Understanding Policy Decisions and Their Implications Regarding Preventive Interventions for Respiratory Syncytial Virus (RSV) Infection in Canadian Infants: A Primer for Nurses

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ABSTRACT

Respiratory syncytial virus (RSV) is a leading cause of morbidity and hospitalization in young children, and prevention is the primary management strategy. At present, palivizumab, a monoclonal antibody providing immediate passive immunity, rather than a vaccine that induces active immunity, is the only preventive intervention used in routine practice internationally. In Canada, access varies across the country. Prophylaxis policies are mainly driven by cost-effectiveness analyses, and it is crucial that the full costs and benefits of any intervention are captured. Positive results from a new Canadian cost-effectiveness analysis of palivizumab will help address the current inequality in use while providing a framework for future models of RSV preventives. Nurses are the principal educators for parents about the risks of childhood RSV and optimal prevention *via* basic hygiene, behavioral and environmental measures, and seasonal prophylaxis. Nurses should be provided not only with regular, up-to-date, and accurate information on RSV and the clinical aspects of emerging interventions but be informed on the decision-making governing the use of preventive strategies.

Keywords: infection; NICU care; education; evidence-based practice; family-centered care/parenting; quality improvement

Respiratory syncytial virus (RSV) is a common respiratory pathogen that typically causes infections during the fall and winter months in Canada and other Northern Hemisphere countries, although such episodes can occur at any time throughout the year. Almost all children will have their first RSV infection by the time they are 2 years old, and any child can be infected more than once.[1] While most RSV infections result in mild cold-like symptoms lasting one to 3 weeks, neonates and infants can suffer severe lower-respiratory tract disease requiring urgent medical care and, sometimes, hospital admission.[2,3] At present, there are no effective treatments for severe RSV infections and medical care is predominantly supportive. Prevention, therefore, is paramount. Alongside basic

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hygiene and behavioral measures, there are now two licensed preventive interventions available—the monoclonal antibodies palivizumab and, very recently, nirsevimab—with several more on the horizon, including maternal and pediatric RSV vaccines.[3,4] There are important differences in the protection afforded by these various preventive interventions that should be recognized. The monoclonal antibodies provide immediate passive immunity for neonates and young infants that lasts up to 5 months when administered monthly (palivizumab) or as a single dose (nirsevimab, with an extended half-life), during the RSV season.[5] In contrast, pediatric vaccines, which induce active immunity, have the advantage of potentially providing years of protection. However, they are typically administered to infants older than 6 months of age who can generate an adequate immunological response, and bypass those who are at greatest risk for severe RSV disease during the first few months of life. Maternal vaccines appear to provide a similar duration of protection as the extended half-life monoclonal antibodies, although this is more limited in infants less than 30 weeks' gestational age (wGA), where maternal RSV antibody transfer is incomplete. Infants born several months outside the RSV season might also have a limited level of immunity from a maternal vaccine. This has implications for the optimal deployment of these preventive interventions and it is likely that a combination of strategies will be needed, particularly when parental choice is taken into consideration.[5–7]

As with all medicines, access to these preventive interventions requires careful consideration of their financial costs *versus* clinical benefits. It is important, therefore, that such decision-making considers all relevant information and data. Unfortunately, it has been reported that there is considerable variability in access to palivizumab both between and within countries since its first launch in 1998. [8–10] In Canada, access to palivizumab varies across the 10 provinces and three territories,[8] despite the product being available for more than 20 years. A new Canadian economic analysis of palivizumab has recently been published with the aim of providing up-to-date evidence to address this inequality.[11] The aim of this article is to provide pediatric and neonatal nurses with an overview of the key considerations that should underpin the economic evaluations of RSV preventive interventions in order to better inform their discussions with parents and health care providers.

