SUPPLEMENTAL MATERIAL

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Table S1. Detailed hospitalization input parameter values and ranges for uncertainty analyses

	Palivizumab-eligible Infants	**Preterm Infants**	**Term Infants**
Hospitalization rates	Hospitalizations* [1-3]	Hospitalizations* [2, 4]	Hospitalizations* [2, 4, 5]
0 months	14.2%	3.6%	2.02% (1.35%-4.89%)
1 months	27.2%	6.8%	3.87% (2.59%-4.89%)
2 months	15.0%	3.8%	2.14% (1.43%-4.89%)
3 months	10.8%	2.7%	1.54% (1.03%-2.84%)
4 months	9.3%	2.4%	1.33% (0.89%-2.84%)
5 months	5.0%	1.3%	0.72% (0.48%-2.84%)
6 months	4.3%	1.1%	0.61% (0.41%-1.34%)
7 months	5.9%	1.5%	0.84% (0.56%-1.34%)
8 months	3.6%	0.9%	0.51% (0.34%-1.34%)
9 months	4.0%	1.0%	0.57% (0.38%-1.34%)
10 months	3.9%	1.0%	0.55% (0.37%-1.34%)
11 months	3.0%	0.8%	0.43% (0.29%-1.34%)
Per-inpatient risk (ICU)	ICU	ICU	ICU [6]
0–2 months	50%	62%	31% (20%-42%)
3–5 months	29%	27%	23% (12%-38%)
6–11 months	19%	18%	17% (4%-31%)
Outpatient rates	ER† [7]		PC Visits† [7]
0 months	2.0% (1.7%-2.2%)		8.5% (7.1%-9.9%)
1 months	6.4% (5.5%-7.3%)		18.8% (15.7%-21.9%)
2 months	7.2% (6.2%-8.3%)		23.4% (19.5%-27.3%)
3 months	10.5% (9.0%-12.0%)		23.3% (19.4%-27.1%)
4 months	11.6% (9.9%-13.3%)		26.5% (22.1%-30.9%)
5 months	7.1% (6.1%-8.2%)		28.9% (24.1%-33.7%)
6 months	8.2% (7.0%-9.4%)		26.5% (22.1%-30.9%)
7 months	5.6% (4.8%-6.4%)		20.7% (17.3%-24.2%)
8 months	5.6% (4.8%-6.4%)		27.8% (23.2%-32.4%)
9 months	5.6% (4.8%-6.4%)		22.7% (18.9%-26.5%)
10 months	4.0% (3.5%-4.6%)		24.2% (20.2%-28.2%)
11 months	5.6% (4.8%-6.4%)		25.8% (21.5%-30.1%)
Mortality rate	RSV Mortality† [8]		
0–5 months	0.0024% (0.0012%-0.0029%)		
6–11 months	0.0024% (0.0012%-0.0029%)		

*Input parameters for the per-patient risk of hospitalization includes the risk of an ICU admission and MV stemming from an initial hospitalization event.

†Due to data limitations, data stratified by subpopulation was unavailable. As a result, the same inputs are applied equally for all subpopulations in the analysis (including lower- and upper-bound values leveraged for sensitivity analyses).

Abbreviations: ER = emergency room; ICU = intensive care unit; MV = mechanical ventilation; PC = primary care; RSV = respiratory syncytial virus

Table S2. Respiratory syncytial virus-related health events by population subgroup under current standard of care, and prevented events with nirsevimab. Values in brackets indicate uncertainty ranges associated with RSV rates.

Parameter	Palivizumab eligible infants	Preterm Infants	Term Infants	Total
Standard of care				
Hospitalizations	1,704 (1,704-1,704)	1,302 (1,302-1,302)	27,607 (21,575-46,278)	**30,613 (24,581-49,284)**
ICU	1,319 (1,319-1,319)	1,433 (1,433-1,433)	10,660 (4,038-31,855)	**13,411 (6,789-34,607)**
MV	396 (396-396)	488 (488-488)	2,374 (1,589-4,510)	**3,257 (2,472-5,393)**
ER visits	1,463 (1,253-1,674)	5,471 (4,685-6,260)	122,136 (104,581-139,730)	**129,070 (110,519-147,663)**
PC visits	4,008 (3,342-4,674)	14,988 (12,496-17,479)	334,567 (278,946-390,161)	**353,563 (294,784-412,313)**
Total	**8,890 (8,013-9,766)**	**23,682 (20,404-26,960)**	**497,344 (410,728-612,533)**	**529,915 (439,145-649,260)**
Immunization with nirsevimab				
Hospitalizations	1,429 (1,429-1,429)	581 (581-581)	12,261 (9,582-20,647)	**14,272 (11,593-22,658)**
ICU	1,102 (1,102-1,102)	632 (632-632)	4,714 (1,780-14,163)	**6,448 (3,514-15,898)**
MV	331 (331-331)	215 (215-215)	1,047 (701-1,998)	**1,593 (1,247-2,544)**
ER visits	1,227 (1,051-1,404)	2,437 (2,087-2,789)	54,409 (46,589-62,247)	**58,074 (49,727-66,440)**
PC visits	3,365 (2,806-3,925)	6,688 (5,576-7,800)	149,299 (124,478-174,107)	**159,353 (132,861-185,831)**
Total	**7,455 (6,719-8,191)**	**10,555 (9,092-12,017)**	**221,731 (183,130-273,162)**	**239,741 (198,942-293,371)**
Prevented events				
Hospitalizations	274 (274-274)	720 (720-720)	15,346 (11,993-25,631)	**16,341 (12,988-26,626)**
ICU	216 (216-216)	800 (800-800)	5,946 (2,258-17,692)	**6,963 (3,274-18,709)**
MV	65 (65-65)	273 (273-273)	1,326 (888-2,512)	**1,664 (1,225-2,850)**
ER visits	236 (202-269)	3,034 (2,598-3,471)	67,727 (57,992-77,483)	**70,996 (60,792-81,223)**
PC visits	643 (536-750)	8,300 (6,920-9,679)	185,268 (154,468-216,054)	**194,210 (161,923-226,482)**
Total	**1,434 (1,293-1,575)**	**13,127 (11,311-14,943)**	**275,613 (227,598-339,372)**	**290,174 (240,203-355,890)**

Abbreviations: ER = emergency room; ICU = intensive care unit; MV = mechanical ventilation; PC = primary care

Table S3. Costs of health events by population subgroup, under current standard of care, with nirsevimab, and prevented direct costs (USD 2021 millions). Values in brackets indicate uncertainty ranges associated with RSV rates.

