HUMAN VACCINES & IMMUNOTHERAPEUTICS
2025, VOL. 21, NO. 1, 2480875
https://doi.org/10.1080/21645515.2025.2480875

Taylor & Francis
Taylor & Francis Group

RESEARCH ARTICLE

OPEN ACCESS Check for updates

Health economic evaluation of implementing a universal immunization program with nirsevimab compared to standard of care for the prevention of respiratory syncytial virus disease in Canadian infants

Thomas Shin[a,b], Jason Kh Lee[a,c]*, Alexia Kieffer[a], Michael Greenberg[a], and Jianhong Wu[b]

[a]Medical Affairs, Sanofi, US; [b]Department of Mathematics and Statistics, York University, Toronto, ON, Canada; [c]Leslie Dan School of Pharmacy, University of Toronto, Toronto, ON, Canada

ABSTRACT

Respiratory syncytial virus (RSV) is a highly contagious pathogen and a leading cause of severe lower respiratory tract illness (LRTI) in infants and young children, irrespective of risk factors. Nirsevimab, an extended half-life monoclonal antibody, was approved in Canada in 2023 as a passive immunizing agent for the prevention of RSV LRTI. This study evaluated the optimal price per dose (PPD) at commonly accepted willingness-to-pay (WTP) thresholds among Canadian infants compared to the current standard of care (i.e. palivizumab for preterm infants and those with specific medical conditions). A static decision tree model was developed to assess the impact of nirsevimab on RSV-related health and economic outcomes among Canadian infants – including outpatient physician and emergency department visits, inpatient hospitalizations including intensive care unit (ICU) admissions and mechanical ventilation, and the associated healthcare costs of these outcomes. The model utilized Canadian epidemiological and cost inputs where possible, adopting a societal perspective. Compared to the standard of care, nirsevimab was expected to prevent 47,609 RSV-related health events, including 2,296 hospitalizations and a reduction of approximately $45 million in direct healthcare costs. At a WTP threshold of $50,000 per quality-adjusted life-year (QALY), the estimated base case PPD was $536, based on average cost assumptions across several costing scenarios. These findings suggest that universal immunization with nirsevimab could significantly reduce the health and economic burden of RSV among Canadian Infants.

ARTICLE HISTORY
Received 28 March 2024
Revised 26 February 2025
Accepted 8 March 2025

KEYWORDS
Respiratory syncytial virus (RSV); nirsevimab; infants; Canada; cost-effectiveness; health economics; vaccine

Introduction

Respiratory syncytial virus (RSV) is a highly contagious seasonal pathogen and a leading cause of medically attended lower respiratory tract illness (MA-LRTI) in infants.[1,2] While typically mild, RSV can progress to bronchiolitis and pneumonia, particularly in vulnerable populations such as infants and young children.[3,4] In Canada, RSV is the primary cause of hospitalization among children under two, with 80% of cases occurring in full-term infants without underlying conditions.[5,6] Although preterm infants, especially those with congenital or chronic health conditions, are at the highest risk for RSV MA-LRTI, healthy full-term infants bear the most significant disease burden due to their larger population size.[7] Early RSV infection has also been linked to long-term respiratory issues, including recurrent wheezing and asthma.[8] Nearly all children contract RSV by age two, and the highest risk of severe disease occurs during their first RSV season.[9,10] Given its high prevalence, severity, and potential long-term impact, effective prevention is critical.

Until recently, palivizumab (Synagis®, AstraZeneca) was the only available RSV prophylaxis, limited to high-risk infants.[11] Nirsevimab (Beyfortus®, Sanofi), an extended half-life monoclonal antibody, was developed to protect all infants from RSV disease. It neutralizes RSV by binding to the fusion protein, preventing viral entry.[12] Clinical trials and real-world studies have shown that nirsevimab significantly reduces RSV-related hospitalizations and severe LRTI.[13–15] Griffin et al. reported that, among healthy preterm infants (29–34 weeks gestation), nirsevimab reduced RSV MA-LRTI by 70.1% (95% CI: 52.3%, 81.2%) and RSV LRTI hospitalizations by 78.4% (95% CI: 51.9%, 90.3%).[14] Hammitt et al. found 74.5% efficacy (95% CI: 49.6%, 87.1%) against MA-LRTI in late preterm and term infants (≥35 weeks gestation).[13] Post-pandemic follow-up demonstrated continued efficacy: 76.4% (95% CI: 62.3%, 85.2%) for MA-LRTI, 76.8% (95% CI: 49.4%, 89.4%) for hospitalizations, and 78.6% (95% CI: 48.8%, 91%) for severe MA-LRTI.[16] A European pragmatic trial reported 83.2% efficacy (95% CI: 67.8%, 92%) against RSV LRTI hospitalizations.[15] Since 2023, real-world studies from France, Spain, and the US have reinforced these findings.[17–25]

In Canada, the National Advisory Committee on Immunization (NACI) recommended building toward a universal RSV immunization program for all infants.[26] Note that the recommendation is to build towards universal programs based on supply, cost effectiveness and affordability. The recommendation over RSVpreF was based on efficacy, safety and duration of protection.[26] Similarly, the US Advisory Committee on Immunization Practices (ACIP)

CONTACT Thomas Shin thomas.shin@sanofi.com Medical Affairs, Sanofi, 1755 Steeles Ave W, North York, ON M2R 3T4, Canada.
*Jason KH Lee is a co-first author.

recommended nirsevimab for all infants <8 months and high-risk infants 8–19 months entering their second RSV season.[27]

Given RSV's burden and seasonality, evaluating cost-effectiveness across implementation strategies is essential. This study employed an externally validated economic model to compare nirsevimab to the standard of care in Canada, estimating the optimized price per dose (PPD) based on willingness-to-pay (WTP) thresholds for reducing medically attended RSV infections and hospitalizations.

Methods

Overview

A static decision tree model of the Canadian infant birth cohort is split into three subgroups based on risks for severe RSV disease: 1) palivizumab-eligible infants (as defined by Canadian-specific criteria;[28] see Appendix Figure A1); 2) preterm infants (born between 29 weeks gestational age (wGA) and 34 weeks 6 days GA, not eligible for palivizumab; 3) term or late preterm infants (≥35 wGA). Based on Canadian RSV surveillance data, the RSV season was assumed to increase in activity from November to the end of the following March.[26] In the base case scenario, all infants born outside and inside the RSV season were administered nirsevimab during their first RSV season in the treatment arm, with a portion of preterm infants who remained at increased risk of RSV receiving follow-up treatment in the subsequent season. The comparator arm was the standard of care (i.e., palivizumab), which only applied to a small proportion of infants meeting Canada's strict eligibility criteria.[28] The model simulated the patient trajectory of RSV infection with health outcomes, including RSV-related hospitalization, intensive care admission (ICU), mechanical ventilation (MV), emergency room and general practitioner admissions (ER, GP), and RSV-related mortality. Direct and indirect costs associated with RSV MA-LRTI were integrated into the model, adopting a societal perspective. All mortality-related costs and outcomes were discounted at a rate of 1.5%, as recommended by national guidelines.[29]

The model integrated the following elements: population data (segmented by palivizumab-eligible, preterm, and term infants), seasonality of RSV, coverage and adherence rates, clinical profiles of therapies, RSV-related health outcomes (e.g., hospitalization, ICU, MV), outcome-related utility values, and outcome-specific costs. To accurately model RSV seasonality, subgroup-specific nirsevimab implementation scenarios (e.g., in-season and out-of-season births, stratified by palivizumab eligibility, preterm, and term status), and price-per-dose estimates, the economic model incorporated granular monthly data inputs. These inputs included birth rates, RSV infection probabilities, and RSV-related health outcomes. A comprehensive list of model parameters is provided in Table 1.

Health outcome parameters

The gray and peer-reviewed literature was systematically reviewed to identify ongoing and completed health economic, clinical, and epidemiological studies related to RSV and palivizumab. Population-based data, with the subgroups of interest and the monthly probability of infection, were derived from national statistics and surveillance data.[30,32] All inputs for nirsevimab were derived from clinical and epidemiological studies, while the gray literature provided insights into palivizumab's cost and clinical profile.[13,14,16,28,45] Where possible, only up-to-date Canadian inputs were utilized to populate the model; however, in the complete absence of such data, US-specific inputs were adopted (e.g. data related to RSV-specific QALY loss and mortality outcomes). Data associated with RSV-related inpatient hospitalization, ICU admissions, and patients requiring MV were generated per infant subgroup, using a combination of average Canadian inputs and distributions of monthly US data (0–36 months age of infection). Importantly, ICU and MV admissions were modeled as conditional fractions of overall hospitalizations rather than applied to the entire population, ensuring internal consistency in healthcare utilization estimates. This distinction is further illustrated in Table 5, where total inpatient hospitalizations encompass ICU and MV cases, which are also separately delineated for clarity. Informed by expert opinion, we assumed US-based monthly distributions as an acceptable proxy for generating "Canadianized" values per subgroup. Figure 1 illustrates the distributional conversion formula for generating Canadian values, utilizing an average of Canadian-specific inputs (see Table 2). Furthermore, for ER and primary care admissions, US-based monthly percentages (0–36 months age of infection) were utilized without monthly data for Canada.[23] RSV-related input parameters are provided in Tables 1 and 2.

Economic parameters

All costs are outlined in Table 3 with inflation adjustments using the Canadian Consumer Price Index (CPI) and adjusted to 2023 Canadian dollars. Although the model adopts a national scope, most RSV-specific costs within the past 5 years were from Ontario, Alberta, and Quebec-specific peer-reviewed sources attributed to availability.[46–56] Furthermore, gray literature on the cost-effectiveness and recommended use of palivizumab provided overall support for model parametrization.[28,45] Direct healthcare costs per RSV-related health outcome required the establishment of a costing matrix with an average cost per health outcome by subgroup (i.e. palivizumab-eligible, preterm, and term infants). ER, GP, and direct non-medical costs per hospitalization (i.e., travel, meals, childcare, and out-of-pocket expenses attributed to RSV-related hospitalization) were assumed to be uniform across subgroups and remained constant regardless of scenario analysis. In contrast, inpatient hospitalization, ICU, and MV costs required calculations based on different sources. The primary costing scenario (S_0) was used for base case modeling; intended to represent a broader Canadian costing perspective, it was generated by averaging all costing scenarios (S1a, S1b, S2, S3, and S4, as described below). For the majority of the scenarios, the distribution of costs per subgroup was derived by McLaurin et al.[52] For Scenario S1a and S1b, the recent Canadian literature from Rafferty et al. provided average RSV-attributable lab-confirmed hospitalization costs within 30 days and 365 days post-diagnosis by age group.[47] Utilizing matrix algebra, the case-weighted cost for infants <1 year was applied to the distribution from McLaurin et al.'s study to establish

Table 1. Key model inputs.

