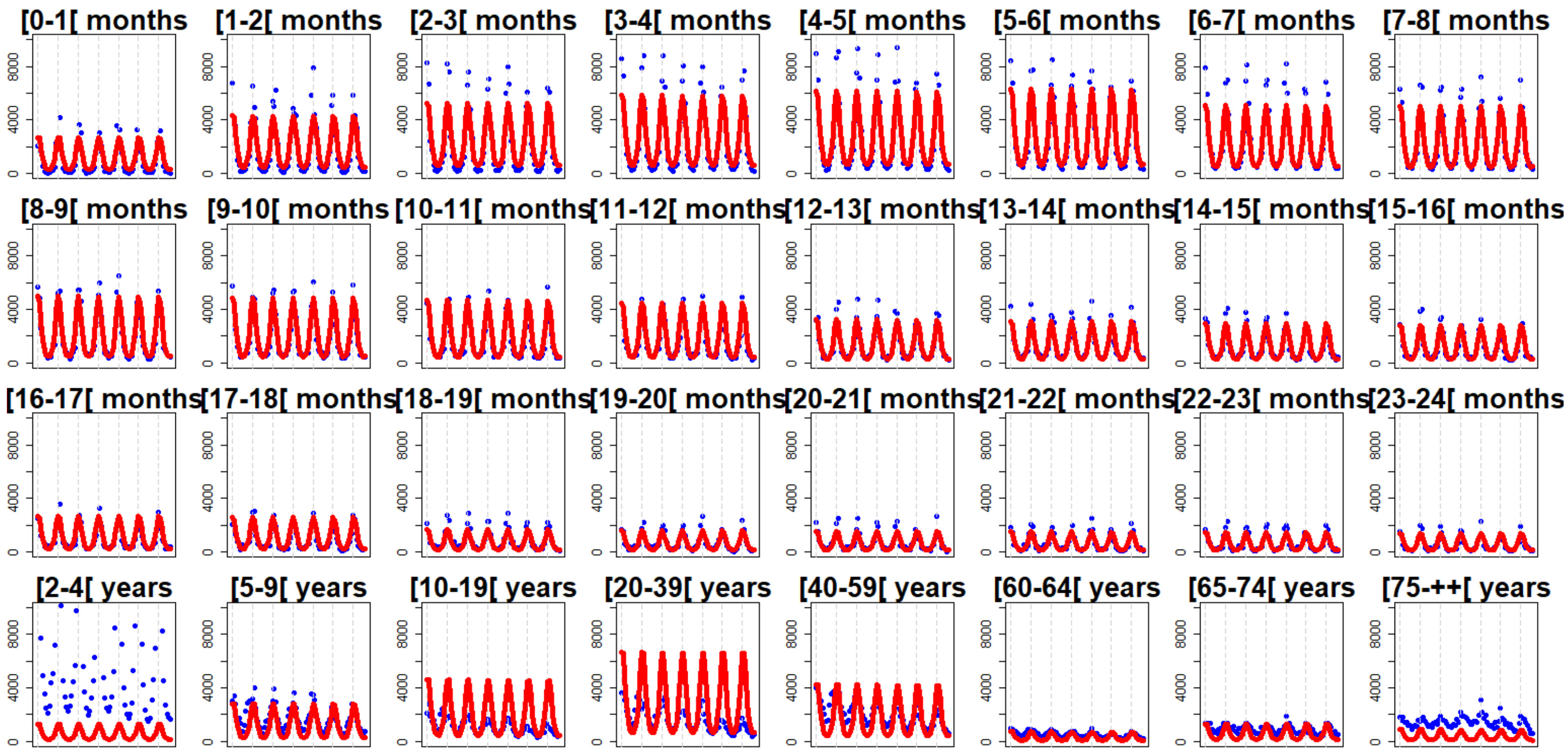
The model's outputs closely mirrored the observed data for all but the 2–4 years age group (**Supplementary Figure S5**). In accordance with this, the age-specific RMSE varied between 215.7 and 1650.8 for 31 age groups; but deviated for the 2–4 years age group, with a RMSE of 7371.9 (**Supplementary Figure S6**). The overall R^2 was 92.2% (varying between 41.8% and 93.1% depending on age groups) indicating strong similarity between observed and modelled data.

Supplementary Figure S5 Observed and modelled overall number of RSV-MALRTIs by age group in the US

A. For the entire period, 2009 to 2015 by age group up to 75+ years



B. By season and age group up to 24 months

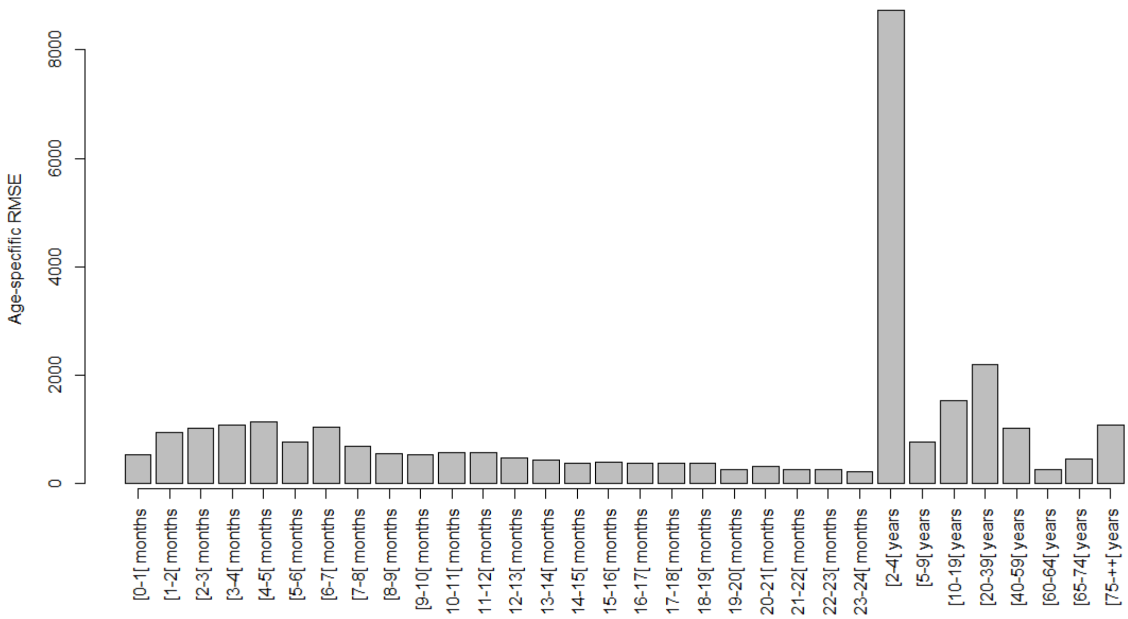


Observed data are plotted as blue dots; modelled data are in red. Y-axes represent the same scale for each age group (0 to 15000 MALRTIs); months are plotted on the x-axis, representing 7 seasons from 2009 to 2015.

