Cost-effectiveness of Palivizumab for Respiratory Syncytial Virus: A Systematic Review

Stephen Mac, MBiotech, BSc,[a,b] Amanda Sumner, MA, BA,[c] Samuel Duchesne-Belanger, BSc,[c] Robert Stirling, MD, FRCPC, MHSc, MSc, BScH,[c] Matthew Tunis, PhD, BSc,[c] Beate Sander, PhD[a,b,d,e]

abstract

CONTEXT: Palivizumab prophylaxis is used as passive immunization for respiratory syncytial virus (RSV). However, because of its high cost, the value of this intervention is unclear.

OBJECTIVE: To systematically review the cost-effectiveness of palivizumab prophylaxis compared with no prophylaxis in infants <24 months of age.

DATA SOURCES: Medline, Embase, and Cochrane Library up to August 2018.

STUDY SELECTION: Two reviewers independently screened results to include economic evaluations conducted between 2000 and 2018 from Organization for Economic Cooperation and Development countries.

DATA EXTRACTION: Two reviewers independently extracted outcomes. Quality appraisal was completed by using the Joanna Briggs Institute checklist. Costs were adjusted to 2017 US dollars.

RESULTS: We identified 28 economic evaluations (20 cost-utility analyses and 8 cost-effectiveness analyses); most were from the United States (n = 6) and Canada (n = 5). Study quality was high; 23 studies met >80% of the Joanna Briggs Institute criteria. Palivizumab prophylaxis ranged from a dominant strategy to having an incremental cost-effectiveness ratio of $2 526 203 per quality-adjusted life-year (QALY) depending on study perspective and targeted population. From the payer perspective, the incremental cost-effectiveness ratio for preterm infants (29–35 weeks' gestational age) was between $5188 and $791 265 per QALY, with 90% of estimates <$50 000 per QALY. Influential parameters were RSV hospitalization reduction rates, palivizumab cost, and discount rate.

LIMITATIONS: Model design heterogeneity, model parameters, and study settings were barriers to definitive conclusions on palivizumab's economic value.

CONCLUSIONS: Palivizumab as RSV prophylaxis was considered cost-effective in prematurely born infants, infants with lung complications, and infants from remote communities.

[a]*Toronto Health Economics and Technology Assessment Collaborative, University Health Network, Toronto, Canada;* [b]*Institute of Health Policy, Management, and Evaluation, University of Toronto, Toronto, Canada;* [c]*Public Health Agency of Canada, Ottawa, Canada;* [d]*Institute of Clinical Evaluative Sciences, Toronto, Canada; and* [e]*Public Health Ontario, Toronto, Canada*

Mr Mac contributed to conceptualization of the study, critically appraising the scientific literature, analysis, and drafting and revising the manuscript; Ms Sumner contributed to conceptualization of the study, critically appraising the scientific literature, and analysis; Mr Duchesne-Belanger contributed to critically appraising the scientific literature; Dr Stirling contributed to conceptualization of the study and review of the manuscript; Dr Tunis contributed to conceptualization of the study, review of the manuscript, and supervision of the study; Dr Sander contributed to conceptualization of the study, critically appraising the scientific literature, critical revision of the manuscript, and supervision of the study; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

To cite: Mac S, Sumner A, Duchesne-Belanger S, et al. Cost-effectiveness of Palivizumab for Respiratory Syncytial Virus: A Systematic Review. *Pediatrics*. 2019;143(5): e20184064

Respiratory syncytial virus (RSV) is the most common cause of lower respiratory tract infections in infants and young children worldwide.[1] It is a ubiquitous virus that nearly 100% of infants will contract within 2 years after birth.[2–4] RSV is a seasonal respiratory infection that is a significant cause of morbidity and mortality, with the virus estimated to cause up to 90% of pediatric bronchiolitis hospitalizations and up to 50% of pediatric hospitalizations for pneumonia.[1,5] Risk factors for severe RSV in infants include preterm birth, congenital heart disease (CHD), bronchopulmonary dysplasia (BPD) or chronic lung disease (CLD), cystic fibrosis, Down syndrome, and a weakened immune system.[6–8]

Although there is currently no vaccine available to prevent RSV infection, since 1998, passive prophylaxis has been available with palivizumab.[9] Palivizumab is a humanized murine monoclonal antibody administered monthly as an intramuscular injection and has shown a significant reduction in the overall rate of hospitalization due to RSV infection.[10] However, because of its high acquisition costs, there has been considerable debate surrounding the cost-effectiveness of this intervention. Since 2000, the cost-effectiveness of palivizumab has been summarized in 8 reviews, of which half were completed >10 years ago.[11–14] In a recent study in 2013, Andabaka et al[15] reported that the economic evaluation results are inconsistent across studies, ranging from highly cost-effective to not cost-effective depending on the scenario. Our objective for this study was to provide an update on the cost-effectiveness of palivizumab passive immunization for the prevention of RSV in infants and children up to 24 months of age and, when possible, to stratify results by at-risk populations to inform policy decisions for these groups. We conducted a systematic scientific-literature review for economic evaluations conducted in high-income countries from the Organization for Economic Cooperation and Development (OECD) to limit heterogeneity in population baseline health, health care systems, and quality of care and included studies conducted after 2000. With this review, we provide a much-needed update to support health-policy decision-making for palivizumab prophylaxis, with particular emphasis on cost-effectiveness results according to gestational age at birth for preterm infants, which has historically been an area of clinical and policy uncertainty.[11,16,17]

METHODS

Search Strategy

We conducted our systematic review by following the Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines.[18] The search strategy was developed with a Public Health Agency of Canada librarian. We conducted a scientific literature search for English- and French-language studies published in 3 electronic databases: Medline and Epub Ahead of Print and Medline In-Process & Other Non-Indexed Citations (Ovid interface), Embase (Ovid interface), and the Cochrane Library, which included the Health Technology Assessment Database, the National Health Service (NHS) Economic Evaluation Database, and the Database of Abstracts of Reviews of Effects. In our search, we used medical-subject headings and text words related to the following concepts: respiratory syncytial virus, palivizumab, economic evaluations, and cost-effectiveness. The primary search strategy was developed in Medline and adapted to other databases to account for database-specific vocabulary and functionality. A complete list of search terms and the full search strategy for Medline are summarized in Supplemental Table 4. We manually searched the reference lists from relevant articles and systematic reviews.

Eligibility Criteria

The protocol and eligibility criteria for studies are published on PROSPERO (identifier CRD42018104977). We included full economic evaluations (eg, cost-benefit analysis, cost-effectiveness analysis, and cost-utility analysis) in which palivizumab prophylaxis for RSV was compared with any comparator (eg, no prophylaxis) for infants up to 24 months of age on the basis of current guidelines from Canada's National Advisory Committee on Immunization.[19] We included economic evaluations that were conducted in OECD countries between 2000 and present and reported outcomes related to an incremental ratio of cost per unit (eg, cost per quality-adjusted life-year [QALY], cost per case averted, cost per life-year gained [LYG], and cost-benefit ratio). We excluded cost-minimization studies, cost-of-illness studies, and budget-impact analyses. We excluded studies conducted outside of OECD countries, studies published in a language other than English or French, and studies published before 2000.

Data Extraction and Analysis

Screening, data extraction, and quality appraisal were completed in duplicate (by S.M. and A.S.). All levels of screening were completed using DistillerSR (Evidence Partners, Ottawa, Canada). Conflicts were discussed and resolved through consensus. Data extraction was guided by Consolidated Health Economics Evaluation and Reporting Standards statement.[20] We collected study characteristics (publication year, country, study design, study perspective, time horizon, discounting, primary and secondary outcomes, use of cost-effectiveness thresholds, and funding sources), study population characteristics (age range, gestational age, health

conditions, and setting), key parameters (RSV incidence and/or hospitalization rates, mortality rates, sequelae, cost of palivizumab, and number of doses), and results (base-case incremental cost-effectiveness ratios [ICERs], scenario analyses, type of sensitivity analysis, and influential parameters). The quality of included studies was assessed by using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Economic Evaluations.[21] We classified a study as high quality if it met >80% of the JBI checklist criteria.[22]

We descriptively summarized the study characteristics and population characteristics. Cost-effectiveness outcomes were adjusted to 2017 US dollars (USDs) by using purchasing power parity rates from the OECD[23] and US inflation rates from the US Department of Labor. Unadjusted and adjusted ICERs were summarized. We conducted subgroup analyses to summarize the cost-effectiveness for studies conducted from remote regions of the Canadian Arctic and studies in which cost-effectiveness was reported in costs per QALY for preterm infants. For studies that included preterm infants, we stratified on the basis of gestational age at birth (weeks) and plotted this against the adjusted ICERs to visually identify the spread of ICER estimates and possible trends related to gestational age. The number of estimates and the proportion of them being cost-effective at various thresholds were summarized. A meta-analysis of cost-effectiveness was inappropriate because of the heterogeneity of the study setting, model designs, parameters used, population, and perspective taken in the studies.

RESULTS

Our systematic literature search identified 237 deduplicated records, of which 30 met our eligibility criteria and were included in our review (Fig 1).[14,24–52] Conclusions of 2 studies[31,51] were updated by using more recent data,[32,39] which excluded them from our review's analysis and conclusions. The 28 studies included were published between 2000 and 2018, with most conducted in the United States (n = 6), Canada (n = 5), Netherlands (n = 3), United Kingdom (n = 3), and Spain (n = 3). The rest of the studies were conducted in Austria (n = 2), Germany (n = 2), Italy (n = 1), Mexico (n = 1), New Zealand (n = 1), and Sweden (n = 1). Study characteristics are summarized in Table 1.

Most studies (83%) met >80% of the JBI quality appraisal checklist criteria (Supplemental Table 5). The 2 checklist items that were least met were whether the study results included all issues of concerns to users (39%) and whether all relevant costs and outcomes were identified (75%). Overall, studies included in this review were considered relatively high quality (Fig 2).