	Palivizumab eligible Infants	**Preterm Infants**	**Term Infants**	**Total**
Standard of care				
Hospitalizations	$65.8 ($65.8-$65.8)	$21.0 ($21.0-$21.0)	$255.4 ($199.6-$428.1)	**$342.2 ($286.4-$514.9)**
ICU	$87.1 ($87.1- $87.1)	$67.1 ($67.1-$67.1)	$366.3 ($138.8-$1,094.6)	**$520.5 ($292.9-$1,248.8)**
MV	$48.4 ($48.4-$48.4)	$39.6 ($39.6-$39.6)	$184.8 ($123.8-$351.1)	**$272.8 ($211.8-$439.2)**
ER visits	$0.7 ($0.6-$0.8)	$2.7 ($2.3-$3.1)	$61.2 ($52.4-$70.0)	**$64.7 ($55.4-$74.0)**
PC visits	$0.5 ($0.4-$0.6)	$1.8 ($1.5-$2.1)	$39.4 ($32.9-$46.0)	**$41.7 ($34.7-$48.6)**
Total	**$202.5 ($202.3-$202.7)**	**$132.2 ($131.5-$132.9)**	**$907.1 ($547.3-$1,989.8)**	**$1,241.8 ($881.1-$2,325.4)**
Immunization with nirsevimab				
Hospitalizations	$55.2 ($55.2-$55.2)	$9.4 ($9.4-$9.4)	$113.4 ($88.6-$191.0)	**$178.0 ($153.2-$255.6)**
ICU	$72.8 ($72.8-$72.8)	$29.7 ($29.7-$29.7)	$162.0 ($61.2-$486.7)	**$264.4 ($163.5-$589.1)**
MV	$40.5 ($40.5-$40.5)	$17.5 ($17.5-$17.5)	$81.5 ($54.6-$155.5)	**$139.5 ($112.5-$213.5)**
ER visits	$0.6 ($0.5-$0.7)	$1.2 ($1.1-$1.4)	$27.3 ($23.4-$31.2)	**$29.1 ($24.9-$33.3)**
PC visits	$0.4 ($0.3-$0.5)	$0.8 ($0.7-$0.9)	$17.6 ($14.7-$20.5)	**$18.8 ($15.7-$21.9)**
Total	**$169.5 ($169.3-$169.7)**	**$58.5 ($58.2-$58.8)**	**$401.8 ($242.4-$884.9)**	**$629.7 ($469.9-$1,113.3)**
Prevented Costs				
Hospitalizations	$10.6 ($10.6-$10.6)	$11.6 ($11.6-$11.6)	$142.0 ($111.0-$237.1)	**$164.2 ($133.2-$259.3)**
ICU	$14.3 ($14.3-$14.3)	$37.5 ($37.5-$37.5)	$204.3 ($77.6-$608.0)	**$256.1 ($129.3-$659.7)**
MV	$8.0 ($8.0-$8.0)	$22.1 ($22.1-$22.1)	$103.3 ($69.1-$195.6)	**$133.3 ($99.2-$225.7)**
ER visits	$0.1 ($0.1-$0.1)	$1.5 ($1.3-$1.7)	$34.0 ($29.1-$38.8)	**$35.6 ($30.5-$40.8)**
PC visits	$0.08 ($0.06-$0.09)	$1.0 ($0.8-$1.1)	$21.8 ($18.2-$25.5)	**$22.9 ($19.1-$26.7)**
Total	**$33.0 ($33.0-$33.0)**	**$73.7 ($73.3-$74.1)**	**$505.3 ($304.9-$1,104.9)**	**$612.1 ($411.3-$1,212.1)**

Abbreviations: ER = emergency room; ICU = intensive care unit; MV = mechanical ventilation; PC = primary care

Table S4: Respiratory syncytial virus-related health events per age at start of season under current standard of care and with nirsevimab

	Inpatient hospitalizations (incl. ICU and MV)	***LCV***	***HCV***	**ER visits**	***LCV***	***HCV***	**Primary Care Visits**	***LCV***	***HCV***
Standard of Care									
March (7mo)	1,985	*1,422*	*4,389*	7,687	*6,581*	*8,789*	21,779	*18,159*	*25,396*
April (6mo)	2,584	*1,849*	*5,263*	10,823	*9,266*	*12,376*	28,376	*23,662*	*33,092*
May (5mo)	2,181	*1,561*	*4,425*	9,584	*8,207*	*10,962*	24,382	*20,331*	*28,435*
April (4mo)	2,402	*1,719*	*5,446*	12,024	*10,299*	*13,757*	32,347	*26,971*	*37,722*
July (3mo)	3,180	*2,276*	*7,353*	16,197	*13,873*	*18,533*	44,554	*37,150*	*51,959*
August (2mo)	4,214	*3,016*	*8,924*	18,915	*16,199*	*21,644*	49,095	*40,938*	*57,257*
September (1mo)	5,744	*4,110*	*10,818*	18,379	*15,738*	*21,033*	48,132	*40,132*	*56,133*
October (0mo)	7,523	*5,383*	*12,929*	15,479	*13,252*	*17,712*	42,714	*35,610*	*49,812*
November (0mo)	7,438	*5,323*	*12,187*	10,407	*8,908*	*11,906*	30,481	*25,408*	*35,543*
December (0mo)	5,711	*4,087*	*9,864*	6,022	*5,155*	*6,888*	19,376	*16,149*	*22,591*
January (0mo)	3,205	*2,295*	*5,592*	2,768	*2,369*	*3,165*	9,434	*7,862*	*10,999*
February (0mo)	1,113	*800*	*2,093*	785	*672*	*898*	2,895	*2,412*	*3,374*
Total	**47,281**	***33,842***	***89,284***	**129,070**	***110,519***	***147,663***	**353,563**	***294,784***	***412,313***
Nirsevimab									
March (7mo)	1,036	*758*	*2,226*	3,450	*2,953*	*3,944*	9,875	*8,233*	*11,514*
April (6mo)	1,232	*903*	*2,456*	4,950	*4,238*	*5,660*	13,009	*10,848*	*15,171*
May (5mo)	1,044	*765*	*2,060*	4,322	*3,701*	*4,944*	11,107	*9,261*	*12,953*
April (4mo)	1,148	*841*	*2,512*	5,437	*4,656*	*6,220*	14,591	*12,166*	*17,015*
July (3mo)	1,508	*1,105*	*3,369*	7,282	*6,237*	*8,332*	20,070	*16,735*	*23,405*
August (2mo)	2,007	*1,471*	*4,085*	8,479	*7,261*	*9,702*	21,948	*18,302*	*25,597*
September (1mo)	2,704	*1,982*	*4,951*	8,308	*7,115*	*9,508*	21,609	*18,018*	*25,201*
October (0mo)	3,535	*2,591*	*5,996*	7,057	*6,042*	*8,075*	19,790	*16,498*	*23,078*
November (0mo)	3,453	*2,532*	*5,522*	4,579	*3,919*	*5,238*	13,411	*11,179*	*15,638*
December (0mo)	2,650	*1,943*	*4,459*	2,649	*2,267*	*3,030*	8,524	*7,105*	*9,939*
January (0mo)	1,486	*1,089*	*2,525*	1,217	*1,042*	*1,392*	4,149	*3,458*	*4,837*
February (0mo)	512	*375*	*939*	345	*295*	*394*	1,272	*1,060*	*1,482*
Total	**22,314**	***16,354***	***41,100***	**58,074**	***49,727***	***66,440***	**159,353**	***132,861***	***185,831***

Abbreviations: ER = emergency room; ICU = intensive care unit; MV = mechanical ventilation; PC = primary care; LCV = lowest credible value; HCV = highest credible value

Table S5: Costs (in million USD 2021) of health events per age at start of the season, under current standard of care and with nirsevimab