Parameter	Input	Range	Source
Population			
Total annual births in Canada	367,684	–	Statistics Canada[30]
Estimated number of PVZ-eligible infants	6,711 (1.83%)	–	Calculations based on Statistics Canada[30] and IQVIA[31]
Estimated number of preterm infants (<37 wGA)	22,497 (6.12%)	–	Calculation based on Statistics Canada[30]
Estimated number of term infants (≥37 wGA)	338,476 (92.06%)	–	Calculation based on Statistics Canada[30]
Percent of first-dose PVZ-eligible recipients who may require a subsequent dose in their 2nd RSV season due to elevated risk of severe RSV	10%	–	Expert opinion
Seasonality of Disease			
April	7.81%	–	Public Health Agency of Canada[32]
May	3.32%	–	
June	1.70%	–	
July	0.58%	–	
August	0.75%	–	
September	2.33%	–	
October	5.20%	–	
November	6.76%	–	
December	17.37%	–	
January	21.40%	–	
February	18.23%	–	
March	14.56%	–	
Clinical Profile			
Nirsevimab duration of protection	5 months	–	Griffin et al.[14] Hammitt et al.[13] Muller et al.[16] Drysdale et al.[15]
Efficacy of nirsevimab among PVZ-eligible preterm infants (inpatient and outpatient)[1]	51%	–	Andabaka et al.[33]
Efficacy of nirsevimab among preterm infants (inpatient and outpatient)	83.2%, 86.2%[3]	–	Drysdale et al.[15] FDA (2023)[34]
Efficacy of nirsevimab among term infants (inpatient and outpatient)	83.2%, 74.5%[4]		Drysdale et al.[15] Hammitt et al.[13]
Efficacy of PVZ	51%	–	Andabaka et al.[33]
First and second-season coverage rate of PVZ among PVZ-eligible preterm infants	81%, 10%	–	Chan et al.[35] Butt et al.[36] modified with expert opinion (second season coverage)
First and second-season coverage rate of nirsevimab among PVZ-eligible preterm infants	81%, 10%	–	Assumption based on palivizumab
First season coverage rate for nirsevimab among preterm and term infants[2]	80%	–	Assumption
All-cause mortality among infants by age (per 1000)			
0–5 months	0.004		Statistics Canada[37]
6–11 months	0.0003		Statistics Canada[37]
12–59 months	0.0002		Statistics Canada[38]
Overall risk of RSV-related mortality			
Preterm infants (including those PVZ-eligible)	0.03%		NACI[28]
Term infants	0.0024%		Hansen et al.[39]
Lifetime QALY loss per RSV event			
Inpatient hospitalizations	0.017	0.0101–0.0726	Hutton et al.[40]
ICU admission	0.017	0.0101–0.0726	
Mechanical ventilation (MV)	0.017	0.0101–0.0726	
Emergency room (ER) visit	0.0134	0.0079–0.0455	
Primary care (GP) visit	0.0085	0.0049–0.0455	
Parent/caregiver QALY loss	0.005		
Lifetime QALY loss with Premature Death			
PVZ-eligible, preterm, and term infants	41.697	–	Calculation based on Guertin et al.[41] Statistics Canada,[42] and Hodgson et al.[43]
Discount rate	1.5%	–	CADTH[44]

[1]PVZ refers to palivizumab; In the absence of published evidence, we assumed nirsevimab was equal in efficacy to palivizumab.
[2]Assumption that first season coverage of nirsevimab among healthy preterm and term infants would mirror palivizumab given the current national recommendations for nirsevimab.
[3]The efficacy of nirsevimab in preterm infants was sourced from a post-hoc analysis of all randomized infants in phase 2b weighing <5 kg at baseline and who received the recommended dose of nirsevimab. The results for Trial 03, 70.1%, were not dose-optimized based on weight-band dosing (<5 kg vs ≥5 kg). If we considered weight-band dosing for those <5 kg (50 mg dose), which was the proposed dose subpopulation (i.e. 50 mg dose), the efficacy of MA-RSV-LRTI was 86.2%.
[4]Efficacy based on primary endpoint – medically attended lower respiratory tract infection 150 days after injection.

values within the costing matrix S1a and S1b.[52] In Scenario 2 (S2), cost outcomes were based on Thampi et al. (2021), with cost differentials between palivizumab-eligible, preterm, and term infants but not across the different health outcomes (e.g., inpatient hospitalization, ICU, MV).[46] Scenario 3 (S3), derived inputs from Buchan et al. (2019), applied a similar costing approach as S2.[47] Scenario 4 (S4) utilized the detailed costs from Papenberg et al. (2020)'s study, where direct and indirect RSV-related costs were sourced from multiple Quebec-specific resources (e.g. the Quebec government's health insurance board Régie de l'assurance maladie du Québec [RAMQ], McGill University Health Centre).[48]

$$HI_{i,j} = \alpha\left(\frac{X_i}{\bar{X}_i}\right) * \left(\frac{X_i}{Z_i}\right)$$

$Let\ X = palivizumab - eligible\ infants; Y = preterm\ infants;$
$Z = term\ infants\ (point\ of\ reference)$

$HI_{i,j}$: $Canadian\ health\ input\ (e.g. inpatient\ hospitalization)\ for\ infant\ subgroup\ i\ and\ age\ at\ time\ of\ infection\ j$
α: $Canadian\ modification\ value$
X_i: $Infant\ subgroup\ X\ (e.g. palivizumab - eligible\ infants) for\ age\ at\ time\ of\ infection\ i$
$\bar{X}$: $Average\ \%\ of\ health\ input\ for\ infant\ subgroup\ X\ (e.g. palivizumab - eligible\ infants)$
Z_i: $Point\ of\ reference\ infant\ subgroup\ (i.e. term\ infants)\ for\ age\ at\ time\ of\ infection\ i$

Figure 1. Modification formula for health-related inputs. The formula in Figure 1 was constructed to utilize average Canadian values and generate data points specific to health outcome, age of infection, and sub-group of interest, assuming a similar distribution of cases to the United States.

Table 2. Health-related inputs.

Inpatient hospitalization				
Age at time of infection (months)	PVZ-eligible infants	Preterm infants	Term Infants	Source
0	13.18%	3.32%	1.89%	Feltes et al.[49]
1	25.28%	6.37%	3.63%	Hall et al.[50]
2	13.96%	3.52%	2.00%	IMPACT RSV Study Group[51]
3	10.05%	2.53%	1.44%	McLaurin et al.[52]
4	8.69%	2.19%	1.25%	Schanzer et al.[5]
5	4.68%	1.18%	0.67%	
6	4.00%	1.01%	0.57%	
7	5.47%	1.38%	0.78%	
8	3.32%	0.84%	0.48%	
9	3.71%	0.93%	0.53%	
10	3.61%	0.91%	0.52%	
11	2.83%	0.71%	0.41%	
12–24	2.50%	0.59%	0.20%	
25–36	2.50%	0.59%	0.20%	
Mean	7.41%	1.86%	1.04%	
Intensive Care Unit (ICU)				
0	43.36%	60.35%	18.81%	Arriola et al.[53]
1	43.36%	60.35%	18.81%	Mitchell et al.[54]
2	43.36%	60.35%	18.81%	
3	19.66%	15.43%	13.95%	
4	19.66%	15.43%	13.95%	
5	19.66%	15.43%	13.95%	
6	11.42%	9.28%	10.31%	
7	11.42%	9.28%	10.31%	
8	11.42%	9.28%	10.31%	
9	11.42%	9.28%	10.31%	
10	11.42%	9.28%	10.31%	
11	11.42%	9.28%	10.31%	
12–24	18.67%	31.26%	10.92%	
25–36	18.67%	31.26%	10.92%	
Mean	21.06%	24.68%	13.00%	
Mechanical Ventilation (MV)				
0	14.62%	22.20%	8.20%	Arriola et al.[53]
1	14.62%	22.20%	8.20%	Buchan et al.[47]
2	14.62%	22.20%	8.20%	
3	5.69%	6.80%	1.82%	
4	5.69%	6.80%	1.82%	
5	5.69%	6.80%	1.82%	
6	5.69%	4.72%	1.82%	
7	5.69%	4.72%	1.82%	
8	5.69%	4.72%	1.82%	
9	5.69%	4.72%	1.82%	
10	5.69%	4.72%	1.82%	
11	5.69%	4.72%	1.82%	
12–24	1.37%	1.13%	2.73%	
25–30	1.37%	1.13%	2.73%	
Mean	6.99%	8.40%	3.32%	

(*Continued*)

Table 2. (Continued).

Inpatient hospitalization				
Age at time of infection (months)	PVZ-eligible infants	Preterm infants	Term Infants	Source
Emergency Room (ER)				
0	1.96%	1.96%	1.96%	Lively et al.[55]
1	6.42%	6.42%	6.42%	
2	7.24%	7.24%	7.24%	
3	10.52%	10.52%	10.52%	
4	11.60%	11.60%	11.60%	
5	7.13%	7.13%	7.13%	
6	8.18%	8.18%	8.18%	
7	5.61%	5.61%	5.61%	
8	5.56%	5.56%	5.56%	
9	5.56%	5.56%	5.56%	
10	4.04%	4.04%	4.04%	
11	5.56%	5.56%	5.56%	
12–24	5.30%	5.30%	5.30%	
25–36	5.30%	5.30%	5.30%	
Mean	6.43%	6.43%	6.43%	
Primary Care (GP)				
0	8.52%	8.52%	8.52%	Lively et al.[55]
1	18.79%	18.79%	18.79%	
2	23.42%	23.42%	23.42%	
3	23.26%	23.26%	23.26%	
4	26.50%	26.50%	26.50%	
5	28.92%	28.92%	28.92%	
6	26.47%	26.47%	26.47%	
7	20.72%	20.72%	20.72%	
8	27.78%	27.78%	27.78%	
9	22.72%	22.72%	22.72%	
10	24.17%	24.17%	24.17%	
11	25.81%	25.81%	25.81%	
12–24	18.03%	18.03%	18.03%	
25–36	18.03%	18.03%	18.03%	
Mean	22.37%	22.37%	22.37%	

Abbreviation PVZ: palivizumab.

