

Cost-effectiveness and public health impact of universal prophylaxis with nirsevimab against respiratory syncytial virus (RSV) infections in all infants in Japan

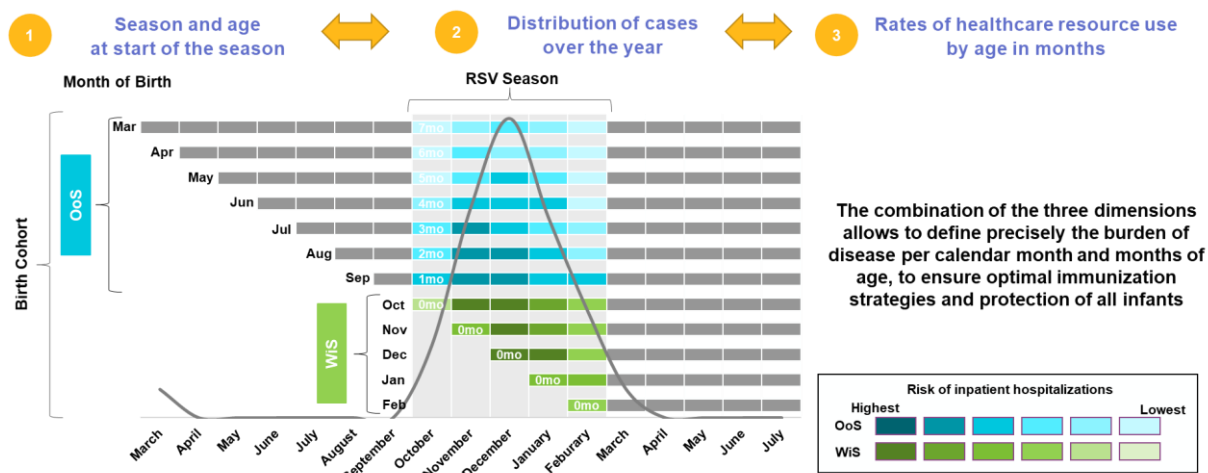
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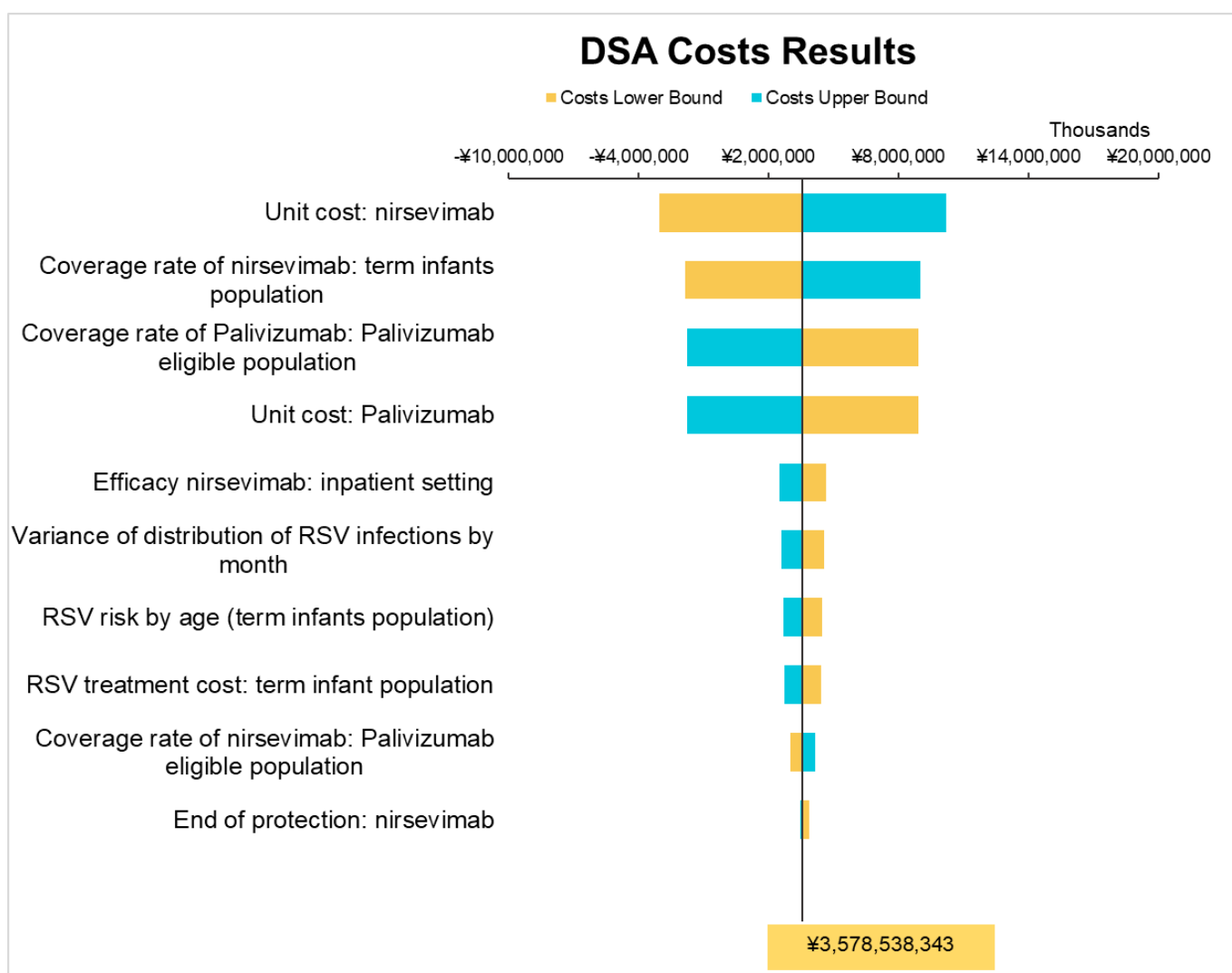
Supplementary materials