BURDEN OF RESPIRATORY SYNCYTIAL VIRUS

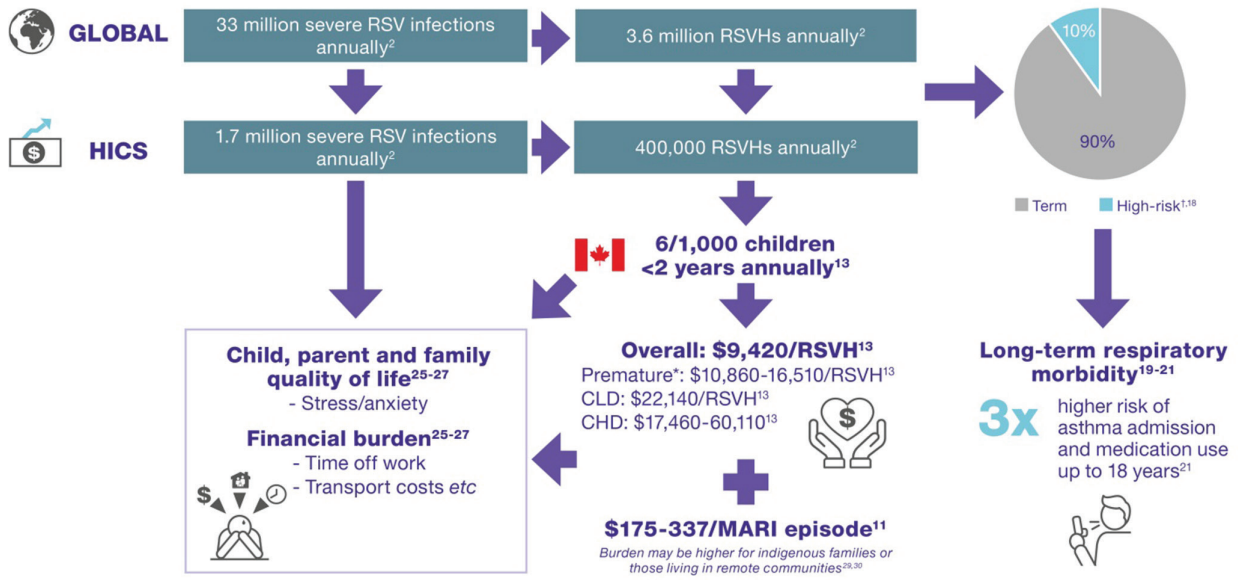
RSV infection can cause a significant burden to health care systems, individuals, and society. Globally, it has been estimated that RSV is responsible for around 33 million severe respiratory infections, resulting in 3.6 million hospital admissions (RSVH) and more than 100,000 deaths in children <5 years of age every year (Figure 1).[2] Approximately 1.7 million of these RSV infections and more than 400,000 of the RSVHs occur in high-income countries.[2] It has been estimated that an average of 56,927 (range: 43,846–66,155) infants are hospitalized with RSV infection in the United States every year.[12] In Canada, an estimated 6 of every 1,000 children <2 years of age are hospitalized with RSV each year.[13] Some children are particularly vulnerable to severe RSV infection, including those children born prematurely and with certain comorbidities, such as bronchopulmonary dysplasia (BPD) or chronic lung disease (CLD), hemodynamically significant congenital heart disease (HS-CHD), neuromuscular impairments, and the immunocompromised.[14–17] Importantly, however, it should be recognized that approximately 90 percent of RSVHs occur in healthy infants born at term, without risk factors.[18]

Every infant hospitalized with RSV is estimated to cost the Canadian health care system, on average, an additional CAN$ 9,240 compared with a matched nonhospitalized infant (2020 values).[13] For infants born prematurely (mean cost for 22–35 wGA: $12,280) or with comorbidities (CLD: $22,140; CHD: $24,130) the cost is even higher. Over a 10-year period, the total cost of RSVH in Ontario was $134,931,900, of which $117,886,720 (87 percent) was attributed to infants born 36–43 wGA.[13] These costs exclude those related to medically attended RSV infections (MARI) treated in outpatient clinics or emergency rooms (ERs), which have been calculated to be between $175 and $337 per episode.[11]

It is now well-established that RSV infections can have significant effects on the long-term health of children. Several studies have shown that RSV infection in early childhood is associated with long-term wheezing and asthma and impaired lung function.[19–21] RSV infection in infancy may also set the stage for a suboptimal lung function trajectory in adulthood resulting in chronic obstructive lung disease.[22] Preterm infants especially those with BPD and who are of very low birth weight have even greater compromised lung function at 26–30 years of age compared with a control cohort of term infants[23]; superimposed RSV infection adds further to pulmonary morbidity.[24] A Scottish study that included 740,418 children followed up to 18 years reported a three-fold higher risk of asthma admission and medication use (4.8 percent, 1.5 percent; relative risk 3.1, 95 percent confidence interval [CI]: 2.9, 3.3; $p < .0001$) in those with a prior history of RSVH at ≤2 years compared with controls.[21] Such long-term sequelae can negatively impact the overall quality of life of children and their families, as well as place further strain on the health care system.