Costing scenarios

The price per dose optimization scenarios were based on four WTP thresholds (incremental cost per quality-adjusted life years [QALY]) of $40,000, $50,000, $70,000, and $100,000 per QALY, which represent the commonly accepted thresholds by North American health technology assessment (HTA) bodies, such as Canada's Drug and Technology Agency (CADTH), Institut national d'excellence en santé en services sociaux (INESSS), National Advisory Committee of Immunization (NACI), and Institute for Clinical and Economic Review (ICER).[29,44,57,58] The primary costing scenario (S_0) attempted to represent a pan-Canadian perspective by averaging the costing matrices of all scenarios. Scenarios S1a and S1b utilized the average RSV-attributable lab-confirmed hospitalization costs within 30 days and 365 days (for those <1 year of age), which we applied to the costing matrix provided by McLaurin et al. (see Figure 2). Two additional scenarios (S2, S3) derived inputs from Ontario-specific sources with no assumptions regarding the underlying cost distributions.[46,47] In S2, costs were derived from Ontario's RSV-focused population-based match cohort study.[46] Costs for inpatient hospitalization, ICU, and MV among the preterm infants eligible for palivizumab were calculated based on the weighted mean adjusted costs for congenital heart disease (CHD), hemodynamically significant CHD, congenital lung disease (CLD), and birth between 22 and 28 wGA. Similar calculations were applied to preterm infants (29–35 wGA) and term infants (36–43 wGA or full-term with no comorbidities). Relative to the S_0, S1a, S1b, and S2, the Ontario-based costing data in S3 was less granular, providing two average costs for young children ≤59 months with and without ≥1 comorbidity.[47] S4 was based on Quebec-specific data providing the granular hospitalization costs attributed to RSV (e.g. pediatric unit, perinatal ICU, neonatal ICU, short-stay unit, ER) across a wide scope of cost outcomes ranging from hospital stay, administration, procedural, specialist, hospital discharge, outpatient resource use, productivity, and out-of-pocket auxiliary costs.[48]

Implementation scenarios

For all costing scenarios (S_0, S1a, S1b, S2, S3, S4), analyses were conducted to explore the price per dose contingent on the scope of program implementation. The scope included four implementation scenarios: 1) all infants (i.e. palivizumab-eligible, preterm, and term) born within and outside of the RSV season (base case scenario); 2) palivizumab-eligible and preterm infants born within and outside of the RSV season (with the exclusion of term infants); 3) palivizumab-eligible and preterm infants born within and outside of the RSV season, and term infants 0–3 months entering their first RSV season and born during the RSV season; and 4) palivizumab-eligible and preterm infants born within and outside of the RSV season with term infants born during the RSV season (Figure 3).

Table 3. Cost-related inputs.

Direct Costs[1]					
		Average cost per event (CAD)			
Health Outcomes	Scenarios	PVZ-eligible infants	Preterm infants	Term infants	Source[1]
ER visits	All scenarios		$836		Weighted average costs based on Thampi et al.[46] and Papenburg et al.[48]
Primary care (GP) visits	All scenarios		$94		Papenburg et al.[48]
Direct non-medical costs per inpatient hospitalization	All scenarios	$652	$652	$220	Papenburg et al.[48]
Inpatient hospitalization	S_0[2]	$24,310	$11,380	$8,134	Rafferty et al.[56]
ICU admission		$48,301	$27,661	$21,238	Thampi et al.[46]
Mechanical ventilation		$130,943	$98,165	$40,601	Buchan et al.[47] Papenberg et al.[48]
Inpatient hospitalization	S1a[2]	$25,918	$8,374	$5,968	Rafferty et al.[56]
ICU admission		$54,693	$24,381	$23,326	
Mechanical ventilation		$89,667	$39,251	$49,039	
Inpatient hospitalization	S1b[2]	$52,333	$16,908	$12,050	
ICU admission		$110,434	$49,229	$47,100	
Mechanical ventilation		$181,052	$79,254	$99,018	
Inpatient hospitalization	S2	$25,529	$13,848	$9,462	Thampi et al.[46]
ICU admission		$25,529	$13,848	$9,462	
Mechanical ventilation		$25,529	$13,848	$9,462	
Inpatient hospitalization	S3	$9,268	$9,268	$6,104	Buchan et al.[47]
ICU admission		$9,268	$9,268	$6,104	
Mechanical ventilation		$9,268	$9,268	$6,104	
Inpatient hospitalization	S4	$8,503	$8,503	$7,086	Papenberg et al.[48]
ICU admission		$41,581	$41,581	$20,196	
Mechanical ventilation		$349,202	$349,202	$39,384	
Cost of Prophylaxis					
PVZ	All scenarios		$1,599		NACI[28]
Indirect Costs					
Average hourly earnings of all employees	All scenarios		$25.39		Papenburg et al.[48]
Number of hours per workday	All scenarios		8 hours		Mitchell et al.[54]
Lost days per RSV episode (Inpatient)	All scenarios	5.35 days		2.56 days	Mitchell et al.[54]
Lost days per RSV episode (Outpatient)	All scenarios	1.30 days		1.40 days	Papenburg et al.[48]

Abbreviation PVZ: palivizumab.
[1]All costs from each source were adjusted for inflation to 2023 based on the latest consumer price index (CPI).
[2]S1a, S1b costing matrix was modeled based on the cost distribution from McLaurin et al.[52] For S1a, the average case-weighted within 30 day RSV-attributable cost was $14,138 (6% CPI adjusted) for infants <1 year of age. For S1b, the average case-weighted within 365 day RSV-attributable cost was $28,546 (6% CPI adjusted) for infants <1 year of age. For each scenario, the average case-weighted costs were used to generate the costing matrix according to McLaurin et al.[52]

$$Modifier\ \mathrm{M} = \frac{\sum \Theta_{ij}\,\mu}{\sum_{ij} X_{ij} Y_{ij}}$$

$$Cost\ Input_{ij} = \mathrm{M} * Y_{ij}$$

i: $subgroup\ (i.e.\ high-risk\ palivizumab-eligible, preterm, term)$
j: $health\ outcome\ (i.e.\ inpatient\ hospitalization, ICU, mechanical\ ventilation)$
X: $total\ number\ of\ in-season\ and\ out-season\ cases\ generated\ by\ the\ static\ model$
Y: $multiplier\ (reference)\ values\ based\ on\ the\ US\ costing\ distribution\ matrix$
Θ: $Case\ counts\ of\ healthcare\ utilization$
μ: $Average, median, or\ midpoint\ values\ derived\ from\ the\ Canadian\ literature$

Figure 2. Modification formula for cost-related inputs [scenarios S1a, S1b based on Rafferty et al. (2023)]. The formula in Figure 2 was constructed to utilize existing aggregate Canadian costs and generate specific outcome and sub-group specific costing data for RSV-related hospitalization, ICU admission, and mechanical ventilation, assuming a similar distribution of costs to the United States.

Deterministic sensitivity analyses

A univariate sensitivity analysis was conducted to understand which variables significantly impacted the price per dose. The lower and upper bounds from the 95% confidence intervals (CI) were used where available; alternatively, we utilized a variance of ± 20%.

Results

Clinical and cost impact

The burden of RSV MA-LRTIs on Canadian infants under the current standard of care is estimated to be 184,432 cases annually, including 138,981 primary care and 40,254

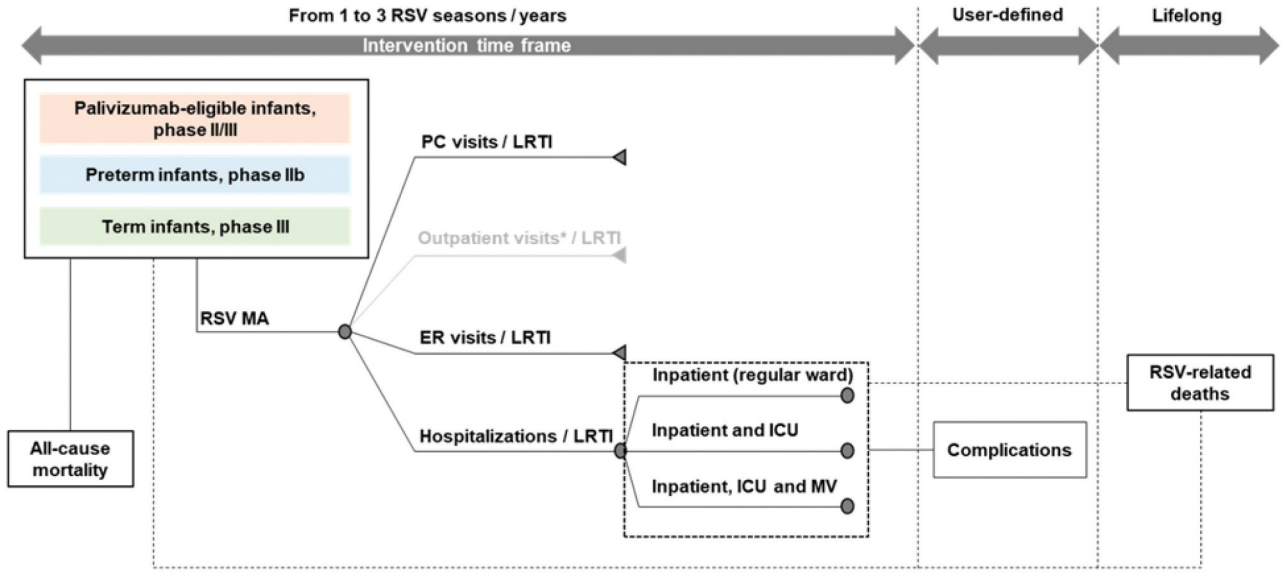

Figure 3. Model structure. The population includes infants less than 2 years of age, and it is divided into three subgroups to account for the differential individual risks of lower respiratory tract infection (LRTIs) and for the groups assessed in the nirsevimab clinical trials: Palivizumab-eligible infants, Preterm infants, and Late Preterm or Term infants. Infants experience different health events and require medical resources such as primary care (PC) and emergency room (ER) visits, as well as hospitalizations. During the inpatient health state, infants might be in a standard pediatric ward, admitted to an intensive care unit (ICU) and requiring mechanical ventilation (MV). Abbreviations: MA = medically attended; ER = emergency room; ICU = intensive care unit; LRTI = lower respiratory tract disease; MV = mechanical ventilation; PC = primary care; RSV = respiratory syncytial virus; wGA = week of gestational age. Figure 3 provides a visual illustration of the static model with the corresponding subgroups, health outcomes, and timeframe of interest

ER visits, and 5,532 hospital admissions – of which 1,328 were ICU admissions, 320 cases required mechanical ventilation, and 16 inpatient deaths (Table 4). The direct health costs, including palivizumab, were estimated to be $171 million annually and $295 million (including societal costs).