	Inpatient hospitalizations (incl. ICU and MV)	***LCV***	***HCV***	**ER visits**	***LCV***	***HCV***	**Primary Care Visits**	***LCV***	***HCV***
Standard of Care									
March (7mo)	$38.03	*$25.49*	*$90.04*	$3.85	*$3.30*	*$4.41*	$2.57	*$2.14*	*$2.99*
April (6mo)	$46.41	*$30.61*	*$103.53*	$5.42	*$4.64*	*$6.20*	$3.34	*$2.79*	*$3.90*
May (5mo)	$39.50	*$26.14*	*$88.27*	$4.80	*$4.11*	*$5.49*	$2.87	*$2.40*	*$3.35*
April (4mo)	$44.67	*$29.87*	*$111.18*	$6.03	*$5.16*	*$6.89*	$3.81	*$3.18*	*$4.44*
July (3mo)	$61.09	*$41.33*	*$154.06*	$8.12	*$6.95*	*$9.29*	$5.25	*$4.38*	*$6.12*
August (2mo)	$87.35	*$59.91*	*$198.65*	$9.48	*$8.12*	*$10.85*	$5.78	*$4.82*	*$6.75*
September (1mo)	$135.81	*$94.66*	*$266.35*	$9.21	*$7.89*	*$10.54*	$5.67	*$4.73*	*$6.61*
October (0mo)	$197.25	*$138.94*	*$348.25*	$7.76	*$6.64*	*$8.88*	$5.03	*$4.20*	*$5.87*
November (0mo)	$203.61	*$144.02*	*$342.16*	$5.22	*$4.46*	*$5.97*	$3.59	*$2.99*	*$4.19*
December (0mo)	$159.52	*$113.06*	*$280.44*	$3.02	*$2.58*	*$3.45*	$2.28	*$1.90*	*$2.66*
January (0mo)	$90.46	*$64.24*	*$160.03*	$1.39	*$1.19*	*$1.59*	$1.11	*$0.93*	*$1.30*
February (0mo)	$31.76	*$22.73*	*$59.83*	$0.39	*$0.34*	*$0.45*	$0.34	*$0.28*	*$0.40*
Total	**$1,135.46**	***$790.99***	***$2,202.78***	**$64.69**	***$55.39***	***$74.01***	**$41.66**	***$34.73***	***$48.58***
Nirsevimab									
March (7mo)	$22.54	*$16.12*	*$49.18*	$1.73	*$1.48*	*$1.98*	$1.16	*$0.97*	*$1.36*
April (6mo)	$24.34	*$17.27*	*$50.39*	$2.48	*$2.12*	*$2.84*	$1.53	*$1.28*	*$1.79*
May (5mo)	$20.78	*$14.77*	*$42.84*	$2.17	*$1.86*	*$2.48*	$1.31	*$1.09*	*$1.53*
April (4mo)	$23.41	*$16.77*	*$53.18*	$2.72	*$2.33*	*$3.12*	$1.72	*$1.43*	*$2.00*
July (3mo)	$31.73	*$22.93*	*$73.13*	$3.65	*$3.13*	*$4.18*	$2.36	*$1.97*	*$2.76*
August (2mo)	$45.33	*$33.07*	*$94.45*	$4.25	*$3.64*	*$4.86*	$2.59	*$2.16*	*$3.02*
September (1mo)	$69.43	*$51.28*	*$127.08*	$4.16	*$3.57*	*$4.77*	$2.55	*$2.12*	*$2.97*
October (0mo)	$100.39	*$74.73*	*$168.43*	$3.54	*$3.03*	*$4.05*	$2.33	*$1.94*	*$2.72*
November (0mo)	$102.60	*$76.64*	*$162.94*	$2.29	*$1.96*	*$2.63*	$1.58	*$1.32*	*$1.84*
December (0mo)	$80.30	*$60.06*	*$132.96*	$1.33	*$1.14*	*$1.52*	$1.00	*$0.84*	*$1.17*
January (0mo)	$45.36	*$33.95*	*$75.67*	$0.61	*$0.52*	*$0.70*	$0.49	*$0.41*	*$0.57*
February (0mo)	$15.63	*$11.70*	*$27.86*	$0.17	*$0.15*	*$0.20*	$0.15	*$0.12*	*$0.17*
Total	**$581.85**	***$429.29***	***$1,058.11***	**$29.11**	***$24.92***	***$33.30***	**$18.78**	***$15.65***	***$21.90***

Abbreviations: ER = emergency room; ICU = intensive care unit; MV = mechanical ventilation; PC = primary care; LCV = lowest credible value; HCV = highest credible value

Table S6. Burden of the second RSV season for infants born during the first RSV season

	RSV-LRTI Hospitalizations			RSV MA LRTIs		
Month of Birth	**First RSV season**	**Second RSV season (up to 11 months old)**	**Total (0-11 months old)**	**First RSV season (up to 11 months old)**	**Second RSV season (up to 11 months old)**	**Total (0-11 months old)**
November	7,438	108	7,546	48,326	2,439	50,765
December	5,711	465	6,175	31,109	9,524	40,633
January	3,205	1,070	4,275	15,407	20,212	35,619
February	1,113	1,412	2,525	4,793	25,035	29,828

Abbreviations: LRTI = lower respiratory tract infection; MA = medically attended; RSV = respiratory syncytial virus

Table S7. Per-patient risk of wheezing following inpatient hospitalization and its associated cost

***Per-patient risk (wheezing)* [9]**	**Wheezing following inpatient hospitalization**
Year 1	31%
Year 2	27%
Year 3	17%
Cost of management of wheezing (over 1 year)	Equal to 5.5 primary care appointments

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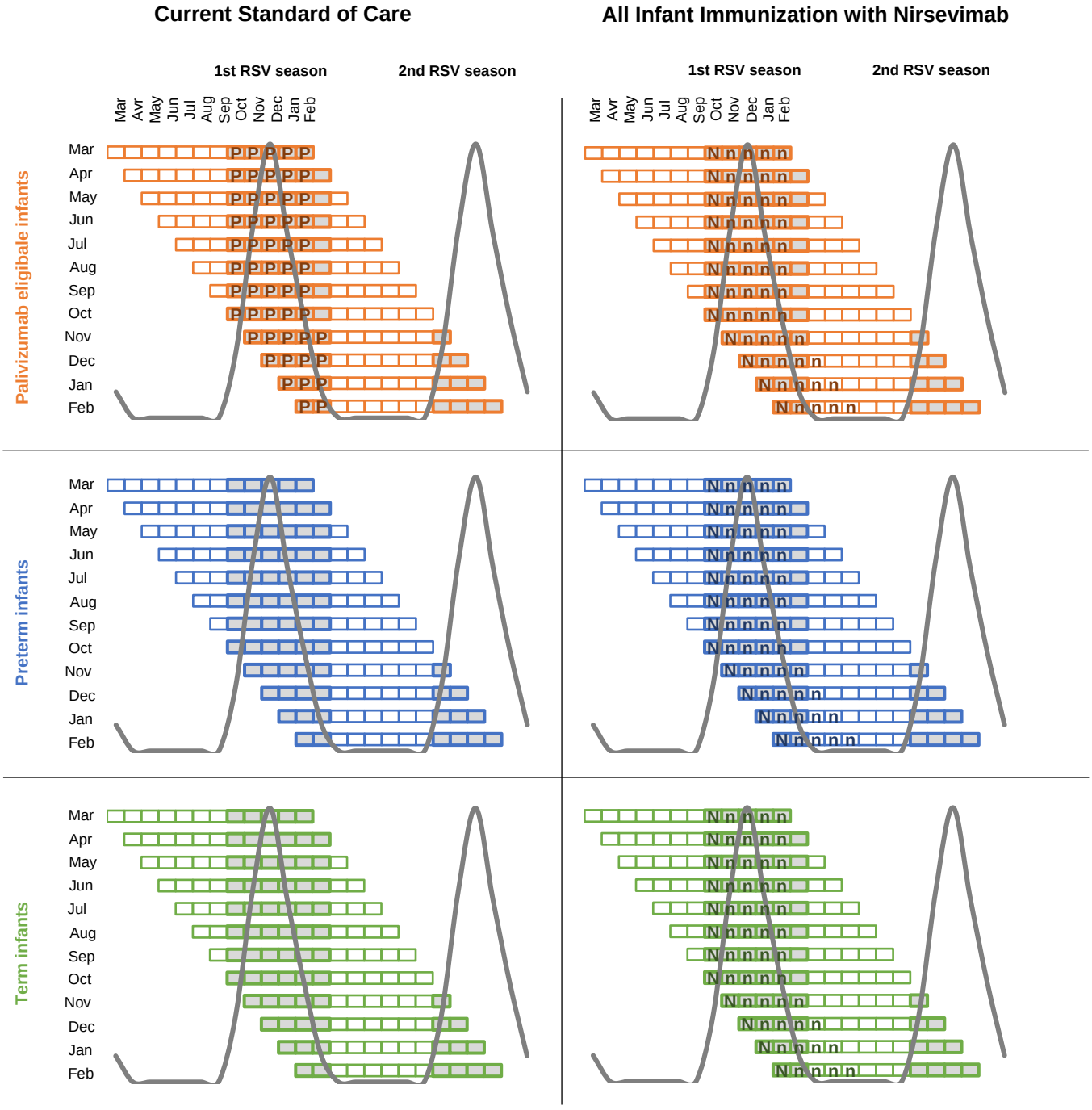
Figure S1. Immunization Strategies