Study Population

In 14 studies, the subject's chronological age was explicitly reported to be <24 months, whereas in the other 14 studies, it was assumed that the cost-effectiveness of palivizumab was assessed in infants

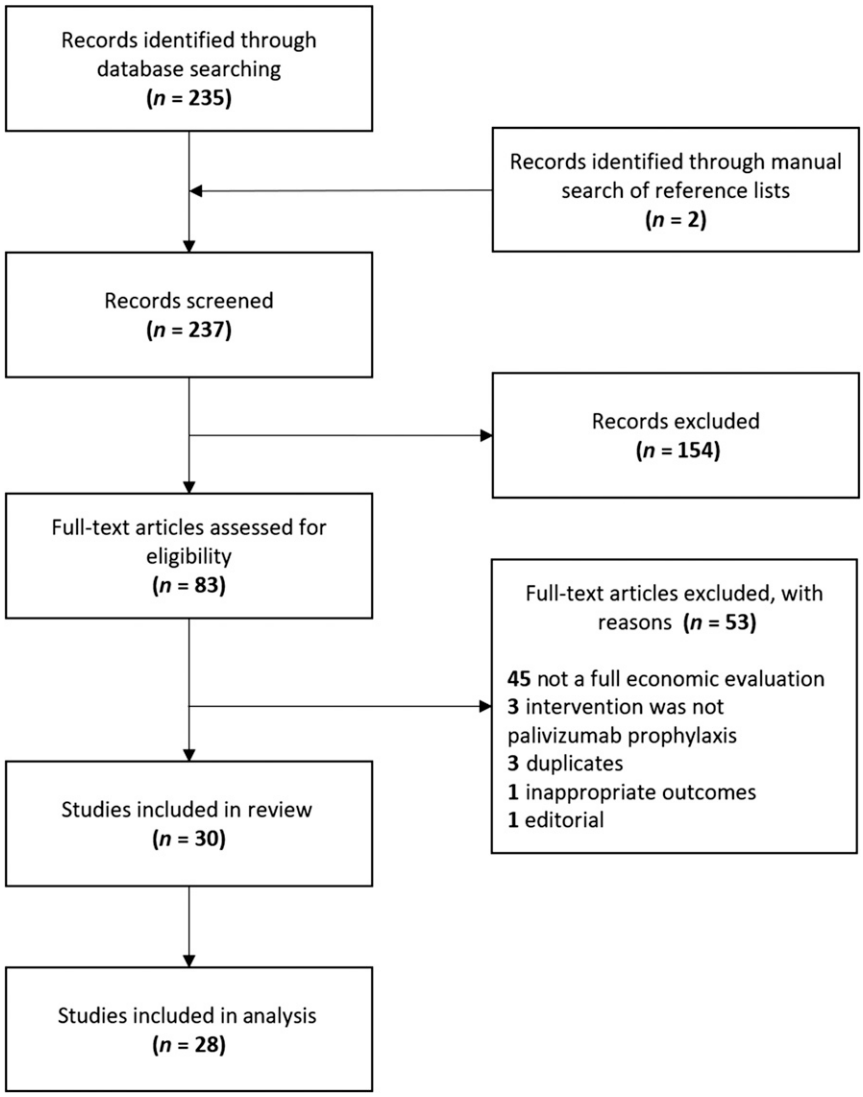

FIGURE 1
Literature search and study selection.

TABLE 1 Study Characteristics

Author, y	Country	Perspective	Type of Analysis	Outcome Measure	Population	Time Horizon	Discount Rate	Industry Funding
Banerji et al[24] 2016	Canada	Payer	CEA	Cost per HA	Term infants	6 mo	N/A	Abbott and MedImmune, LLC (grants)
Bentley et al[35] 2013	United Kingdom	Payer	CUA	Cost per QALY	Preterm infants with CHD, and CLD	Lifetime	3.5%	AbbVie
Blanken et al[46] 2018	Netherlands	Societal	CUA	Cost per QALY	Preterm infants	1 y	N/A	Unknown: grants for investigator-initiated studies from MedImmune and AbbVie, including the MAKI trial, from which data for this CEA were derived
Chirico et al[47] 2009	Italy	Payer	CUA	Cost per QALY	Preterm infants with BPD	Lifetime	3%	Abbott
Elhassan et al[44] 2006	United States	Societal	CUA; CBA	Cost per QALY	Preterm infants without CLD	8 y	3%	None
Hampp et al[48] 2011	United States	Payer	CEA	Cost per HA	Preterm and term infants (both with and without CHD and CLD)	NR	NR	None
Harris et al[49] 2011	Canada	Societal	CEA; CBA	Cost per day of HA	Infants with CHD	5 y[a]	NR	Unknown: honorarium (<$1000) from Abbott Laboratories
Hascoet et al[50] 2008	France	Societal (BC) and payer	CEA; CBA	Cost per LYG	Preterm infants with CHD or BPD	Lifetime	3%	Abbott France
Lofland et al[45] 2000	United States	Payer	CEA	Cost per RSV infection avoided	Preterm infants with CLD	6 mo	N/A	MedImmune, LLC
Mahadevia et al[52] 2012	United States	Societal	CUA	Cost per QALY	Preterm infants	Lifetime	3%	MedImmune, LLC
McGirr et al[25] 2017	Canada	Payer	CUA	Cost per QALY	Term infants with cystic fibrosis	Lifetime	5%	None
Neovius et al[26] 2011	Sweden	Societal	CUA	Cost per QALY	Preterm infants	Lifetime	3%	Abbott Scandinavia
Nuijten et al[30] 2009	Germany	Societal (BC) and payer	CUA	Cost per QALY	Infants with CHD	Lifetime	5%	Abbott
Nuijten et al[29] 2009	Netherlands	Payer (BC) and societal	CUA	Cost per QALY	Preterm infants with BPD and CHD	Lifetime	4%, 1.5%[b]	Abbott GmbH & Co KG (Ludwigshafen, Germany)
Nuijten et al[28] 2010	Spain	Payer (BC) and societal	CUA	Cost per QALY	Preterm infants	Lifetime	3%	Abbott GmbH & Co KG (Ludwigshafen, Germany)
Nuijten et al[27] 2007	United Kingdom	Payer (BC) and societal	CUA	Cost per QALY; cost per HA	Preterm infants with BPD and CHD	Lifetime	3.5%	Abbott GmbH & Co KG (Ludwigshafen, Germany)
Resch et al[31,32] 2008, 2012	Austria	Payer (BC) and societal	CUA	Cost per QALY	Preterm infants with BPD and CHD	Lifetime	5%	None
Rietveld et al[33] 2010	Netherlands	Societal	CEA	Cost per HA	Preterm infants with BPD	1 y	N/A	None
Roeckl-Wiedmann et al[34] 2003	Germany	Societal	CEA	Cost per HA	Preterm infants with risk factors	1 y	N/A	Abbott Laboratories, Germany
Salinas-Escudero et al[36] 2012	Mexico	Payer	CUA	Cost per QALY	Preterm infants	Lifetime	3%	Abbott Laboratories of Mexico
Sanchez-Luna et al[37] 2017	Spain	Payer (BC) and societal	CUA	Cost per QALY	Preterm infants with risk factors	6 y	3%	None
Schmidt et al[38] 2017	Spain	Societal	CUA	Cost per QALY	Infants with CHD	Lifetime	3%	AbbVie (grant)
Smart et al[39,51] 2010	Canada	Payer (BC) and societal	CUA	Cost per QALY	Preterm infants with risk factors	Lifetime	5%	Unknown: financial and other relationships with Abbott but not funded for this study

TABLE 1 Continued

Author, y	Country	Perspective	Type of Analysis	Outcome Measure	Population	Time Horizon	Discount Rate	Industry Funding
Tam et al[40] 2009	Canada	Payer (BC) and societal	CUA	Cost per QALY	NR	Lifetime	5%	Abbott Laboratories and Abbott International (grant)
Vogel et al[41] 2002	New Zealand	Societal	CEA; CBA	Cost per case averted	Preterm infants with CLD	3 y[a]	NR	Abbott (grant)
Wang et al[14] 2008	United Kingdom	Payer (BC) and societal	CUA	Cost per QALY	Preterm infants with BPD, CHD, or CLD; term infants with risk factors	Lifetime	3.5%	None
Weiner et al[42] 2012	United States	Societal	CUA	Cost per QALY	Preterm infants with risk factors	Lifetime	3%	MedImmune, LLC
Yount et al[43] 2004	United States	Societal	CUA; CBA	Cost per QALY	Infants with CHD	Lifetime	3%	None

BC, base case; CBA, cost-benefit analysis; CEA, cost-effectiveness analysis; CUA, cost-utility analysis; NR, not reported; N/A, not applicable.

[a] Not clearly reported; assumed on the basis of data used for cohorts.

[b] Four percent for economic outcomes and 1.5% for clinical outcomes.

<24 months of age on the basis of their respective country guidelines on palivizumab use. High-risk infant populations were often studied, and, in some cases, overlapped: preterm infants (≤35 weeks' gestational age [wGA]) (n = 19), BPD or CLD (n = 13), CHD (n = 11), and other risk factors (n = 6).

Study Outcomes

Base-case analyses were almost equally conducted from a societal perspective (n = 13) or health care–payer perspective (n = 15). In 8 of the 15 payer-perspective studies, additional analyses were performed from a societal perspective. Time horizon ranged from 6 months to lifetime; a time horizon was not reported in 1 study.[48] (Table 1) Discount rates ranged between 3% and 5%; in 5 studies, the authors did not discount because of a limited time horizon,[24,33,34,45,46] and a discount rate was not reported in 3 studies.[41,48,49] The majority of studies were industry sponsored (n = 17; 61%). Cost-effectiveness was mostly reported as cost per QALY (n = 20) and cost per hospitalization averted (HA) (n = 5). For the remainder of this review, we described results using adjusted ICERs (2017 USDs); original unadjusted ICERs are summarized in Table 2.