Comparing the clinical and cost impact of a universal infant nirsevimab immunization program with ~80% uptake rate (base case scenario) to the standard of care, the base case implementation strategy could avoid 47,609 RSV-related health outcomes, including 10,633 ER visits, 34,672 GP visits, 2,296 inpatient hospitalizations, and seven inpatient deaths (Table 4). The

Table 4. Comparative clinical and cost outcomes between existing therapy and nirsevimab for all newborn infants (born within and outside the RSV season).

	Current available standard of care[1]			Nirsevimab[2]			
	PVZ-eligible infants	Preterm infants	Term infants	PVZ-eligible infants	Preterm infants	Term infants	Total Difference[3]
Health outcomes							
Inpatient hospitalizations (including ICU and MV)	513	564	4,455	500	325	2,410	−2,296
ICU	177	269	883	171	141	448	−569
MV	40	66	215	39	30	106	−146
ER visits	609	2,471	37,174	600	1,712	27,308	−10,633
GP visits	2,120	8,530	128,332	2,097	6,055	96,156	−34,672
Inpatient deaths	1	7	8	1	3	5	−7
Total health outcomes	3,244	11,571	169,969	3,199	8,096	125,879	−47,609
Cost outcomes based on S_0 (average of all scenarios)[3]							
Inpatient hospitalizations	$8,138,909	$3,335,739	$28,971,652	$7,965,313	$2,081,645	$15,877,489	-$14,521,853
ICU	$6,574,719	$5,610,191	$14,159,441	$6,360,151	$3,041,336	$7,229,300	-$9,713,564
MV	$5,238,737	$6,461,737	$8,699,545	$5,048,839	$2,982,198	$4,287,090	-$8,081,891
ER visits	$504,667	$2,050,234	$30,677,383	$497,209	$1,416,270	$22,478,992	-$8,839,812
GP visits	$197,813	$797,013	$11,991,538	$195,689	$564,122	$8,963,150	-$3,263,402
Direct non-medical costs per inpatient hospitalization	$332,940	$366,068	$979,036	$324,447	$210,642	$528,433	-$614,523
Total direct costs	$57,426,853	$18,620,983	$95,478,594	$25,563,448	$27,215,223	$313,921,110	$195,173,352
Total indirect costs (excluding mortality)	$1,269,823	$3,494,828	$49,046,778	$1,247,342	$2,381,778	$36,025,583	-$14,156,726
Cost of inpatient death	$7,415,311	$27,932,561	$33,620,971	$7,368,019	$22,653,531	$28,129,324	-$10,817,968
Total Cost	$66,111,986	$50,048,371	$178,146,343	$34,178,809	$52,250,532	$378,076,018	$170,198,657

Abbreviation PVZ: palivizumab.
[1]Current available standard of care is palivizumab, which is only offered, under strict criteria, to high-risk preterm infants who meet the age, comorbidity, seasonal, and/or geographic community for prophylaxis.
[2]In the base case scenario, nirsevimab is offered to all infants entering the RSV season born within or outside the RSV season.
[3]The base case scenario represents a wide spectrum of short-term and long-term costs across Canada (i.e. Alberta, Ontario, Quebec) specific to RSV-related hospitalization among infants.

reduction of health outcomes was associated with a potential cost-savings of approximately $70 M for both direct and non-direct costs (including mortality-related costs), of which 64% could be attributed to a reduction in direct costs, primarily derived from the avoidance of hospitalization and severe hospitalization-related outcomes. The majority of total health outcomes avoided (99.9%) and resultant cost-savings (98.7%) were attributed to nirsevimab administered to healthy full-term and preterm infants who are not eligible for palivizumab.

Price per dose (PPD)

Table 5 illustrates the PPD of nirsevimab at the four WTP thresholds for all costing and implementation scenarios. Using a WTP threshold of $50,000 per QALY, immunizing all infants born in and out of season would be cost-effective from a societal perspective at a PPD of $536 for the primary costing scenario (S_0) and ranged from $475 to $617 depending on the source of costing input; at the highest WTP threshold of 100,000/QALY, the PPD increased to $706 (range: $646 to $787). Of all costing scenarios, S3, which derived its costing input from an Ontario-based RSV study that calculated costs for all children <59 months (stratified by the presence or absence of at least one comorbidity) rather than more granular age groups, consistently yielded the lowest PPDs; the highest PPDs were generated by S1b, a scenario that used the average RSV-attributable lab-confirmed hospitalization costs within one year.

Among the four implementation scenarios at the various WTP thresholds, immunizing only palivizumab-eligible children and those preterm born in and out of RSV season generated the highest PPD for nirsevimab. At $50,000/QALY, the base case PPD was $2,641, ranging from 2,401 to 3,074 and threshold (i.e., $100,000/QALY).

Deterministic sensitivity analysis

The results of the univariate sensitivity analysis for the base case scenario (nirsevimab provided to all infants within and outside the RSV season) at the $40,000 WTP threshold are displayed in the Tornado diagram in Figure 4. The factors resulting in the most variation in PPD were the discount rate, the variance of the distribution of monthly RSV, the coverage rate of nirsevimab for infants born at term, and the cost of palivizumab.

Discussion

The approval of nirsevimab as an option for RSV prophylaxis in Canada represents a valuable source of protection for infants against a disease that is associated with significant healthcare resource utilization. Our study demonstrates that compared to scenarios where only specific segments of the infant population receive nirsevimab, administering nirsevimab to all infants during their first RSV season with a PPD of $536 at a $50,000/QALY willingness-to-pay threshold may be a cost-effective strategy. Compared to the current standard of care, the base case could avoid 47,609 RSV-related medical outcomes for a cost savings of approximately $70 M, factoring in direct and indirect costs as well as mortality. Our model estimates that passive immunization of all infants with nirsevimab could prevent approximately 2,296 hospitalizations, with the majority of hospitalization burden avoided among

Table 5. Scenario-based price per dose ($CAD) of nirsevimab at various willingness-to-pay (WTP) thresholds.

		Implementation Scenarios			
Costing Scenarios[1]	Willingness-to-pay threshold ($ CAD/QALY)	All-infants born in & out-season (BASE CASE)	PVZ-eligible & preterm born in & out-season	PVZ-eligible & preterm born in & out-season, term infants (0–3 months) in first season and term infants born in-season	PVZ-eligible & preterm born in & out-season, term infants born in-season
S_0	40,000	$ 502	$ 2,559	$ 600	$ 723
S1a		$ 486	$ 2,441	$ 579	$ 696
S1b		$ 583	$ 2,666	$ 705	$ 849
S2		$ 470	$ 2,376	$ 554	$ 660
S3		$ 441	$ 2,320	$ 519	$ 619
S4		$ 529	$ 2,992	$ 641	$ 792
S_0	50,000	$ 536	$ 2,641	$ 634	$ 756
S1a		$ 520	$ 2,522	$ 614	$ 730
S1b		$ 617	$ 2,748	$ 740	$ 882
S2		$ 504	$ 2,458	$ 589	$ 693
S3		$ 475	$ 2,401	$ 554	$ 653
S4		$ 563	$ 3,074	$ 676	$ 825
S_0	70,000	$ 604	$ 2,804	$ 704	$ 823
S1a		$ 588	$ 2,685	$ 683	$ 796
S1b		$ 685	$ 2,911	$ 809	$ 949
S2		$ 572	$ 2,621	$ 658	$ 760
S3		$ 544	$ 2,565	$ 623	$ 720
S4		$ 631	$ 3,237	$ 745	$ 892
S_0	100,000	$ 706	$ 3,048	$ 808	$ 924
S1a		$ 690	$ 2,930	$ 787	$ 897
S1b		$ 787	$ 3,156	$ 913	$ 1,049
S2		$ 674	$ 2,865	$ 762	$ 860
S3		$ 646	$ 2,809	$ 727	$ 820
S4		$ 733	$ 3,481	$ 849	$ 992

Abbreviation PVZ: palivizumab.