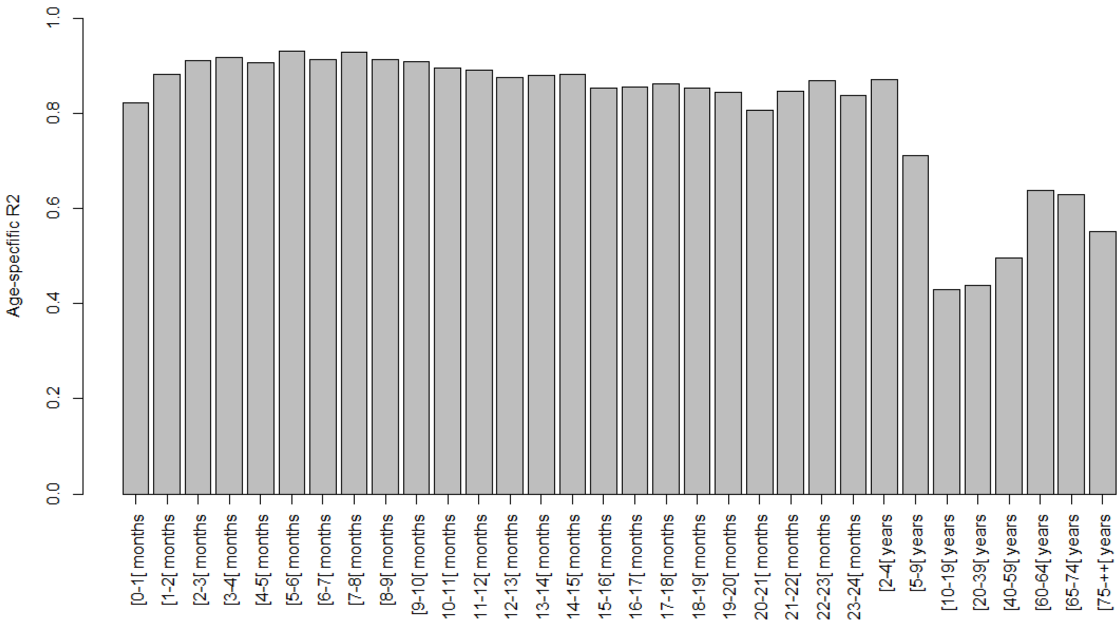
Supplementary figure S6. Model calibration.

The number of RSV-MALRTIs in each age group during each calendar month was assumed to follow a Poisson distribution, assuming the mean of RSV-MALRTIs for any single age group is equal to the model-predicted number of RSV episodes for that age group. Numerical goodness-of-fit was determined by calculating the root mean square error (RMSE) and R-squared.

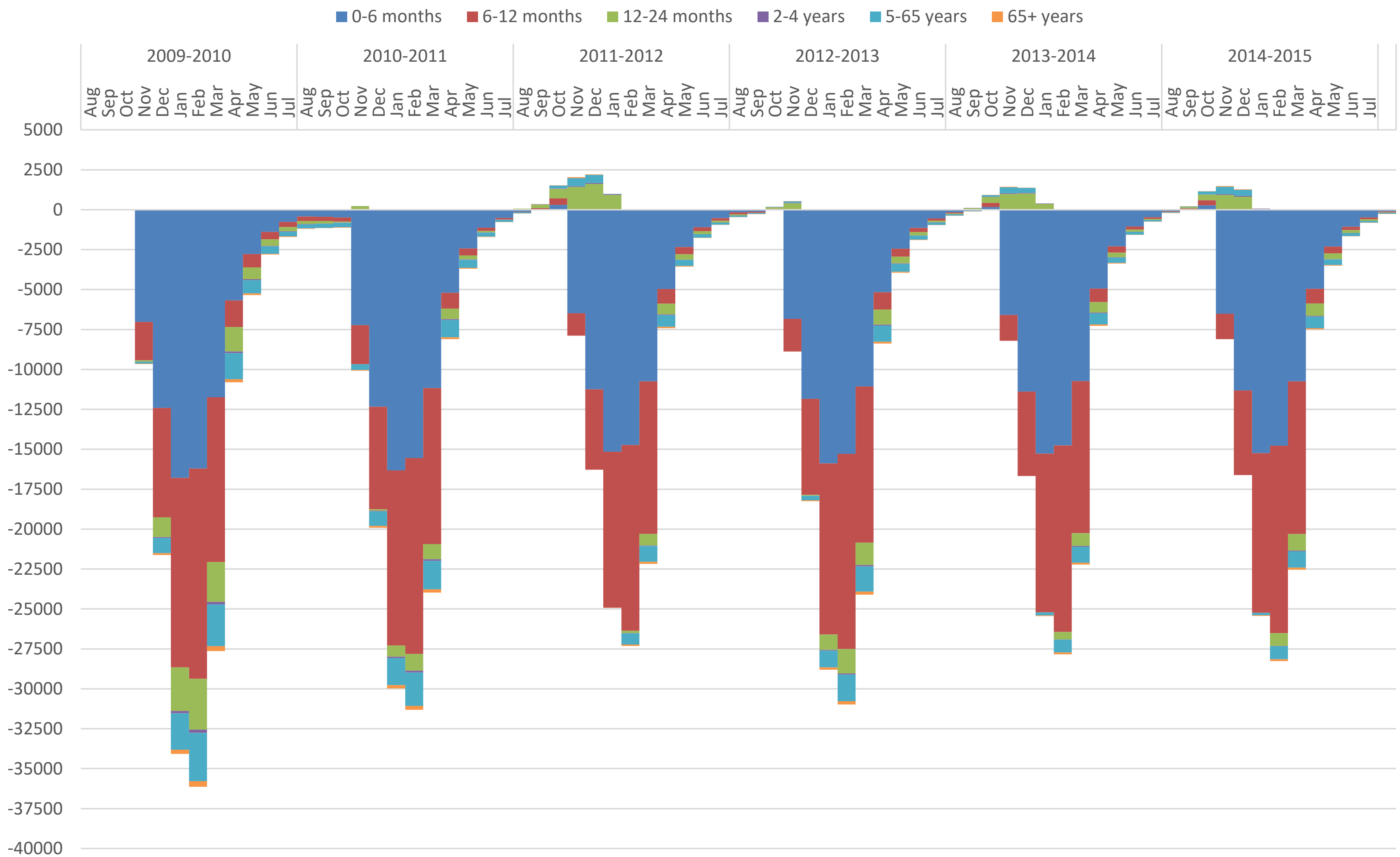
A. Goodness-of-fit as determined by age-specific root mean square error