Cost-effectiveness Reported in Cost per QALY

For studies in which cost-effectiveness was reported in cost per QALY units, we summarized the number of estimates, the ICER ranges, and the proportion of estimates under selected thresholds of $50 000 to $200 000 per QALY, stratified by population subgroups and study perspective in Table 3. From a health care–payer perspective, there were 22 varying cost-effectiveness estimates for preterm infants, ranging between $5188 and $791 265 per QALY.* The subgroups with the next highest estimates were preterm infants with risk factors (n = 14),[25,37,39,40] in which the ICER was between $177 and $169 103 per QALY; infants with CHD (n = 10),[14,27,29,30,32,35] in which the ICER was between $9837 and $139 051 per QALY; and infants with BPD or CLD (n = 6),[27,29,32,35,47] in which the ICER was between $3984 and $40 036 per QALY. At a threshold of $100 000 per QALY, 86% of estimates for preterm infants, 86% of estimates for preterm infants with risk factors, 90% of estimates for infants with CHD, and 100% of estimates for infants with BPD or CLD were considered cost-effective. Other risk factors considered in preterm infants included chronological age at the beginning of the RSV season, school-aged siblings, day care attendance, smoking during pregnancy, male sex, and cystic fibrosis (in term infants only).[25,37,39,42,52] From a societal perspective, palivizumab prophylaxis was considered a dominant strategy (ie, the strategy provided additional clinical benefit and was cost saving) in some instances for preterm infants,[28,42,52] term infants (with and without other risk factors),[40] and infants with CHD.[29]

* Refs 14,27–29,32,36,37,39,47

Cost-effectiveness Reported in HAs

There were 5 studies in which cost-effectiveness was reported in cost per HA,[14,24,33,34,48] of which 2 were industry funded.[24,34] In the study by Banerji et al,[24] the authors studied healthy term infants from a payer perspective in different regions of the Canadian Arctic and compared 2 scenarios of palivizumab prophylaxis for infants who were <6 months of age. The ICER for palivizumab prophylaxis ranged from being dominant (in specific Arctic regions) to $479 242 per HA in the Northwest Territories.[24] Also from the payer perspective, Hampp et al[48] assessed cost-effectiveness in preterm infants

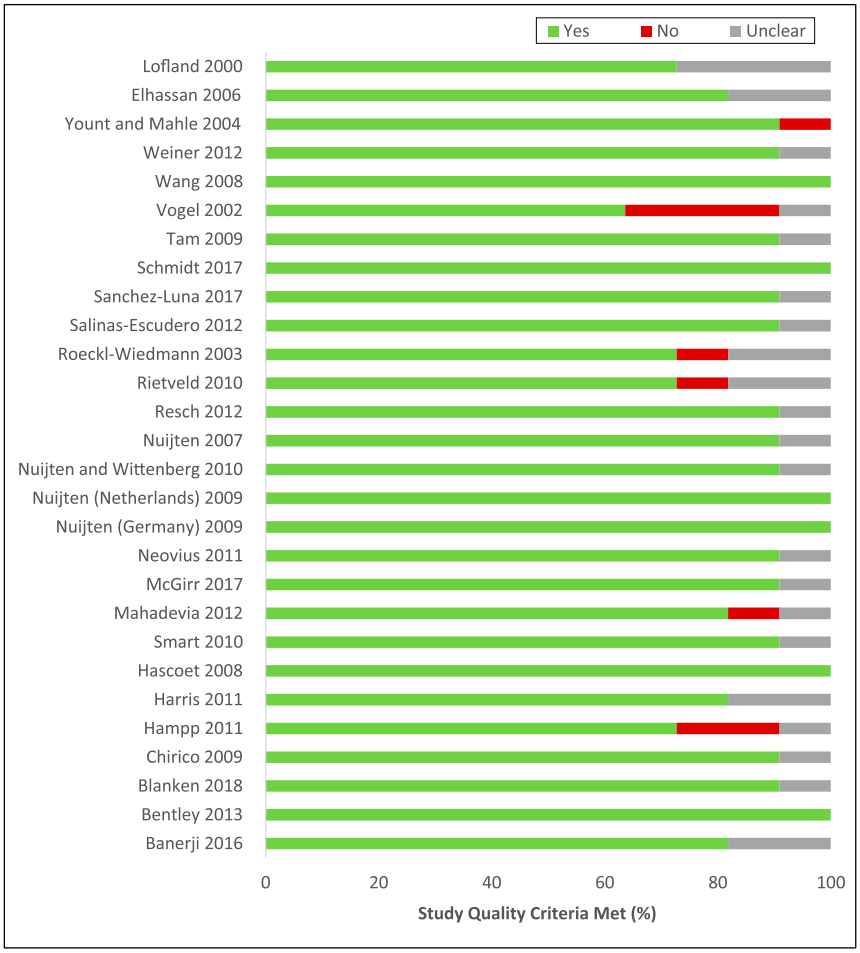

FIGURE 2
Quality appraisal results.

(<32 wGA) and term infants with CHD, CLD, and combinations of all 3 risk factors in a Florida setting. The ICERs were between $339 852 (preterm infants) and $2 406 129 per HA (healthy term infants without CLD or CHD).[48]

From a societal perspective, the study by Rietveld et al[33] in 2010 from southwest Netherlands studied preterm infants (<28 wGA) with additional risk factors (male sex, birth weight <2500 g, and BPD). The ICER ranged between $21 066 and $1 331 529 per HA depending on the month of the prophylaxis. The most cost-effective month for palivizumab prophylaxis (lowest ICER) was December, whereas the least cost-effective month was October. In this study, the authors recommended a restricted immunization policy on the basis of their results.[33] Roeckl-Wiedmann et al[34] conducted a study in 2003 from southern Germany on preterm infants (<35 wGA) with additional risk factors. ICERs ranged between $10 011 and $308 658 per HA for preterm infants with CLD and preterm infants with risk factors (male sex, no CLD, and no siblings in school), respectively. In this study, the authors also recommended a restricted use of palivizumab in preterm infants with CLD.[34]

Cost-effectiveness in Other Outcomes

Authors of 4 studies reported cost-effectiveness of palivizumab prophylaxis in other units: cost to prevent 1 day of hospitalization,[49] cost per LYG,[50] cost per case averted,[41] and cost per RSV infection episode avoided.[45] In 3 of 4 studies, authors conducted analyses from a societal perspective.[41,49,50] Harris et al[49] conducted an economic evaluation on term infants with CHD in western Canada. The base-case ICER was $15 111 per 1 day of hospitalization prevented.[49] Hascoet et al[50] studied preterm infants (<32 wGA) with BPD or significant CHD in France. The base-case ICER was $36 971 per LYG and $28 198 per LYG for preterm infants with BPD and preterm infants with cardiopathy (CHD), respectively. The authors of this study used a cost-effectiveness threshold (unadjusted) of 45 000 Euros per LYG and considered prophylaxis cost-effective for both subgroups in France.[50] In New Zealand, Vogel et al[41] studied preterm infants (<28 and 29–31 wGA) and infants with CLD. The ICER ranged between $28 265 per case avoided for preterm infants discharged from the hospital on oxygen and $164 176 per case avoided for preterm (29–31 wGA) infants with CLD. The authors concluded that the intervention was more cost-effective for preterm infants discharged from the hospital on oxygen followed by preterm infants of ≤28 weeks' gestation.[41] Lastly, Lofland et al[45] studied preterm infants with CLD in the United States. Their model used a reduction in incidence of RSV infection instead of a hospitalization reduction approach, ranging from a 50% ($56 313 per RSV infection episode avoided) to 83% reduction, in which palivizumab prophylaxis was considered a dominant strategy (ie, cost savings).[45]

Cost-effectiveness in Preterm Infants

The cost-effectiveness of palivizumab prophylaxis compared with no palivizumab prophylaxis ranged from being a dominant strategy to $2 526 203 per QALY in preterm infants. Because studies estimated cost-effectiveness for varying ranges

TABLE 2 Study Outcomes

Author, y	Country or Original Currency, y	ICER (Original)	ICER (Adjusted), 2017 USD	Outcome Measure	Results (Context)	Type of Sensitivity Analysis	Study Conclusions
Banerji et al[24] 2016	CAD 2011	4633	4073	Cost per HA	Scenario B, Nunavut without Iqaluit[a]	Deterministic	Palivizumab was cost-effective in the Kitikmeot and Kivalliq regions and in Nunavik. Scenario B (compared with Scenario A) was more cost-effective in all regions except the Kitikmeot region.
		14 545	12 787		Scenario B, Nunavut[a]		
		15 601	13 716		Scenario B, Nunavik[a]		
		22 954	20 180		Scenario A, Kivalliq region[a]		
		28 580	25 126		Scenario A, Nunavut without Iqaluit[a]		
		30 230	26 577		Scenario A, Nunavik[a]		
		41 404	36 401		Scenario A, Nunavut[a]		
		105 259	92 539		Scenario B, Qikiqtaaluk region without Iqaluit[a]		
		133 407	117 286		Scenario B, Qikiqtaaluk region[a]		
		166 600	146 468		Scenario A, Qikiqtaaluk region without Iqaluit[a]		
		211 444	185 893		Scenario A, Qikiqtaaluk region[a]		
		326 441	286 993		Scenario B, NWT[a]		
		545 115	479 242		Scenario A, NWT[a]		
		Dominant	Dominant		Scenario A, Kitikmeot region[a]		
		Dominant	Dominant		Scenario B, Kitikmeot region[a]		
		Dominant	Dominant		Scenario B, Kivalliq region[a]		
Bentley et al[35] 2013	GBP 2010	3845	6165	Cost per QALY gained	Preterm infants (<29 wGA)	Deterministic; probabilistic	Prophylactic palivizumab represents an economically viable use of NHS resources for infants (aged <24 mo) with CHD, infants (aged <24 mo) with CLD, preterm infants born at ≤32 wGA, and preterm infants born 33–35 wGA when additional risk factors are considered.
		19 168	30 734		Infants with CLD		
		30 205	48 430				
		33 216	53 258		Infants with CHD		
		99 056	158 824		Preterm infants (33–35 wGA)		
Blanken et al[46] 2018	Netherlands 2015	214 748	272 654	Cost per QALY gained	Preterm (32–35 wGA)	Deterministic; probabilistic	—
Chirico et al[47] 2009	Italy 2007	2732	3984	Cost per QALY gained	BPD	Deterministic	Compared with no prophylaxis, palivizumab is cost-effective in the prevention of RSV infection among high-risk preterm infants.
		8677	12 653		Preterm (<35 wGA, mix) with BPD		
		9380	13 679		Preterm (<33 wGA)		
		14 937	21 783		Preterm (33–35 wGA)		
Elhassan et al[44] 2006	USD 2002	103 053	140 341	Cost per QALY gained	Base case, preterm (26 wGA), targeted use policy	Deterministic	Our model supports implementing more restrictive guidelines for palivizumab prophylaxis. Palivizumab was cost-effective for some infants in an analysis used to account for increased risk of severe asthma after RSV infection. We found evidence that long-term health consequences of RSV are central to the determination of the cost-effectiveness of the intervention.

