Cost-Effectiveness of Nirsevimab for Respiratory Syncytial Virus in Infants and Young Children

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abstract

BACKGROUND AND OBJECTIVES: Respiratory syncytial virus (RSV) causes substantial hospitalization in US infants. The Advisory Committee on Immunization Practices recommended nirsevimab in infants younger than 8 months born during or entering their first RSV season and for children aged 8 to 19 months at increased risk of RSV hospitalization in their second season. This study's objective was to evaluate the cost-effectiveness of nirsevimab in all infants in their first RSV season and in high-risk children in their second season.

METHODS: We simulated healthcare utilization and deaths from RSV with and without nirsevimab among infants aged 0 to 7 months and those 8 to 19 months old over a single RSV season. Data came from published literature, US Food and Drug Administration approval documents, and epidemiologic surveillance data. We evaluated societal outcomes over a lifetime discounting at 3% and reporting in 2022 US dollars. Sensitivity and scenario analyses identified influential variables.

RESULTS: We estimated that 107 253 outpatient visits, 38 204 emergency department visits, and 14 341 hospitalizations could be averted each year if half of the US birth cohort receives nirsevimab. This would cost $153 517 per quality-adjusted life year (QALY) saved. Nirsevimab in the second season for children facing a 10-fold higher risk of hospitalization would cost $308 468 per QALY saved. Sensitivity analyses showed RSV hospitalization costs, nirsevimab cost, and QALYs lost from RSV disease were the most influential parameters with cost-effectiveness ratios between cost-saving and $323 788 per QALY saved.

CONCLUSIONS: Nirsevimab for infants may be cost-effective, particularly among those with higher risks and costs of RSV.

WHAT'S KNOWN ON THIS SUBJECT: Respiratory syncytial virus (RSV) causes substantial hospitalization in US infants and nirsevimab has been shown to reduce lower respiratory illness from RSV in infants and children.

WHAT THIS STUDY ADDS: Nirsevimab for infants may reduce 107 253 outpatient visits and 14 341 hospitalizations per year at a cost of $153 517 per quality-adjusted life year saved in the United States. Cost-effectiveness is influenced by hospitalization costs, nirsevimab cost, and RSV quality-of-life.

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Respiratory syncytial virus (RSV) causes substantial morbidity in infants in the United States. It is estimated that hospitalization for RSV in infants costs the US society $472 million per year.[1] The disease and economic burden of severe RSV is particularly high for infants in their first few months of life.[2–4]

In July 2023, the US Food and Drug Administration approved a monoclonal antibody, nirsevimab, for use in infants and young children to prevent RSV lower respiratory tract infection (LRTI). Nirsevimab is an immunoglobulin G1 antibody that binds to the prefusion conformation of the RSV F protein and was engineered to have a prolonged half-life.[5] In clinical trials, nirsevimab effectiveness against medically attended (MA) RSV LRTI for up to 150 days was 79.0%; side effects were rare and included rash and injection site reactions.[6] In August 2023, the Advisory Committee on Immunization Practices (ACIP) recommended nirsevimab for all infants aged <8 months born during or entering their first RSV season and for infants and children aged 8 to 19 months who are at increased risk for severe RSV disease and entering their second RSV season.[6] Before approval, palivizumab was the only available monoclonal antibody immunization, but it requires multiple costly doses, and has been only recommended to be given during the RSV season for a very small subset of infants who are high-risk premature or those born with certain heart or lung conditions. Because the duration of protection is limited and RSV is highly seasonal,[7] nirsevimab is intended to be administered as a single dose at birth for infants born during the RSV season or shortly before the RSV season begins, typically in October or November, for children born outside of the RSV season to provide these children protection during their first RSV season.[6] In September 2023, ACIP recommended a maternal RSV vaccine for use during pregnancy to prevent infant LRTI. Either use of the maternal RSV vaccine or infant receipt of nirsevimab was recommended, but both are not needed for most infants.[8]

The ACIP incorporates cost-effectiveness information into its decision-making process when developing immunization recommendations. The findings of our analysis were presented to ACIP as part of its deliberations on nirsevimab recommendations.[9]

The objective of this analysis was to evaluate the cost-effectiveness of nirsevimab for infants in their first RSV season. In a secondary analysis, we evaluated the cost-effectiveness of nirsevimab administration to high-risk young children in their second RSV season. In an additional secondary analysis, we evaluated the use of nirsevimab in infants born to mothers who had been vaccinated with the maternal RSV vaccine. Overall, we aim to provide further transparency on the methods and results of our cost-effectiveness study used by ACIP as part of its deliberations leading to the 2023 policy recommendation on nirsevimab. A separate article evaluates maternal vaccination.[10]

METHODS

To evaluate the projected health benefits and cost-effectiveness of nirsevimab, we did not collect direct patient data, but instead created a decision analytical model using secondary data that simulates the short- and long-term impacts of RSV on infants with and without nirsevimab. For the base case scenario with nirsevimab, we assumed 50% uptake of nirsevimab, administered at birth for those born between October 1 and March 31 and administered in October (for those born in April, June, and August) or in November (for those born in May, July, or September) to correspond with routine well-child visits at about 2, 4, and 6 months of age. Since we do not simulate transmission, the resulting value per person immunized is not affected by uptake. RSV disease and economic outcomes were estimated using a societal perspective in the base case.

Model Description

Assuming a uniform monthly distribution of US births in an annual birth cohort, the model simulates the number of births throughout each month over a 1-year time frame and accounts for lifetime outcomes (eg, lives and life-years lost because of RSV). The cohort of infants would face variable risk of RSV MA-LRTI on the basis of the specific month of birth and RSV seasonality (Supplemental Fig 4). The model incorporated RSV-associated disease outcomes along with resource utilization such as outpatient visits, emergency department (ED) visits, hospitalizations, and deaths (Fig 1). Likewise, we included adverse events from nirsevimab such as injection site reactions, systemic reactions, or theoretical serious adverse events. Each disease and adverse event outcome was associated with costs and health-related quality-of-life losses.

Epidemiology Inputs

Annual RSV incidence was estimated from a variety of epidemiologic studies of RSV (Table 1). RSV inpatient incidence came from 2016 to 2020 data from the Centers for Disease Control and Prevention's New Vaccine Surveillance Network.[4] We assumed 100% of RSV hospitalizations were because of LRTI.[11] ED and outpatient incidence came from several New Vaccine Surveillance Network epidemiologic studies in young children and infants.[2,3,12] Because these were less severe outcomes, a fraction of those events were assumed to be because of LRTI (whereas the remaining were assumed to be because of upper respiratory tract infections [URTIs]).[11] Death could happen for those hospitalized with RSV, with mortality rates based on data among all infants hospitalized with RSV (both high risk and low risk).[12–15] We did not incorporate potential long-term sequelae of RSV infection (eg, asthma). Monthly RSV seasonality was derived from prepandemic (2015–2019) proportion of RSV detections per month from the National Respiratory and Enteric Virus Surveillance System[16] (Supplemental Fig 4).