B. Goodness-of-fit as determined by R-squared

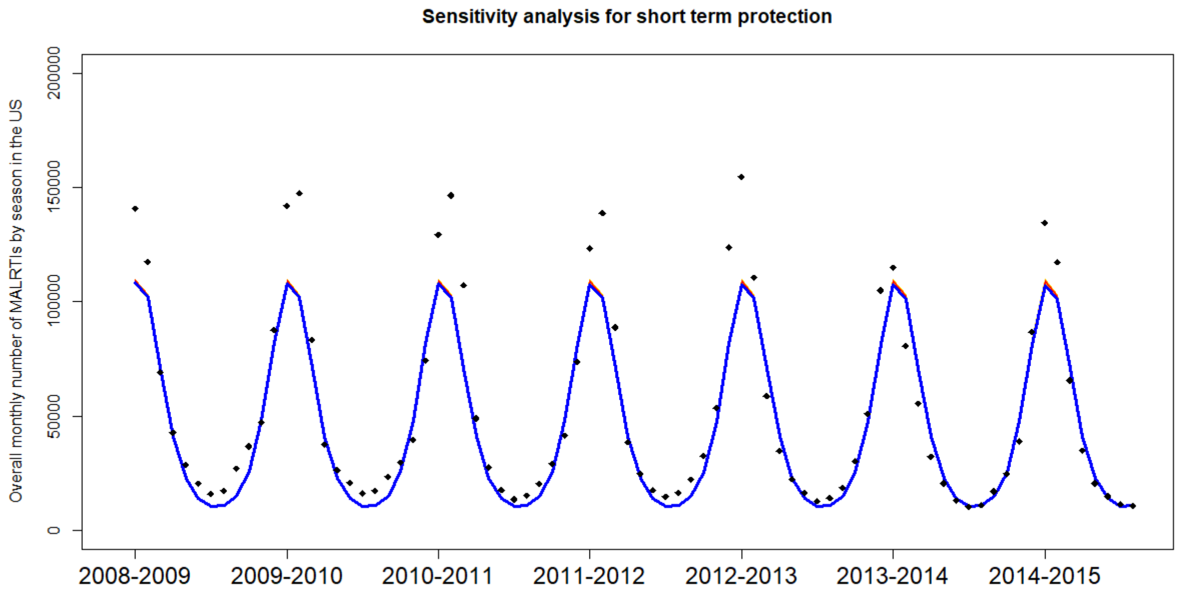


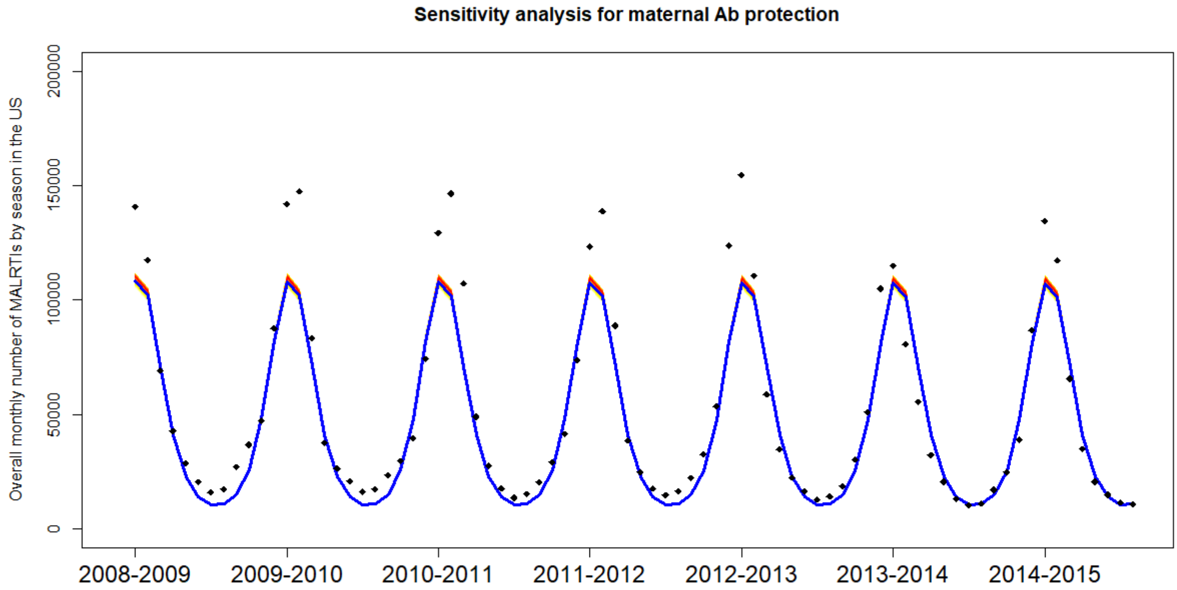
Supplementary Figure S7. Potential impact of nirsevimab (scenario 2) on expected number of RSV-MALTRIs per month, by age group

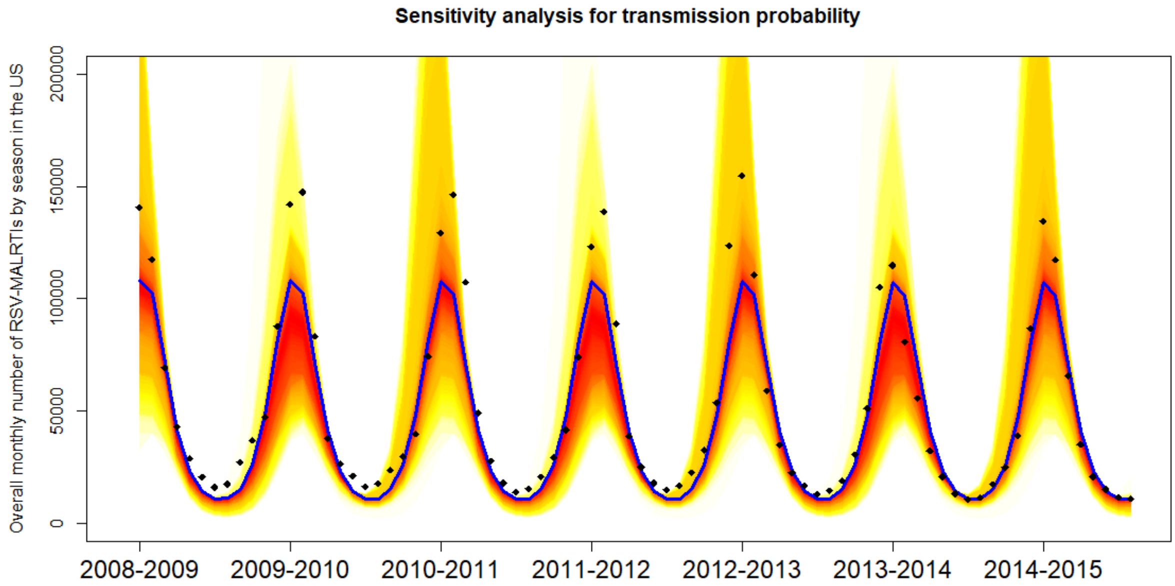


Supplementary Figure S8. Sensitivity analyses

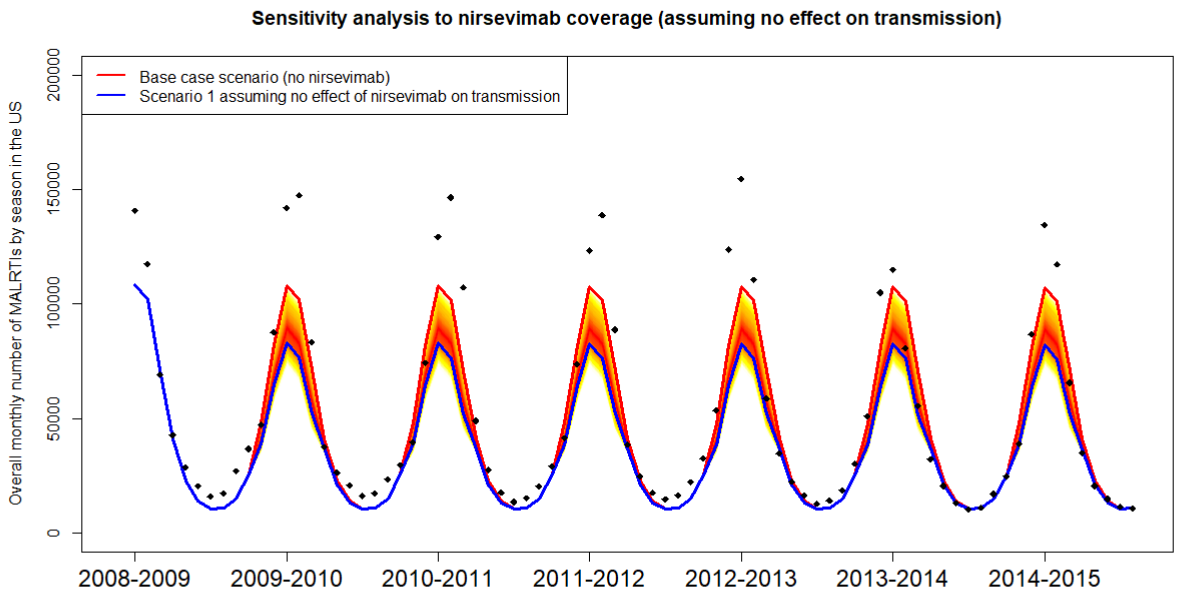
Univariate probabilistic sensitivity analyses were performed to assess the potential impact of the duration of maternal protective immunity between 1 and 3 months, the duration of short-term protection between 6 and 24 months, and the transmission parameter between $\boldsymbol{\beta 0}/2$ and 1.5*$\boldsymbol{\beta 0}$ on the model with no intervention. For each parameter assessed a uniform distribution was used for sampling and 100 runs were performed. Results were reported as fanplots based on percentiles of the results distribution.