TABLE 2 Continued

Author, y	Country or Original Currency, y	ICER (Original)	ICER (Adjusted), 2017 USD	Outcome Measure	Results (Context)	Type of Sensitivity Analysis	Study Conclusions
		216 830	295 287		Base case, preterm (28 wGA), targeted use policy		
		280 083	381 427		Base case, preterm (29–30 wGA), targeted use policy		
		675 780	920 300		Base case, preterm (29–30 wGA)		
		830 152	1 130 530		Base case, preterm (26 wGA)		
		1 212 497	1 651 220		Base case, preterm (31 wGA)		
		1 295 781	1 764 639		Base case, preterm (27 wGA)		
		1 500 351	2 043 230		Base case, preterm (28 wGA)		
		1 855 000	2 526 203		Base case, preterm (32 wGA)		
Hampp et al[48] 2011	USD 2010	302 103	339 852	Cost per HA	Preterm (<32 wGA)	Deterministic; probabilistic	The cost of immunoprophylaxis with palivizumab far exceeded the economic benefit of preventing hospitalizations, even in infants at highest risk for RSV infection.
		361 727	406 926		Preterm (<32 wGA) and CHD		
		368 048	414 037		Preterm (<32 wGA) and CLD		
		522 490	587 777		Term, CLD, and CHD		
		823 868	926 813		Term and CHD only		
		920 033	1 034 994		Any risk factor (indication)		
		1 322 422	1 487 663		Term and CLD only		
		2 138 870	2 406 129		No risk factor (indication)		
Harris et al[49] 2011	CAD 2007	8292	8077	Cost to treat 1 child per RSV season	Base case	Deterministic	With our study, we contribute to the growing body of literature in which it is suggested that palivizumab is not cost-effective in children <2 y old with hemodynamically significant CHD.
		15 513	15 111	Cost to prevent 1 d of hospitalization	Base case		
Hascoet et al[50] 2008	France 2006	10 172	13 798	Cost per LYG	Preterm (<32 wGA), with BPD (health care)	Deterministic; probabilistic	Prophylaxis with palivizumab for RSV in premature children with BPD or hemodynamically significant CHD can be considered cost-effective in France.
		20 788	28 198		Preterm (<32 wGA), with cardiopathy (societal)		
		27 255	36 971		Preterm (<32 wGA), with BPD (societal)		
Lofland et al[45] 2000	USD 2000	1008	1434	Cost per RSV-infection episode avoided	Base case, preterm (NR wGA), 81% reduction incidence of RSV infection (5% vs 26%)	Deterministic	The incremental cost per RSV-infection episode avoided ranged from $0 (cost savings) to $39 591 for palivizumab prophylaxis costs of $2500 and from $2702 to $79 706 for palivizumab prophylaxis costs of $4500. Clinicians may use this information to help determine if prophylactic palivizumab therapy is cost-effective in their clinical practice setting.
		39 591	56 313		Preterm (NR wGA), 50% reduction incidence of RSV infection (5% vs 10%)		
		Dominant	Dominant		Preterm (NR wGA), 83% reduction incidence of RSV infection (5% vs 28%)		

TABLE 2 Continued

Author, y	Country or Original Currency, y	ICER (Original)	ICER (Adjusted), 2017 USD	Outcome Measure	Results (Context)	Type of Sensitivity Analysis	Study Conclusions
Mahadevia et al[52] 2012	USD 2010	44 774	50 369	Cost per QALY gained	Group 2, preterm (32–35 wGA) with risk factors[b]	Deterministic	Palivizumab remained cost-effective for guideline-eligible high-risk infants across both public and private sectors. Guideline-eligible infants included infants of <32 wGA, 32–34 wGA with 2009 AAP risk factors, and 32–35 wGA with 2006 AAP risk factors. Palivizumab was not cost-effective in infants of 32–35 wGA with 1 risk factor.
		79 477	89 408		Group 3, preterm (32–35 wGA) with risk factors[b]		
		464 476	522 514		Group 4, preterm (32–35 wGA) with risk factors[b]		
		Dominant	Dominant		Group 1, preterm (<32 wGA)[b]		
McGirr et al[25] 2017	CAD 2013	157 332	135 207	Cost per QALY gained	High-risk CF <2 y (high risk for severe RSV disease)	Deterministic	Palivizumab is not cost-effective in Canada by commonly used thresholds. However, given the rarity of CF and the relatively small budget impact, consideration may be given.
		652 560	560 792		All CF < 2 y		
Neovius et al[26] 2011	SEK 2009	148 293	19 000	Cost per QALY gained	Preterm (<29 wGA), adding wheezing to asthma	Deterministic; probabilistic	On the basis of a willingness-to-pay threshold of 500 000 SEK per QALY, palivizumab was found to be cost-effective compared with no prophylaxis for infants born at <29 wk if severe RSV infection was assumed to increase subsequent asthma or mortality risk.
		195 420	25 038		Base case, preterm (<29 wGA)		
		383 825	49 178		Preterm (<29 wGA), excluding indirect effect on asthma		
		492 430	63 093		Preterm (<29 wGA), excluding indirect effect on mortality		
		8 856 829	1 134 793		Preterm (<29 wGA), excluding the indirect effect of mortality and asthma		
Nuijten et al[30] 2009_DEU	Germany 2006	2221	3180	Cost per QALY gained	Base case, Cardiac Study parameters, societal	Deterministic; probabilistic	This analysis revealed that palivizumab represents a cost-effective means of prophylaxis against severe RSV infection requiring hospitalization in infants with hemodynamically significant CHD.
		9528	13 643		Base case, Cardiac Study parameters, including asthma, payer		
		9529	13 644		Base case, societal		
		11 126	15 931		Base case, Cardiac Study parameters, excluding asthma, payer		
		16 673	23 874		Base case, direct medical costs (including asthma), payer		
		18 266	26 155		Base case, direct medical costs (excluding asthma), payer		
		123 439	176 749				

TABLE 2 Continued

Author, y	Country or Original Currency, y	ICER (Original)	ICER (Adjusted), 2017 USD	Outcome Measure	Results (Context)	Type of Sensitivity Analysis	Study Conclusions
					Base case, excluding mortality, societal		
Nuijten et al[29] 2009_NLD	Netherlands 2006	7067	9837	Cost per QALY gained	Base case: CHD	Deterministic; probabilistic	Palivizumab provides cost-effective prophylaxis against RSV in high-risk infants. The use of palivizumab in these children results in positive short- and long-term health-economic benefits.
		11 336	15 779		Base case: preterm (<35 wGA, mix), with BPD (total costs, societal)		
		18 563	25 838		Preterm (<35 wGA, mix)		
		20 236	28 167		Base case: preterm (<35 wGA, mix), with BPD		
		23 461	32 655		Subpopulations with BPD		
		Dominant	Dominant		Base case: CHD (total costs, societal)		
Nuijten and Wittenberg[28] 2010	Spain 2006	6498	10 715	Cost per QALY gained	Base case, preterm (<32 wGA), inclusion of costs of sequelae treatment	Deterministic; probabilistic	Palivizumab provides a cost-effective method of prophylaxis against severe RSV disease among preterm infants in Spain.
		12 814	21 130		Base case, preterm (<32 wGA)		
		Dominant	Dominant		Base case, preterm (<32 wGA), societal perspective		
Nuijten et al[27] 2007	GBP 2003	6664	12 733	Cost per QALY gained	CHD	Deterministic; probabilistic	This study reveals that palivizumab prophylaxis against severe RSV infection in children at high risk may be cost-effective from the NHS perspective
		11 494	21 962		Base case, preterm (<35 wGA), with indirect costs (societal)		
		14 883	28 438		Preterm (<35 wGA)		
		16 720	31 948		Base case, preterm (<35 wGA), with BPD		
		20 953	40 036		BPD only		
Resch et al[31,32] 2008, 2012	Austria 2010	3045	4071	Cost per QALY gained	Base case, CHD, including recurrent wheezing treatment, societal	Deterministic	Our results, which are based on nationwide long-term epidemiological data, reveal that palivizumab is cost-effective in the prevention of RSV disease in high-risk infants.
		7818	10 452		Base case, CHD, including recurrent wheezing treatment		
		8484	11 343		Base case, CHD		
		15 800	21 124		Base case, for all preterm (<35 wGA, mix), including recurrent wheezing treatment, societal		
		15 992	21 380		Base case, preterm (33–35 wGA), including recurrent wheezing treatment, societal		
		17 554	23 469				

TABLE 2 Continued

Author, y	Country or Original Currency, y	ICER (Original)	ICER (Adjusted), 2017 USD	Outcome Measure	Results (Context)	Type of Sensitivity Analysis	Study Conclusions
					Base case, BPD, including recurrent wheezing treatment, societal		
		18 133	24 243		Base case, preterm (<33 wGA), including recurrent wheezing treatment, societal		
		21 669	28 970		Base case, for all preterm (<35 wGA, mix), including recurrent wheezing treatment		
		21 862	29 228		Base case, preterm (33–35 wGA), including recurrent wheezing treatment		
		22 515	30 101		Base case, BPD, including recurrent wheezing treatment		
		23 833	31 863		Base case, preterm (<33 wGA), including recurrent wheezing treatment		
		24 392	32 611		Base case, preterm (33–35 wGA)		
		24 654	32 961		Base case, BPD		
		26 212	35 044		Base case, for all preterm (<35 wGA, mix)		
		26 292	35 151		Base case, preterm (<33 wGA)		
Rietveld et al[33] 2010	Netherlands 2000	13 190	21 066	Cost per HA	Male infant, preterm (<28 wGA), birth wt <2500 g, with BPD (December)	Deterministic	Every mo, costs per HA were higher for children without BPD and children with higher gestational ages. Incremental costs per HA were always high. Passive immunization was always most cost-effective in December. A restrictive immunization policy requiring immunization of only children with BPD in high-risk months is therefore recommended. The costs of passive immunization would have to be considerably reduced to achieve cost-effectiveness.
		30 795	49 184		Male infant, preterm (<28 wGA), birth wt <2500 g, with BPD (January)		
		31 055	49 599		Male infant, preterm (<28 wGA), birth wt <2500 g, with BPD (November)		
		47 145	75 297		Male infant, preterm (<28 wGA), birth wt <2500 g, with BPD (February)		
		105 120	167 892		Male infant, preterm (<28 wGA), birth wt <2500 g, with BPD (March)		
		395 860	632 245				

