Cost-effectiveness analysis of prevention strategies for pediatric respiratory syncytial virus infection in Japan

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BACKGROUND

- Respiratory syncytial virus (RSV) is a common cause of respiratory infections in infants and the leading cause of viral bronchiolitis and pneumonia and that majority of burden occur among healthy term infants[1].
- The standard of care (SoC), a monoclonal antibody (mAb), palivizumab, was licensed for the prevention of RSV infection for infants with risk of RSV infection* and premature infants born ≤35 weeks gestational age (wGA)[2].
- In 2024, the bivalent RSV prefusion F protein-based (RSVpreF) vaccine was approved for the prevention of RSV infection in infants by active immunization of pregnant individuals in Japan[3]. Furthermore, a second mAb, nirsevimab, was approved for administration to infants to prevent RSV infection was approved in Japan[3].

*bronchopulmonary dysplasia (BPD), congenital heart disease (CHD), Down's syndrome, or a compromised immune system

OBJECTIVE

- To assess the cost effectiveness of various prevention strategies including RSVpreF vaccine, palivizumab and nirsevimab for pediatric RSV infection in Japan

METHODS

Overview

- A previously published Markov model[4] estimated the clinical and economic outcomes due to medically attended RSV infections from birth through 11 months. Incremental cost-effectiveness ratios (ICERs) and quality-adjusted life years (QALYs) were evaluated from a healthcare payer's perspective over a lifetime horizon at a 2% discount rate[5].
- Key model inputs were shown in **Table 1** and intervention strategies tested in this analysis were shown in **Table 2**.

Model Outcomes

- Health outcomes: RSV cases, stratified by care setting (hospitalization, emergency department visit, and outpatient visit), and RSV-related death.
- Economic outcomes: Medical care costs, and intervention costs (RSVpreF vaccine, palivizumab, and nirsevimab).

Table 1. Key model inputs

	Value												Ref
Number of pregnant women	718,912												6
Number of infants born	729,692												7, 8
Percentage of infants with risk	2.58%												9
	Full term (≥37 wGA)		Preterm (32-36wGA)		Preterm (28-31 wGA)		Preterm (≤27 wGA)						
Distribution of births	94.27%		5.01%		0.48%		0.25%						6, 7
Percentage of infants stillborn	0.10%		1.54%		9.97%		47.53%						7, 8
	Infant age (month)												
RSV incidence (per 1,000 person years) *	<1	1-<2	2-<3	3-<4	4-<5	5-<6	6-<7	7-<8	8-<9	9-<10	10-<11	11-<12	
Hospitalization	28.6	50.5	36.2	40.2	.35.1	28.1	23.7	19.7	18.0	20.7	14.8	14.8	10
Emergency department	4.9	7.4	8.7	26.8	29.5	18.1	38.6	26.5	26.3	26.3	19.1	26.3	
Outpatient	21.9	19.4	18.1	46.0	52.4	57.2	59.9	62.9	62.9	51.4	54.7	58.4	
Proportion of RSV with LRTI	91.6%						91.6%						11
Hospitalization	65.0%						50.0%						12
Emergency department	65.0%						30.0%						12
Outpatient													
	Infant age (month)												
Baseline mortality (per 1,000 live births) *	<1	1-<2	2-<3	3-<4	4-<5	5-<6	6-<7	7-<8	8-<9	9-<10	10-<11	11-<12	13
	0.83	0.18	0.13	0.12	0.12	0.12	0.08	0.08	0.06	0.05	0.04	0.04	
CFR due to RSV (per 100 cases) *													14
Hospitalization	0.141												
Emergency department/Outpatient	0												
Disutility due to RSV													15
Hospitalization	0.0157												
Emergency department/Outpatient	0.0061												15
RSVpreF vaccine uptake rate (once)	80% (Equally year-round)												16
	Full term (≥37 wGA)		Preterm (32-36wGA)		Preterm (≤31 wGA)		High risk						
Palivizumab prescription rate (6 times, once a month)	0%		90% (32-35 wGA) 0% (36wGA)		90%		95%						17-19
Nirsevimab prescription rate (once)	0%		90% (32-35 wGA) 0% (36wGA)		90%		95%						assumption
	Infant age (month)												
RSVpreF vaccine effectiveness (Inpatient)	<1	1-<2	2-<3	3-<4	4-<5	5-<6	6-<7	7-<8	8-<9	9-<10	10-<11	11-<12	
Full term/preterm (32-36 wGA)	82.3%	76.9%	68.5%	59.2%	50.2%	42.1%	34.9%	28.8%	23.7%	19.3%	15.8%	12.8%	20
Preterm (≤31wgA)/High-risk	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	
RSVpreF vaccine effectiveness (Outpatient)													
Full term/preterm (32-36 wGA)	61.3%	57.0%	50.7%	43.9%	37.2%	31.2%	25.9%	21.3%	17.5%	14.3%	11.7%	9.5%	20
Preterm (≤31wgA)/High-risk	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	
	Month after prescription												
	<1	1-<2	2-<3	3-<4	4-<5	5-<6	6-<7	7-<8	8-<9	9-<10	10-<11	11-<12	
Palivizumab effectiveness	56.0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	21
Nirsevimab effectiveness	87.6%	83.5%	76.4%	67.6%	58.1%	49.0%	40.7%	33.4%	27.2%	21.9%	17.6%	14.1%	20
Duration before getting nirsevimab effectiveness	1 week												22
Intervention costs (per shot)													
RSVpreF vaccine	Vaccine price (¥23,948) + administration cost (¥3,310)												4, 23
Palivizumab	Palivizumab price (¥148,366) + administration cost (¥1,802)												9, 23
Nirsevimab	Nirsevimab price (¥521,541) + administration cost (¥3,910)												23, 24
	Age group (month)												
Medication cost (per episode)	<1		1-<2		2-<6		6-<12						
Hospitalization	¥601,980		¥387,088		¥358,595		¥358,424						9
Emergency department	¥17,015		¥16,449		¥18,404		¥17,676						9
Outpatient	¥7,005		¥9,527		¥10,874		¥11,274						9