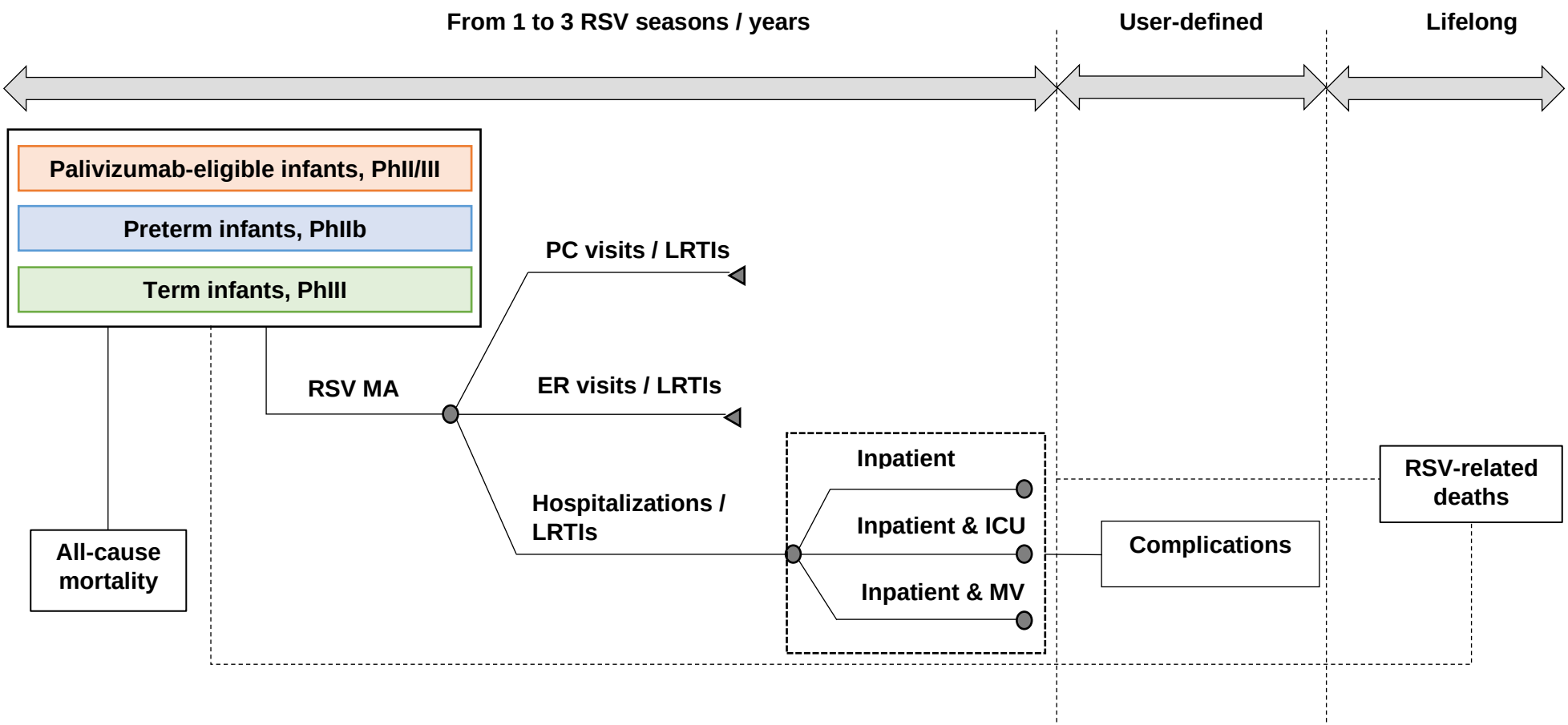


P: Immunization with palivizumab; N: immunization with nirsevimab; n: protection from nirsevimab

Shape of the RSV season

Abbreviations: Apr = April; Aug = August; Dec = December; Feb = February; Jan = January; Jul = July; Jun = June; Mar = March; Nov = November; Oct = October; RSV = respiratory syncytial virus; Sep = September

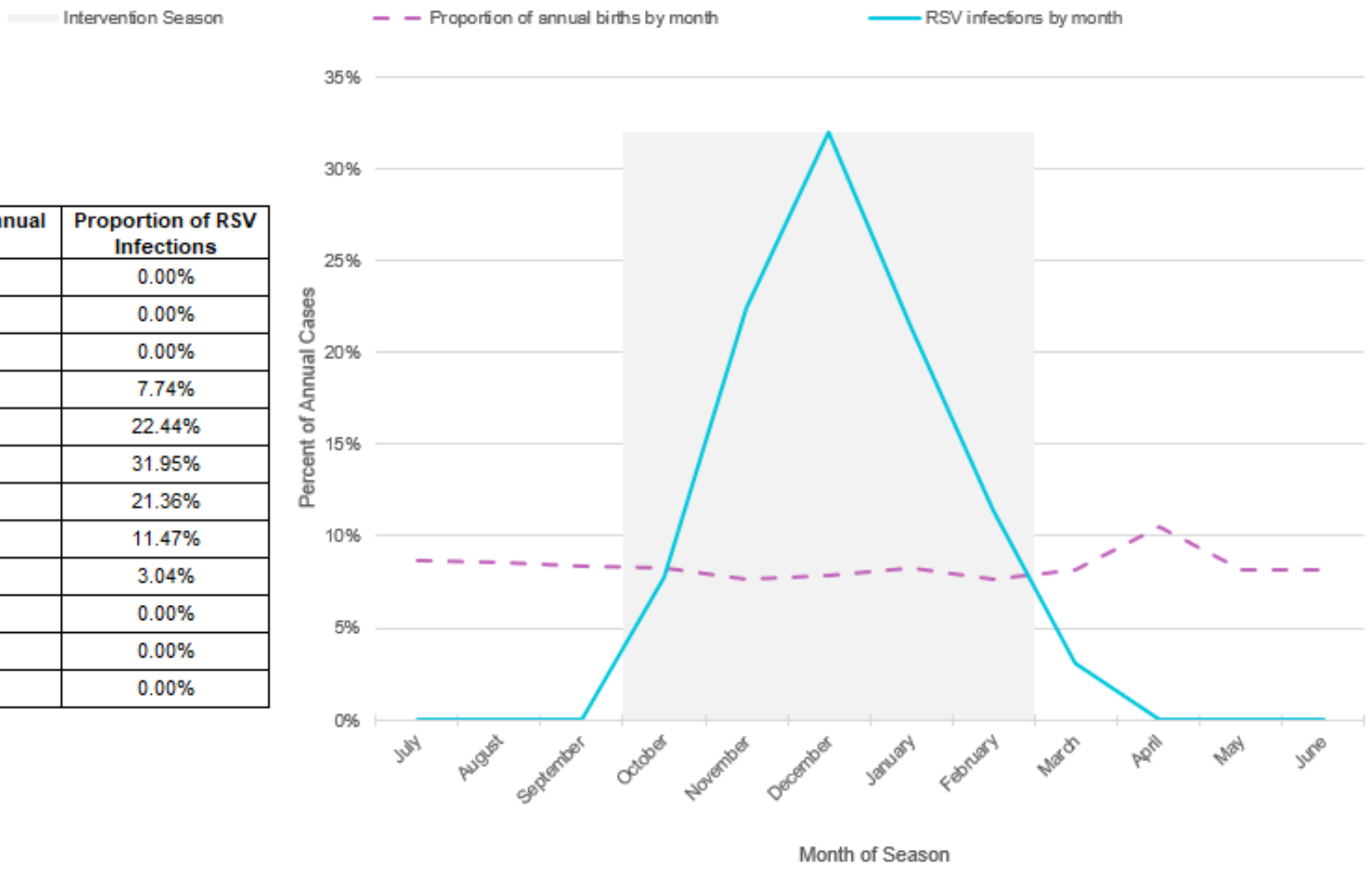
Figure S2. Model Overview



Abbreviationd: RSV = respiratory syncytial virus; ER = Emergency Room; MA = Medically-attended; LRTI = Lower respiratory tract infections; ICU = Intensive care unit; MV = mechanical ventilation