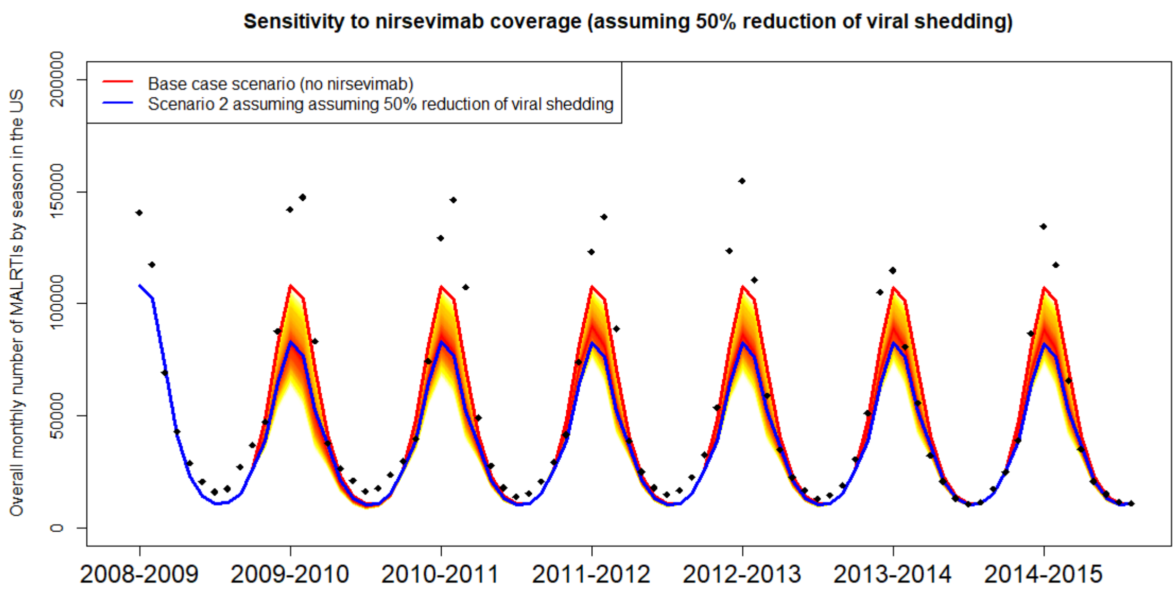



Sensitivity analysis for maternal Ab protection
Overall monthly number of MALRTIs by season in the US
0
50000
100000
150000
200000
2008-2009
2009-2010
2010-2011
2011-2012
2012-2013
2013-2014
2014-2015

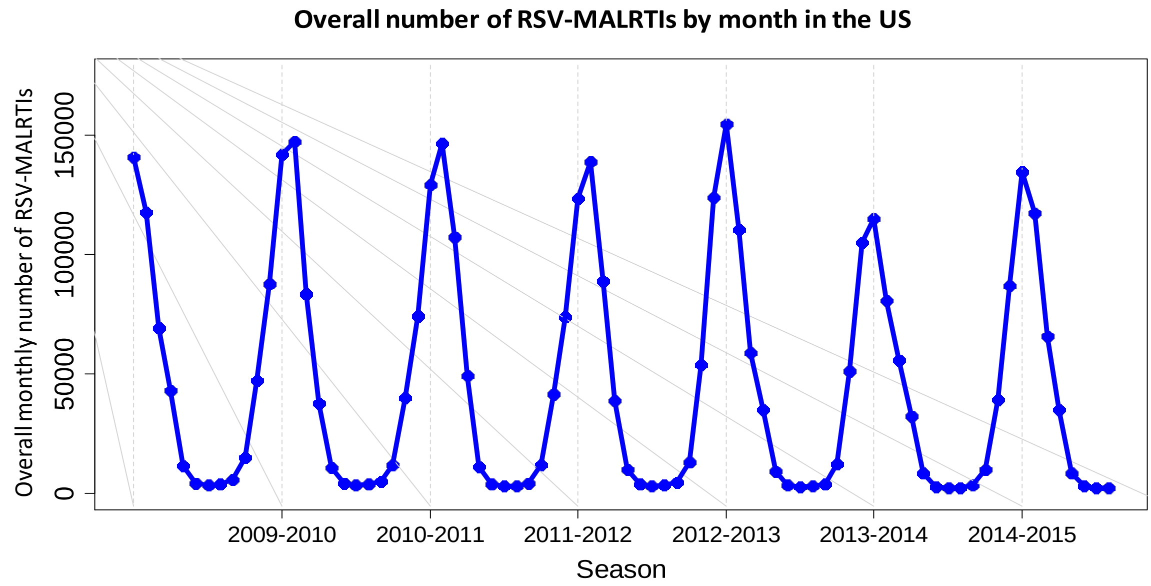

Sensitivity analysis for transmission probability
Overall monthly number of RSV-MALRTIs by season in the US
0
50000
100000
150000
200000
2008-2009
2009-2010
2010-2011
2011-2012
2012-2013
2013-2014
2014-2015

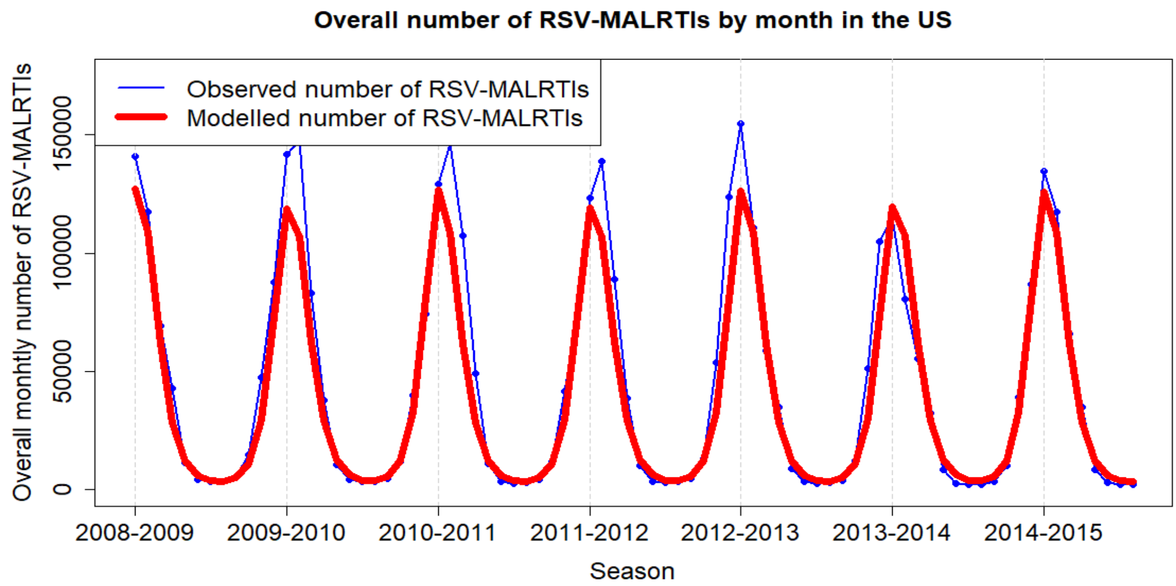
For the models with interventions (scenarios 1 and 2), univariate probabilistic sensitivity analyses were performed for a coverage rate of nirsevimab varying between 0% and 100%, and for a potential reduction in transmission varying from 0% to100%. A uniform distribution was used for sampling and 100 runs were performed. Results were reported as fanplots based on percentiles of the results distribution.