RSV infections can also have a devastating impact on families, causing high levels of stress and anxiety during hospital admission as well as longer-term concerns about their infant's health.[25–27] The impact on parents and families of having an infant hospitalized with severe RSV was assessed in a Canadian survey undertaken in 2020.[28] It was

FIGURE 1 ■ Key information on the burden of respiratory syncytial virus in children.



*Born 22–35 weeks' gestational age; †prematurity, CHD, CLD, and so forth.

Abbreviations: CHD = congenital heart disease; CLD = chronic lung disease; HIC = high-income countries; MARI = medically attended RSV infection (family doctor/emergency room); RSV = respiratory syncytial virus; RSVH = RSV-related hospitalization.

reported that most parents of preterm infants (86 percent) believed that RSV was a very serious condition. The parents also identified RSV-related bronchitis and pneumonia as the main cause of hospitalization in young infants <1 year of age during the winter season (92 percent), but struggled to internalize this information.[28] In addition to the mental and emotional strain caused by RSV,[25] families face difficulties related to the financial burden of lost work time, costs of child care for siblings at home, travel, parking, and eating out when caring for their infant in the hospital.[26]

The burden associated with RSV can be particularly large for indigenous families or those living in remote communities. A higher prevalence of environmental and sociodemographic risk factors is often found in these populations, resulting in increased rates of RSV infection and hospitalization.[29] They may also face additional difficulties in accessing health care, such as increased distances to local hospitals and the need for air transport to hospitals out-of-region for intensive care. Furthermore, these populations are often underrepresented in current national surveillance systems to monitor RSV outbreaks.[30]

Preventive Interventions

Passive Immunoprophylaxis. Passive immunoprophylaxis is defined as the administration of externally produced antibodies to prevent infection.[31] As noted earlier, protection is typically short-lived (e.g., 1 and 5 months for a single dose of palivizumab and nirsevimab, respectively) as the antibody supply is not replenished by the body's immune system.[5,31] Monoclonal antibodies for the prevention of RSV have been developed to target the RSV fusion protein and inhibit binding to cellular receptors and fusion of the viral envelope to airway epithelium, thereby interrupting RSV entry into host cells.[32]

Palivizumab has been proven safe and effective in two randomized controlled clinical trials for the prevention of severe RSV in high-risk infants (preterm ≤35 wGA, BPD/CLD, and HS-CHD).[33,34] The evidence from a recent Cochrane systematic review, involving 3,343 subjects, confirmed that palivizumab reduces RSVHs by 56 percent overall (Table 1).[35] These results were confirmed in another recent meta-analysis, which reported palivizumab was also associated with a significant reduction in intensive care unit (ICU) admissions (reduced by 5 per 1,000 infants versus placebo/no prophylaxis; 95 percent CI, −7, 0) and supplemental oxygen use (reduced by 55 per 1,000 infants; 95 percent CI, −61, −41).[36] There is no evidence, however, that palivizumab reduces mortality,[35,36] albeit this should be taken in the context of an overall RSV-related mortality rate of 0.1 percent in industrialized countries.[2] The benefit of palivizumab in the second year of life for children with BPD/CLD is often debated, although real-world evidence indicates that targeting those at the highest risk, such as those still on or weaned off supplemental oxygen 3–6 months prior to the onset of the RSV season, is an effective strategy and is supported by position statements.[37–44]

TABLE 1 ■ Preventive Interventions Against Childhood RSV That Are Market Approved or in Ongoing Phase 3 Development

	Status	Population	Posology	Effectiveness
Passive immunoprophylaxis				
Palivizumab[33,34]	Approved	Preterm ≤35 wGA and <6 months; CLD/BPD; HS - CHD	15 mg/kg IM, monthly during RSV season	Preterm: 78% (95% CI: 66%, 90%; $p < .001$) RRR in RSVH; CLD/BPD: 39% (95% CI: 20%, 58%; $p < .038$) RRR in RSVH; HS-CHD: 45% (95% CI: 23%, 67%; $p < .03$) RRR in RSVH
Nirsevimab[45–47]	Approved	Newborns and children during their first RSV season	<5 kg: 50 mg; ≥5 kg: 100 mg IM before the start of the RSV season	79.5% (95% CI: 65.9%, 87.7%; $p < .0001$) RRR in MARI; 77.3% (95% CI: 50.3%, 89.7%; $p < .001$) RRR in RSVH
Clesrovimab[48,49]	Phase 3	Healthy preterm and full-term infants; high-risk infants and children	Single IM dose	Ongoing Phase 3 studies: 3,300 healthy pre/term infants (NCT04767373), because of complete August 2024; 1,000 high-risk infants (NCT04938830), because of complete April 2026. No interim results published to date
Vaccine				
RSVpreF (PF-06928316)[50,51]	Phase 3	Pregnant women	120 µg IM at between 24 and 36 wGA	Ongoing Phase 3 study: 14,741 participants (NCT04424316), because of complete November 2023. Interim results: 57.1% (95% CI: 14.7%, 79.8%) and 51.3% (95% CI: 29.4%, 66.8%) RRR in MARI at 90 days and 6 months of life, respectively; 81.8% (95% CI: 40.6%, 96.3%) and 69.4% (95% CI: 44.3%, 84.1%) RRR in severe MARI at 90 days and 6 months, respectively (no *p*-values reported)