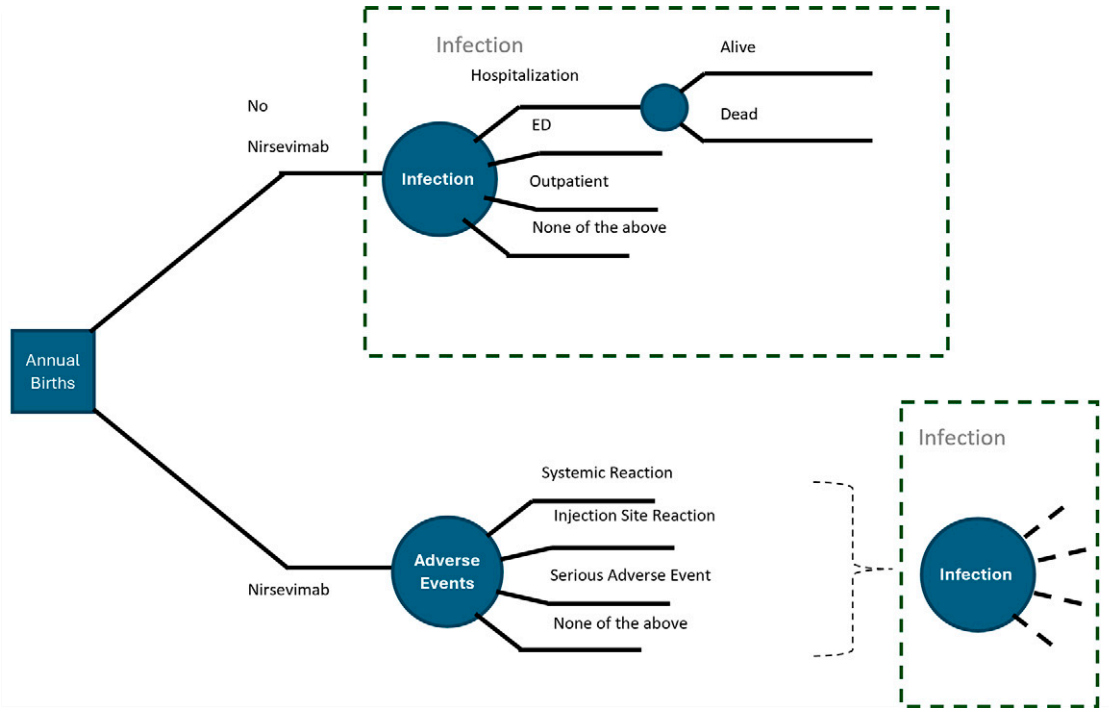

FIGURE 1
Decision tree model diagram.

Efficacy and Safety Inputs

Nirsevimab efficacy was estimated on the basis of pooled results from the phase 2b and phrase 3 clinical trials (Table 1).[17] After administration, we assumed that efficacy follows a sigmoid function over the first 150 days, declining to an efficacy of 25% by day 150 and then reaching 0% efficacy at month 10 (Supplemental Fig 5). The average efficacy in the first 150 days matches the reported efficacy against RSV-associated MA-LRTI. Because the trial results measured efficacy against RSV MA-LRTI and efficacy against URTI is unknown, we assumed that nirsevimab only protected against RSV MA-LRTI and offered no protection against RSV URTI. In a sensitivity analysis, we assumed flat efficacy during days 0 through 150, then immediately declining to 0% efficacy. Rates of adverse events including systemic reaction and injection site reaction came from clinical trials (Table 1). Severe adverse events (eg, anaphylaxis or Guillain-Barre) were not observed in trials and, in general, rare events may not be observed in clinical trials because of the limited number of enrolled participants. However, to account for unobserved risks in larger populations, we assumed a 1 in 1 million rate of hypothetical serious adverse events.[18]

Costs Inputs

The model included costs associated with nirsevimab and RSV MA-LRTI outcomes. The cost of nirsevimab was based on an anticipated commercial price of $495 and a Vaccines for Children price of $395.[19] We assumed 50% of doses would be purchased through Vaccines for Children,[20–22] so we used a weighted average of $445 per dose as our base case cost (Table 1). Because the dose was anticipated to be given at birth or a routine outpatient visit (well-child checkup), we did not include costs of an extra health care visit to administer nirsevimab, but we included $22.27 for counseling and administration. We based adverse event costs on a recent analysis of MarketScan data[23] and included productivity losses from workdays lost by caregivers for these adverse events (Table 1).[24] The comparator arm of no nirsevimab assumes a standard of care that includes palivizumab use among eligible high-risk infants (Table 1). In the nirsevimab strategy, uptake of nirsevimab was assumed to be the same in all infants, including those that are palivizumab eligible, so eligible high-risk infants who do not receive nirsevimab may still receive palivizumab.

Costs for RSV came from a systematic literature review of RSV costs in infants (Table 1).[1] To account for total societal costs, we also included days of work lost for caregivers and the dollar value of lifetime medical costs and productivity losses in infants associated with RSV-related premature deaths using the human capital approach (Table 1 and Supplemental Table 5).[25–27]

Quality of Life Inputs

The health-related quality of life associated with RSV outcomes of hospitalization, ED visits, and outpatient visits in infants is