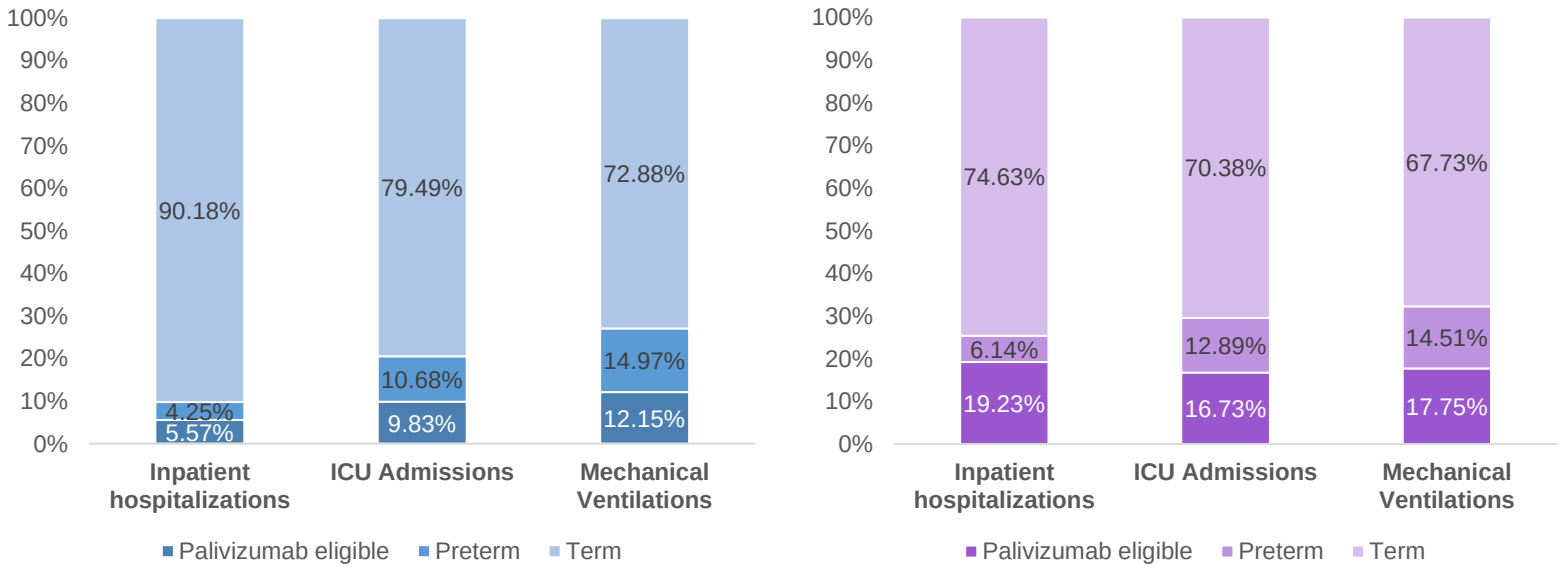
Figure S3. Proportion of respiratory syncytial virus infections by month in the United States

Month	Proportion of Annual Births	Proportion of RSV Infections
July	8.65%	0.00%
August	8.60%	0.00%
September	8.38%	0.00%
October	8.22%	7.74%
November	7.60%	22.44%
December	7.81%	31.95%
January	8.22%	21.36%
February	7.63%	11.47%
March	8.14%	3.04%
April	10.51%	0.00%
May	8.11%	0.00%
June	8.14%	0.00%



Abbreviation: RSV = respiratory syncytial virus

Figure S4. Distribution of respiratory syncytial virus-related lower respiratory tract infection hospitalizations by population groups (A); distribution of respiratory syncytial virus-related lower respiratory tract infection hospitalizations costs by population groups (B)

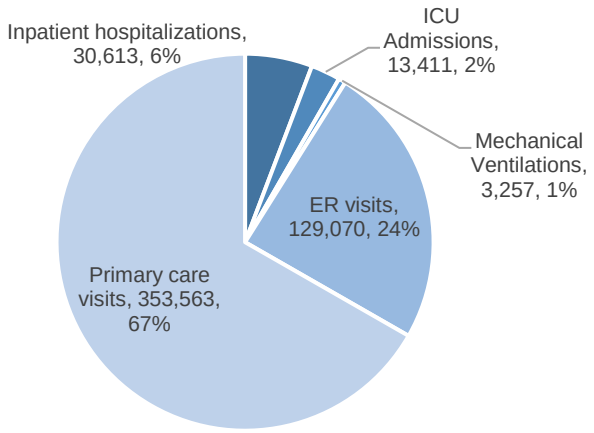


A. Hospitalizations by population groups

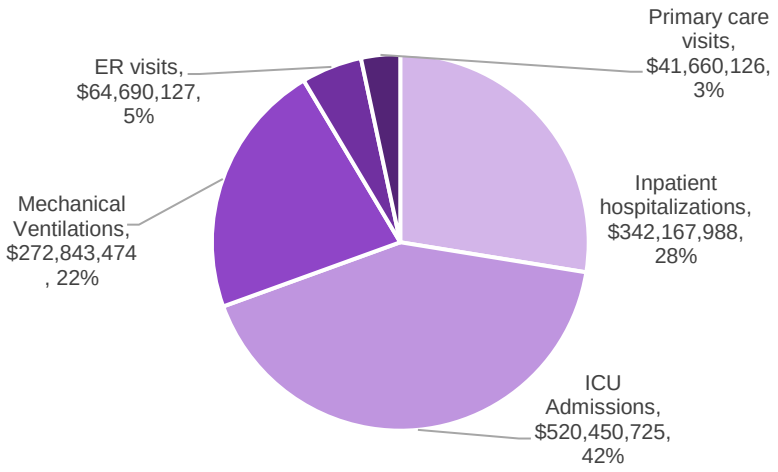
B. Hospitalization costs by population groups (in 2021 USD)

Abbreviation: ICU = intensive care unit

Figure S5. Distribution of respiratory syncytial virus medically-attended lower respiratory tract infections by (A) health event and (B) related direct medical costs over the first respiratory syncytial virus season of US infants



