EPH163

Modeling the Public Health Impact of Nirsevimab and Maternal Vaccination with RSVpreF Against Infant Respiratory Syncytial Virus Infection in Germany

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Key Takeaways

All-infant immunization with nirsevimab is projected to have a substantially greater public health impact in Germany, preventing 2.7-fold more medically attended RSV LRTI cases than year-round maternal vaccination across all birth months

OBJECTIVE

Compare the public health impact of nirsevimab for all-infants and year-round maternal vaccination (MV) with the respiratory syncytial virus prefusion F subunit vaccine (RSVpreF) versus palivizumab for high-risk infants in Germany

CONCLUSIONS

Our model suggests that an all-infant immunization strategy with nirsevimab provides substantially greater public health impact compared with year-round MV with RSVpreF in Germany, preventing 2.7-fold more medically attended respiratory syncytial virus (RSV) lower respiratory tract infection (LRTI) cases at equally standardized coverage rates

Our model estimates nirsevimab would achieve greater public health benefits than MV for infants born in any month of the year, indicating consistent protection potential across all monthly birth cohorts

BACKGROUND

- RSV is a leading cause of LRTI worldwide, particularly in newborns and infants
- Nirsevimab, an extended half-life monoclonal antibody, and RSVpreF, a maternal vaccine, have recently been authorized, and evaluating their potential public health impact is essential for evidence-based decision-making

METHODS

Model type: static, population-based decision-analytic model following monthly German birth cohorts through their first RSV season

Population: entire German birth cohort (April-March), stratified into:
- Healthy term infants (≥35 weeks of gestational age [wGA]): 89.8% of total births[1]
- Otherwise healthy preterm infants (29-<35 wGA): 6.7% of total births[1]
- Palivizumab-eligible infants (<29 wGA with hemodynamically significant congenital heart disease, or with bronchopulmonary dysplasia): 3.5% of total births[1]

Strategies Compared:
- All-infant approach with nirsevimab: catch-up immunization in October for pre-RSV season births and immediate post-birth administration for in-season births
- Year-round MV with RSVpreF at 32–36 weeks' gestation (assuming equal distribution within 5-week window) plus nirsevimab for palivizumab-eligible infants
- Comparator: pre-2024 standard of care (SoC), palivizumab for eligible infants; no prophylaxis for non-eligibles

RSV LRTI incidence: derived from German statutory health insurance claims (2012–2013 to 2018–2019)[2] (**Figure 1**)

Efficacy inputs: from meta-analyses and clinical trials[3-6] (**Table 1**)

Efficacy waning: modeled time-dependent vaccine/monoclonal antibody efficacy assuming a sigmoid decay function fitted to clinical trial data via least squares optimization in R, following Hutton et al.[7] and Bugden et al.[8]

Preterm adjustment: antibody transfer factor applied to MV with RSVpreF efficacy, assuming 2-4 weeks until full antibody transfer (Rainisch et al.)[9]

Coverage rates: standardized at 80% for nirsevimab in infants and RSVpreF in pregnant women (intention-to-vaccinate) with no combined strategies modeled to ensure a precise comparison of the potential public health impact of each preventive measure

Outcomes: number of medically attended RSV LRTI cases averted (comprising hospitalizations and cases treated only in the outpatient setting)

Sensitivity analysis: probabilistic sensitivity analysis (PSA) with 5000 iterations was conducted with:
- RSV LRTI incidence randomly sampled from 7 seasons (2012-2013 to 2018-2019)
- Efficacy varied within 95% confidence intervals reported in clinical studies assuming a beta distribution

Figure 1: Base case incidence of medically attended RSV LRTI episodes in German infants during the first season of life by birth month and infection month (2012–2013 to 2018–2019)

Birth month	Hospitalized RSV LRTI cases (n/1000)								Outpatient RSV LRTI cases (n/1000)							
	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May
Apr	0.1	0.3	2.1	2.1	2.4	1.5	0.5	0.1	3.1	9.4	45.8	76.0	87.3	56.1	18.3	3.4
May	0.1	0.4	2.1	2.4	2.7	1.6	0.4	0.1	3.1	9.3	45.2	75.0	86.2	55.4	18.1	3.4
Jun	0.3	0.7	2.3	4.1	3.9	1.9	0.6	0.1	3.1	9.1	44.6	74.1	85.1	54.7	17.8	3.3
Jul	0.2	0.7	2.8	4.4	4.7	2.5	0.6	0.1	2.9	8.8	42.7	71.0	81.5	52.4	17.1	3.2
Aug	0.4	1.0	3.2	4.5	4.6	2.8	0.6	0.1	2.7	8.0	38.8	64.5	74.1	47.6	15.5	2.9
Sep	0.5	1.1	3.8	5.7	5.5	3.5	0.9	0.2	2.3	6.9	33.5	55.6	63.8	41.0	13.4	2.5
Oct	0.2	0.9	5.9	7.2	7.2	4.2	1.1	0.2	1.9	5.6	27.3	45.4	52.1	33.5	10.9	2.0
Nov		0.5	6.7	10.4	8.2	4.3	1.6	0.2		4.4	21.6	35.9	41.2	26.5	8.6	1.6
Dec			1.9	10.8	13.3	7.0	1.6	0.3			15.4	25.6	29.4	18.9	6.1	1.2
Jan				3.1	13.7	9.3	2.4	0.3				15.7	18.1	11.6	3.8	0.7
Feb					2.9	7.7	3.0	0.7					7.8	5.0	1.6	0.3
Mar						1.8	2.9	0.7						1.4	0.5	0.1

Infection month

Note: risk group stratification is not displayed in figure

Table 1: Base case efficacy/effectiveness inputs for nirsevimab and MV with RSVpreF from clinical trials