TABLE 1 Model Parameters				
Model Input Parameter	**Base case**	**Range**	**Distribution**	**Source**
Category of RSV incidence per 100 000				
Inpatient				
Age 0 mo	1760	1560–1970	Lognormal	CDC NVSN[4,a]
Age 1 mo	3110	2850–3390	Lognormal	
Age 2 mo	2230	2030–2450	Lognormal	
Age 3 mo	1560	1390–1740	Lognormal	
Age 4 mo	1360	1200–1520	Lognormal	
Age 5 mo	1090	960–1250	Lognormal	
Age 6 mo	960	810–1120	Lognormal	
Age 7 mo	800	640–960	Lognormal	
Age 8 mo	730	600–880	Lognormal	
Age 9 mo	840	680–990	Lognormal	
Age 10 mo	600	480–730	Lognormal	
Age 11 mo	600	490–730	Lognormal	
Age 12 mo	630	500–750	Lognormal	
Age 13 mo	500	380–620	Lognormal	
Age 14 mo	580	470–700	Lognormal	
Age 15 mo	540	430–660	Lognormal	
Age 16 mo	400	290–510	Lognormal	
Age 17 mo	370	270–460	Lognormal	
Age 18 mo	370	260–480	Lognormal	
Age 19 mo	340	250–450	Lognormal	
Age 20 mo	280	190–370	Lognormal	
Age 21 mo	210	140–290	Lognormal	
Age 22 mo	180	120–260	Lognormal	
Age 23 mo	290	200–380	Lognormal	
Proportion with LRTI				
Age 0–5 mo	1	0.5–1.0	—	Assumption based on Rainisch 2020[10]
Age 6–23 mo	1	0.5–1.0	—	Assumption based on Rainisch 2020[10]
ED				
Age 0–5 mo	7500	5500–7500	Lognormal	Lively 2019 (base case and range),[3] Hall 2009 (range)[2]
Age 6–11 mo	5800	5700–5800	Lognormal	Lively 2019 (base case and range),[3] Hall 2009 (range)[2]
Age 12–23 mo	3200	3200–5300	Lognormal	Hall 2009 (base case and range),[2] Lively 2019 (range)[3]
Proportion with LRTI				
Age 0–5 mo	0.65	0.25–1.0	Beta	Assumption based on Rainisch 2020[10]
Age 6–23 mo	0.5	0.25–1.0	Beta	Assumption based on Rainisch 2020[10]
Medically attended outpatient				
Age 0–5 mo	21 600	13 200–21 600	Lognormal	Lively 2019 (base case and range),[3] Hall 2009 (range)[34]
Age 6–11 mo	24 600	17 700–24 600	Lognormal	
Age 12–23 mo	18 440	6600–29 620	Lognormal	Lively 2019 (base case and range),[3] Jackson 2021 (range),[11] Hall 2009 (range)[34]
Proportion with LRTI				
Age 0–5 mo	0.65	0.25–1.0	Beta	Assumption based on Rainisch 2020[10]
Age 6–23 mo	0.3	0.1–1.0	Beta	Assumption based on Rainisch 2020[10]
RSV mortality per hospitalization				
Age 0–5 mo	0.0010	0.0004–0.0020	Beta	Doucette 2016,[12] Hansen 2022[14]
Age 6–11 mo	0.10	0.0004–0.0020	Beta	—
Age 12–23 mo	0.003	0.0028–0.0034	Beta	Gupta 2016[13]
Intervention efficacy				
Initial efficacy (mo 1–5) against RSV-associated LRTI	79.0%	68.5%–86.1%	Beta	Phase 3 trial, phase 2b[16]

TABLE 1 Continued

Model Input Parameter	Base case	Range	Distribution	Source
Effectiveness mo 6–10	25%	0%–50%	Beta	—
Effectiveness after 10 mo	0%	—	—	—
Adverse events				
Nirsevimab	—	—	—	—
Probabilities of pediatric adverse events	—	—	—	—
Systemic reaction	0.005	0.00486–0.00525	Beta	AstraZeneca ACIP data request
Probability of outpatient visit given Systemic reaction	0.1	—	—	Assumption; Deluca 2023[22]
Anaphylaxis	0	0–0.0000010	—	AstraZeneca ACIP data request
Injection site reaction	0.002	0.0026–0.0028	Beta	AstraZeneca ACIP data request
Probability of outpatient visit given Injection site reaction	0.1	—	—	Assumption; Deluca 2023[22]
Serious adverse event	0.000001	—	Beta	(Guillain-Barre) Prosser 2006[17]
Pediatric QALY lost because of adverse events				
Systemic reaction	0.0056	0.00051–0.0061	Lognormal	Deluca 2023[22]
Anaphylaxis	0.0137	0.0135–0.0139	Lognormal	—
Serious adverse event	0.141	0.092–0.199	Lognormal	(Guillain-Barre) Prosser 2006[17]
Costs because of adverse events				
Cost of outpatient visit for systemic reaction (non-high–risk)	$313	$27–$1337	Lognormal	Marketscan unpublished; Deluca 2023[22]
Cost of outpatient visit for injection site reaction	$367.76	$33.15–$1758	Lognormal	Marketscan unpublished; Deluca 2023[22]
Recipient time for office visit (h)	2	1–3	Normal	Ray 2015[35]
Anaphylaxis medical costs	$7706	$89–$23 414	Lognormal	Marketscan unpublished; Deluca 2023[22]
Parent time for anaphylaxis (d)	1	1–3	Normal	Shimabukuo 2021[36]
Serious adverse event	$36 163.76	$10 372.31–$122 145.60	Lognormal	Prosser 2006[17]
Daily productivity for caregivers	190	169.41–211.03	Lognormal	Grosse 2019[23,b]
Cost inputs				
Palivizumab costs (for high-risk infants not receiving nirsevimab)				
Fraction of children that are high-risk	1.6%	0%	1.6%	Sanofi[37]
Fraction of children at high risk receiving palivizumab	75%	0%	100%	Sobi 2021[38]
Palivizumab cost per dose	$1228[c]	—	—	Shahabi 2018[39]
Doses per patient	4.167[d]	—	—	Assumption
RSV costs				
RSV-specific inpatient costs (per inpatient outcome)				
Age 0–11 mo	$11 487	4804–86 646	Lognormal	Bowser 2022[40]
Age 12–23 mo	$11 469	4804–86 646	Lognormal	
D lost productivity	7.4	0–14	Lognormal	Fragaszy 2018,[24] Petrie 2016,[25] Van Wormer 2017[26]
RSV-specific ED costs (per ED visit)				
Age 0–11 mo	$563	544–581	Lognormal	Bowser 2022[40]
Age 12–23 mo	563	544–581	Lognormal	—
D lost productivity	2.5	0–5	Lognormal	Fragaszy 2018,[24] Petrie 2016,[25] Van Wormer 2017[26]
RSV-specific outpatient costs (outpatient visit)				
Age 0–11 mo	$82	46–118	Lognormal	Bowser 2022[1]
Age 12–23 mo	$82	46–118	Lognormal	—
D lost productivity	2.5	0–5	Lognormal	Fragaszy 2018,[24] Petrie 2016,[25] Van Wormer 2017[26]
Lifetime productivity for those <1 y old	$1 795 936	1 346 951–2 244 919	Lognormal	Grosse 2019[23,e]
Nirsevimab-related costs				
Nirsevimab per dose	$445[f]	$50–$600	—	—

TABLE 1 Continued

Model Input Parameter	Base case	Range	Distribution	Source
Nirsevimab administration	$22.27	$16.70–$27.84	Lognormal	Medicare CPT 96380, administration and counseling
Proportion of patients requiring specific visit for immunization	0	—	—	Assumed part of regularly scheduled office visits
Discount rate	0.03	0.0–0.07	—	—
Quality-of-life lost because of RSV				
Quality-adjusted life d lost from acute RSV				Glaser[27] (base case), Regnier[28] (lower bound), JIVE COVID-19/RSV utilities (unpublished)
Outpatient				
Child	3.1	1.8–16.6	Lognormal	
Caregiver	1.5	0–9.1	Lognormal	
ED				
Child	4.9	2.9–16.6[g]	Lognormal	
Caregiver	2.5	0–9.1	Lognormal	
Hospitalized				
Child	6.2	3.7–26.5	Lognormal	
Caregiver	2.4	0–13.6	Lognormal	
Discounted QALY lost from death in the				Calculated from y 2020 life tables[41]
First year of life	28.40	—	—	—
Second year of life	28.38	—	—	—