[1]**S_0**: costing scenario used in base case with average costs derived from S1a, S1b, S2, S3, and S4; S1a: Costs derived from Rafferty et al. (2023) representing costs within 30 days post-RSV infection; S1b: costs derived from Rafferty et al. (2023) representing costs within 365 days post-RSV infection; S2: scenario based on costs derived from Thampi et al;[46] S3: scenario based on costs derived from Buchan et al;[47] S4: scenario based on costs derived from Papenberg et al.[48]

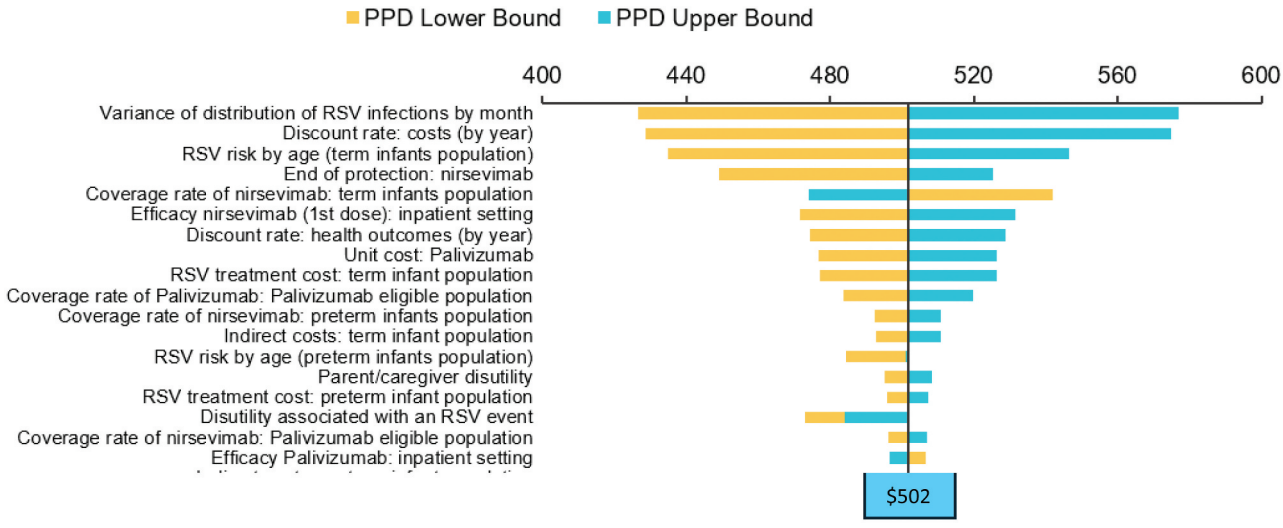

Figure 4. Deterministic sensitivity analysis for price per dose (PPD). Abbreviations PPD: price per dose; DSA: deterministic sensitivity analysis The DSA was executed for all scenarios. Since each scenario only applies variations in the costing matrix, providing one DSA (base case) was considered appropriate to understand how each parameter affects the price per dose. Figure 3 was provided to illustrate the base case scenario for all infants within and outside the RSV season at the $40,000 cost per QALY threshold

term and healthy preterm children. While premature infants are at the highest risk for severe RSV-related outcomes requiring hospitalization,[59,60] they comprise only a small percentage of the birth cohort (and therefore a smaller overall health and cost burden) compared to healthy term and preterm infants.

Our sensitivity analysis revealed that increasing the discount rate, variations in monthly disease incidence and risk of infection (particularly among term infants), duration of protection of nirsevimab, decreasing nirsevimab coverage rate (among term infants), and increasing nirsevimab's hospitalization-related efficacy, would each result in a higher PPD (see Figure 4). Immunization programs are often sensitive to discounting since benefits may not be realized immediately, as with conventional curative therapies.[61] Instead, there are often time delays between the dose administration and when the disease is averted, and discount rates become more impactful. Our coverage rate assumption for nirsevimab across the subgroups (i.e. 80%) was derived from the palivizumab coverage rate. As nirsevimab becomes routinely administered as a prophylaxis for RSV in Canada and the United States, a more informed coverage rate assumption will be possible. Unlike many other diseases, the seasonality of RSV translates to a substantial variation in the risk of infection from month to month. Previous studies have demonstrated that RSV-associated hospitalizations and healthcare costs were the highest for children born between September and February, who, therefore, had early exposure to the virus, with rates peaking in December and declining into April and after.[62–65] Due to this monthly change in viral risk combined with granularity in palivizumab and nirsevimab's current indications for use in Canada, we strived to derive and utilize monthly data inputs for our Canadian model. Given the lack of such data but similar seasonality and potential incidence of RSV among infants in Canada and the United States,[66,67] we opted to extrapolate US-based health outcomes and cost inputs and modify them using average Canadian values.

Throughout the process of modeling the PPD for nirsevimab (relative to standard or care; palivizumab), we utilized numerous Canadian-based RSV-related economic models to help inform our analysis. The analysis by Rafferty et al. – rooted in healthcare data specific to Alberta, Canada – provided 30 and 365-day RSV-related costs. Thampi et al. examined direct medical costs in Ontario, Canada, among infants <24 months over 12 months, incorporating attributable costs ranging from ER visits, inpatient hospitalizations, inpatient rehabilitation, same-day surgery, physician services, and outpatient diagnostics. Similar to Thampi et al., Buchan et al. examined hospitalization costs in Ontario, Canada, among children under 5 years of age hospitalized with lab-confirmed influenza or RSV from 2009 to 2014. In Quebec, Papenburg et al. focused on infants under 6 months at the start of or born during the RSV season, assessing costs up to 30 days post-discharge. Given the variation in model inputs, based on age and geography (i.e. provinces) across Canada, our base case analysis utilized an average of these costing scenarios to provide a comprehensive, pan-Canadian perspective.

We calculated the optimal PPD of nirsevimab at various WTP thresholds, as Canada does not adhere to one official cost-effectiveness threshold to inform national and provincial recommendations and decisions. While our model generated a base case PPD of $536 CAD (range: $475 to $617), the current public CDC vaccine price list (per dose) indicates a $395 USD public price and a $519.75 USD private list price, regardless of the dose concentration.[68] Costing models from the United States Centers for Disease Control (CDC) and Prevention's Advisory Committee on Immunization Practices (ACIP) have utilized a list price of $445 USD (i.e. $600 to $618 CAD depending on conversion rate) per dose of nirsevimab.[68] The Sanofi US health economic model for nirsevimab vs. standard of care assumed a price of $500 USD,[68] which is the approximate current private market list price in the U.S.[69] To note, the lowest price of $395 USD (i.e. CDC public price) is approximately $553 CAD. Given the emerging health economic literature on nirsevimab, we recognize that our findings

differ from other recent economic analyses.[40,43,70–72] These discrepancies reflect key methodological variations, as each analysis incorporated different perspectives (i.e. healthcare, societal, or both), target populations, cost inputs, and assumptions about effectiveness and duration of protection. Compared to other models, our model was unique in several ways. First, we were solely focused on price per dose (PPD) optimization for nirsevimab and different permutations of program implementation compared to one sole comparator (i.e. palivizumab for high-risk infants). Furthermore, the PPD analysis was provided in three dimensions – underlying cost assumptions, infant subgrouping, and willingness-to-pay threshold (see Table 5). Second, we combined both US and Canadian epidemiological data inputs to derive granular distributions of health outcomes by age at risk of infection. This provided the ability to surgically adjust the timing of program implementation based on our nirsevimab strategies. Third, our team thoroughly vetted and derived costs per outcome per at-risk infant subgroup from a pan-Canadian perspective. This may be a limitation or a strength; however, our team wanted to differentiate the costs associated with general and severe RSV-related hospital admissions. Finally, based on the nirsevimab published literature on duration of protection, we did not adopt a sigmoidal nor exponential waning curve. Altogether these characteristics are unique to our model and may contributed to the outcome disparities. Shoukat et al., for instance, examined individual and combined approaches for nirsevimab and RSVpreF programs in Canada, incorporating various modeling nuances such as (1) perspectives (healthcare vs. societal), (2) efficacy profiles (sigmoidal vs. constant), (3) product uptake rates (100% vs. 80%), and (4) monetary loss due to infant mortality. In the main text of their analysis, the PPD was stated as $285–$290 PPD from a societal perspective for combined infant and maternal immunization with a $50,000/QALY WTP threshold. When adjusted to reflect a standalone nirsevimab program incorporating the societal costs of RSV-related infant mortality, the PPD was aligned with our base case analysis, ranging from $575 CAD to $595 CAD at coverage rates of 100% and 80%, as reported in the supplementary materials in Shoukat et al.[70] Since Shoukat et al. used a no-vaccination comparator, the PPD would likely increase if the standard of care for palivizumab-eligible infants was utilized in the comparator arm. In the UK, Hodgson et al. utilized a dynamic transmission model spanning 10 years, with a 3.5% discount rate, to establish a two-dimensional cost-effectiveness frontier to evaluate nirsevimab and RSVpreF. Hodgson et al. introduced a time-varying factor for waning immunity, with efficacy decreasing exponentially from day 0 to day 300. This diverged from our methodological approach on multiple levels, which assumed constant efficacy over the first 5 months, followed by linear waning. Hodgson et al.'s findings were further influenced by a Bayesian framework that incorporated the price per dose (PPD) of RSVpreF in tandem with nirsevimab, producing optimal strategies based on incremental net monetary benefit (NMB) rather than the incremental cost-effectiveness ratio (ICERs). As a result of the stark differences in context, modeling approach, interventions, and costing inputs, it would be challenging to draw comparisons with our study results.

Gebretekle et al. conducted a health economic analysis, focusing on nirsevimab and RSVPreF, ranking vaccine strategies from lowest to highest cost, and calculating the ICER by comparing each strategy to the next least costly alternative.[71] Their analysis established a cost-effectiveness PPD for an all-infant nirsevimab program ranging from $110 to $190. Upon comparison to the results of our base case PPD (i.e. $536 at $50,000 per QALY), the difference may have been attributed to variations in both model structure and inputs. For example, in our current analysis, we attempted to utilize granular Canadian-specific costs, with stratifications for gestational age and RSV severity, while Gebretekle et al. assumed broader (lower) hospitalization rates and cost offsets. Additionally, we assumed constant efficacy for five months, followed by linear waning, whereas Gebretekle et al. applied an exponential decay in efficacy over 300 days, signaling a more rapid decline in protection. Furthermore, our analysis compared nirsevimab-specific strategies to a common comparator (i.e., standard of care). In contrast, Gebretekle et al. did not anchor their RSV strategies to a single reference intervention, as they ranked multiple prevention strategies in a stepwise fashion. In their analysis of seasonal nirsevimab for all infants with catch-up, Gebretekle et al. compared this nirsevimab strategy with year-round RSV PreF for infants at high risk.