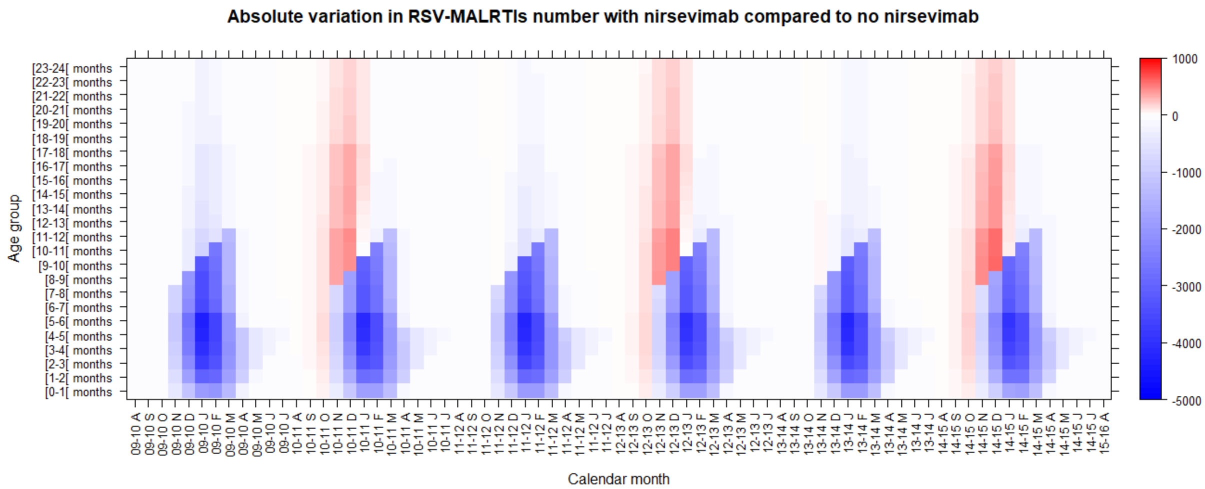




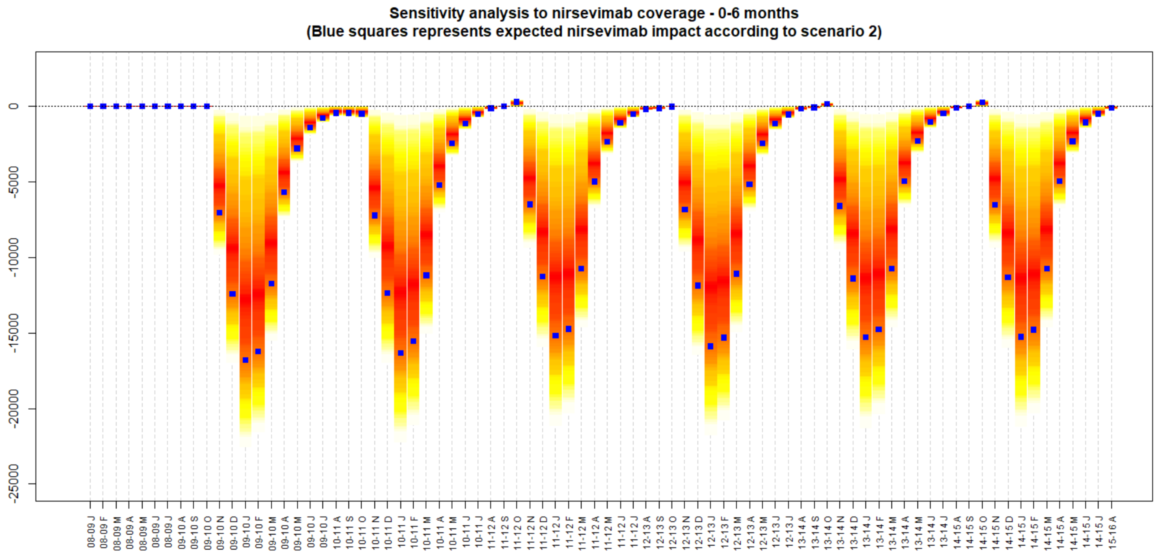
Supplementary Figure S9. Sensitivity analyses. Impact of a potential overdiagnosis of RSV during RSV inter-seasons, we re-calibrated the model assuming a 5-fold reduction of RSV-MALRTIs incidence in between April and October each RSV season.

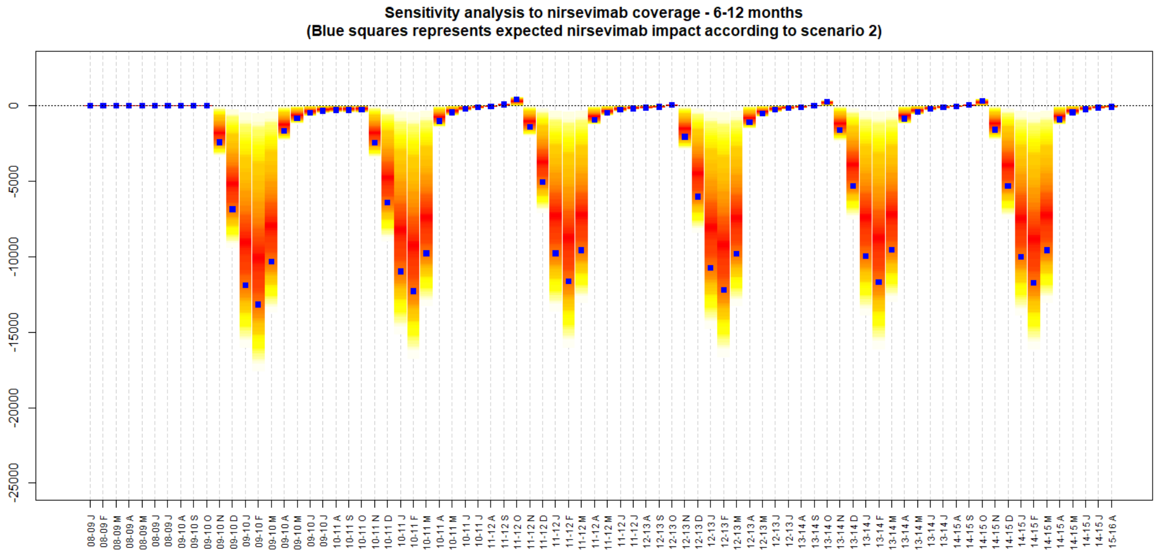

Overall number of RSV-MALRTIs by month in the US
Overall monthly number of RSV-MALRTIs
0
50000
100000
150000
2009-2010
2010-2011
2011-2012
2012-2013
2013-2014
2014-2015
Season


Overall number of RSV-MALRTIs by month in the US
Observed number of RSV-MALRTIs
Modelled number of RSV-MALRTIs
Overall monhtly number of RSV-MALRTIs
0
50000
100000
150000
2008-2009
2009-2010
2010-2011
2011-2012
2012-2013
2013-2014
2014-2015
Season