Distribution is used for the probabilistic sensitivity analysis. The mean is the same as the base case value with an SD of one-quarter of the range. Efficacy estimates are based on pooled estimates from the phase 2b and phase 3 trials. In the phase 2b trial, all infants received 50 mg of nirsevimab. Because nirsevimab is approved for a dose of 50 mg for infant weighing <5 kg and for a dose of 100 mg for infants weighing ≥5 kg or more, pooled efficacy estimated excluded infants who weighed ≥5 kg in the phase 2b trial. The phase 3 trial used the approved dosing regimen. A QALY is 1 365th of a QALY (QALY efficacy is for hospitalization, ED, and outpatient outcomes, but it is assumed to be effective against LRTI only in the base case; we assume 0% efficacy against upper-respiratory outcomes). CDC, Centers for Disease Control and Prevention; COVID-19, coronavirus disease 2019; CPT, Current Procedural Terminology; JIVE, Joint Initiative in Vaccine Economics; NVSN, New Vaccine Surveillance Network.

[a] CDC New Vaccine Surveillance Network hospitalization rates for children <2 years of age from December 2016 to September 2020.

[b] Daily productivity rate calculated by dividing mean annual total productivity (both market and nonmarket) for ages 15 to 99 by 365 days and inflated from 2016 to 2022 value using the Federal Reserve Gross Domestic Product implicit price deflator.

[c] Palivizumab cost per dose is the drug costs. We do not include costs (or quality-of-life losses) associated with adverse events from palivizumab administration.

[d] Based on an assumption 66% receive 5 doses and 8.3% each receive 4, 3, 2, and 1 doses.

[e] Lifetime productivity taken from Table 2 of Grosse for age 0 lifetime total productivity (both market and nonmarket) assuming 1% annual productivity growth and a 3% discount rate and inflated from 2016 to 2022 dollars using the Federal Reserve GDP implicit price deflator.

[f] The cost of nirsevimab was based on an anticipated commercial price of $495 and a Vaccines for Children price of $395. We assumed 50% of doses would be purchased through Vaccines for Children to calculate an average of $445 per dose as our base case cost.

[g] Upper bound for sensitivity analysis utilities was not directly measured for ED in the JIVE/coronavirus disease 2019 RSV utilities study, but outpatient values were used.

particularly challenging to evaluate because infants cannot be queried directly, and there may be spillover effects on families. So, in addition to quality-adjusted life years (QALYs) lost to the child, we also incorporated QALYs lost from caregivers. We used a systematic review of literature on child and caregiver quality of life[28] for our base case QALYs losses. However, for the lower-bound values, we resorted to a study by Regnier[29] and to an unpublished preference elucidation survey of parents of RSV patients for our upper-bound values (Table 1).

Analysis Plan

Health and Economic Outcomes

The model simulated RSV MA-LRTI–associated outpatient visits, ED visits, hospitalizations, and deaths to calculate total medical and productivity costs and QALYs lost. The main summary measure is the incremental cost-effectiveness ratio (ICER) in terms of dollars per QALYs gained. This metric tells us how much money is spent per year of life in perfect health (QALY) gained with the use of nirsevimab. Assuming spending less on health is better, a lower ICER is preferred. We also estimated the number needed to immunize to prevent an undesirable RSV disease outcome (eg, number of infants needed to be immunized with nirsevimab to prevent an RSV-associated hospitalization or death). Other intermediate outcomes included numbers of outpatient visits, ED visits, hospitalizations, medical and indirect costs, and total cost per outcome averted. Costs are reported in 2022 US dollars for a 1-year time frame, and future costs and health outcomes are discounted at 3% annually. We used Microsoft Excel 365 for all calculations.

Primary Analysis: Infants Born During or Entering Their First RSV Season

The primary analysis estimated the ICER of nirsevimab compared with no nirsevimab in the first RSV season.

Secondary Analysis: High-Risk Children Entering Their Second RSV Season

The secondary analysis evaluated the ICER of nirsevimab compared with no nirsevimab in the month of October

before the second RSV season for children 8 to 19 months of age for a variety of risk levels. Few data are available on the incidence of RSV MA-LRTI and RSV hospitalization by risk condition. For this analysis, we created theoretical risk groups that had an RSV-associated hospitalization incidence of 2, 3, 6, or 10 times the incidence in the general population. We conservatively assumed that the incidence of outpatient visits, ED visits, death per hospitalization, and cost of health care visits were the same as those of the general population. We assumed children currently eligible for palivizumab in their second season would already receive nirsevimab, given the higher efficacy, lower cost, and implementation profile of nirsevimab (single dose versus monthly dosing). Therefore, we focused the analysis for the second season on children not already eligible for palivizumab, and thus savings from palivizumab were not included in this analysis.[30–32] We assumed the cost of nirsevimab is doubled because 2 100 mg doses of nirsevimab would be required in this group.

Sensitivity and Scenario Analyses

We conducted 1-way, 2-way, and probabilistic sensitivity analyses. Parameter ranges for sensitivity analysis can be found in Table 1, as well as Supplemental Fig 4. Probabilistic sensitivity analysis assigned distributions to input parameters (see Table 1) and using 1000 Monte Carlo simulation iterations, calculated overall uncertainty using cost-effectiveness acceptability curves. The results of these simulations are also used to create 95% credible intervals for outcome estimates. We also explored scenarios where there were no savings from palivizumab (a policy for a population not currently eligible to receive palivizumab and where there was lower risk of mortality), and where nirsevimab might have an equivalent prevention efficacy on URTI as on LRTI. Finally, we explored an additional tertiary analysis where we assume the pregnant mother had received the US Food and Drug Administration-approved RSVpreF vaccine more than 14 days before delivery (inputs in Supplemental Table 6).[10] In that scenario, because there are no data available on the efficacy of nirsevimab when given to infants born to vaccinated mothers, we assumed the efficacy of adding nirsevimab on top of RSVpreF vaccine protection would be the higher efficacy of either nirsevimab or RSVpreF (Supplemental Fig 6).

RESULTS

Outcomes, Outcomes Averted, and Number Needed to Immunize

Without nirsevimab, our model projects RSV-associated illness among the annual US birth cohort would result in 47 758 hospitalizations, with 48 deaths occurring among inpatients (Table 2). If nirsevimab was given in the first RSV season to half of an annual US birth cohort, our model projects that 30% of hospitalization visits and deaths would be averted (Table 2). It would take 128 immunized with nirsevimab to prevent a hospitalization.