[a]Infants and children at increased risk for severe RSV infection are recommended to receive palivizumab in accordance with national or local guidelines or professional society recommendations.

[b]Further details of dosing in children are publicly unavailable.

[c]Not defined, but in Phase 2b study,[52] severe MARI was defined as MARI with the presence of one of the following signs of severe RSV disease: tachypnea (respiratory rate ≥70 breaths per minute in infants younger than 2 months [60 days] of age or ≥60 breaths per minute in those between 2 and 12 months of age); oxygen saturation <93% while the infant was breathing ambient air; use of oxygen delivered through a high-flow nasal cannula or mechanical ventilation; admission to an intensive care unit for more than 4 hours; and unresponsiveness or unconsciousness.

Abbreviations: BPD/CLD = bronchopulmonary dysplasia/chronic lung disease (CLD) ; CI = confidence interval; HS-CHD = hemodynamically significant congenital heartdisease; IM = intramuscular; MARI = medically attended respiratory syncytial virus infection; NCT = national clinical trial; Phase 3 trial = tests the safetyand how well a new intervention works compared with a standard treatment; RR = risk ratio; RRR = relative risk reduction; RSV = respiratory syncytialvirus; RSVH = respiratory syncytial virus-related hospitalization; RSVpreF = RSV prefusion F protein-based subunit vaccine; wGA = weeks' gestational age.

Palivizumab received marketing authorization from Health Canada in 2002, following approval by the U.S. Food and Drug Administration agency in 1998. Extensive data on its use are available from the Canadian Registry of Synagis (CARESS), a prospective, observational, multicenter study conducted over 12 years (2005–2017).[53] A total of 25,003 infants who received 109,579 palivizumab injections were enrolled in CARESS across 32 centers, with an overall RSVH rate of 1.6 percent. Of note, 17.8 percent of infants that received palivizumab were not those with core labeled indications (preterm ≤35 wGA, BPD/CLD, and HS-CHD), but a variety of different medical conditions that were approved provincially because of their vulnerability to severe RSV infection, including trisomy 21, airway anomalies, pulmonary disorders, cystic fibrosis, neurological impairments, and being immunocompromised. Palivizumab is dosed by weight (15 mg/kg) and is usually administered in five moly injections during the RSV season. Adherence, as measured by expected versus actual doses plus correct inter-dose interval for the RSV season, was reported as 64.7 percent in CARESS.[53]

In October 2022, nirsevimab became the second monoclonal antibody that was granted approval by the European Medicines Agency (EMA) for the prevention of RSV infection in neonates and infants during their first RSV season.[3] Of note, this indication covers all infants under the age of 1 year, not just those at the highest risk of infection. At the time of writing (March 2023), nirsevimab remains under review by the U.S. Food and Drug Administration and Health Canada.[54,55] Efficacy rates of 79.5 percent and 77.3 percent have been reported in clinical studies of nirsevimab for MARI and RSVH, respectively.[45–47] As with palivizumab, nirsevimab

has not been associated with a reduction in mortality.[36] The longer half-life of nirsevimab (63, 73 days[56] versus 17–27 days for palivizumab[57]) and maintenance of efficacy against RSV Subtype A and B strains for 150 days after dosage imply that a single injection (50 mg for those <5 kg and 100 mg for ≥5 kg) provides coverage for the RSV season, and this is reflected in the EMA approved posology.[3]

The options for passive immunoprophylaxis are due to expand over the next few years with five further monoclonal antibodies in development.[4] Most notably, this includes another extended half-life monoclonal, clesrovimab, for which two ongoing Phase 3 studies are anticipated to complete in August 2024[48] and April 2026.[49] By definition, Phase 3 studies evaluate the safety and efficacy of a new treatment such as clesrovimab compared with a standard treatment or placebo.