In the US, the ACIP model applied aggregated hospitalization rates for children under two, adopted a broader RSV seasonality pattern based on CDC data from 2016 to 2019, and assumed a sigmoid decay in efficacy over 10 months. In contrast, our analysis incorporated age-specific hospitalization rates, granular Canadian cost inputs stratified by preterm and term subgroups and outcome severity, an RSV seasonality assumption ending in February, and a constant nirsevimab efficacy for the first 5 months, followed by linear waning. Differences in assumptions – such as age-specific data, seasonality, and duration of protection – led to divergent outcomes. Multiple study comparisons reveal common elements which can contribute to the variability among the studies and pose challenges for direct comparisons: 1) complexity in modeling, including the granularity of analysis; 2) assumptions around duration of protection of nirsevimab; 3) variable costing assumptions; 4) co-analysis of multiple interventions (nirsevimab and RSVPreF); 5) disparities in the baseline comparator (no intervention, palivizumab); 6) multiple nirsevimab-based strategies; and 7) differing modeling perspectives (e.g. healthcare, societal, inclusion or exclusion of infant mortality).

Compared to other models, our model was unique in several ways. First, we were solely focused on price per dose (PPD) optimization for nirsevimab and different permutations of program implementation compared to one sole comparator (i.e. palivizumab for high-risk infants). Furthermore, the PPD analysis was provided in three dimensions – underlying cost assumptions, infant subgrouping, and willingness-to-pay threshold (see Table 5 in manuscript). Second, we combined both US and Canadian epidemiological data inputs to derive granular distributions of health outcomes by age at risk of infection. This provided the ability to surgically adjust the timing of program implementation windows based on our nirsevimab strategies. Third, our team thoroughly vetted and derived costs per outcome per at-risk infant subgroup from

a pan-Canadian perspective. This may be a limitation or a strength; however, our team wanted to differentiate the costs associated with general and severe RSV-related hospital admissions. Finally, based on the nirsevimab published literature on duration of protection, we did not adopt a sigmoidal or exponential waning curve.

Our analysis had several strengths, including incorporating a broad range of hospitalization cost data, a costing matrix to account for hospitalization-related costs by RSV risk level, and the assessment of multiple immunization scenarios. Additionally, our model stratified the infant population by gestational age at birth and included various medically attended health outcomes and mortality. The basis of our analysis, which focused solely on the PPD of nirsevimab relative to standard of care, can make the results more intuitive for decision-makers versus ICER values.

However, our model also possessed several limitations. As stated earlier, we assumed that Canadian RSV health-related inputs would follow a US-based distribution; while this assumption was supported by the similar incidence rates of RSV in both countries, differences in healthcare delivery, practice patterns and healthcare-seeking behavior may have led to variations that we did not consider. We also assumed that healthcare costs would differ between subgroups and adjusted our model's hospitalization-related inputs according to the costing matrix; using US data to inform the matrix may have introduced differences in our model. However, Canadian literature suggests that hospitalization length of stay, need for ICU stay, and use of mechanical ventilation vary considerably based on wGA and underlying conditions, with the implication of significant differences in cost between risk subgroups by province.[48] Based on our guidance from external experts, we deemed that integrating this into our model would enhance its accuracy. In the event that data was being pulled from tertiary care hospitalization data, it would be important to highlight the potential biases toward severe hospitalizations. Our model assumed that infants with RSV infection would be immune for the rest of the study period and did not account for reinfection; the impact is likely low, given that previous studies report that reinfection is typically mild.[10] Our model did not include the RSV-related costs associated with long-term sequelae such as asthma, wheezing, otitis media, and reduced pulmonary function incurred after hospitalization, which has been linked to RSV.[73]

Overall, relative to the current nirsevimab-related health economic literature, our analysis attempted to provide a Canada-specific, price-optimized assessment of nirsevimab's PPD relative to the standard of care. By incorporating granular pan-Canadian epidemiological data, costing inputs, and product data, our objective was to provide a range of economically justifiable prices at multiple willingness-to-pay thresholds to help provide insights regarding nirsevimab's health economic value. As such, our study demonstrates that a passive immunization strategy for all infants with nirsevimab could be cost-effective at a WTP threshold of $50,000/QALY, provided the nirsevimab PPD is less than $536. Most importantly, an all-infant program may lead to significant reductions in the health and economic burden of RSV in Canada compared to the current standard of care (i.e. palivizumab administered to certain at-risk infants only).

Acknowledgments

Sanofi would like to acknowledge the input and feedback from various clinical and health economic experts from multiple advisory boards across Canada for the refinement and development of this costing model.

Disclosure statement

TS, JKL, AK, MG are employees of Sanofi. JW holds research grants from Sanofi.

Funding

This work was supported by Sanofi and AstraZeneca.

Notes on contributor

Thomas Shin is the North American Health Economics Lead for Sanofi Vaccines. Prior to his current role, he served as a senior health economist for the Ontario (Canada) government, supporting the management of the public drug formulary for oncology, non-oncology, and pipeline therapies. He holds master's degrees in Medical Anthropology, Epidemiology and Statistics from the University of Toronto and York University.

AI disclosure

Microsoft Copilot was utilized to optimize word count, enhance tone and language, as well as detect grammatical and spelling errors. As such, Copilot was enlisted as a post-hoc editorial tool and was not utilized in any other capacity.

Author contributions

Study conception, design, analysis, interpretation and manuscript development were led and supported by TS, JKHL, MG and AK; JW provided expertise in methodology and model validation. All authors reviewed and approved the final version of the manuscript and are accountable for all aspects of the work.

Ethics approval

This study did not involve human participants

References

1. Li Y, Wang X, Broberg EK, Campbell H, Nair H, European RSV Surveillance Network. Seasonality of respiratory syncytial virus and its association with meteorological factors in 13 European countries, week 40 2010 to week 39 2019. Euro Surveill. 2022;27 (16):2100619. doi: 10.2807/1560-7917.ES.2022.27.16.2100619.
2. Radhakrishnan D, Ouedraogo A, Shariff SZ, McNally JD, Benchimol EI, Clemens KK. The association between climate, geography and respiratory syncytial virus hospitalizations among children in Ontario, Canada: a population-based study. BMC Infect Dis. 2020;20(1):157. doi: 10.1186/s12879-020-4882-6.
3. La Vla WV, Marks MI, Stutman HR. Respiratory syncytial virus puzzle: clinical features, pathophysiology, treatment, and