Cost-Effectiveness

Without nirsevimab, $225 million would be spent on palivizumab for roughly 1.2% of the birth cohort, $755 million on RSV medical care, and $671 million on productivity losses, for $1651 million in total costs (Table 3). A combination of nirsevimab immunization for 50% of

TABLE 2 Cost-Effectiveness Outcomes for Use of Nirsevimab

	RSV Outcomes						
	LRTI or Total	No. Outpatient Visits	No. ED visits	No. Inpatient Visits	No. Deaths	Costs (Millions)	QALYs Lost
Natural history	LRTI	392 446 (143 969–641 886)	142 449 (71 910–198 938)	47 758 (41 803–53 998)	48 (18–96)	—	—
	Total	846 451 (570 447–881 128)	243 675 (205 206–249 996)	47 758 (41 803–53 998)	48 (18–96)	1651 (857–3857)	18 151 (6844–42 113)
Nirsevimab[a]	LRTI	285 193 (97 840–482 578)	104 245 (52 497–146 998)	33,417 (27 666–39 451)	33 (15–81)	—	—
	Total	739 199 (506 623–800 399)	205 471 (169 765–224 312)	33 417 (27 666–39 451)	33 (12–67)	2085 (1447–3607)	15 324 (5569–36 362)
Difference	LRTI	107 253 (−178 103 to −40 827)	38 204 (−59 478 to −17 207)	14 341 (−18 999 to −10 672)	14 (−30 to −5)	—	—
	Total	107 253 (−178 103 to −40 827)	38 204 (−59 478 to −17 207)	14 341 (−18 999 to −10 672)	14 (−30 to −5)	434 (−292 to −623)	−2827 (−6578 to −1 075)
Cost per outcome averted	Total	4047 (−2756–12 922)	11 361 (−7457 to 30 127)	30 264 (−19 111–52 294)	30 263 954 (−19 309 to 397 815 665)	N/A	153 517 (−106 281 to 490 747)

Negative numbers in the difference row indicate gains or events saved with the nirsevimab arm as compared with natural history. Positive numbers mean worse outcomes like increased costs. LRTI, Lower Respiratory Tract Infection; N/A, not applicable; No., number; RSV, Respiratory Syncytial Virus; QALY, Quality-Adjusted Life-Year. —, costs and QALYs lost are only reported in totals.

[a] Nirsevimab given to 50% of US infants aged <8 months entering their first RSV season.

TABLE 3 Resulting Costs (in Millions of 2022 US Dollars) in US Infants Aged <8 Months Entering Their First RSV Season, Without and With Nirsevimab Among 50% of US Birth Cohort

	Medical Costs (Millions of 2022 US Dollars)						Productivity Costs (Millions of 2022 US Dollars)					
	Intervention Costs	Outpatient Costs	ED Costs	Inpatient Costs	Total RSV Medical Costs	Total Health System Costs	Outpatient Costs	ED Costs	Inpatient Costs	Death Costs	Total Productivity Costs	Total Costs
Natural history	225 (103–398)	69 (38–102)	137 (116–142)	549 (25–2716)	755 (217–2932)	980 (387–3166)	402 (122–876)	116 (39–260)	67 (24–146)	86 (31–175)	671 (338–1164)	1651 (857–3857)
Nirsevimab[a]	969 (868–1 023)	61 (33–89)	116 (95–127)	384 (17–1908)	560 (179–2078)	1529 (1087–3024)	351 (105–762)	98 (32–219)	47 (17–101)	60 (21–122)	556 (270–987)	2085 (1447–3607)
Difference	744 (619–777)	−9 (−17 to −3)	−22 (−34 to −10)	−165 (−838 to −8)	−195 (−870 to −33)	549 (−158 to 711)	−51 (−131 to −11)	−18 (−46 to −5)	−20 (−46 to −7)	−26 (−56 to −9)	−115 (−208 to −57)	434 (−292 to 623)

Negative numbers in the difference row indicate savings with the nirsevimab arm as compared with natural history. The natural history comparator policy intervention costs include palivizumab use in this cost category. Because we assume 50% of infants get nirsevimab in the nirsevimab strategy, the other 50% might (if they are high risk) get palivizumab. Therefore, the nirsevimab intervention number includes both nirsevimab and palivizumab costs.

[a] Nirsevimab given to 50% of US infants aged <8 months entering their first RSV season.

the birth cohort and palivizumab for 0.6% (half of the 1.2% who did not receive nirsevimab) would lead to $969 million in intervention costs (330% higher), $560 million in RSV medical care (26% lower), and $556 million in productivity costs (17% lower) for $2085 million in total costs (26% higher) (Table 3). Although costs are higher with nirsevimab, the model projects 2827 more net QALYs gained (Table 4), leading to a societal ICER of $153 517 per QALY gained (Table 1). Costs per event averted are in Table 1.

In our secondary analysis focused on the second RSV season, the ICER depends greatly on the risk of severe outcomes. For an average risk child, receiving nirsevimab costs >$1.6 million per QALY gained; however, for young children with a 10-fold risk of hospitalization, the cost would be $308 468 per QALY gained (Supplemental Figs 7 and 8).

Sensitivity and Scenario Analyses

The results are sensitive to several parameters (Fig 2). If the cost of nirsevimab dropped to $50 per dose, nirsevimab was cost-saving, but if it rose to $600 per dose, the cost rose to $253 964 per QALY gained (Fig 3). The range of costs per hospitalization were wide (ie, a base case of $11 487 but ranging from $4804 to $86 646). Using the highest cost assumption, use of nirsevimab in infants aged <8 months became cost-saving. The quality-of-life associated with RSV outcomes also had a big impact. If RSV has a larger burden for children and their caregivers (ie, the highest QALY losses per RSV-associated hospitalization, ED, and outpatient), then the cost dropped to $35 659 per QALY gained. However, if the impact of RSV on quality of life is low, then the cost increased to $323 788 per QALY gained. Efficacy of nirsevimab was important: if it was high, the ICER was $98 183 per QALY gained, and if low, it was $243 556 per QALY gained. If nirsevimab were just as effective at preventing URTI as it has been shown to prevent MA-LRTI, then the estimated societal cost would be $78 420 per QALY gained (Fig 3). If efficacy was a flat 79% efficacy through day 150 and then immediately dropping to 0%, the ICER would be $152 651 per QALY gained. Finally, the use of palivizumab had an impact on the ICER because nirsevimab was assumed to reduce palivizumab use. If none of the population under consideration needed palivizumab, the ICER rose to $193 310 per QALY gained (Fig 2).