	Hospitalization efficacy	Outpatient efficacy
Palivizumab[3]	56% (95% CI: 36–70)[a]	
Nirsevimab[4,5]	82.7% (95% CI: 67.8–91.5) *180 days*	79.5% (95% CI: 65.9–87.7) *150 days*
MV with RSVpreF[6]	69.7% (95% CI: 37.1-86.7) *90 days*	57.6% (95% CI: 31.3–74.6) *90 days*

[a]*Implemented as mean 5 doses of palivizumab administered monthly during the RSV season with a duration of protection of one month per dose*

RESULTS

- The model estimated that nirsevimab could prevent ~82,000 medically attended RSV LRTI cases annually, comprising 8600 hospitalizations (63.2% reduction compared with the previous SoC) and 73,400 outpatient cases (59.5% reduction)
- In comparison, year-round MV with RSVpreF, at the same coverage rate, was projected to prevent 29,900 medically attended cases, including 4000 hospitalizations (29.2% reduction) and 25,900 outpatient cases (21.2% reduction)
- When analyzed by monthly birth cohort, nirsevimab demonstrated a consistently greater reduction in medically attended RSV LRTI cases compared to MV (**Figure 2**)

Figure 2: Cumulative RSV LRTI cases during the first season of life by prevention strategy and monthly birth cohort

Bars show the cumulative number of RSV LRTI cases by monthly birth cohort, i.e., the sum of all cases occurring within the first season across all infection months (typically October to May in Germany, see Figure 1)

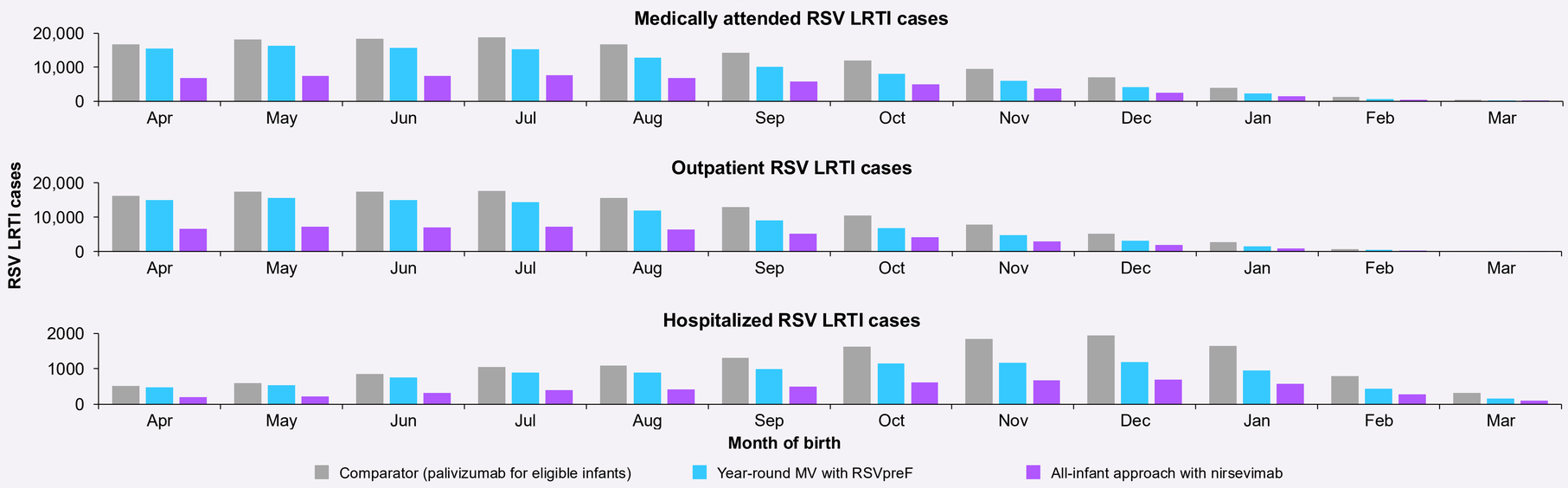
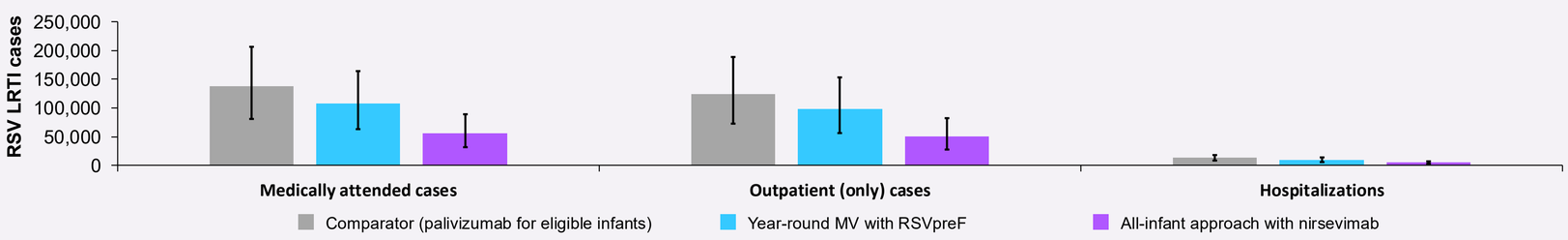


Figure 3: RSV LRTI cases during the first season of life by prevention strategy with 95% uncertainty intervals from 5000 model runs



- The PSA indicated wide 95% uncertainty intervals, primarily reflecting the substantial seasonal variability in RSV disease burden, with naturally occurring severe and mild seasons (**Figure 3**)
- Nevertheless, the PSA estimated a 96.3% probability that nirsevimab would prevent more RSV LRTI hospitalizations than year-round MV, and a >99.9% probability for outpatient cases

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