Figure S1. Three dimensions considered for RSV modelling; Exemplary figure not reflecting Japanese seasonality



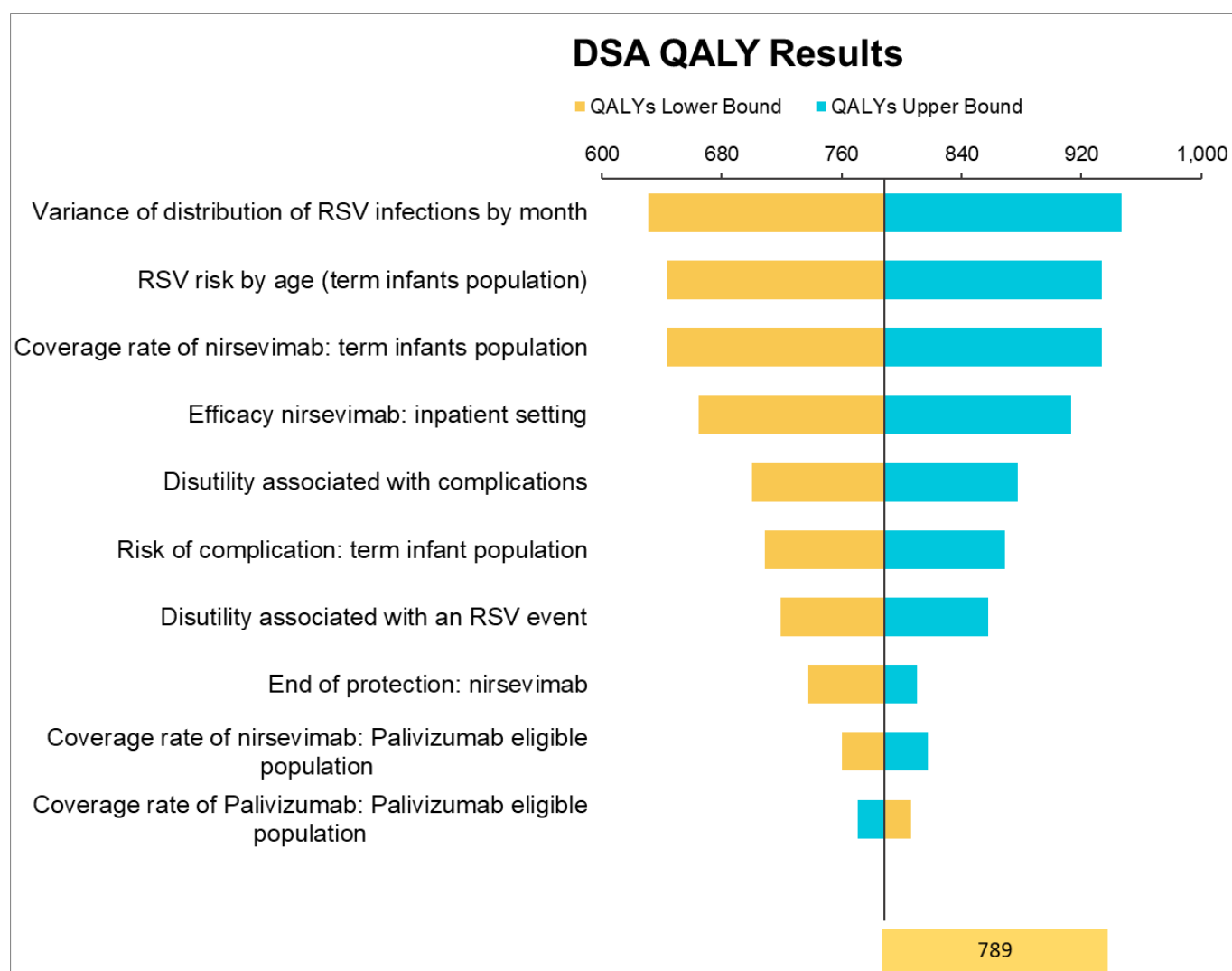
mo, month(s); OoS, out of season; RSV, respiratory syncytial virus; WiS, within a season