We examined several scenarios. If we exclude productivity costs to evaluate health system costs alone, the ICER increases to $194 198 per QALY gained (Supplemental Table 7). In 1 scenario, we examined the combined effects of RSV mortality and savings because of reduced palivizumab use (Supplemental Table 8). In the first part of this scenario, we considered infants at low risk of dying. If the population were not high risk (ie, with a 0.04% risk of death, if

TABLE 4 Resulting Quality Adjusted Life Years (QALYs) Lost From RSV in US Infants Aged <8 Months Entering Their First RSV Season and Their Caregivers, Without and With Nirsevimab Among 50% of US Birth Cohort

	Adverse Events	Outpatient		ED		Inpatient		Deaths	Total		Grand Total
		Child	Caregiver	Child	Caregiver	Child	Caregiver	Child	Child	Caregiver	
Natural history	0 (0–0)	7153 (628–26 624)	3580 (213–17 252)	3290 (760–9012)	1645 (238–5543)	807 (127–2861)	320 (24–1352)	1356 (509–2717)	12 606 (4130–32 528)	5545 (1053–19 610)	18 151 (6844–42 113)
Nirsevimab to 50% of the birth cohort	52 (47–58)	6246 (548–23 313)	3127 (189–15 166)	2774 (636–7519)	1387 (198–4637)	565 (87–1983)	224 (17–949)	949 (350–1900)	10 586 (3317–27 793)	4738 (870–16 892)	15 324 (5569–36 362)
QALYs gained	−52 (−58 to −47)	906 (65–3663)	454 (23–2323)	516 (96–1555)	258 (31–946)	242 (38–885)	96 (7–424)	407 (148–862)	2020 (710–5012)	808 (156–2811)	2827 (1075–6578)

Negative numbers in the QALYs gained row indicate losses with the Nirsevimab arm as compared with natural history.

hospitalized), then the societal cost increased to $174 026 per QALY gained. In the second part of this scenario, we examined palivizumab use. If administering nirsevimab did not replace palivizumab (eg, in a population not initially eligible for palivizumab), then the cost rose to $193 310 per QALY gained. Finally, in the combined part of this scenario, if the population had low risk of mortality and would have never received palivizumab, then the cost for receiving nirsevimab was $217 584 per QALY gained. Additional scenarios related to the timing of administration of nirsevimab are shown in Supplemental Figs 9 and 10.

In the probabilistic sensitivity analysis of the primary analysis, we found 20% of simulations had an incremental cost of <$100 000 per QALY gained, 54% of simulations had an incremental cost of <$200 000 per QALY gained, and 97% had an incremental cost of <$500 000 per QALY gained (Supplemental Fig 11).

Finally, we examined a scenario where we assumed the pregnant mother had received an RSVpreF vaccine >14 days before delivery. In that scenario, the societal cost increased to $435 114 per QALY gained because the marginal benefit of adding nirsevimab protection above the existing RSVpreF protection was smaller (Supplemental Fig 12). However, the value of adding nirsevimab on top of RSVpreF protection varied by the month of birth of the child and the risk level of the child (Supplemental Fig 13).

DISCUSSION

Our analysis shows administering nirsevimab to infants <8 months of age before entering their first RSV season in the United States is expected to decrease RSV LRTI-associated medical events (ie, outpatient and ED patient visits, hospitalizations, and deaths) and could potentially be a cost-effective way to reduce RSV burden in infants in their first RSV season with a societal cost of $153 517 per QALY gained. The results of this analysis were incorporated into the ACIP's decisions for recommendations for infants and young children in their first RSV season.[8] Administering nirsevimab to all young children in their second season is unlikely to be cost-effective, but it may be cost-effective for certain young children at a significantly higher risk of severe outcomes from RSV (eg, chronic lung disease or severe immunocompromise). On the basis of these results and other data, the ACIP recommended nirsevimab for the second RSV season only in children who the American Academy of Pediatrics deems eligible for palivizumab in their second year of life.[8] ACIP also recommended nirsevimab for American Indian and Alaska Native children entering their second RSV season because of studies showing an increased risk of RSV hospitalization in this population.[6]

There are no other published cost-effectiveness studies on nirsevimab in US infants. However, another unpublished

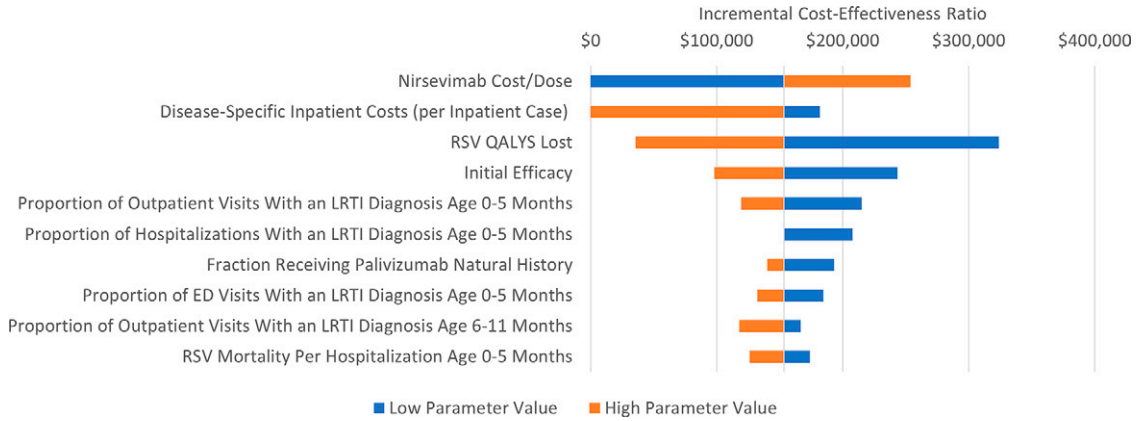

FIGURE 2

One-way sensitivity analysis. Note: The ICER measures the cost per QALY saved with nirsevimab use in US infants aged <8 months. The colored bars show how the ICER can change as the parameter assumptions change. This figure ranks parameters by their influence on the base case ICER. For example, if the inpatient costs associated with RSV are low (blue bar), then the ICER rises to $181 908 per QALY gained. If the initial efficacy high (orange bar), then the ICER drops such that using nirsevimab is cost-saving. Bars that go to 0 mean nirsevimab is cost-saving. "Fraction receiving palivizumab natural history" is the fraction of infants receiving palivizumab in the natural history arm. If many children are receiving expensive palivizumab in the natural history arm, there is a greater potential to avoid that expense if nirsevimab is used instead.

and manufacturer-sponsored cost-effectiveness analysis was also discussed and summarized for the ACIP's consideration in February 2023.[33] That analysis had similarities in modeling approach with our model, but came to the conclusion that nirsevimab had a societal cost of $70 430 per QALY gained. That analysis incorporated assumptions more favorable for nirsevimab cost-effectiveness compared with the analysis in our study. Higher incidence of hospitalization, much higher costs of hospitalization, and higher costs associated with outpatient visits were among the more influential assumptions.