TABLE 2 Continued

Author, y	Country or Original Currency, y	ICER (Original)	ICER (Adjusted), 2017 USD	Outcome Measure	Results (Context)	Type of Sensitivity Analysis	Study Conclusions
					Male infant, preterm (<28 wGA), birth wt <2500 g, with BPD (April)		
		833 695	1 331 529		Male infant, preterm (<28 wGA), birth wt <2500 g, with BPD (October)		
Roeckl-Wiedmann et al[34] 2003	Germany 2000	6639	10 011	Cost per HA	Group A, preterm (<35 wGA)[c]	Deterministic	Because of the findings of our cost-effectiveness analysis, we would recommend a restricted use of palivizumab prophylaxis in premature infants with CLD in their risk combination. The results of this cost-effectiveness analysis do not justify the widespread use of palivizumab among preterm infants. Palivizumab was most cost-effective among male infants with CLD who had siblings visiting day care groups and who were discharged between October and December.
		25 288	38 134		Group B, preterm (<35 wGA), with risk factors[c]		
		52 838	79 678		Group C, preterm (<35 wGA), with risk factors[c]		
		204 684	308 658		Group D, preterm (<35 wGA), with risk factors[c]		
Salinas-Escudero et al[36] 2012	USD 2009	4539	5188	Cost per QALY gained	Partial coverage, preterm (<29 wGA)	Deterministic; probabilistic	Palivizumab prophylaxis for preterm newborn patients born at ≤32 wk resulted in a cost-effective alternative. When evaluating the ICER per QALY and LYG against the USD $50 000 threshold, all age groups within the prophylaxis group are cost-effective.
		7294	8337		Partial coverage, preterm (29–32 wGA)		
		17 532	20 038		Full coverage, preterm (<29 wGA)		
		20 760	23 728		Full coverage, preterm (29–32 wGA)		
Sanchez-Luna et al[37] 2017	Spain 2016	11 550	17 792	Cost per QALY gained	Subgroup A (payer)[d]	Deterministic; probabilistic	Of 1000 Monte Carlo simulations, 85.7% of the cases presented an ICUR <€30 000 per QALY. Palivizumab is efficient for preventing RSV infections in preterm infants 32 1/7 to 35 0/7 wGA in Spain, including specific high-risk subgroups.
		14 177	21 839		Subgroup B (payer)[d]		
		17 153	26 424		Base case (societal), preterm (32–35 wGA)		
		18 938	29 173		Subgroup C (payer)[d]		
		19 698	30 344		Base case (payer), preterm (32–35 wGA)		
Schmidt et al[38] 2017	Spain 2016	15 748	24 259	Cost per QALY gained	Base case	Deterministic; probabilistic	PSA revealed that the probability of palivizumab prophylaxis being cost-effective at a €30 000-per-QALY threshold was 92.7%. The ICER remained below this threshold for most extreme-scenario analyses. Palivizumab prophylaxis was shown to be

TABLE 2 Continued

Author, y	Country or Original Currency, y	ICER (Original)	ICER (Adjusted), 2017 USD	Outcome Measure	Results (Context)	Type of Sensitivity Analysis	Study Conclusions
							a cost-effective health care intervention according to the commonly accepted standards of cost-effectiveness in Spain (ICER below the threshold of €30 000 per QALY).
Smart et al[39,51] 2010	CAD 2010	192	177	Cost per QALY gained	Preterm (32–35 wGA), ≥4 risk factors	Deterministic; probabilistic	Palivizumab ICERs remained fairly stable from 2007 to 2010. The original recommendation stating that palivizumab is cost-effective in infants born between 32 and 35 wGA with ≥2 risk factors or in infants who are at a moderate to high risk on the basis of a risk-assessment model, does not change.
		5274	4859		Preterm (32–35 wGA), risk-scoring tool, high risk (65–100 score)		
		20 814	19 175		Base case, preterm (32–35 wGA), including asthma		
		26 701	24 598		Preterm (32–35 wGA), 3 risk factors		
		31 360	28 890		Base case, preterm (32–35 wGA), excluding asthma		
		34 438	31 726		Preterm (32–35 wGA), risk-scoring tool, medium risk (49–64 score)		
		48 495	44 675		Base case, preterm (32–35 wGA), mortality rate (1.2%)		
		50 434	46 462		Base case, preterm (32–35 wGA), mortality rate (1.0%)		
		82 732	76 216		Preterm (32–35 wGA), 2 risk factors		
		146 218	134 701		Preterm (32–35 wGA), 1 risk factor		
		183 561	169 103		Preterm (32–35 wGA), risk-scoring tool, low risk (0–48 score)		
		820 701	756 060		Preterm (32–35 wGA), 0 risk factors (preterm only)		
Tam et al[40] 2009	CAD 2007	334	325	Cost per QALY gained	High risk area (defined as having hospitalization rates over 500/1000 live births) and <1 y	Deterministic; probabilistic	Palivizumab is a cost-effective option for the prevention of RSV for Inuit infants on Baffin Island, is highly cost-effective in Arctic infants <1 y of age specifically residing outside of Iqaluit, and is a dominant strategy for those <6 mo of age in remote areas. However, palivizumab is not cost-effective compared with no treatment of infants of all ages residing in Iqaluit.
		7822	7619		Infants from Baffin Island <6 mo, societal		
		10 190	9926		Infants from Baffin Island <6 mo		
		22 383	21 803		Outside of Iqaluit (remote areas) <1 y, societal		
		24 750	24 109		Outside of Iqaluit (remote areas) <1 y		
		37 070	36 110				

TABLE 2 Continued

Author, y	Country or Original Currency, y	ICER (Original)	ICER (Adjusted), 2017 USD	Outcome Measure	Results (Context)	Type of Sensitivity Analysis	Study Conclusions
					All infants from Baffin Island <1 y, societal		
		39 435	38 414		All infants from Baffin Island <1 y		
		100 872	98 260		Residing in Iqaluit <6 mo, societal		
		103 235	100 561		Residing in Iqaluit <6 mo		
		149 782	145 903		Residing in Iqaluit <1 y, societal		
		152 145	148 205		Residing in Iqaluit <1 y		
		Dominant	Dominant		Infants in remote areas <6 mo		
		Dominant	Dominant		High-risk areas, <6 mo		
		Dominant	Dominant		High-risk areas, <1 y, societal		
		Dominant	Dominant		Infants in remote areas <6 mo, societal		
		Dominant	Dominant		High-risk areas, <6 mo, societal		
Vogel et al[41] 2002	NZD 2000	28 700	28 265	Cost per case averted	Preterm (32–35 wGA), with CLD, discharged from the hospital on oxygen	Deterministic	If value is placed on preventing morbidity, the priority groups for palivizumab prophylaxis are preterm infants discharged from the hospital on oxygen followed by preterm infants of ≤28 wk gestation.
		32 000	31 515		Preterm (≤28 wGA), no CLD		
		60 000	59 091		Total cohort, preterm (32–35 wGA), with CLD, societal		
		65 000	64 016		Preterm (≤28 wGA), with CLD		
		98 000	96 516		Preterm (29–31 wGA), no CLD		
		166 700	164 176		Preterm (29–31 wGA), with CLD		
Wang et al[14] 2008	GBP 2006	51 800	90 261	Cost per HA	Preterm infants (<35 wGA) and children without CLD	Deterministic	According to this model, prophylaxis with palivizumab is not a cost-effective strategy for preterm infants and children with CHD compared with no prophylaxis from both an NHS perspective and a societal perspective. These findings are robust to probabilistic and other sensitivity analyses. Prophylaxis with palivizumab is also not a cost-effective strategy for preterm infants or infants with CLD who have no other risk factors. Subgroup analyses revealed that prophylaxis with palivizumab for children with CLD may be cost-effective at a willingness-to-pay threshold of £30 000 per QALY.
		63 800	111 171	Cost per QALY gained	Preterm infants (<35 wGA) and children with CLD		
		66 900	116 573		Preterm infants (<35 wGA) and children with CLD (societal)		
		67 600	117 792	Cost per HA	Preterm infants (<35 wGA) and children with CLD		
		78 600	136 960		CHD		
		79 800	139 051	Cost per QALY gained	CHD		
		83 200	144 975		CHD (societal)		

TABLE 2 Continued

Author, y	Country or Original Currency, y	ICER (Original)	ICER (Adjusted), 2017 USD	Outcome Measure	Results (Context)	Type of Sensitivity Analysis	Study Conclusions
		454 100	791 265		Preterm infants (<35 wGA) and children without CLD		
		475 600	828 728		Preterm infants (<35 wGA) and children without CLD (societal)		
Weiner et al[42] 2012	USD 2010	16 037	18 041	Cost per QALY gained	Base-case group 2, preterm (32–34 wGA), with risk factors[e]	Deterministic; probabilistic	Palivizumab, when dosed consistently with the FDA-approved labeling, was either cost saving or cost-effective among current guideline-eligible infants in the Medicaid population. Palivizumab did not reveal cost-effectiveness in infants of 32–35 wGA with ≤1 risk factor.
		38 244	43 023		Base-case group 3, preterm (32–35 wGA), with risk factors[e]		
		281 892	317 115		Base-case group 4, preterm (32–35 wGA), with risk factors[e]		
		Dominant	Dominant		Base-case group 1, preterm (<32 wGA)[e]		
Yount and Mahle[43] 2004	USD 2002	114 337	155 708	Cost per QALY gained	Base case, term, CHD	Deterministic	The cost of palivizumab prophylaxis was high relative to benefits realized. Given the large No. CHD patients who might be considered candidates for RSV prophylaxis (>6000 patients per y in the United States), routine use of palivizumab in young children with CHD needs to be evaluated further.

CAD, Canadian dollar; CF, Cystic fibrosis; FDA, Food and Drug Administration; GBP, Great Britain pound; ICUR, Incremental cost-utility ratio; NR, not reported; NWT, Northwest Territories; NZD, New Zealand dollar; PSA, Probabilistic sensitivity analysis; SEK, Swedish krona; —, not applicable.

[a] Scenario A[24]: universal palivizumab prophylaxis for all healthy term infants who were <6 mo of age as of January 1, 2009, was compared with no prophylaxis; Scenario B: palivizumab prophylaxis for infants up to 5 mo of age only (for 6 mo of protection) was compared with no prophylaxis.

[b] Group 1[52]: <32 wGA and <6 mo chronological age; group 2: 32–34 wGA and ≤3 mo chronological age, with 2009 AAP risk factors; group 3: 32–35 wGA and ≤6 mo chronological age, with 2006 AAP risk factors; group 4: 32–35 wGA and ≤6 mo chronological age, with ≤1 risk factor.

[c] Group A[34]: Male infants, siblings in day care, discharged between October and December, CLD; group B: male infants, siblings in day care, discharged between October and December; group C: male infants, siblings in day care; group D: male infants.

[d] Subgroup A: preterm (32–35 wGA), with risk factors (2 major, 2 minor); Subgroup B: preterm (32–35 wGA), with risk factors (2 major, 1 minor); Subgroup C: preterm (32–35 wGA), with risk factors (2 major risk factors)

[e] Base-case group 1[42]: <32 wGA and ≤6 mo chronological age; base-case group 2: 32–34 wGA and ≤3 mo chronological age, with 2009 AAP risk factors (ie, having siblings <5 y of age and/or attending day care); base-case group 3: 32–35 wGA and ≤6 mo chronological age, with 2006 AAP risk factors (any 2 of the following: exposure to environmental air pollutants, congenital abnormalities of the airways, severe neuromuscular disease, school-aged siblings, and day care attendance); base-case group 4: 32–35 wGA and ≤6 mo chronological age, with ≤1 risk factor.