*Relative risk of RSV encounters[25], infant mortality[8] and death due to RSV[26, 27] were applied to adjust RSV incidence, baseline mortality and CFR due to RSV, respectively.
CFR; Case-fatality rate, LRTI; lower respiratory tract infection, RSV; respiratory syncytial virus, RSVpreF; RSV prefusion F protein-based, wGA; weeks gestational age

RESULTS

- Strategies #1, #2 and #3 were dominant (more effective and less costly) compared with SoC. (**Table 2**).
- With SoC (palivizumab for infants with risk and premature infants born ≤35 wGA), 39,193 medically attended RSV cases (17,464 hospitalizations, 8,078 emergency department visits, and 13,650 outpatient visits) and 21 deaths were estimated, with a corresponding total cost of 38.2 billion yen (**Table 3**).
- Nirsevimab usage restricted to the same population (infants with risk and premature infants born ≤35 wGA) was a dominant strategy over SoC, but majority of infants remain unprotected against RSV infection (**Table 2, 3**).
- A year-round RSVpreF vaccination (strategy #2) was the most cost-saving strategy and year-round RSVpreF vaccine with the supplementary administration of nirsevimab (strategy #3) was the most effective strategy (**Table 3, Figure 1**).
- Strategy #3 reduced 12,106 medically attended RSV cases (6,944 hospitalizations, 1,780 emergency department visits, and 3,381 outpatient visits), 8 deaths and 5.5 billion yen over SoC (**Table 3**).
- In one-way sensitivity analysis for strategy #4, the parameters that had the greatest impact on ICER was the cost of palivizumab (**Figure 2**).