Figure S2. Results of deterministic sensitivity analysis: Tornado chart for costs.



DSA, deterministic sensitivity analysis; QALY, quality-adjusted life year; RSV, respiratory syncytial virus

Figure S3. Results of deterministic sensitivity analysis: Tornado chart for QALY results.



DSA, deterministic sensitivity analysis; QALY, quality-adjusted life year; RSV, respiratory syncytial virus

Table S1. The model inputs

Parameters	Input values	Reference
Population as % of total birth: • PEP • preterm • term	5.526% 1.29% 93.19%	MHLW, Demographic Survey 2022 [1] Kobayashi 2022 [2]
Total annual births	770,747	MHLW, vital statistics 2022 [3]
Distribution of infant birth by month Jan Feb Mar Apr May Jun Jul Aug Sep Oct Nov Dec	8.45% 7.42% 8.17% 7.89% 8.15% 8.06% 8.51% 9.26% 9.07% 8.78% 8.22% 8.02%	MHLW, vital statistics 2022 [3]
Efficacy Palivizumab Nirsevimab	51.0% 79.5%	Andabaka 2013 [4] Simoes 2023 [5]
Coverage rate, first year, second year		Benchmarked with other pediatric vaccines in Japan
Palivizumab	90% ^a , 70% ^a	
Nirsevimab	90%, 70% ^a	
Probability of hospitalization by age at time of infection, PEP, preterm and term 0M 1M 2M 3M 4M 5M 6M 7M 8M 9M 10M 11M 12-24M	 14.17%, 0.75% 27.19%, 5.06% 15.01%, 5.82% 10.81%, 4.22% 9.34%, 3.18% 5.04%, 2.52% 4.30%, 2.16% 5.88%, 2.09% 3.57%, 1.84% 3.99%, 1.87% 3.88%, 1.79% 3.04%, 1.82% 3.04%, 1.40%	PEP: Feldes 2005 [6] Impact-RSV Study 1998 [7] Hall 2013 [8] Preterm and term: Arashiro 2023 submitted [9] (hospitalization pattern), Kobayashi 2022 [2] (0-11, 12-24M, incidence rate)
Probability of ER visit by age at time of infection, PEP, preterm and term 0M 1M 2M 3M 4M 5M 6M 7M 8M	 1.70% 0.09% 3.26% 0.61% 1.80% 0.70% 1.30% 0.51% 1.12% 0.39% 0.60% 0.31% 0.52% 0.26% 0.71% 0.25% 0.43% 0.22%	Sruamsiri 2018 [10]

Parameters	Input values	Reference
9M 10M 11M 12-24M	0.48% 0.23% 0.47% 0.22% 0.36% 0.22% 0.36% 0.17%	
Probability of GP visit by age at time of infection, all subgroups 0-2M 3-5M 6-11M 12-24M	5.29% 10.43% 9.68% 6.65%	Kobayashi 2022 [2]
Proportion of ICU utilization of hospitalization, all subgroups 0-2M 3-11M 12-24M	0.2% 0.0% 0.2%	Kobayashi 2022 [2]
Proportion of MV utilization of hospitalization, all subgroups 0-5M 6-11M 12-24M	8.9% 9.2% 2.8%	Kobayashi 2022 [2]
Probability of wheezing First year Second year Third year	31.6%	Mochizuki 2017 [11]
Background mortality 0-11M 12-24M	0.174% 0.025%	Japanese life table [12]
Mortality associated with RSV hospitalization	0.034%	Arashiro 2023 submitted [9]
QALY loss per event Hospitalization ICU MV ER Outpatient wheezing	0.0101 0.0101 0.0101 0.0063 0.0063	Mao 2023 [13]
Annual QALY loss Wheezing	0.0392	Li 2022 [14]
Lifetime QALY loss associated with premature death	39.72 QALY	Shiroiwa 2016 [15] Japanese life tables [12]
Cost per dose Palivizumab Nirsevimab	¥102,099 ¥45,000	MHLW price list (2024) [16] Sanofi's estimation
Administration fee Palivizumab Nirsevimab	¥2,910 ¥3,930	MHLW, medical fee (2024) [17]
Health event costs Hospitalization ICU MV ER Outpatient visit Wheezing	¥391,648 2,022,198 ¥270,899 ¥10,613 ¥2,910 ¥18,333	Arashiro 2023 submitted [9] Ikumi 2023 [18] Sruamsiri 2018 [10] Igarashi 2023 [19] MHLW, medical fee, 2024 [17] ERCA report [20]