TABLE 3 Summary of Cost-effectiveness Estimates by Health Condition and Perspective

	Health Conditions						
	BPD or CLD	CHD	Healthy	Preterm	Preterm With BPD or CLD	Preterm With Risk Factors	Other Risk Factors[a]
Payer perspective							
No. estimates	6	10	6	22	4	14	4
ICER (minimum)	3984	9837	Dominant	5188	12 653	177	Dominant
ICER (maximum)	40 036	139 051	148 205	791 265	111 171	169 103	560 792
Proportion of estimates' CE <$50 000 per QALY	1.00	0.80	0.67	0.86	0.75	0.79	0.50
Proportion of estimates' CE <$100 000 per QALY	1.00	0.90	0.67	0.86	0.75	0.86	0.50
Proportion of estimates' CE <$200 000 per QALY	1.00	1.00	1.00	0.91	1.00	1.00	0.75
Societal perspective							
No. estimates	1	8	6	23	3	6	2
ICER (minimum)	23 469	Dominant	Dominant	Dominant	15 779	18 041	Dominant
ICER (maximum)	23 469	176.749	145 903	2 526 203	116 573	522 514	Dominant
Proportion of estimates' CE <$50 000 per QALY	1.00	0.63	0.67	0.43	0.67	0.33	1.00
Proportion of estimates' CE <$100 000 per QALY	1.00	0.63	0.83	0.48	0.67	0.67	1.00
Proportion of estimates' CE <$200 000 per QALY	1.00	1.00	1.00	0.52	1.00	0.67	1.00

All ICERs are reported in 2017 USDs per QALY. CE, cost-effective.

[a] Cystic fibrosis, major risk factors (chronological age <10 wk at beginning of RSV season [being born during first 10 wk of the season], school-aged siblings, and day care attendance), and minor risk factors (mother smoking during pregnancy and male sex).

of wGA, we were unable to group all estimates into predefined intervals. For example, we did not group <29 wGA estimates under the <32 wGA estimates because we could not infer or reasonably assume the breakdown of the wGA in each preterm group. From the payer perspective, the ICER for palivizumab prophylaxis for infants born at <29 wGA (n = 3) ranged between $5188 and $20 038 per QALY.[35,36] For infants born at 29 to 32 wGA, the ICER (n = 3) ranged between $8337 and $48 430 per QALY.[35,36] At <32 wGA and <33 wGA, 2 estimates ($10 715–$21 130 per QALY)[28] and 3 estimates ($13 679–$35 151 per QALY) were identified, respectively.[32,47] In the 32- to 35-wGA range (includes 2 estimates at 32–35 wGA and 4 estimates at 33–35 wGA), there were 6 ICER estimates for preterm infants ($21 783–$756 060 per QALY)[32,35,37,39,47] and 14 ICER estimates for preterm infants with additional risk factors ($177–$169 103 per QALY).[37,39] For preterm infants born at <35 wGA, there were 5 estimates between $25 838 and $791 265 per QALY.[14,27,29,32] All preterm infants with BPD or CLD were estimated in this <35-wGA group, in which the 4 estimates were between $12 653 and $111 171 per QALY.[14,27,29,47]

From a societal perspective, estimates of preterm infants born at 26 to 28 wGA were entirely extracted from Elhassan et al,[44] with ICERs between $140 341 and $2 043 230 per QALY. For preterm infants born at <29 wGA, there were 5 ICER estimates between $19 000 and $1 134 793 per QALY.[26] The cost-effectiveness of palivizumab from a societal perspective varied across studies for preterm infants born between 29 and 35 wGA, with ICER estimates between $381 427 and $920 300 per QALY (29–30 wGA),[44] being a dominant strategy (ie, cost savings and provides clinical benefits for <32 wGA),[28,42,52] $26 424 and $272 654 per QALY (32–35 wGA),[37,46] and $21 124 and $828 728 per QALY (<35 wGA).[14,32] In preterm infants (<35 wGA) with lung complications, 3 studies reported separate ICER estimates between $15 779 and $116 573 per QALY.[14,27,29] Six estimates were reported for preterm infants with risk factors between $18 401 and $522 514 per QALY ($18 401–$50 369 per QALY for two 32–34-wGA estimates and $43 023–$522 514 per QALY for four 32–35-wGA estimates).[42,52]

We stratified and plotted the ICERs for palivizumab prophylaxis expressed in cost per QALY in preterm infants by wGA in Fig 3; we presented 57 of 72 ICER estimates, stratified by study perspective, that were estimated <$200 000 per QALY.[†] In Fig 3, 51 of the 57 (89%) ICER estimates for preterm infants (with or without other RSV risk factors) were below the $100 000-per-QALY threshold. Of the 15 ICER estimates excluded from Fig 3, 8 (ie, more than half) were from a single study by Elhassan et al,[44] whereas the rest were single estimates from other studies.[14,26,35,39,42,46,52]

Cost-effectiveness in Infants From Remote Regions of the Canadian Arctic

Authors of 2 studies investigated the cost-effectiveness of palivizumab prophylaxis in Arctic (remote) regions of Canada.[24,40] In the study by Tam et al,[40] palivizumab was cost-effective from a health care–payer perspective for all infants from Baffin Island who were <1 year of age ($38 414 per QALY) or <6 months of age ($9926 per QALY), infants <1 year of age and from high risk areas for RSV ($325 per QALY), infants <1 year of age from remote areas ($24 109 per QALY), infants

[†] Refs 14,26–29,31,32,35–37,39,42,44,47,51,52.

<6 months of age from remote areas (dominant), and infants <6 months of age from high risk areas for RSV (dominant). However, when compared with a $100 000-per-QALY threshold, it was not cost-effective for infants <6 months or for infants <1 year of age residing in Iqaluit.[40] Similarly, Banerji et al[24] concluded that their proposed palivizumab programs would be cost-effective in some but not all Arctic regions. The authors of both studies attributed the likelihood of these results to the higher hospitalization rates and transportations costs associated with hospitalization from remote areas to hospitals.[24,40]

Key Parameters

Reduction in RSV hospitalization used in models ranged between 39% for infants with CLD in the United Kingdom[35] and 96% in healthy infants in a Canadian Arctic setting.[24] Mortality was reported in 19 studies, ranging between 1%[40,50] and 8.11%[32] for various infant populations. The number of palivizumab doses per season was between an average of 3.88 doses in a 5-month season in Spain[37] and 6 doses in a 6-month RSV season.[24] Authors of most studies evaluated cost-effectiveness assuming 5 palivizumab doses per RSV seasons (n = 17), whereas the authors of 3 studies did not report the dose schedule.[35,46,48] The cost of a 100-mg vial of palivizumab in 2017 USDs was between $904 (from a UK study)[35] and $1866 (from a US study).[44]

Influential Parameters

The most influential parameters reported across the 28 studies were the following: RSV hospitalization rates (43%),‡ cost of palivizumab (36%),§ discount rate (32%),[26–30,32,35,36,38] and efficacy of palivizumab (29%).[33–35,41,42,46,48,52] Other parameters that were influential in multiple studies included the following: mortality rate reduction, incidence of RSV (and/or sequelae), drug wastage resulting from vial usage, utility values (quality of life), and dosage scheme.

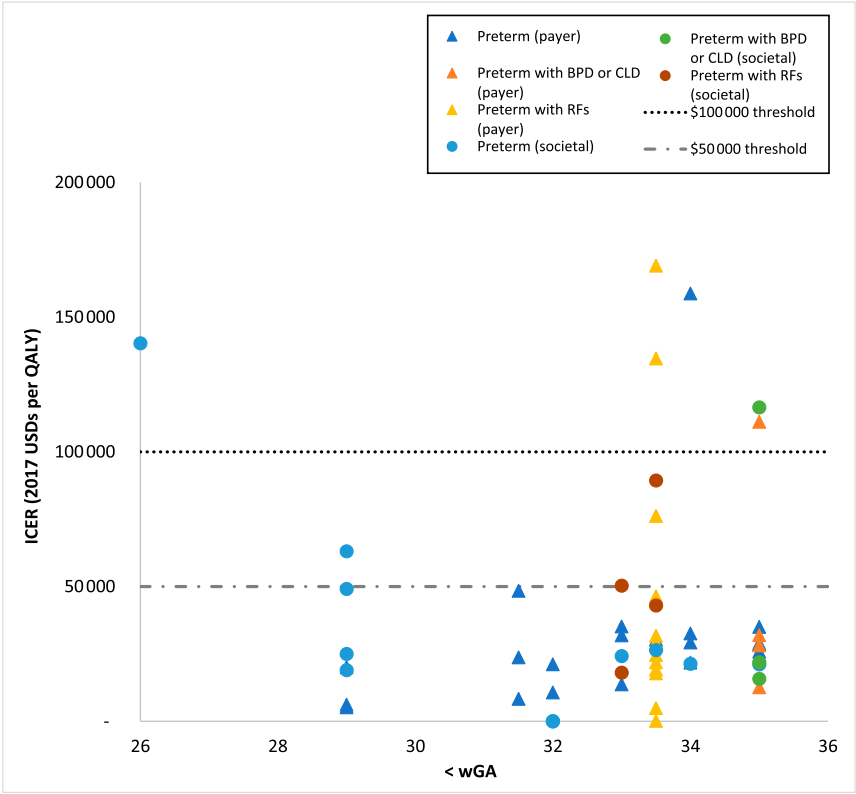

FIGURE 3

Cost-effectiveness of palivizumab in preterm infants in which the ICER was <$200 000 per QALY. The total number of estimates in the scatterplot (n = 57). ICERs >$200 000 per QALY were not captured in this figure (n = 15): From the payer perspective, the following were excluded: preterm (<35 wGA): $791 265 per QALY[14] and preterm (32–35 wGA): $756 060 per QALY.[39] From the societal perspective, the following were excluded: preterm (26 wGA): $1 130 530 per QALY,[44] preterm (27 wGA): $1 764 639 per QALY,[44] preterm (28 wGA): $2 043 230 per QALY,[44] preterm (28 wGA): $295 287 per QALY,[44] preterm (<29wGA): $1 134 793 per QALY,[26] preterm (29–30 wGA): $920 300 per QALY,[44] preterm (29–30 wGA): $381 427 per QALY,[44] preterm (31 wGA): $1 651 220 per QALY,[44] preterm (32 wGA): $2 526 203 per QALY,[44] preterm (32–35 wGA): $272 654 per QALY,[46] preterm (<35 wGA): $828 728 per QALY,[14] and preterm (32–35 wGA) with RFs: $522 514 per QALY[52] and $317 115 per QALY.[42] RF, risk factor.