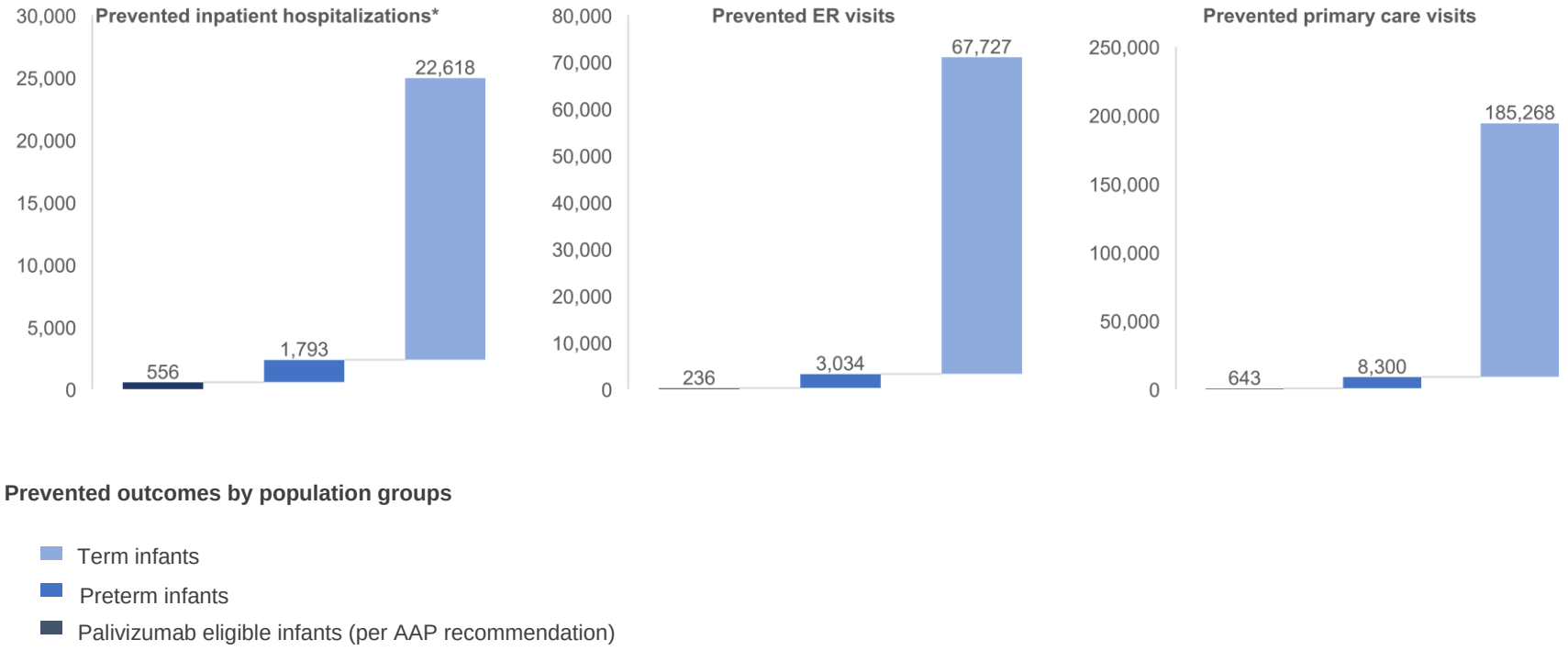
A. Number of Health events



B. Direct medical costs of health events (in 2021 USD)

Abbreviations: ER = emergency room; ICU = intensive care unit

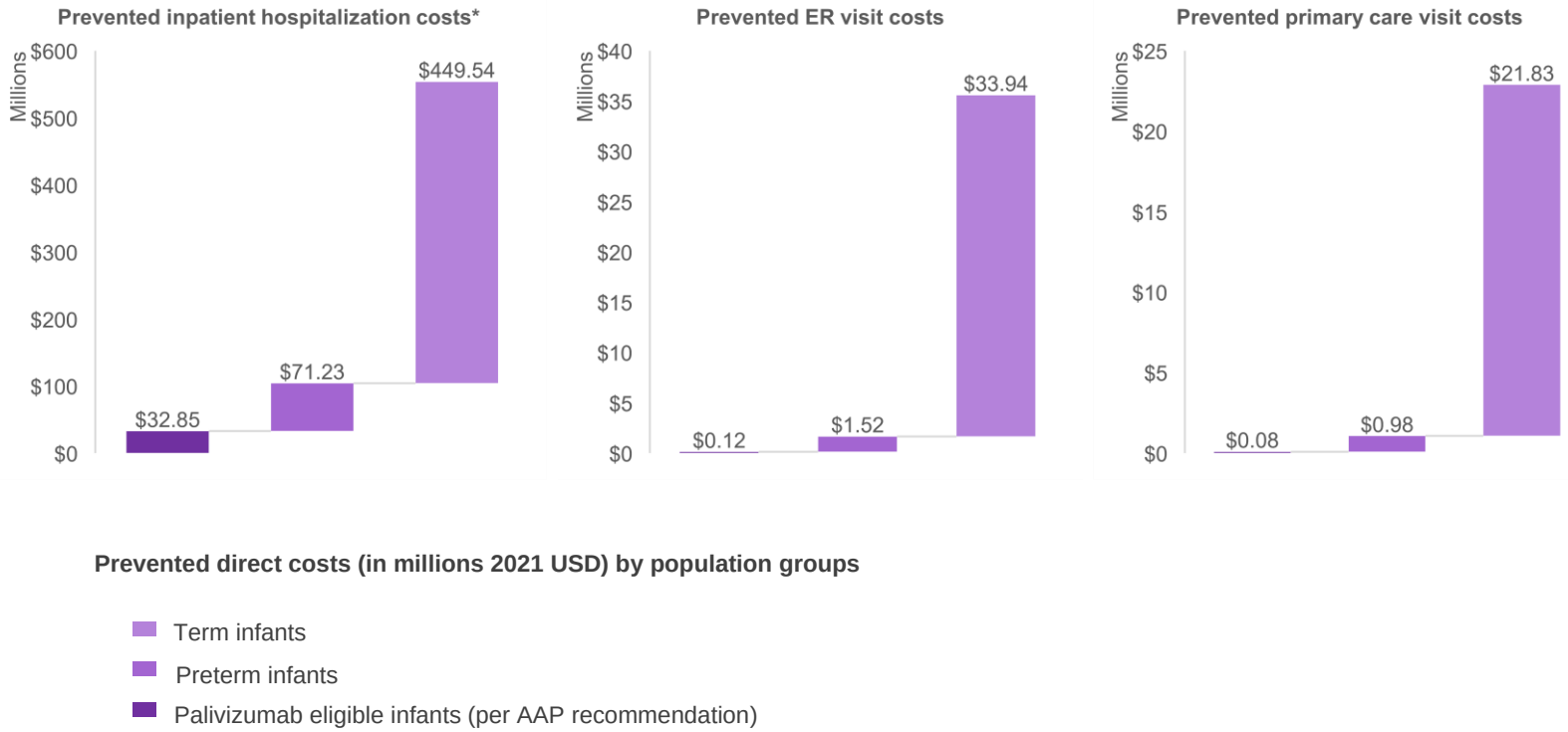
Figure S6. Prevented respiratory syncytial virus-related health events with nirsevimab immunization all US infants in their first RSV season, by health events and population groups



*Note: Estimates for prevented inpatient hospitalizations include hospitalizations that resulted in an ICU admission or MV.