Parameters	Input values	Reference
Cost of productivity loss	¥67,494,682	Igarashi 2023 [19]

^a – in PEP only

ER, emergency room; ERCA, Environmental Restoration and Conservation Agency; ICU, intensive care unit; MHLW, Ministry of Health, Labour and Welfare; M, month(s); MV, mechanical ventilation; PEP, palivizumab-eligible patients; QALY, quality-adjusted life year, RSV, respiratory syncytial virus

Table S2. Probability of RSV infection by month [21]

Month	Base case After COVID-19 seasonality: 2023	Scenario Before COVID-19 seasonality: 2017
Jan	2.78%	4.30%
Feb	2.74%	2.15%
Mar	3.54%	1.91%
Apr	7.77%	2.36%
May	16.54%	2.45%
Jun	25.63%	2.37%
Jul	28.61%	9.70%
Aug	7.23%	19.58%
Sep	2.98%	25.76%
Oct	1.17%	15.78%
Nov	0.54%	7.02%
Dec	0.50%	6.62%

COVID-19, coronavirus disease; RSV, respiratory syncytial virus

Table S3. Indirect costs input table

Input	Value	Source
Average hourly earnings of all employees	¥1,874	MHLW Survey 2021 [22]
Number of hours per workday	8 hours	Labor Standards Act [23]
Lost days of work per RSV episode (inpatient)	6.0 days	Igarashi 2023 [19]
Lost days of work per RSV episode (outpatient)	1.0 day	Igarashi 2023 [19]
Average age of retirement	65	MHLW 2021 [24]
Discount rates for costs	2%	C2H guidelines [25]
Average number of hours per year	246 days	In 2024: 366 days – 16 days of public holidays – 104 days of Saturdays/Sundays = 246
Labor force rate	78.80%	Labor force survey 2022 [23]
Unemployment rate	2.50%	Labor force survey monthly (June 2024) [26]

C2H, Center for Outcomes Research and Economic Evaluation for Health; MHLW, Ministry of Health, Labour and Welfare; RSV, respiratory syncytial virus

Table S4. Sensitivity analysis input table

Parameter	Base value	DSA		PSA
		Low value	High value	Distribution ^a
Variance of distribution of RSV infections by month	Set of values	0.8	1.2	Dirichlet
End of protection (months): nirsevimab	5	4	6	Normal
End of protection (months): palivizumab	1	0.8	1.2	Normal
Efficacy nirsevimab	79.5%	63.6%	95.4%	Beta
Efficacy palivizumab	51.0%	40.8%	61.2%	Beta
RSV risk by age	Set of values	0.8	1.2	Beta
Coverage rate of nirsevimab (1 st year/2 nd year)	90%/70%	72%/56%	100%/84%	Normal
Coverage rate of palivizumab (1 st year/2 nd year)	90%/70%	72%/56%	100%/84%	Normal
Risk of complication	31.6%	25.3%	37.9%	Beta
RSV mortality risk	Set of values	0.8	1.2	Normal
Lifetime QALY loss associated with premature death	39.72	31.78	47.66	Beta
QALY loss associated with RSV event	Set of values	0.8	1.2	Beta
QALY loss associated with complications	0.0392	0.0314	0.0470	Beta
Unit cost: nirsevimab, ¥	45,000	36,000	54,000	- ^b
Unit cost: palivizumab, ¥	102,099	81,679	122,519	- ^b
RSV treatment cost, ¥	Set of values	0.8	1.2	Gamma
Cost associated with infant death, ¥	67,494,682	53,995,746	80,993,618	Gamma
Cost associated with complications, ¥	18,333	14,666	22,000	Gamma