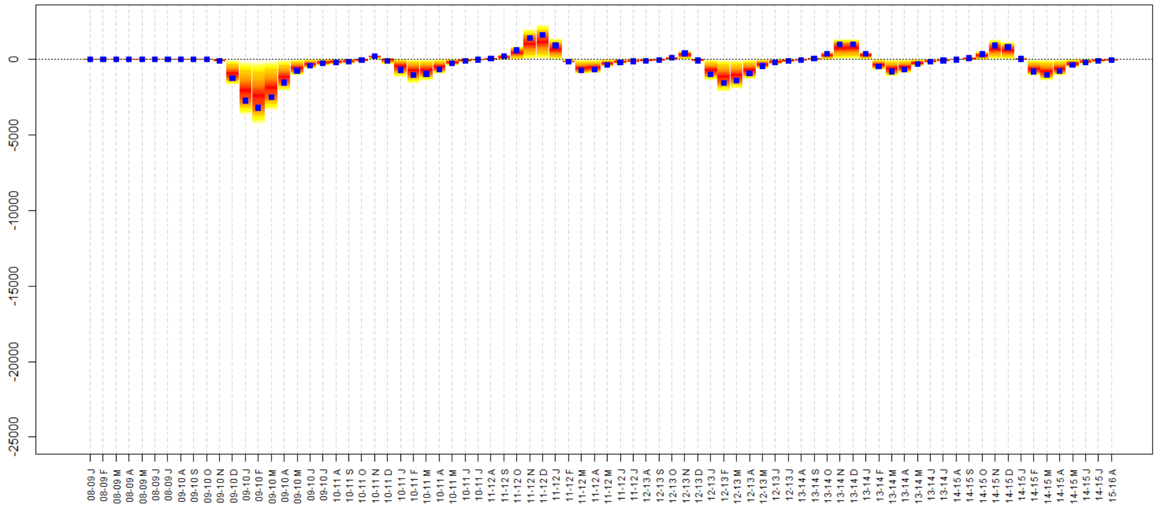

Absolute variation in RSV-MALRTIs number with nirsevimab compared to no nirsevimab
Age group
[23-24[months
[22-23[months
[21-22[months
[20-21[months
[19-20[months
[18-19[months
[17-18[months
[16-17[months
[15-16[months
[14-15[months
[13-14[months
[12-13[months
[11-12[months
[10-11[months
[9-10[months
[8-9[months
[7-8[months
[6-7[months
[5-6[months
[4-5[months
[3-4[months
[2-3[months
[1-2[months
[0-1[months
Calendar month
1000
0
-1000
-2000
-3000
-4000
-5000

Supplementary Figure S10. Sensitivity analysis per age group on coverage rate

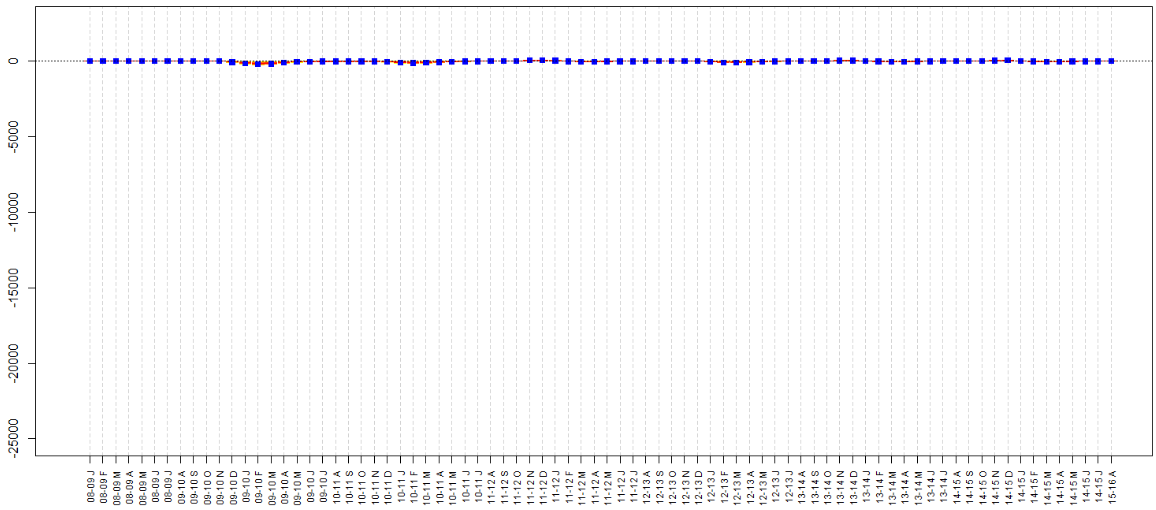




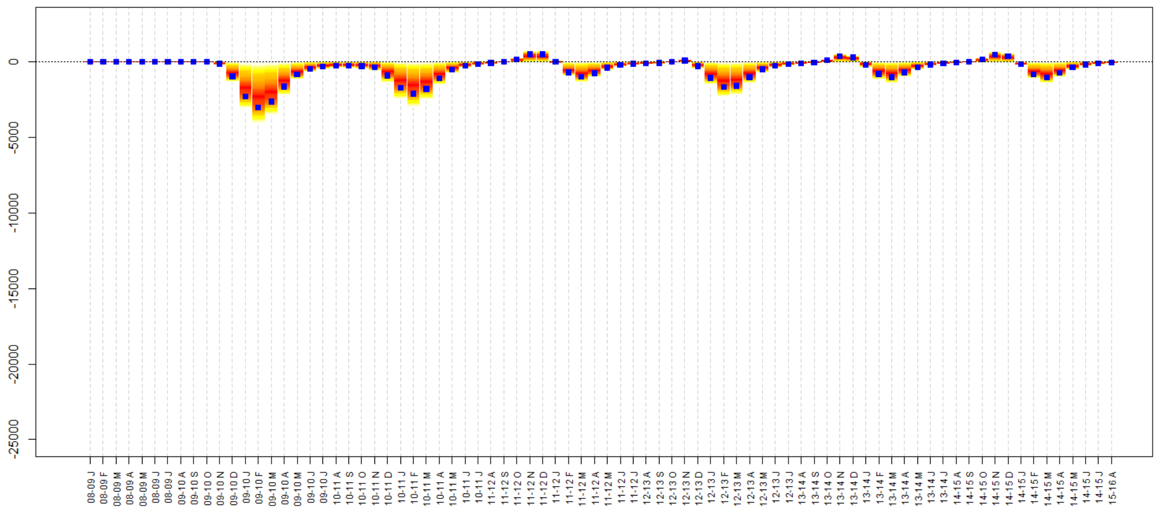
Sensitivity analysis to nirsevimab coverage - 12-24 months
(Blue squares represents expected nirsevimab impact according to scenario 2)



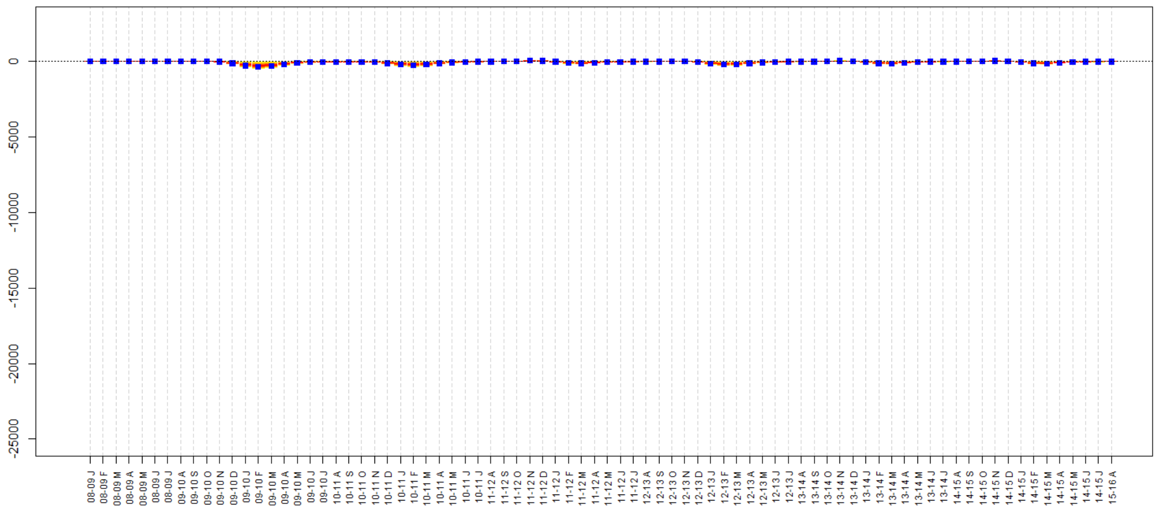
Sensitivity analysis to nirsevimab coverage - 2-4 years
(Blue squares represents expected nirsevimab impact according to scenario 2)