Abbreviations: ER = emergency room; ICU = intensive care unit; RSV = respiratory syncytial virus

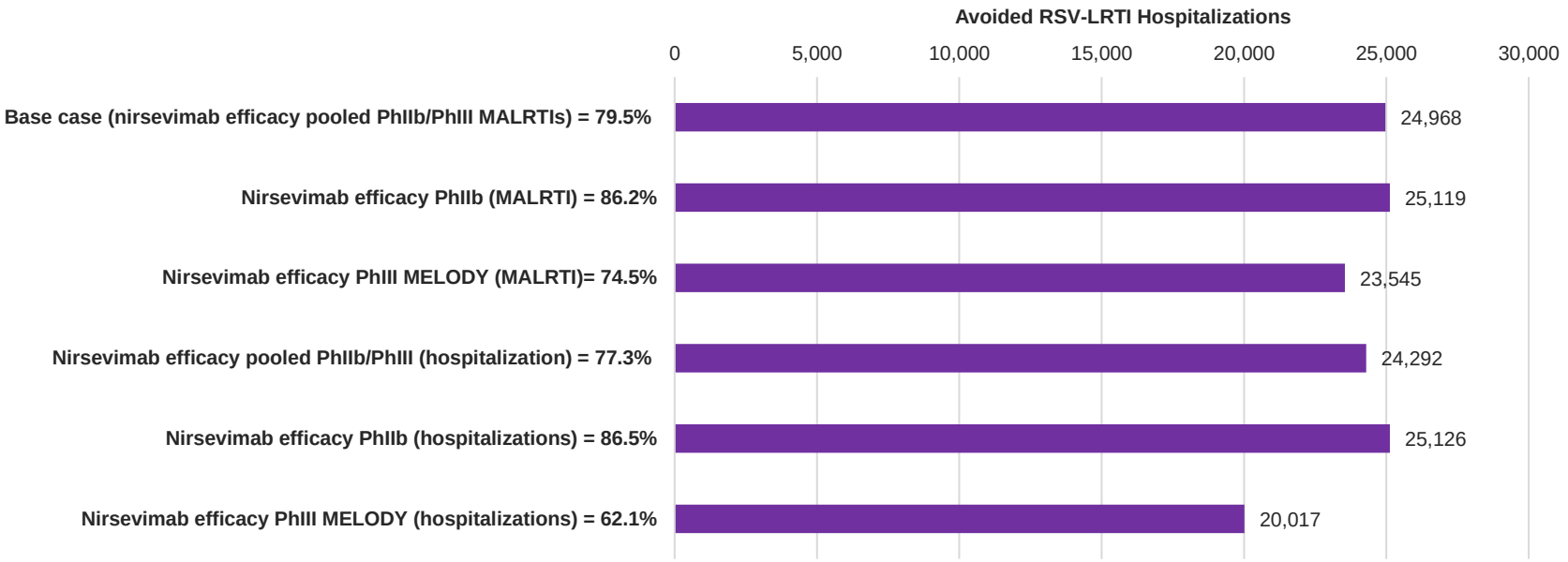
Figure S7. Prevented respiratory syncytial virus-related direct costs with nirsevimab immunization all US infants in their first RSV season, by health events and population groups



*Note: Cost estimates for prevented inpatient hospitalizations include the costs associated with hospitalizations that resulted in an ICU admission or MV.

Abbreviations: AAP = American Academy of Pediatrics; ER = emergency room; ICU = intensive care unit; USD = United States dollar

Figure S8. Sensitivity analysis on efficacy of nirsevimab based on phase IIB and phase III trial endpoints



Abbreviation: MALRTI = medically attended lower-respiratory tract infection

Supplemental Materials

Model inputs

Inpatient hospitalization rates for the palivizumab-eligible population prior to the introduction of palivizumab were informed by Feltes 2005 [1] and the IMpact-RSV study group 1998 studies [3]. Feltes 2005 [1] estimated the hospitalization rate for infants with congenital heart disease (CHD) while the IMpact-RSV study group 1998 studies [3] provided estimates for the hospitalization rate of infants with chronic lung disease (CLD) as well as those born <29 weeks gestational age (wGA). The point estimate for the hospitalization rate among palivizumab-eligible infants was then calculated as the weighted average of the hospitalization rate for infants born with CHD, with CLD, or <29 wGA and the percent of live births in the United States (US) which fall into each category as based on Rainisch 2019 [10] and internal Sanofi data on file. The McLaurin 2016 study [4] was used to inform the hospitalization rates among preterm and term infants. However, these sources only provided the hospitalization rate by weeks of gestation or as an overall estimate and not by month of age as required to inform the model. Hall 2013 [2] estimated inpatient hospitalizations by month of age, but for an all-infant population. Therefore, to get the inpatient hospitalization rates for each infant subpopulation by month of age, a monthly trend from Hall 2013 [2] was first estimated by calculating the ratio between the mean rate for the first year and the rates each month. This monthly trend was then applied to the point estimate derived from Feltes 2005 [1] and IMpact-RSV 1998 [3] for the palivizumab-eligible population and to the raw point estimates from McLaurin 2016 [4] for preterm and term infants to determine the rate of inpatient hospitalizations by month of age for each infant subpopulation. Additionally, 100% of inpatient hospitalizations for all ages were assumed to be LRTIs.

The rates for both emergency room (ER) and primary care visits by month of age were informed by Lively 2019 [7]. Due to a lack of data corresponding to the individual subpopulations included in this analysis, the estimates from Lively 2019 for an overall infant population less than 12 months in age were applied equally across each subpopulation.

A total of 65% of ER visits were assumed to be LRTIs for the first five months of age followed by 50% starting in month 6 [10]. Similarly, 65% of primary care visits were assumed to be LRTIs in the first five months of age followed by 30% starting at six months [10]. The remaining cases were considered as

upper respiratory infections, for which nirsevimab is not expected to have an impact as per clinical trial endpoints.

The proportion of hospital admissions requiring intensive care unit (ICU) admission or mechanical ventilation (MV) was informed by Arriola et al. 2020 [6]. The rates were presented in age ranges for the first year (zero to two months, three to five months, six to 12 months) by subpopulation. Therefore, to estimate the rate of ICU and MV by month of age, the model applied the same rate across each month in the respective age ranges for each subpopulation. (**Table S1**)

The cost of health events was differentiated by subpopulation and derived from published sources. McLaurin et al. 2016 [4] was used to inform the costs associated with the treatment of RSV in an inpatient hospitalization requiring an ICU visit or MV. The study provided costs by payer type, which were weighted using an average of 58% for commercial and 42% for Medicaid and inflated to 2021 costs for use in the model [11]. Costs associated with an ER or primary care visit were also derived as a weighted average of Medicaid and commercial costs informed from InHealth Professional Services, Agency for Healthcare Research and Quality 2017 for Commercial and the Centers for Medicare & Medicaid Services Physician Fee Schedule Look-Up Tool for Medicare [12-14].

Second RSV Season

Infants born from November to February will partly experience a second RSV season before turning 1 year of age. The impact of immunization during the first versus second RSV season for these infants is presented in Table S4. Based on the results the benefit of immunization for infants born in February for their first RSV season is slightly less favorable than targeting their second RSV season when looking at hospitalizations and this is even more marked when considering all RSV-MALRTIs. The model can inform the optimal timing for immunization and may raise the need to immunize part of the birth cohort for two seasons instead of one, depending on seasonality and potential circulation of RSV outside the season.

Sensitivity analysis

The sensitivity analysis evaluated the impact of a parameter's high and low ranges on model results, informed from the source of the model input or by varying the parameter by an assumed range of ±20%.

Three sets of analysis were conducted. In the first analysis, the impact of uncertainty in the rates of RSV-MALRTIs and nirsevimab coverage was examined. Analyses were run by health event and results were presented as the total number of events avoided. In the second analysis, all model parameters were varied, and results were presented as incremental total costs by infant subpopulation. The most influential parameters were presented in tornado diagrams for each subpopulation. The third set of analysis varied the efficacy of nirsevimab based on the results of the phase IIB and phase III trials. Results were presented as the total number of prevented MALRTIs and hospitalizations.

The multivariate deterministic sensitivity analysis (DSA) for occurrences of health events measured the impact to the estimated number of cases by varying two input parameters of focus: the risk of RSV-MALRTI, and the coverage rate of nirsevimab. The upper and lower bound for the risk of hospitalizations for term infants were extracted from Hall 2013[2] and Stockman 2012[5]; a 95% confidence interval (CI) from Arriola 2020[6] was used for ICU visits for term infants. The 95% CI for ER and primary care visits for all subgroups. The upper and lower bounds of coverage rate for nirsevimab were extracted from the published estimates of other respiratory infections. The upper bound was based on Hepatitis B vaccination in children 2-5 years from 2011-2016 (86.8% [15]); lower bound was extracted from influenza vaccination in children from 6 months to 4 years old from 2017-2018 (68% [16]).