The cost-effectiveness of administering nirsevimab to infants is sensitive to a variety of factors. The cost per dose of nirsevimab could be highly influential as to whether nirsevimab is cost-effective or not. Uncertainty in RSV-associated health care costs and quality-of-life remain sizable and highly correlated with nirsevimab cost-effectiveness. If RSV hospitalizations were more expensive, or if quality-of-life losses from RSV were higher, then nirsevimab may be more cost-effective.

Our results on the cost-effectiveness of administering nirsevimab to infants of vaccinated mothers should be interpreted with caution; the added protection of adding nirsevimab is unknown. Our base case ICER would apply to infants whose gestational parent was not vaccinated with RSVpreF within 14 days of delivery, and are given

FIGURE 3

Impact of varying nirsevimab cost per dose on the ICER for preventing RSV LRTI (base case) or when assuming equal efficacy also preventing RSV URTI (scenario). The dots represent the base case cost per dose of $445.

nirsevimab. However, our preliminary scenario analysis suggests that administering nirsevimab to infants whose mothers received RSVpreF vaccine ≥14 days before giving birth may be much less cost-effective than when administered to unvaccinated mothers, but potentially could be cost-effective if administered to the highest-risk populations, or if nirsevimab provides increased or longer protection against RSV-associated MA-LRTI. ACIP recommended that nirsevimab may be considered for infants born to vaccinated mothers if the health care provider assesses that additional protection is warranted because the infant is at substantial increased risk for severe RSV disease.

A natural question is how do nirsevimab and RSVpreF immunization compare when used alone. In our analysis of maternal RSVpreF immunization, we found ICERs of $163 513 per QALY saved when administered September through January or $396 280 when administered year-round, suggesting nirsevimab may be more cost-effective compared with maternal RSVpreF immunization alone;[10] however, differences in the trials may make the products difficult to directly compare.

There are several limitations to our analysis. Although in some scenarios we evaluate varying levels of hospitalization risks, our model structure does not include specific clinically-defined risk groups because of lack of available data. We also do not include any impact on reducing person-to-person transmission of RSV. If nirsevimab reduced RSV transmission (to other infants or to the elderly), nirsevimab might be more cost-effective. Although a theoretical model of RSV transmission suggests that vaccination of infants may reduce transmission to other groups,[34] that study is based on theoretical assumptions seldom supported by epidemiologic studies that trace RSV transmission, and we lack clinical evidence that nirsevimab (or future RSV vaccine products for these age groups) reduces transmission. In analyzing the cost-effectiveness of immunization in the second season for children at high risk, our assumption that risks of outpatient visits, ED visits, or deaths given hospitalization did not increase may underestimate costs and health outcomes for individuals with high-risk conditions, thus underestimating the value of nirsevimab immunization. Additional research on RSV disease transmission along with its medical costs, quality-of-life impact, as well as real-world performance of nirsevimab, may be helpful to better understand the health benefits and cost-effectiveness of nirsevimab.

CONCLUSIONS

Nirsevimab to prevent RSV MA-LRTI in infants and young children is likely to sizably decrease RSV disease burden. Although subject to key factors, nirsevimab could also be societally cost-effective for all infants entering the first RSV season, and in the second season for certain young children facing a greater risk of severe disease.

ABBREVIATIONS

ACIP: Advisory Committee on Immunization Practices
ED: emergency department
ICER: incremental cost-effectiveness ratio
LRTI: lower respiratory tract infection
MA: medically attended
QALY: quality-adjusted life year
URTI: upper respiratory tract infections

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REFERENCES

1. Bowser DM, Rowlands KR, Hariharan D, et al. Cost of respiratory syncytial virus infections in US infants: systematic literature review and analysis. *J Infect Dis*. 2022;226(Suppl 2): S225–S235
2. Hall CB, Weinberg GA, Iwane MK, et al. The burden of respiratory syncytial virus infection in young children. *N Engl J Med*. 2009;360(6):588–598
3. 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(3):284–286

4. Curns AT, Rha B, Lively JY, et al. Respiratory syncytial virus associated hospitalizations among children <5 years old: 2016 to 2020. *Pediatrics*. 2024;153(3):e2023062574

5. Hammitt LL, Dagan R, Yuan Y, et al. MELODY Study Group. Nirsevimab for prevention of RSV in healthy late-preterm and term infants. *N Engl J Med*. 2022;386(9):837–846

6. Jones J. Use of nirsevimab for the prevention of respiratory syncytial virus disease among infants and young children: recommendations of the Advisory Committee on Immunization Practices–United States, 2023. *MMWR Morb Mortal Wkly Rep*. 2023;72(34):920–925

7. Hamid S, Winn A, Parikh R, et al. Seasonality of respiratory syncytial virus–United States, 2017–2023. *MMWR Morb Mortal Wkly Rep*. 2023;72(14):355–361

8. Fleming-Dutra KE, Jones JM, Roper LE, et al. Use of the Pfizer respiratory syncytial virus vaccine during pregnancy for the prevention of respiratory syncytial virus–associated lower respiratory tract disease in infants: recommendations of the Advisory Committee on Immunization Practices–United States, 2023. *MMWR Morb Mortal Wkly Rep*. 2023;72(41):1115–1122

9. Centers for Disease Control and Prevention. ACIP presentation slides: August 3, 2023 meeting. Available at: https://www.cdc.gov/vaccines/acip/meetings/slides-2023-08-3.html. Published 2023. Accessed November 11, 2023

10. Hutton DW, Prosser LA, Rose AM, et al. Cost effectiveness of maternal vaccination to prevent respiratory syncytial virus illness. *Pediatrics*. 2024;154(6):e2024066481

11. 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(2):251–257

12. Jackson ML, Scott E, Kuypers J, Nalla AK, Roychoudury P, Chu HY. Epidemiology of respiratory syncytial virus across 5 influenza seasons among adults and children 1 year of age and older-Washington state, 2011/2012–2015/2016. *J Infect Dis*. 2021;223(1):147–156

13. Doucette A, Jiang X, Fryzek J, Coalson J, McLaurin K, Ambrose CS. Trends in respiratory syncytial virus and bronchiolitis hospitalization rates in high-risk infants in a United States nationally representative database, 1997–2012. *PLoS One*. 2016;11(4):e0152208

14. Gupta P, Beam BW, Rettiganti M. Temporal trends of respiratory syncytial virus-associated hospital and ICU admissions across the United States. *Pediatr Crit Care Med*. 2016;17(8):e343–e351

15. 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(2):e220527

16. AstraZeneca and Sanofi. Nirsevimab for the prevention of RSV in all infants. ACIP presentation, October 2022. Available at: https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2022-10-19-20/02-RSV-Mat-Ped-Felter-508.pdf. Accessed October 12, 2023

17. Prosser LA, Bridges CB, Uyeki TM, et al. Health benefits, risks, and cost-effectiveness of influenza vaccination of children. *Emerg Infect Dis*. 2006;12(10):1548–1558