DISCUSSION

In our systematic review, we identified 28 relevant economic evaluations from OECD countries assessing the cost-effectiveness of palivizumab prophylaxis compared with no prophylaxis. The greatest number of cost-effectiveness estimates came from preterm infants, which was expected given their higher risk for RSV.[6,8] The majority of estimates for infants with or without additional risk factors (eg, BPD and CHD) were below the $100 000-per-QALY threshold. The only exception to this was the estimates for preterm infants from the societal perspective, in which only 48% of the estimates were <$100 000 per QALY. This exception was likely a result of a large group of estimates (n = 8; 35% of subgroup) extracted from 1 study, with estimates between $295 287 and $2 526 203 per QALY.[44] Possible reasons for the higher ICERs in this study may include: using the highest adjusted cost for a 100-mg vial of palivizumab at $1866, following infants only up to 8 years of age, and,

‡ Refs 24,27,29,30,33–35,39,40,42,48,52.

§ Refs 25,30,33,34,42,44,45,48,49,52.

as suggested by the authors, overestimating the quality of life (utility) for subsequent asthma onset. Separate sensitivity analyses reducing the palivizumab cost by 25% and reducing the health-state utility value of asthma afforded ICERs <$200 000 per QALY and <$100 000 per QALY, respectively.[44]

On the basis of our review, the cost-effectiveness of palivizumab prophylaxis varies depending on the population and setting. To facilitate comparisons and summarize our findings, we adjusted all ICERs to 2017 USDs per QALY and stratified them on the basis of gestational age at birth and risk factors for RSV in Fig 3. For term and preterm infants with BPD or CLD, the ICER was <$50 000 per QALY in 9 of the 10 estimates from a payer perspective. All other subgroups of infants (term, preterm, and with CHD or other risk factors) resulted in inconsistent results for palivizumab prophylaxis, with the intervention being dominant at times and having an ICER up to $791 265 per QALY in other scenarios. When stratifying for preterm births by wGA, we noticed lacking evidence for infants born at <28 wGA, especially from the payer perspective. No specific trend was depicted between the wGA and the ICER, overall or stratified by perspective. However, we should note that although preterm estimates were available across 26 to 35 wGA, estimates for preterm infants with additional risk factors or BPD or CLD were limited to 33 to 35 wGA. Generally, one would expect ICERs from a societal perspective to be lower than those from a payer perspective, but on the basis of our review, this trend does not exist for 2 potential reasons: (1) payer and societal perspective estimates were coming from different studies and (2) there was heterogeneity in model designs and differences between setting-specific costs and RSV epidemiology.

Because palivizumab prophylaxis was determined to be cost-effective in some settings but not cost-effective in others, we summarized the most frequently reported influential parameters affecting the ICER, which were the RSV hospitalization rates and cost of palivizumab used. Reduction in RSV hospitalization varied drastically between 39% and 96% depending on the population of interest and the source of the data. The cost of a 100-mg vial of palivizumab also ranged between $904 and $1866 (2017 USDs). The influential nature of both parameters was expected given that reduction in RSV and RSV hospitalization is essential to reduction in costs and future sequelae, whereas the costs of palivizumab is directly related to the ICER. However, it was interesting to note that vial usage and dosage scheme only affected the ICER in 4[27,28,38,41] and 3 studies,[37,41,47] respectively. In studies where drug wastage through vial usage was addressed, ICERs fluctuated up to 50% depending on the assumed vial usage. In a New Zealand study, assuming no vial sharing (the entire 100-mg vial is used per injection) increased costs up to 50%,[41] whereas authors of a study from Spain reported a lower ICER when 50-mg vials were used instead of 100-mg vials.[28] It has been suggested in the literature and by physicians that vial-usage efficiency can be achieved for palivizumab.[53] Authors of many studies did not assess scenarios in which the vial usage became more efficient or the number of assumed doses was reduced, which remains a question that can be addressed in future studies.

The cost-effectiveness of palivizumab prophylaxis has been explored in multiple reviews in the past 2 decades,[11,12,14] but only 4 have been published between 2010 and 2013.[15,54–56] Our results and conclusions are consistent with those in other reviews and are most comparable with the systematic review by Smart et al[54] published in 2010 in which the authors reported ICERs (in 2009 Canadian dollars) for palivizumab prophylaxis varying between being dominant and $3 365 768 per QALY depending on the study population, outcomes, and model parameters. We added onto this review by capturing studies from 2010 to mid-2018 but limited our scope to OECD countries and adjusted for inflation differences by using the purchasing power parity rates from the OECD. In their reviews, Andabaka et al[15] and Prescott et al[56] similarly concluded that cost-effectiveness of palivizumab was inconsistent. Hussman et al[55] conducted a review on RSV prophylaxis overall and included studies in which palivizumab and other interventions (eg, respiratory syncytial virus immune globulin intravenous) were compared. To our knowledge, our review is the first to provide an update on the cost-effectiveness of palivizumab prophylaxis compared with no prophylaxis since the 2014 American Academy of Pediatrics (AAP) guideline update.[57]

Our review has several limitations. Differences in model designs, RSV hospitalization rates used, disease progress, study perspectives, and settings prevented us from providing definitive conclusions on the value of this intervention. We attempted to summarize the cost-effectiveness of this intervention from 2000 to 2018 but acknowledge that changes in AAP recommendations in the United States (and decision-makers in other respective countries) over time can affect model design and input data. Lastly, our review may be subject to publication and language bias because we did not search the gray literature or include articles not in English or French.

Despite these limitations, with our review, we provide a comprehensive summary of the cost-effectiveness of palivizumab prophylaxis from OECD countries to inform decision-makers of the estimated value of this intervention in term infants, preterm infants, and infants at high risk for RSV (eg, CHD and BPD or CLD). We extracted all base-case results and

scenario analyses to create Fig 3, which gives a sense of the number of studies (and estimates) that fall under specific cost-effectiveness thresholds from both payer and societal perspectives. We standardized all estimates to 2017 USDs, which allowed us to group, stratify, and compare the cost-effectiveness estimates in costs per QALY. These adjusted ICERs should be useful for program decision-makers because costs can be significantly underestimated if not appropriately inflated.

CONCLUSIONS

Palivizumab prophylaxis for RSV can be considered cost-effective in certain subgroups of infants according to predefined cost-effectiveness thresholds but varied depending on study setting, population of interest, risk factors, and input parameters. From a payer perspective, palivizumab was found to be relatively cost-effective in infants with BPD or CLD, infants with CHD, term infants from specific remote communities, and preterm infants with and without lung complications. Authors of future studies should take into account all influential parameters presented in this review, especially concerns regarding vial usage and dosage because these can drastically reduce the costs associated with the intervention and impact the model outcomes.

ACKNOWLEDGMENT

We thank Public Health Agency of Canada librarian Lynda Gamble for her assistance in developing the search strategy and managing results.

ABBREVIATIONS

BPD: bronchopulmonary dysplasia
CHD: congenital heart disease
CLD: chronic lung disease
HA: hospitalization averted
ICER: incremental cost-effectiveness ratio
JBI: Joanna Briggs Institute
LYG: life-year gained
NHS: National Health Service
OECD: Organization for Economic Cooperation and Development
QALY: quality-adjusted life-year
RSV: respiratory syncytial virus
USD: US dollar
wGA: weeks' gestational age

This review has been registered with PROSPERO (https://www.crd.york.ac.uk/prospero) (identifier CRD42018104977).

DOI: https://doi.org/10.1542/peds.2018-4064

Accepted for publication Feb 12, 2019

Address correspondence to Stephen Mac, MBiotech, BSc, Toronto Health Economics and Technology Assessment Collaborative, Toronto General Hospital, 200 Elizabeth St, Toronto, ON M5G 2C4, Canada. E-mail: sm.mac@mail.utoronto.ca

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: Supported by the Public Health Agency of Canada.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

REFERENCES

1. Meates-Dennis M. Bronchiolitis. *Arch Dis Child Educ Pract Ed*. 2005;90(4):ep81–ep86
2. Collins CL, Pollard AJ. Respiratory syncytial virus infections in children and adults. *J Infect*. 2002;45(1):10–17
3. Glezen WP, Paredes A, Allison JE, Taber LH, Frank AL. Risk of respiratory syncytial virus infection for infants from low-income families in relationship to age, sex, ethnic group, and maternal antibody level. *J Pediatr*. 1981;98(5):708–715
4. Hall CB. Respiratory syncytial virus and parainfluenza virus. *N Engl J Med*. 2001;344(25):1917–1928
5. Paes BA, Mitchell I, Banerji A, Lanctôt KL, Langley JM. A decade of respiratory syncytial virus epidemiology and prophylaxis: translating evidence into everyday clinical practice. *Can Respir J*. 2011;18(2):e10–e19
6. Simoes EA. Respiratory syncytial virus infection. *Lancet*. 1999;354(9181):847–852
7. Sánchez-Solis M, Gartner S, Bosch-Gimenez V, Garcia-Marcos L. Is palivizumab effective as a prophylaxis of respiratory syncytial virus infections in cystic fibrosis patients? A meta-analysis. *Allergol Immunopathol (Madr)*. 2015;43(3):298–303
8. Wang EE, Law BJ, Stephens D. Pediatric Investigators Collaborative Network on Infections in Canada (PICNIC) prospective study of risk factors and outcomes in patients hospitalized with respiratory syncytial viral lower respiratory tract infection. *J Pediatr*. 1995;126(2):212–219
9. American Academy of Pediatrics. Palivizumab granted licensure for prophylaxis of RSV disease. *AAP News*. October 1, 1998. Available at: www.aappublications.org/content/14/10/10.3. Accessed December 19, 2018
10. The IMpact-RSV Study Group. Palivizumab, a humanized respiratory

syncytial virus monoclonal antibody, reduces hospitalization from respiratory syncytial virus infection in high-risk infants. The IMpact-RSV Study Group. *Pediatrics*. 1998;102(3, pt 1): 531–537