Table 2. Base-case results from a healthcare payer's perspective

No.	Intervention strategies			QALYs	Costs (million yen)	Incremental QALYs*	Incremental costs* (million yen)	ICER* (yen/QALY)
	RSVpreF	palivizumab	nirsevimab					
SoC	—	Infants with risk** Premature (≤ 35 wGA)	—	27,595,659	38,188	—	—	—
1	—	—	Infants with risk** Premature (≤ 35 wGA)	27,595,709	25,023	50.4	-13,165	dominant
2	Pregnant women (year-round)	—	—	27,595,920	20,004	261.0	-18,184	dominant
3	Pregnant women (year-round)	—	Infants with risk** Premature (≤ 31 wGA) Unprotected infants (32-35 wGA) ***	27,596,086	32,686	426.9	-5,503	dominant

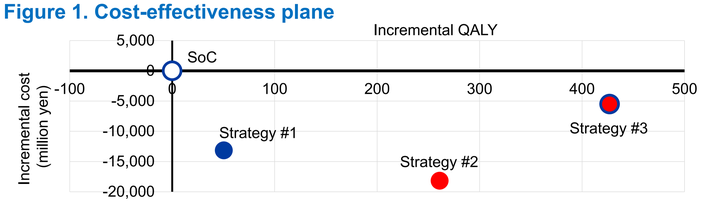
*Incremental QALYs and cost and ICER were calculated based on the comparison with SoC. **bronchopulmonary dysplasia (BPD), congenital heart disease (CHD), Down's syndrome, or a compromised immune system, ***unprotected infants is infants whose mother was unvaccinated, or infants born within 2 weeks after maternal vaccination.
ICER; incremental cost-effectiveness ratio, QALY; quality-adjusted life year, RSV: respiratory syncytial virus; RSVpreF; RSV prefusion F protein-based, SoC; standard of care, wGA; weeks gestational age

Table 3. Detailed analysis results

	SoC	Difference vs SoC		
		Strategy 1	Strategy 2	Strategy 3
Vaccination/Prescription (times)				
RSVpreF vaccine	0	0	578,271	578,271
Palivizumab (6 times/year)	211,692	-211,692	-211,692	-211,692
Nirsevimab	0	35,101	0	25,089
Health outcomes (No. of cases)				
Hospitalization due to RSV	17,464	-253	-6,070	-6,944
Emergency department visit due to RSV	8,078	-151	-1,210	-1,780
Outpatient visit due to RSV	13,650	-225	-2,560	-3,381
Death due to RSV	21.0	-1.2	-3.8	-7.7
Economic outcomes (million yen)				
Intervention				
RSVpreF vaccine	0	0	15,581	15,581
Palivizumab	31,283	-31,283	-31,283	-31,283
Nirsevimab	0	18,210	0	13,010
Total	31,283	-13,073	-15,702	-2,692
Medication costs	6,905	-93	-2,482	-2,811
Total costs	38,188	-13,165	-18,184	-5,503

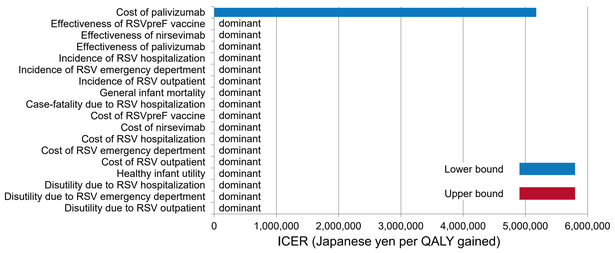
RSV: respiratory syncytial virus; RSVpreF; RSV prefusion F protein-based, SoC; standard of care, wGA; weeks gestational age

Figure 1. Cost-effectiveness plane



QALY, quality-adjusted life year, SoC; standard of care

Figure 2. One-way sensitivity analysis of strategy #3



Upon changing the value ranges of the parameter, ± 25% of each parameter was used as upper and lower bounds. ICER: incremental cost-effectiveness ratio; QALY; quality-adjusted life year, RSV: respiratory syncytial virus; RSVpreF; RSV prefusion F protein-based

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CONCLUSIONS

- While nirsevimab for infants with risk and premature infents was dominant over current SoC, many infants remained unprotected against RSV.
- A strategy containing year-round RSVpreF vaccination, either alone or complement with nirsevimab for risk and unprotected infants, was a more optimal and cost-effective prophylaxis strategy for pediatric RSV infection.

LIMITATIONS

- Effectiveness of RSVpreF vaccine for pregnant women was not considered.
- RSV infections are thought to be associated with the development of bronchial asthma and other conditions; however, reductions of bronchial asthma and other complications were not considered as outcome measures.
- Adverse events of interventions were not considered.

DISCLOSURES

- This study was sponsored by Pfizer Inc.