Based on the results of the DSA, the risk of RSV-MALRTI had the largest impact on the total prevented hospitalizations (including ICU admissions and MVs). Application of the lower and upper bounds for hospitalizations, ICU admissions, and MVs resulted in a variation of -30% and +93% in prevented hospitalizations (including ICU admissions and MVs). The number of ER and primary care visits were most sensitive to variations in nirsevimab coverage rate. The lower bound for nirsevimab coverage rate resulted in 3,113 fewer prevented ER visits and 8,516 fewer prevented primary care visits. Alternately, the upper bound for nirsevimab coverage resulted in 15,817 additional prevented ER visits and 43,267 additional prevented primary care visits. The associated tornado diagrams are presented in **Figure 3**.

The second set of multivariate analyses was conducted to find model parameters with the largest impact on results for each infant subpopulation. The analysis showed that variation in the distribution of births, RSV risk by age, and cost to treat RSV-MALRTI had the largest impact on the total incremental costs for the palivizumab eligible, preterm, and term infants. Results of the sensitivity analysis can be seen in Figure 4.

Finally, sensitivity analyses were conducted around nirsevimab efficacy. Alternate efficacy estimates for preterm and term infants from the phase IIb [17], and phase III MELODY [18] studies were used. Based on the results of the phase IIb study nirsevimab demonstrated an efficacy of 86.2% and 86.5% in the prevention of RSV-MALRTI and RSV-LRTI hospitalization respectively. Results of the phase III MELODY study presented an efficacy of 74.5% and 62.1% in the prevention of RSV-MALRTI and RSV-LRTI hospitalization. Finally the pooled efficacy of 77.3% in the prevention of RSV-LRTI hospitalization from both studies was also studied. Results presented in **Figure S8**, showed that alternative sources for nirsevimab efficacy showed minimal variability in the total number of prevented hospitalizations compared to the base-case.

Number Needed to Immunize Analyses

A common indicator for the effectiveness of prophylaxis measures is the number needed to immunize (NNI) to prevent one additional health outcome. With the introduction of nirsevimab, the estimated NNI to prevent one RSV-MALRTI was 11 for the overall infant population, and seven, 11, and 12 for palivizumab-eligible, preterm, and term infants, respectively. The estimated NNI to prevent one inpatient RSV-LRTI hospitalization was 185, 33, 191, and 203 for the overall infant population, palivizumab-eligible, preterm, and term infants, respectively. Those estimates were consistent with Finelli 2020 [19], which reported that the NNI to avoid one hospitalization ranged from 37 to 280, according to age groups, assuming 70% efficacy of mAbs. The estimated NNI to prevent one RSV-MALRTI was also comparable to results from the phase III MELODY study. In addition, the estimated NNI for nirsevimab was lower than the NNIs observed in the literature for rotavirus vaccine and pneumococcal conjugate vaccine (PCV 13), with 200 [20] and 671 [21] NNI to prevent one hospitalization, respectively.

References

1. Feltes TF, Simoes E. Palivizumab prophylaxis in haemodynamically significant congenital heart disease. Arch Dis Child **2005**; 90:875-7; author reply -7.

2. Hall CB, Weinberg GA, Blumkin AK, et al. Respiratory syncytial virus-associated hospitalizations among children less than 24 months of age. Pediatrics **2013**; 132:e341-8.

3. The IMpact-RSV Study Group. Palivizumab, a humanized respiratory syncytial virus monoclonal antibody, reduces hospitalization from respiratory syncytial virus infection in high-risk infants. Pediatrics **1998**; 102:531-7.

4. McLaurin KK, Farr AM, Wade SW, Diakun DR, Stewart DL. Respiratory syncytial virus hospitalization outcomes and costs of full-term and preterm infants. J Perinatol **2016**; 36:990-6.

5. Stockman LJ, Curns AT, Anderson LJ, Fischer-Langley G. Respiratory syncytial virus-associated hospitalizations among infants and young children in the United States, 1997-2006. Pediatr Infect Dis J **2012**; 31:5-9.

6. Arriola CS, Kim L, Langley G, et al. Estimated Burden of Community-Onset Respiratory Syncytial Virus-Associated Hospitalizations Among Children Aged <2 Years in the United States, 2014-15. J Pediatric Infect Dis Soc **2020**; 9:587-95.

7. Lively JY, Curns AT, Weinberg GA, et al. Respiratory Syncytial Virus-Associated Outpatient Visits Among Children Younger Than 24 Months. J Pediatric Infect Dis Soc **2019**; 8:284-6.

8. Hansen CL, Chaves SS, Demont C, Viboud C. Mortality Associated With Influenza and Respiratory Syncytial Virus in the US, 1999-2018. JAMA Netw Open **2022**; 5:e220527.

9. Li X, Bilcke J, Vazquez Fernandez L, et al. Cost-effectiveness of Respiratory Syncytial Virus Disease Prevention Strategies: Maternal Vaccine Versus Seasonal or Year-Round Monoclonal Antibody Program in Norwegian Children. J Infect Dis **2022**.

10. Rainisch G, Adhikari B, Meltzer MI, Langley G. Estimating the impact of multiple immunization products on medically-attended respiratory syncytial virus (RSV) infections in infants. Vaccine **2020**; 38:251-7.

11. Medicaid and CHIP Payment and Access Communication (MACPAC). Medicaid's Role in Financing Maternity Care. **2020**.

12. Agency for Healthcare Research and Quality. Healthcare Cost and Utilization Project: Costs of Emergency Department Visits in the United States, 2017. Available at: https://www.hcup-us.ahrq.gov/reports/statbriefs/sb268-ED-Costs-2017.pdf. Accessed October 2021.

13. InHealth Professional Services. Physicians' Fee and Coding Guide (Payment Range). ISBN 978-1-60099-114-1, **2021**.

14. Centers for Medicare & Medicaid Services. Physician Fee Schedule Look-Up Tool. National 2021 Payment Amount by HCPCS Code. Available at: www.cms.gov. Accessed October 2021.

15. Le MH, Yeo YH, So S, Gane E, Cheung RC, Nguyen MH. Prevalence of Hepatitis B Vaccination Coverage and Serologic Evidence of Immunity Among US-Born Children and Adolescents From 1999 to 2016. JAMA Netw Open **2020**; 3:e2022388.

16. Hughes MM, Reed C, Flannery B, et al. Projected Population Benefit of Increased Effectiveness and Coverage of Influenza Vaccination on Influenza Burden in the United States. Clin Infect Dis **2020**; 70:2496-502.

17. Hammitt LL, Dagan R, Yuan Y, et al. Nirsevimab for Prevention of RSV in Healthy Late-Preterm and Term Infants. N Engl J Med **2022**; 386:837-46.

18. Simões E, et al.,. Pooled efficacy of nirsevimab against RSV lower respiratory tract infection in preterm and term infants. In: ESPID 2022 Congress. (Hybrid Congress).

19. Finelli L, Choi Y, Goldstein E. Number needed to immunize to prevent RSV with extended half-life monoclonal antibody. Vaccine **2020**; 38:5474-9.

20. Ruiz-Palacios GM, Perez-Schael I, Velazquez FR, et al. Safety and efficacy of an attenuated vaccine against severe rotavirus gastroenteritis. N Engl J Med **2006**; 354:11-22.

21. Palmu AA, Jokinen J, Nieminen H, et al. Vaccine-preventable disease incidence of pneumococcal conjugate vaccine in the Finnish invasive pneumococcal disease vaccine trial. Vaccine **2018**; 36:1816-