11. Embleton ND, Harkensee C, Mckean MC. Palivizumab for preterm infants. Is it worth it? *Arch Dis Child Fetal Neonatal Ed*. 2005;90(4):F286–F289
12. Fenton C, Scott LJ, Plosker GL. Palivizumab: a review of its use as prophylaxis for serious respiratory syncytial virus infection. *Paediatr Drugs*. 2004;6(3):177–197
13. Harkensee C, Brodlie M, Embleton ND, Mckean M. Passive immunisation of preterm infants with palivizumab against RSV infection. *J Infect*. 2006; 52(1):2–8
14. Wang D, Cummins C, Bayliss S, Sandercock J, Burls A. Immunoprophylaxis against respiratory syncytial virus (RSV) with palivizumab in children: a systematic review and economic evaluation. *Health Technol Assess*. 2008;12(36):iii–, ix–x, 1–86
15. Andabaka T, Nickerson JW, Rojas-Reyes MX, Rueda JD, Bacic Vrca V, Barsic B. Monoclonal antibody for reducing the risk of respiratory syncytial virus infection in children. *Cochrane Database Syst Rev*. 2013;(4):CD006602
16. Byington CL, Munoz FM. Palivizumab prophylaxis for healthy preterm infants: more data supporting American Academy of Pediatrics guidelines. *Pediatrics*. 2016;138(2):e20161494
17. Chabra S. Precise gestational age definitions needed for palivizumab prophylaxis in preterm infants. *Am J Respir Crit Care Med*. 2018;197(5):680
18. Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med*. 2009;6(7):e1000097
19. National Advisory Committee on Immunization. Statement on the recommended use of monoclonal anti-RSV antibody (palivizumab) [in French]. *Can Commun Dis Rep*. 2003;29:1–15
20. Husereau D, Drummond M, Petrou S, et al; ISPOR Health Economic Evaluation Publication Guidelines-CHEERS Good Reporting Practices Task Force. Consolidated Health Economic Evaluation Reporting Standards (CHEERS)—explanation and elaboration: a report of the ISPOR Health Economic Evaluation Publication Guidelines Good Reporting Practices Task Force. *Value Health*. 2013;16(2):231–250
21. Gomersall JS, Jadotte YT, Xue Y, Lockwood S, Riddle D, Preda A. Conducting systematic reviews of economic evaluations. *Int J Evid-Based Healthc*. 2015;13(3):170–178
22. Patel H, Sander B, Nelder MP. Long-term sequelae of West Nile virus-related illness: a systematic review. *Lancet Infect Dis*. 2015;15(8):951–959
23. Organization for Economic Cooperation and Development. Purchasing power parities (PPP) (indicator). Available at: https://doi.org/10.1787/1290ee5a-en. Accessed December 19, 2018
24. Banerji A, Panzov V, Young M, et al. Hospital admissions for lower respiratory tract infections among infants in the Canadian Arctic: a cohort study. *CMAJ Open*. 2016;4(4):E615–E622
25. McGirr AA, Schwartz KL, Allen U, Solomon M, Sander B. The cost-effectiveness of palivizumab in infants with cystic fibrosis in the Canadian setting: a decision analysis model. *Hum Vaccin Immunother*. 2017;13(3):599–606
26. Neovius K, Buesch K, Sandström K, Neovius M. Cost-effectiveness analysis of palivizumab as respiratory syncytial virus prophylaxis in preterm infants in Sweden. *Acta Paediatr*. 2011;100(10): 1306–1314
27. Nuijten MJC, Wittenberg W, Lebmeier M. Cost effectiveness of palivizumab for respiratory syncytial virus prophylaxis in high-risk children: a UK analysis. *Pharmacoeconomics*. 2007;25(1):55–71
28. Nuijten MJ, Wittenberg W. Cost effectiveness of palivizumab in Spain: an analysis using observational data. *Eur J Health Econ*. 2010;11(1):105–115
29. Nuijten M, Lebmeier M, Wittenberg W. Cost effectiveness of palivizumab for RSV prevention in high-risk children in the Netherlands. *J Med Econ*. 2009; 12(4):291–300
30. Nuijten M, Lebmeier M, Wittenberg W. Cost effectiveness of palivizumab in children with congenital heart disease in Germany. *J Med Econ*. 2009;12(4): 301–308
31. Resch B, Gusenleitner W, Nuijten MJ, Lebmeier M, Wittenberg W. Cost-effectiveness of palivizumab against respiratory syncytial viral infection in high-risk children in Austria. *Clin Ther*. 2008;30(4):749–760
32. Resch B, Sommer C, Nuijten MJ, et al. Cost-effectiveness of palivizumab for respiratory syncytial virus infection in high-risk children, based on long-term epidemiologic data from Austria. *Pediatr Infect Dis J*. 2012;31(1):e1–e8
33. Rietveld E, Steyerberg EW, Polder JJ, et al. Passive immunisation against respiratory syncytial virus: a cost-effectiveness analysis. *Arch Dis Child*. 2010;95(7):493–498
34. Roeckl-Wiedmann I, Liese JG, Grill E, Fischer B, Carr D, Belohradsky BH. Economic evaluation of possible prevention of RSV-related hospitalizations in premature infants in Germany. *Eur J Pediatr*. 2003;162(4): 237–244
35. Bentley A, Filipovic I, Gooch K, Büsch K. A cost-effectiveness analysis of respiratory syncytial virus (RSV) prophylaxis in infants in the United Kingdom. *Health Econ Rev*. 2013;3(1):18
36. Salinas-Escudero G, Martínez-Valverde S, Reyes-López A, et al. Cost-effectiveness analysis of the use of palivizumab in the prophylaxis of preterm patients in Mexico. *Salud Publica Mex*. 2012;54(1):47–59
37. Sanchez-Luna M, Burgos-Pol R, Oyagüez I, et al. Cost-utility analysis of palivizumab for respiratory syncytial virus infection prophylaxis in preterm infants: update based on the clinical evidence in Spain. *BMC Infect Dis*. 2017; 17(1):687
38. Schmidt R, Majer I, García Román N, Rivas Basterra A, Grubb E, Medrano López C. Palivizumab in the prevention of severe respiratory syncytial virus infection in children with congenital heart disease; a novel cost-utility modeling study reflecting evidence-based clinical pathways in Spain. *Health Econ Rev*. 2017;7(1):47
39. Smart KA, Paes BA, Lanctôt KL. Changing costs and the impact on RSV

prophylaxis. *J Med Econ*. 2010;13(4):705–708

40. Tam DY, Banerji A, Paes BA, Hui C, Tarride JE, Lanctôt KL. The cost effectiveness of palivizumab in term Inuit infants in the Eastern Canadian Arctic. *J Med Econ*. 2009;12(4):361–370
41. Vogel AM, McKinlay MJ, Ashton T, et al. Cost-effectiveness of palivizumab in New Zealand. *J Paediatr Child Health*. 2002;38(4):352–357
42. Weiner LB, Masaquel AS, Polak MJ, Mahadevia PJ. Cost-effectiveness analysis of palivizumab among pre-term infant populations covered by Medicaid in the United States. *J Med Econ*. 2012;15(5):997–1018
43. Yount LE, Mahle WT. Economic analysis of palivizumab in infants with congenital heart disease. *Pediatrics*. 2004;114(6):1606–1611
44. Elhassan NO, Sorbero ME, Hall CB, Stevens TP, Dick AW. Cost-effectiveness analysis of palivizumab in premature infants without chronic lung disease. *Arch Pediatr Adolesc Med*. 2006;160(10):1070–1076
45. Lofland JH, O'Connor JP, Chatterton ML, et al. Palivizumab for respiratory syncytial virus prophylaxis in high-risk infants: a cost-effectiveness analysis. *Clin Ther*. 2000;22(11):1357–1369
46. Blanken MO, Frederix GW, Nibbelke EE, et al; Dutch RSV Neonatal Network. Cost-effectiveness of rule-based immunoprophylaxis against respiratory syncytial virus infections in preterm infants. *Eur J Pediatr*. 2018;177(1):133–144
47. Chirico G, Ravasio R, Sbarigia U. Cost-utility analysis of palivizumab in Italy: results from a simulation model in the prophylaxis of respiratory syncytial virus infection (RSV) among high-risk preterm infants. *Ital J Pediatr*. 2009;35(1):4
48. Hampp C, Kauf TL, Saidi AS, Winterstein AG. Cost-effectiveness of respiratory syncytial virus prophylaxis in various indications. *Arch Pediatr Adolesc Med*. 2011;165(6):498–505
49. Harris KC, Anis AH, Crosby MC, Cender LM, Potts JE, Human DG. Economic evaluation of palivizumab in children with congenital heart disease: a Canadian perspective. *Can J Cardiol*. 2011;27(4):523.e11–523.e15
50. Hascoet JM, Fagnani F, Charlemagne A, Vieux R, Rozé JC, Bendjenana H. Methodological aspects of economic evaluation in pediatrics: illustration by RSV infection prophylaxis in the French setting [in French]. *Arch Pediatr*. 2008;15(12):1739–1748
51. Lanctôt KL, Masoud ST, Paes BA, et al. The cost-effectiveness of palivizumab for respiratory syncytial virus prophylaxis in premature infants with a gestational age of 32-35 weeks: a Canadian-based analysis. *Curr Med Res Opin*. 2008;24(11):3223–3237
52. Mahadevia PJ, Masaquel AS, Polak MJ, Weiner LB. Cost utility of palivizumab prophylaxis among pre-term infants in the United States: a national policy perspective. *J Med Econ*. 2012;15(5):987–996
53. Seeler RA, Schatz B. Palivizumab (Synagis)—cohorting babies to reduce waste. *Pediatrics*. 1999;104(5, pt 1):1170–1171
54. Smart KA, Lanctôt KL, Paes BA. The cost effectiveness of palivizumab: a systematic review of the evidence. *J Med Econ*. 2010;13(3):453–463
55. Hussman JM, Li A, Paes B, Lanctôt KL. A review of cost-effectiveness of palivizumab for respiratory syncytial virus. *Expert Rev Pharmacoecon Outcomes Res*. 2012;12(5):553–567
56. Prescott WA Jr, Doloresco F, Brown J, Paladino JA. Cost effectiveness of respiratory syncytial virus prophylaxis: a critical and systematic review. *Pharmacoeconomics*. 2010;28(4):279–293
57. American Academy of Pediatrics Committee on Infectious Diseases; American Academy of Pediatrics Bronchiolitis Guidelines Committee. Updated guidance for palivizumab prophylaxis among infants and young children at increased risk of hospitalization for respiratory syncytial virus infection [published correction appears in *Pediatrics*. 2014;134(6):1221]. *Pediatrics*. 2014;134(2):415–420

Cost-effectiveness of Palivizumab for Respiratory Syncytial Virus: A Systematic Review

Stephen Mac, Amanda Sumner, Samuel Duchesne-Belanger, Robert Stirling, Matthew Tunis and Beate Sander

Pediatrics 2019;143;
DOI: 10.1542/peds.2018-4064 originally published online April 30, 2019;

PEDIATRICS®
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Cost-effectiveness of Palivizumab for Respiratory Syncytial Virus: A Systematic Review

Stephen Mac, Amanda Sumner, Samuel Duchesne-Belanger, Robert Stirling, Matthew Tunis and Beate Sander

Pediatrics 2019;143;
DOI: 10.1542/peds.2018-4064 originally published online April 30, 2019;