18. Centers for Disease Control and Prevention. CDC vaccine price list. Available at: https://www.cdc.gov/vaccines/programs/vfc/awardees/vaccine-management/price-list/index.html#adult. Accessed December 10, 2023

19. Centers for Disease Control and Prevention. NVSS–birth data. Available at: https://www.cdc.gov/nchs/nvss/births.htm. Accessed June 5, 2024

20. Whitney CG, Zhou F, Singleton J, Schuchat A. Centers for Disease Control and Prevention. Benefits from immunization during the vaccines for children program era–United States, 1994–2013. *MMWR Morb Mortal Wkly Rep*. 2014;63(16):352–355

21. Stoecker C, Hampton LM, Link-Gelles R, Messonnier ML, Zhou F, Moore MR. Cost-effectiveness of using 2 versus 3 primary doses of 13-valent pneumococcal conjugate vaccine. *Pediatrics*. 2013;132(2):e324–e332

22. DeLuca EK, Gebremariam A, Rose A, Biggerstaff M, Meltzer MI, Prosser LA. Cost-effectiveness of routine annual influenza vaccination by age and risk status. *Vaccine*. 2023;41(29):4239–4248

23. Grosse SD, Krueger KV, Pike J. Estimated annual and lifetime labor productivity in the United States, 2016: implications for economic evaluations. *J Med Econ*. 2019;22(6):501–508

24. Fragaszy EB, Warren-Gash C, White PJ, et al. Flu Watch Group. Effects of seasonal and pandemic influenza on health-related quality of life, work and school absence in England: results from the Flu Watch cohort study. *Influenza Other Respir Viruses*. 2018;12(1):171–182

25. Petrie JG, Cheng C, Malosh RE, et al. Illness severity and work productivity loss among working adults with medically attended acute respiratory illnesses: US Influenza Vaccine Effectiveness Network 2012-2013. *Clin Infect Dis*. 2016;62(4):448–455

26. Van Wormer JJ, King JP, Gajewski A, McLean HQ, Belongia EA. Influenza and workplace productivity loss in working adults. *J Occup Environ Med*. 2017;59(12):1135–1139

27. Glaser EL, Hariharan D, Bowser DM, et al. Impact of respiratory syncytial virus on child, caregiver, and family quality of life in the United States: systematic literature review and analysis. *J Infect Dis*. 2022;226(Suppl 2):S236–S245

28. Régnier SA. Respiratory syncytial virus immunization program for the United States: impact of performance determinants of a theoretical vaccine. *Vaccine*. 2013;31(40):4347–4354

29. Cohen J. Two new medicines may curb serious respiratory disease in infants. Available at: https://www.science.org/content/article/two-new-medicines-may-curb-serious-respiratory-disease-infants. Accessed February 15, 2024

30. Domachowske J, Madhi SA, Simões EAF, et al. MEDLEY Study Group. Safety of nirsevimab for RSV in infants with heart or lung disease or prematurity. *N Engl J Med*. 2022;386(9):892–894

31. Wilkins D, Hamrén UW, Chang Y, et al. 1934. Nirsevimab is associated with higher and more sustained RSV neutralizing antibody responses compared with standard of care palivizumab: observations from a 2: 1 randomized, phase 2/3 trial in medically vulnerable children (MEDLEY). [Published online November 27, 2023] *Open Forum Infectious Diseases*. 2023;10(Suppl_2):ofad500.2465

32. Ortega-Sanchez IR. Economics of preventing respiratory syncytial virus lower respiratory tract infections (RSVLRTI) among US infants with nirsevimab. Available at: https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-02/slides-02-23/rsv-pediatric-03-sanchez-508.pdf. Published 2023. Updated February 23, 2023. Accessed November 13, 2023

33. Yamin D, Jones FK, DeVincenzo JP, et al. Vaccination strategies against respiratory syncytial virus. *Proc Natl Acad Sci U S A.* 2016;113(46):13239–13244

34. Werner EF, Hauspurg AK, Rouse D, et al. A cost–benefit analysis of low dose aspirin prophylaxis for the prevention of preeclampsia in the United States. *Obstet Gynecol.* 2015;126(6):1242–1250

35. Petrini JR, Dias T, McCormick MC, Massolo ML, Green MS, Escobar GJ. Increased risk of adverse neurological development for late preterm infants. *The Journal of Pediatrics.* 2009;154(2):169–176.e163

36. Hirvonen M, ojala R, Korhonen P, Haataja P, Eriksson K, Gissler M, et al. Cerebral Palsy Among Children Born Moderately and Late Preterm. *Pediatrics.* 2014;134(6):e1584–e1593

37. Crump C, Sundquist J, Sundquist K. Preterm or early term birth and risk of autism. *Pediatrics.* 2021;148(3):e2020032300

38. Darcy Mahoney A, Minter B, Higgins M, Guo Y, Williams B, Williams LMH, et al. Probability of an autism diagnosis by gestational age. *Newborn and Infant Nursing Reviews.* 2016;16(4):322–326

39. Carroll AE, Downs SM. Improving decision analyses: parent preferences (utility values) for pediatric health outcomes. *The Journal of pediatrics* 2009;155(1):21–25.e25

40. Payakachat N, Tilford JM, Kuhlthau JP, Kovacs E, Bellando J, et al. Predicting health utilities for children with autism spectrum disorders. *Autism Res.* 2014;7(6):649–663

41. Ray KN, Chari AV, Engberg J, Bertolet M, Mehrotra A. Opportunity costs of ambulatory medical care in the United States. *Am J Manag Care.* 2015;21(8):567–574

42. Shimabukuro TT, Cole M, Su JR. Reports of anaphylaxis after receipt of mRNA COVID-19 vaccines in the United States–December 14, 2020–January 18, 2021. *JAMA.* 2021;325(11):1101–1102

43. Sanofi. Nirsevimab: aiming for RSV prophylaxis for all infants. Available at: https://www.sanofi.com/assets/dotcom/content-app/events/investor-presentation/2020/R-D-DAYS-5-5–Nirsevimab-R-D-investor-event/2020_07_30_Nirsevimab_slides_website.pdf. Accessed November 13, 2023

44. Sobi. Annual and sustainability report 2021. Available at: https://www.sobi.com/en/financial-reports/annual-and-sustainability-report-2021. Published 2020. Accessed November 13, 2023

45. Shahabi A, Peneva D, Incerti D, McLaurin K, Stevens W. Assessing variation in the cost of palivizumab for respiratory syncytial virus prevention in preterm infants. *Pharmacoecon Open.* 2018;2(1):53–61

46. Bowser DM, Rowlands KR, Hariharan D, et al. Cost of respiratory syncytial virus infections in US infants: systematic literature review and analysis. *J Infect Dis.* 2022;226(Suppl 2):S225–S235

47. Arias E, Xu J, National Center for Health Statistics. United States life tables, 2020. *National Vital Statistics Reports.* 2022;71(1):1–63