prevention. J Pediatr. 1992;121(4):503–510. doi: 10.1016/s0022-3476(05)81135-7.
4. Chatterjee A, Mavunda K, Krilov LR. Current state of respiratory syncytial virus disease and management. Infect Dis Ther. 2021;10 (Suppl 1):5–16. doi: 10.1007/s40121-020-00387-2.
5. Schanzer DL, Saboui M, Lee L, Nwosu A, Bancej C. Burden of influenza, respiratory syncytial virus, and other respiratory viruses and the completeness of respiratory viral identification among respiratory inpatients, Canada, 2003-2014. Influenza Other Respir Viruses. 2018;12(1):113–121. doi: 10.1111/irv.12497.
6. Pisesky A, Benchimol EI, Wong CA, Hui C, Crowe M, Belair M-A, Pojsupap S, Karnauchow T, O'Hearn K, Yasseen AS, et al. Incidence of hospitalization for respiratory syncytial virus infection amongst children in Ontario, Canada: a population-based study using validated health administrative data. PLOS ONE. 2016;11(3):e0150416. doi: 10.1371/journal.pone.0150416.
7. Reichert H, Suh M, Jiang X, Movva N, Bylsma LC, Fryzek JP, Nelson CB. Mortality associated with respiratory syncytial virus, bronchiolitis, and influenza among infants in the United States: a birth cohort study from 1999 to 2018. J Infect Dis. 2022;226 (Suppl 2):S246–S254. doi: 10.1093/infdis/jiac127.
8. Makrinioti H, Hasegawa K, Lakoumentas J, Xepapadaki P, Tsolia M, Castro-Rodriguez JA, Feleszko W, Jartti T, Johnston SL, Bush A, et al. The role of respiratory syncytial virus- and rhinovirus-induced bronchiolitis in recurrent wheeze and asthma-A systematic review and meta-analysis. Pediatr Allergy Immunol. 2022;33(3):e13741. doi: 10.1111/pai.13741.
9. Shi T, McAllister DA, O'Brien KL, Simoes EAF, Madhi SA, Gessner BD, Polack FP, Balsells E, Acacio S, Aguayo C, et al. Global, regional, and national disease burden estimates of acute lower respiratory infections due to respiratory syncytial virus in young children in 2015: a systematic review and modelling study. Lancet. 2017;390(10098):946–958. doi: 10.1016/S0140-6736(17)30938-8.
10. Glezen WP, Taber LH, Frank AL, Kasel JA. Risk of primary infection and reinfection with respiratory syncytial virus. Am J Dis Child. 1986;140(6):543–546. doi: 10.1001/archpedi.1986.02140200053026.
11. Resch B. Product review on the monoclonal antibody palivizumab for prevention of respiratory syncytial virus infection. Hum Vaccin Immunother. 2017;13(9):2138–2149. doi: 10.1080/21645515.2017.1337614.
12. AstraZeneca Canada Inc, Sanofi Pasteur Ltd. Beyfortus (nirsevimab injection): solution for injection, 100 mg/mL, intramuscular use, 50 mg single-use, pre-filled syringe, 100 mg single-use, pre-filled syringe [product monograph]. Mississauga (ON): AstraZeneca Canada Inc.; 2022 Nov 1.
13. Hammitt LL, Dagan R, Yuan Y, Baca Cots M, Bosheva M, Madhi SA, Muller WJ, Zar HJ, Brooks D, Grenham A, et al. Nirsevimab for prevention of RSV in healthy late-preterm and term infants. N Engl J Med. 2022;386(9):837–846. doi: 10.1056/NEJMoa2110275.
14. Griffin MP, Yuan Y, Takas T, Domachowske JB, Madhi SA, Manzoni P, Esser MT, Khan AA, Dubovsky F, Villafana T, et al. Single-dose nirsevimab for prevention of RSV in preterm infants. New Engl J Med. 2020;383(5):415–425. doi: 10.1056/NEJMoa1913556.
15. Drysdale SB, Cathie K, Flamein F, Knuf M, Collins AM, Hill HC, Kaiser F, Cohen R, Pinquier D, Felter CT, et al. Nirsevimab for prevention of hospitalizations due to RSV in infants. N Engl J Med. 2023;389(26):2425–2435. doi: 10.1056/NEJMoa2309189.
16. Muller WJ, Madhi SA, Seoane Nuñez B, Baca Cots M, Bosheva M, Dagan R, Hammitt LL, Llapur CJ, Novoa JM, Llorens XS, et al. Nirsevimab for prevention of RSV in term and late-preterm infants. N Engl J Med. 2023;388(16):1533–1534. doi: 10.1056/NEJMc2214773.
17. Ares-Gómez S, Mallah N, Santiago-Pérez MI, Pardo-Seco J, Pérez-Martínez O, Otero-Barrós MT, Suárez-Gaiche N, Kramer R, Jin J, Platero-Alonso L, et al. Effectiveness and impact of universal prophylaxis with nirsevimab in infants against hospitalisation for respiratory syncytial virus in Galicia, Spain: initial results of a population-based longitudinal study. Lancet Infect Dis. 2024;24 (8):817–828. doi: 10.1016/S1473-3099(24)00215-9.
18. Barbas Del Buey JF, Íñigo Martínez J, Gutiérrez Rodríguez M, Alonso García M, Sánchez-Gómez A, Lasheras Carbajo MD, Jiménez Bueno S, Esteban Vasallo MD, López Zambrano MA, Calvo Rey C, et al. The effectiveness of nirsevimab in reducing the burden of disease due to respiratory syncytial virus (RSV) infection over time in the Madrid region (Spain): a prospective population-based cohort study. Front Public Health. 2024;12:1441786. doi: 10.3389/fpubh.2024.1441786.
19. Carbajal R, Boelle PY, Pham A, Chazette Y, Schellenberger M, Weil C, Colas A-S, Lecarpentier T, Schnuriger A, Guedj R, et al. Real-world effectiveness of nirsevimab immunisation against bronchiolitis in infants: a case–control study in Paris, France. Lancet Child & Adolesc Health. 2024;8(10):730–739. doi: 10.1016/S2352-4642(24)00171-8.
20. Jimeno Ruiz S, Peláez A, Labourt A, Acuña FM, Linares L, Llana Martín I, Calle Gómez Á, Martínez SN. Evaluating the effectiveness of nirsevimab in reducing pediatric RSV hospitalizations in Spain. Vaccines. 2024;12(10):1160. doi: 10.3390/vaccines12101160.
21. Lassoued Y, Levy C, Werner A, Assad Z, Bechet S, Frandji B, Batard C, Sellam A, Cahn-Sellem F, Fafi I, et al. Effectiveness of nirsevimab against rsv-bronchiolitis in paediatric ambulatory care: a test-negative case–control study. Lancet Reg Health Eur. 2024;44:101007. doi: 10.1016/j.lanepe.2024.101007.
22. López-Lacort M, Muñoz-Quiles C, Mira-Iglesias A, López-Labrador FX, Garcés-Sánchez M, Escribano-López B, Zornoza-Moreno M, Jesús Pérez-Martín J, Alfayate-Miguelez S, Iofrío-De Arce A, et al. Nirsevimab effectiveness against severe RSV infection in the primary care setting. Pediatrics. 2024;155(1). doi: 10.1542/peds.2024-066393.
23. Molina Gutiérrez M, de Miguel Lavisier B, Ruiz Domínguez JA, García de Oteyza M, Velasco Molina VM, Gutiérrez Arroyo A, de Ceano-Vivas M. Impacto de la inmunización con nirsevimab en las infecciones por VRS atendidas en urgencias pediátricas: primeros resultados en un hospital terciario de Madrid. Enfermedades Infecciosas y Microbiología Clínica (English ed). 2024;42(7):367–372. doi: 10.1016/j.eimc.2024.04.010.
24. Perramon-Malavez A, de Rioja VL, Coma E, Hermosilla E, Fina F, Martínez-Marcos M, Mendioroz J, Cabezas C, Montañola-Sales C, Prats C, et al. Introduction of nirsevimab in Catalonia, Spain: description of the incidence of bronchiolitis and respiratory syncytial virus in the 2023/2024 season. Eur J Pediatrics. 2024;183 (12):5181–5189. doi: 10.1007/s00431-024-05779-x.
25. Moline HL, Tannis A, Toepfer AP, Williams JV, Boom JA, Englund JA, Halasa NB, Staat MA, Weinberg GA, Selvarangan R, et al. Early estimate of nirsevimab effectiveness for prevention of respiratory syncytial virus–associated hospitalization among infants entering their first respiratory syncytial virus season — new vaccine surveillance network, October 2023–February 2024. MMWR Morb Mortal Wkly Rep. 2024;73(209–214):209–214. doi: 10.15585/mmwr.mm7309a4.
26. Public Health Agency of Canada (PHAC). National advisory committee on immunization (NACI) statement: guidance for the prevention of respiratory syncytial virus (RSV) disease in infants. Ottawa, Canada: Public Health Agency of Canada; 2024.
27. Jones JM, Fleming-Dutra KE, Prill MM, Roper LE, Brooks O, Sanchez PJ, Kotton CN, Mahon BE, Meyer S, Long SS, et al. 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. doi: 10.15585/mmwr.mm7234a4.
28. National Advisory Committee on Immunization. An advisory committee statement (ACS) national advisory committee on immunization (NACI) - recommended use of palivizumab to reduce complications of respiratory syncytial virus infection in infants. Ottawa, Canada: Public Health Agency of Canada (PHAC), editor; 2022.

29. Public Health Agency of Canada (PHAC). Guidelines for the economic evaluation of vaccination programs in Canada. 1 ed. Ottawa, Canada: National Advisory Committee on Immunization, editor; 2023.
30. Statistics Canada. Table 13-10-0425-01 live births by weeks of gestation 2022. [accessed 2023 Aug 30]. https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=1310042501.
31. IQVIA. Synagis sales by SKU (50MG and 100MG). 2020.
32. Public Health Agency of Canada (PHAC). Respiratory virus detections in Canada 2023. [accessed 2023 Aug 30]. https://www.canada.ca/en/public-health/services/surveillance/respiratory-virus-detections-canada.html.
33. Andabaka T, Nickerson JW, Rojas-Reyes MX, Rueda JD, Vrca VB, Barsic B. Monoclonal antibody for reducing the risk of respiratory syncytial virus infection in children. Cochrane Database Syst Rev. 2013;2013(6):CD006602. doi: 10.1002/14651858.CD006602.pub4.
34. Food and Drug Administration (FDA). Highlights of prescribing information: BEYFORTUS (product monograph). 2023 [accessed 2023 Aug 29]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/761328s000lbl.pdf.
35. Chan P, Li A, Paes B, Abraha H, Mitchell I, Lanctôt KL. Adherence to palivizumab for respiratory syncytial virus prevention in the Canadian registry of palivizumab. Pediatr Infect Dis J. 2015;34(12):e290–7. doi: 10.1097/INF.0000000000000922.
36. Butt ML, Elliott L, Paes BA. Respiratory syncytial virus hospitalization and incurred morbidities the season after prophylaxis. Paediatr Child Health. 2018;23(7):441–446. doi: 10.1093/pch/pxy046.
37. Statistics Canada. Table 13-10-0713-01 infant deaths and mortality rates, by age group.
38. Statistics Canada. Table 13-10-0710-01 mortality rates, by age group.
39. Hansen CL, Chaves SS, Demont C, Viboud C. Mortality associated with influenza and respiratory syncytial virus in the US, 1999-2018. JAMA Network Open. 2022;5(2):e220527. doi: 10.1001/jamanetworkopen.2022.0527.
40. Hutton DW. Economic analysis of nirsevimab in pediatric populations. University of Michigan; 2023 [accessed 2023 Aug 29]. https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-02/slides-02-23/RSV-Pediatric-02-Hutton-508.pdf.
41. Guertin JR, Feeny D, Tarride J-E. Age- and sex-specific Canadian utility norms, based on the 2013-2014 Canadian community health survey. CMAJ. 2018;190(6):E155–E61. doi: 10.1503/cmaj.170317.
42. Statistics Canada. Canadian vital statistics, death database and demography division (population estimates). [accessed 2023 Aug 23]. https://www23.statcan.gc.ca/imdb/p2SV.pl?Function=getSurvey&SDDS=3233.
43. Hodgson D, Atkins KE, Baguelin M, Panovska-Griffiths J, Thorrington D, van Hoek AJ, Zhao H, Fragaszy E, Hayward AC, Pebody R. Estimates for quality of life loss due to respiratory syncytial virus. Influenza and other respiratory viruses. Influenza Other Respir Viruses. 2020;14(1):19–27. doi: 10.1111/irv.12686.
44. CADTH. Methods and guidelines: guidelines for the economic evaluation of health technologies: Canada (4th edition). 2017 [accessed 2023 Aug 28]. https://www.cadth.ca/sites/default/files/pdf/guidelines_for_the_economic_evaluation_of_health_technologies_canada_4th_ed.pdf.
45. Public Health Agency of Canada. Cost-effectiveness of palivizumab prophylaxis for respiratory syncytial virus: a systematic review [Internet]. Ottawa (ON): Public Health Agency of Canada; 2017. https://www.canada.ca/content/dam/phac-aspc/documents/services/publications/vaccines-immunization/cost-effectiveness-palivizumab-prophylaxis-respiratory-syncitial-virus/systemic-review-en.pdf.
46. Thampi N, Knight BD, Thavorn K, Webster RJ, Lanctot K, Hawken S, McNally JD. Health care costs of hospitalization of young children for respiratory syncytial virus infections: a population-based matched cohort study. CMAJ Open. 2021;9(4):E948–e56. doi: 10.9778/cmajo.20200219.
47. Buchan SA, Chung H, Karnauchow T, McNally JD, Campitelli MA, Gubbay JB, Katz K, McGeer AJ, Richardson DC, Simor A, et al. Characteristics and outcomes of young children hospitalized with laboratory-confirmed influenza or respiratory syncytial virus in Ontario, Canada, 2009-2014. Ped Infect Dis J. 2019;38(4):362–369. doi: 10.1097/INF.0000000000002164.
48. Papenburg J, Saleem M, Teselink J, Li A, Caouette G, Massé É, Lanctot KL. Cost-analysis of withdrawing immunoprophylaxis for respiratory syncytial virus in infants born at 33-35 weeks gestational age in Quebec: a multicenter retrospective study. Ped Infect Dis J. 2020;39(8):694–699. doi: 10.1097/INF.0000000000002719.
49. Feltes TF, Simoes E. Palivizumab prophylaxis in haemodynamically significant congenital heart disease. Arch Dis Child. 2005;90(8):875–877. doi: 10.1136/adc.2004.069948.
50. Hall CB, Weinberg GA, Blumkin AK, Edwards KM, Staat MA, Schultz AF, Poehling KA, Szilagyi PG, Griffin MR, Williams JV, et al. Respiratory syncytial virus-associated hospitalizations among children less than 24 months of age. Pediatrics. 2013;132(2):e341–8. doi: 10.1542/peds.2013-0303.
51. 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(3):531–537. doi: 10.1542/peds.102.3.531.
52. 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: Off J Calif Perinatal Assoc. 2016;36(11):990–996. doi: 10.1038/jp.2016.113.
53. Arriola CS, Kim L, Langley G, Anderson EJ, Openo K, Martin AM, Lynfield R, Bye E, Como-Sabetti K, Reingold A, et al. Estimated burden of community-onset respiratory syncytial virus-associated hospitalizations among children aged <2 years in the United States, 2014-15. J Pediatr Infect Dis Soc. 2020;9(5):587–595. doi: 10.1093/jpids/piz087.
54. Mitchell I, Defoy I, Grubb E. Burden of respiratory syncytial virus hospitalizations in Canada. Can Respir J. 2017;2017:1–9. doi: 10.1155/2017/4521302.
55. Lively JY, Curns AT, Weinberg GA, Edwards KM, Staat MA, Prill MM, Gerber SI, Langley GE. Respiratory syncytial virus-associated outpatient visits among children younger than 24 months. J Pediatr Infect Dis Soc. 2019;8(3):284–286. doi: 10.1093/jpids/piz011.
56. Rafferty E, Paulden M, Buchan SA, Robinson JL, Bettinger JA, Kumar M, Swenson LW, MacDonald SE. Canadian immunization research network (CIRN) investigators. Evaluating the individual healthcare costs and burden of disease associated with RSV across age groups. PharmacoEconomics. 2022;40(6):633–645. doi: 10.1007/s40273-022-01142-w.
57. Pichon-Riviere A, Drummond M, Palacios A, Garcia-Marti S, Augustovski F. Determining the efficiency path to universal health coverage: cost-effectiveness thresholds for 174 countries based on growth in life expectancy and health expenditures. Lancet Global Health. 2023;11(6):e833–e42. doi: 10.1016/S2214-109X(23)00162-6.
58. Institute for Clinical and Economic Review (ICER). 2020-2023 Value Assessment Framework. 2020.
59. Lanari M, Anderson EJ, Sheridan-Pereira M, Carbonell-Estrany X, Paes B, Rodgers-Gray BS, Fullarton JR, Grubb E, Blanken M. Burden of respiratory syncytial virus hospitalisation among infants born at 32-35 weeks' gestational age in the Northern Hemisphere: pooled analysis of seven studies. Epidemiol Infect. 2020148:e170. doi: 10.1017/S0950268820001661.
60. Figueras-Aloy J, Manzoni P, Paes B, Simoes EA, Bont L, Checchia PA, Fauroux B, Carbonell-Estrany X. Defining the risk and associated morbidity and mortality of severe respiratory syncytial virus infection among preterm infants without chronic lung disease or congenital heart disease. Infect Dis Ther. 2016;5(4):417–452. doi: 10.1007/s40121-016-0130-1.
61. World Health Organization: Immunization Vaccines and Biologicals. WHO guide for standardization of economic evaluations of immunization programmes. 2019 [accessed 2023 Sep 1].