^aAn SE of 0.2 of the base-case value was applied to each parameter

^bNot tested in the PSA

DSA, deterministic sensitivity analysis; PSA, probabilistic sensitivity analysis; QALY, quality-adjusted life year; RSV, respiratory syncytial virus; SE, standard error

Table S5. Detailed results of the base case

	SoC	Nirsevimab	Incremental
Health outcomes			
Total infant births	770,747	770,747	0
Hospitalizations (including ICU admission and MV)	23,245	11,078	-12,167
ICU ^a , including MV	2,046	952	-1,094
Mechanical ventilation ^a	2,027	943	-1,084
ER visits	2,808	1,337	-1,471
Primary care visits	68,695	34,823	-33,872
Inpatient deaths	8	4	-4
QALY outcomes			
Total QALY loss	2,302.84	1,514.14	-788.70
Total QALY loss per infant birth	0.01	0.01	0.00
Hospitalizations	213.91	102.10	-111.81

	SoC	Nirsevimab	Incremental
ICU ^a	0.18	0.08	-0.10
Mechanical ventilation ^a	20.47	9.52	-10.95
ER visits	17.67	8.41	-9.26
Primary care visits	432.49	219.14	-213.36
QALY loss associated with complications			
Recurrent wheezing (year 1)	287.68	137.00	-150.68
Recurrent wheezing (year 2)	282.04	134.31	-147.72
Recurrent wheezing (year 3)	276.51	131.68	-144.83
QALY loss associated with premature death	0.00	0.00	0.00
Cost outcomes (¥)			
Cost of prophylaxis	27,404,227,300	35,953,477,834	8,549,250,534
Hospitalizations alone	8,294,635,438	3,959,059,323	-4,335,576,115
ICU ^a	36,821,856	16,665,244	-20,156,612
Mechanical ventilation ^a	549,030,710	255,412,737	-293,617,973
ER visits	29,771,750	14,165,837	-15,605,913
Primary care visits	199,770,348	101,219,633	-98,550,715
Total cost of complications	395,601,666	188,396,802	-207,204,863
Total direct costs	36,909,859,067	40,488,397,410	3,578,538,343
Cost associated with inpatient death	0	0	0
Total costs	36,909,859,067	40,488,397,410	3,578,538,343

^aConditional on initial hospitalization

ER, emergency room; ICU, intensive care unit; MV, mechanical ventilation; QALY, quality-adjusted life year; SoC, standard of care

Table S6. RSV related events by month of birth under SoC and with nirsevimab.

Month	Strategy	Hospitalization	Wheezing	ER visits	PC visits
September	Nirsevimab	652	225	86	2,674
	Standard of care	1,378	477	183	6,709
October	Nirsevimab	662	228	87	2,676
	Standard of care	1,393	483	185	6,587
November	Nirsevimab	687	237	91	2,455
	Standard of care	1,413	490	187	6,140
December	Nirsevimab	744	257	98	2,347
	Standard of care	1,534	531	203	5,998
January	Nirsevimab	799	276	105	2,402
	Standard of care	1,766	612	234	6,332
February	Nirsevimab	739	255	97	2,151
	Standard of care	1,804	625	239	5,531
March	Nirsevimab	860	297	114	2,300
	Standard of care	2,325	806	308	5,674
April	Nirsevimab	915	316	121	2,101
	Standard of care	2,461	853	326	4,807
May	Nirsevimab	949	328	125	2,171
	Standard of care	2,431	843	322	4,292
June	Nirsevimab	898	311	119	2,863
	Standard of care	1,871	648	248	4,483
July	Nirsevimab	954	330	126	4,335
	Standard of care	1,366	473	181	5,391
August	Nirsevimab	1,267	438	168	6,348

Month	Strategy	Hospitalization	Wheezing	ER visits	PC visits
	Standard of care	1,458	505	193	6,751

ER, emergency room; Nirs., nirsevimab; PC, primary care; SoC, standard of care

Table S7. Prophylaxis strategy scenario results.

	Scenario 1	Scenario 2	Base Case
Population	PEP only	PEP + Preterm	All infants
Incremental QALYs Saved	54.03	64.37	788.70
Incremental Costs	-¥23,918,914,553	-¥23,552,308,312	¥3,578,538,343
Incremental Cost/QALY Saved	-¥442,689,057 /QALY	-¥365,906,509 /QALY	¥4,537,256 /QALY
ICER (Incremental Cost per QALY Saved)	Dominant	Dominant	¥4,537,256 /QALY

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