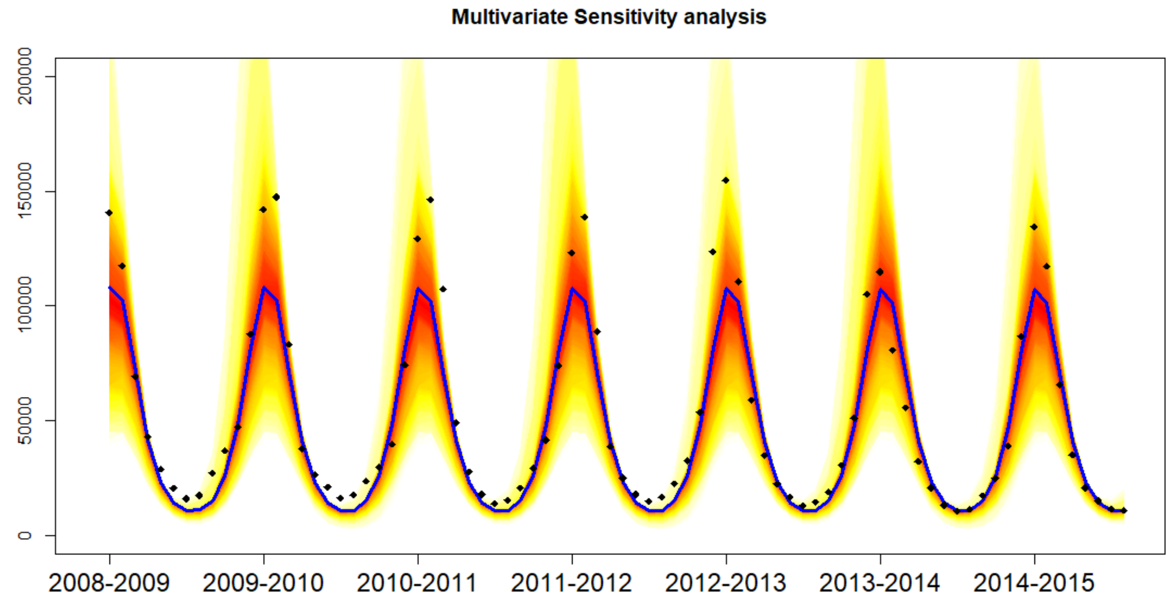
Sensitivity analysis to nirsevimab coverage - 5-65 years
(Blue squares represents expected nirsevimab impact according to scenario 2)

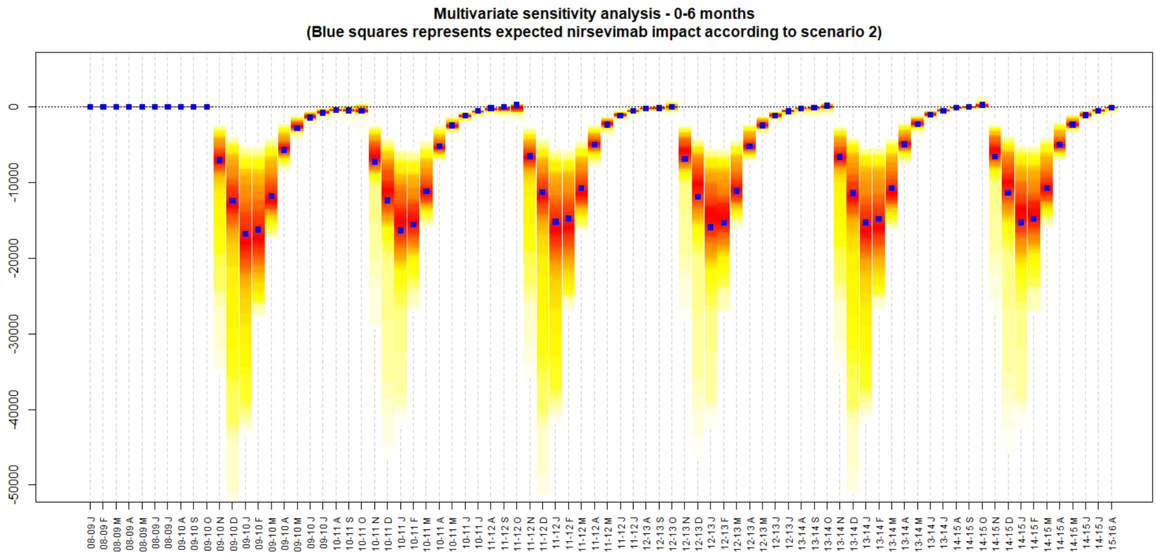


Sensitivity analysis to nirsevimab coverage - 65+ years
(Blue squares represents expected nirsevimab impact according to scenario 2)

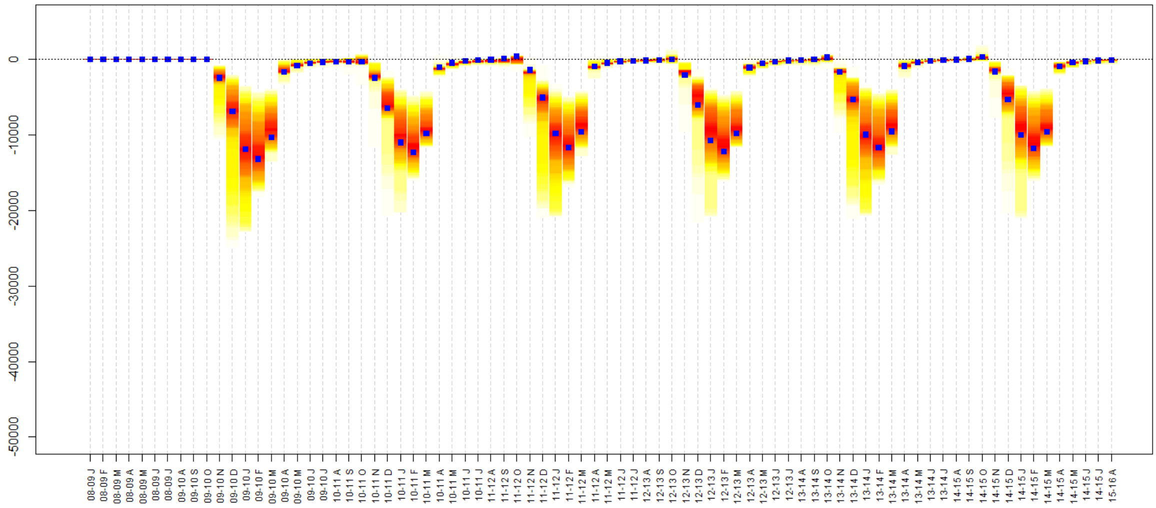


Supplementary Figure S11. Multivariate sensitivity analysis overall and per age groups on duration of maternal protective immunity, duration of short-term protection and transmission probability