https://apps.who.int/iris/bitstream/handle/10665/329389/WHO-IVB-19.10-eng.pdf.
62. Demont C, Petrica N, Bardoulat I, Duret S, Watier L, Chosidow A, Lorrot M, Kieffer A, Lemaitre M. Economic and disease burden of rsv-associated hospitalizations in young children in France, from 2010 through 2018. BMC Infect Dis. 2021;21(1):730. doi: 10.1186/s12879-021-06399-8.
63. Kramer R, Duclos A, Lina B, Casalegno J-S. Cost and burden of rsv-related hospitalisation from 2012 to 2017 in the first year of life in Lyon. Fr Vaccine. 2018;36(45):6591–6593. doi: 10.1016/j.vaccine.2018.09.029.
64. Obando-Pacheco P, Justicia-Grande AJ, Rivero-Calle I, Rodríguez-Tenreiro C, Sly P, Ramilo O, Mejías A, Baraldi E, Papadopoulos NG, Nair H, et al. Respiratory syncytial virus seasonality: a global overview. J Infect Dis. 2018;217(9):1356–1364. doi: 10.1093/infdis/jiy056.
65. Hawkes MT, Lee BE, Kanji JN, Zelyas N, Wong K, Barton M, Mukhi S, Robinson JL. Seasonality of respiratory viruses at northern latitudes. JAMA Netw Open. 2021;4(9):e2124650. doi: 10.1001/jamanetworkopen.2021.24650.
66. McLaughlin JM, Khan F, Schmitt HJ, Agosti Y, Jodar L, Simões EAF, Swerdlow DL. Respiratory syncytial virus-associated hospitalization rates among US infants: a systematic review and meta-analysis. J Infect Dis. 2022 15;225(6):1100–1111. doi: 10.1093/infdis/jiaa752.
67. Buchan SA, Chung H, To T, Daneman N, Guttmann A, Kwong JC, Murti M, Aryal G, Campigotto A, Chakraborty P, et al. Estimating the incidence of first RSV hospitalization in children born in Ontario, Canada. J Pediatr Infect Dis Soc. 2023;12(7):421–430. doi: 10.1093/jpids/piad045.
68. National Center for Immunization and Respiratory Diseases. Economics of preventing respiratory syncytial virus lower respiratory tract infections (RSV LRTI) among US infants with nirsevimab - a summary report comparing models from. Sanofi AND University of Michigan and CDC [accessed 2023 31]. https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-02/slides-02-23/rsv-pediatric-03-sanchez-508.pdf.
69. Centers for Disease Control and Prevention. CDC vaccine price list. [accessed 2024 Mar 25]. https://www.cdc.gov/vaccines/programs/vfc/awardees/vaccine-management/price-list/index.html.
70. Shoukat A, Abdollahi E, Galvani AP, Halperin SA, Langley JM, Moghadas SM. Cost-effectiveness analysis of nirsevimab and maternal RSVpreF vaccine strategies for prevention of respiratory syncytial virus disease among infants in Canada: a simulation study. Lancet Reg Health - Am. 2023;28:100629. doi: 10.1016/j.lana.2023.100629.
71. Gebretekle GB, Yeung MW, Ximenes R, Cernat A, Simmons AE, Killikelly A, Siu W, Rafferty E, Brousseau N, Tunis M, et al. Cost-effectiveness of RSVpreF vaccine and nirsevimab for the prevention of respiratory syncytial virus disease in Canadian infants. Vaccine. 2024;42(21):126164. doi: 10.1016/j.vaccine.2024.126164.
72. Centers for Disease Control and Prevention (CDC). Advisory committee on immunization practices (ACIP). Evidence to recommendation (ETR) framework for nirsevimab [slides]. Presented at: ACIP Meeting; 2023 Aug 3; Atlanta (GA). https://www.cdc.gov/acip/downloads/slides-2023-08-03/02-RSV-jones-508.pdf.
73. Respiratory syncytial virus. In: Kimberlin DW, editor. Red book: 2018 report of the committee on infectious diseases. 31st ed. Elk Grove Village (IL): American Academy of Pediatrics; 2018. p. 682–692.

Appendix

NACI provides the following guidance for public health programs regarding the use of palivizumab (PVZ) to prevent severe RSV disease in high-risk children:

- PVZ is recommended for premature infants born at less than 30 weeks gestational age (wGA) who are under 6 months old at the start or during RSV season. It is also advised for children under 24 months with chronic lung disease of prematurity who have required ongoing oxygen therapy within the past 6 months, infants under 12 months with significant congenital heart disease (CHD), and infants born before 36 wGA and under 6 months old residing in remote northern Inuit communities where air transport would be needed for hospitalization. For children with both CHD and chronic lung disease, recommendations for chronic lung disease should be prioritized.
- PVZ may also be considered for certain groups at high risk: premature infants between 30-32 wGA and under 3 months of age; children under 24 months with severe chronic lung disease due to cystic fibrosis or other conditions requiring recent oxygen therapy or assisted ventilation; infants under 12 months with significant chronic heart conditions other than congenital; children aged 12-24 months awaiting or having received a heart transplant within the past 6 months; and children under 24 months with severe immunodeficiency. It may also be considered for term infants under 6 months old in remote Inuit communities with high RSV hospitalization rates, as well as for infants born before 36 wGA and under 6 months in other remote areas where air transport would be needed. In cases of RSV outbreaks in neonatal intensive care units (NICUs), PVZ can be considered if other control measures fail.
- PVZ should not be provided to otherwise healthy infants born at or after 33 wGA, or to multiple birth siblings who do not meet other criteria. It is also not recommended for routine use in children under 24 months with cystic fibrosis or Down syndrome unless other risk factors are present, or in healthy-term infants in remote northern Inuit communities unless RSV hospitalization rates are extremely high. Furthermore, PVZ is not intended to prevent wheezing or asthma in the absence of other indications.
- For hospital-associated RSV prevention, PVZ is not recommended for hospitalized eligible children, except as a last resort in NICUs where other RSV outbreak control measures have failed.

In Canada, as PVZ is not readily available for individual purchase, NACI does not provide specific recommendations for individual-level use.

Figure A1. The national advisory committee on immunization (NACI) recommended use of palivizumab to reduce complications of respiratory syncytial virus in infants.