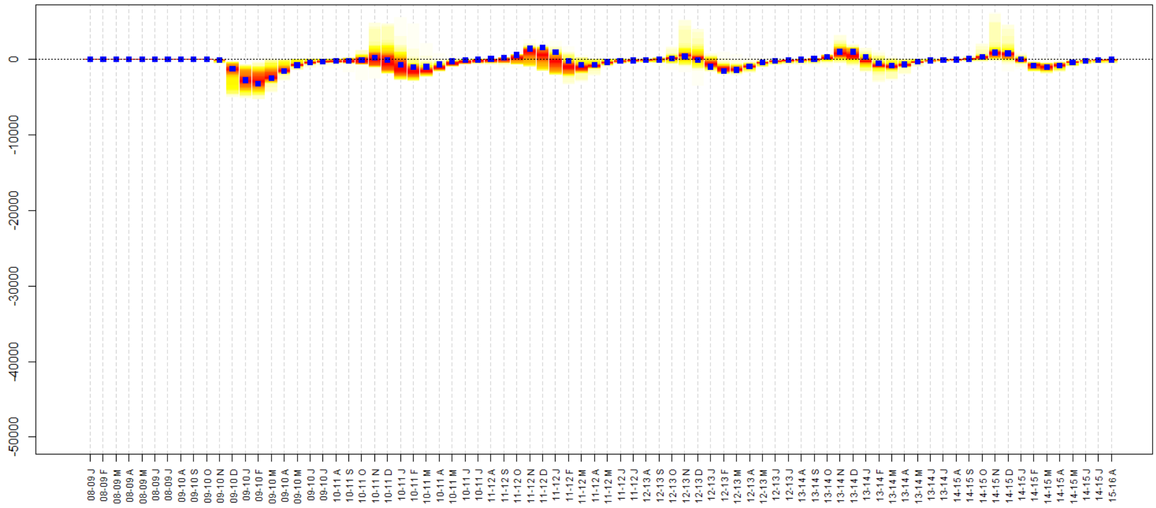




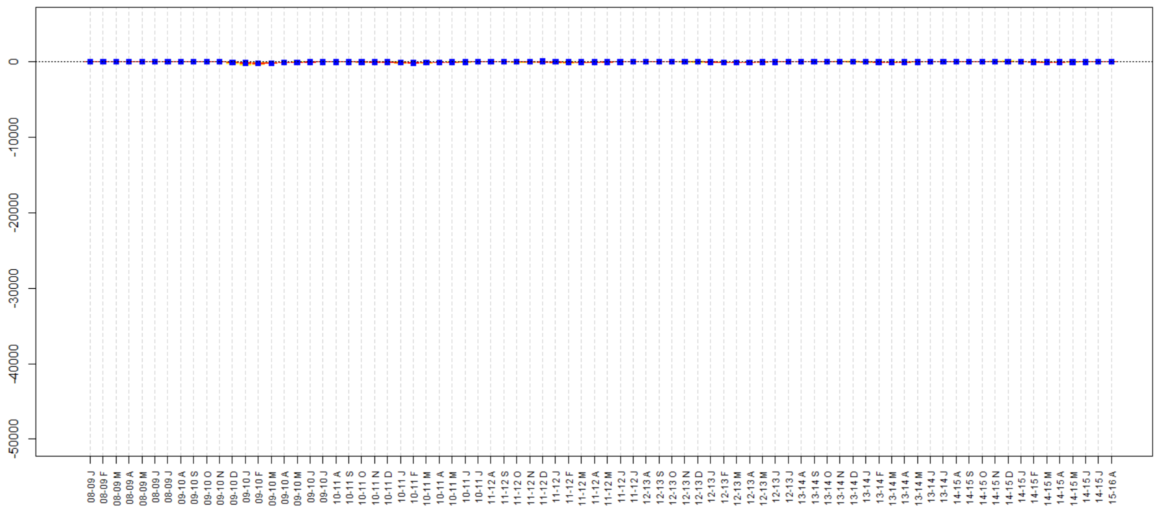
Multivariate sensitivity analysis - 6-12 months
(Blue squares represents expected nirsevimab impact according to scenario 2)

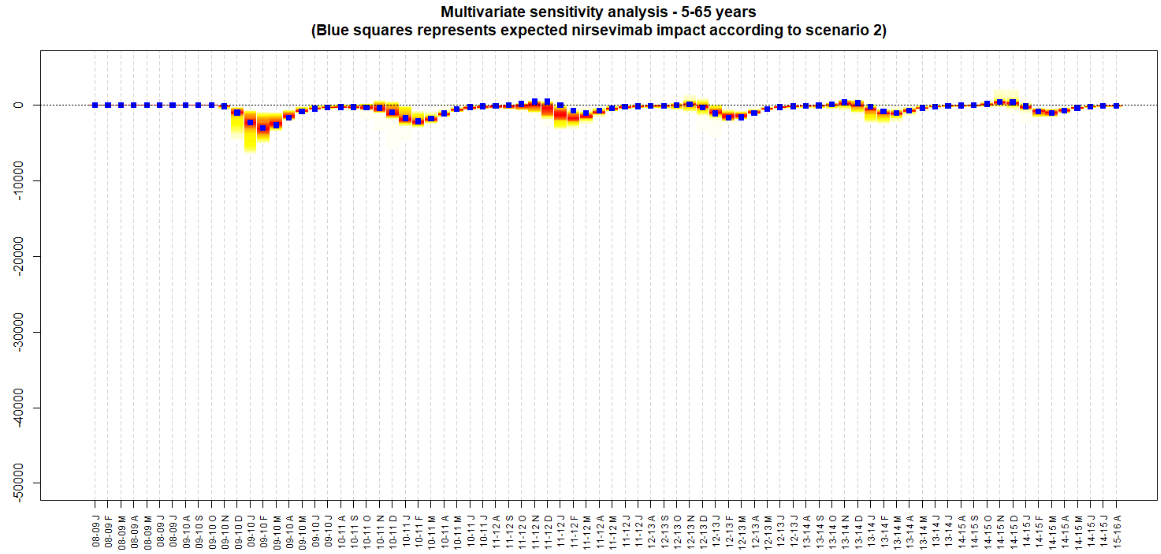


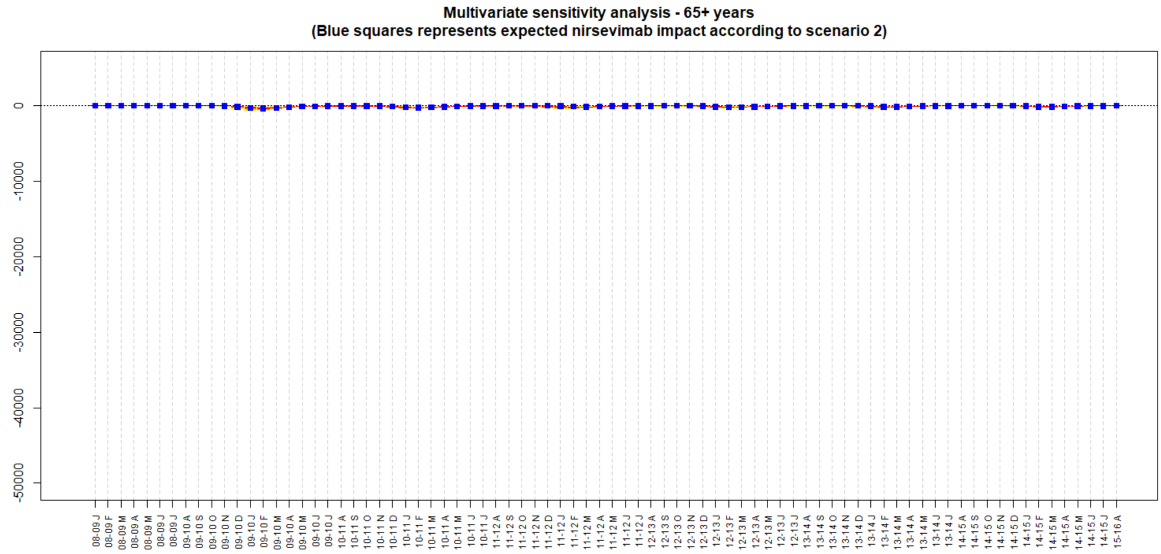
Multivariate sensitivity analysis - 12-24 months
(Blue squares represents expected nirsevimab impact according to scenario 2)



Multivariate sensitivity analysis - 2-4 years
(Blue squares represents expected nirsevimab impact according to scenario 2)




Multivariate sensitivity analysis - 5-65 years
(Blue squares represents expected nirsevimab impact according to scenario 2)
0
-10000
-20000
-30000
-40000
-50000


Multivariate sensitivity analysis - 65+ years
(Blue squares represents expected nirsevimab impact according to scenario 2)
0
-10000
-20000
-30000
-40000
-50000

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