Vaccines. Vaccinations stimulate the body's immune system to produce antibodies. This has led to two prevention strategies: maternal and pediatric RSV vaccines. With maternal vaccines, the mother-to-be is vaccinated (between 24 and 36 wGA) and antibodies produced by her immune system are transferred to the baby via the placenta before birth and through the colostrum and milk after birth;[58] ergo, the immunity the child receives remains passive, with the child's immune system playing no part in generating antibodies. With pediatric vaccines, the child receives the vaccine once the immune system is sufficiently developed after birth to produce antibodies, potentiating more sustained immunity.

There is currently one RSV vaccine for preventing severe RSV infection in infants close to commercial availability, a bivalent RSV prefusion *F* protein-based subunit vaccine (RSVpreF) for maternal immunization between 24 and 36 weeks gestation.[4,52] A Phase 3 study of RSVpreF is ongoing and due to be completed in November 2023.[50] Preplanned, interim results from the study were released in November 2022 and appeared positive, with a 57.1 percent reduction in MARI and 81.8 percent reduction in severe MARI (MARI plus signs of severe disease, e.g., the use of a high-flow nasal cannula or mechanical ventilation) at 3 months after birth.[51] A good level of efficacy was also reported during the 6-month follow-up period: 51.3 percent for MARI and 69.4 percent for severe MARI. Predicated on these results, regulatory submissions for RSVpreF were anticipated from the end of 2022 onwards.[51]

Unfortunately, the Phase 3 trials for another subunit vaccine for maternal immunization, RSVPreF3 (GSK3888550A), were halted because of an adverse safety signal concerning an increase in the risk of preterm birth in the treated group, and an associated increase in infant mortality.[59–63] The clinical development of RSVPreF3 does continue, however, in older adults (≥60 years).[62] On a positive note, there are a further 29 vaccine candidates in earlier-stage development, including four pediatric vaccines (two live-attenuated, one protein-based, and one recombinant vector) in Phase 2 studies.[4]

Health Economics and Policy Decision-Making

International guidelines for RSV prophylaxis are country-specific and the indications vary across North America, Europe, and the Middle East.[39–43,64] In Canada, guidelines for the use of RSV prophylaxis are provided by the Canadian Paediatric Society (CPS) and The National Advisory Committee on Immunization (NACI). For palivizumab, the latest CPS guidelines,[43] reaffirmed in 2021, recommend prophylaxis for: (a) infants with CLD (defined as a need for oxygen at 36 wGA) or CHD in the first year of life and in certain infants with continuing CLD in the second season (those still on or weaned off supplemental oxygen in the 3 months prior to the onset of the season), (b) infants without CLD born ≤30 wGA and who are <6 months at the start of the RSV season, and (c) infants without CLD ≤36 wGA living in remote communities and who are <6 months at the start of the RSV season. The NACI guidelines[44] are similar to those from the CPS, although they state that palivizumab may also be considered for premature infants of 30–32 wGA and age <3 months who are at high risk for RSV infection. How the guidelines are followed and what funding is made available for palivizumab becomes the decision of the health authorities in the individual provinces and territories in Canada, with similar reimbursement systems operating internationally.

An assessment of prophylaxis policies across Canada for the 2018–2019 RSV season reported that no province or territory follows the CPS and NACI guidelines exactly and substantial variation exists across jurisdictions driven primarily by heterogeneity in the use of palivizumab in premature children, particularly those born >30 wGA, and those born with cystic fibrosis or Down syndrome.[8] For preterm infants, policies ranged from not offering palivizumab to any infants born at >30 wGA (three jurisdictions) or to infants born at >33 wGA (one jurisdiction) to offering prophylaxis to all infants born at <35^6 wGA (one jurisdiction). The majority of territories and provinces considered prophylaxis in infants born at $32/33^0$–35^6 based on risk factors (e.g., birth during the RSV season, presence of siblings) and/or chronologic age, although the scoring criteria used varied between jurisdictions.[8] These policy differences are largely driven by cost considerations and potentially create unfairness in the health system, with palivizumab use varying depending on where an infant is born. Such inequalities in access to palivizumab require addressing, and similar issues should not be allowed to arise with the new preventive interventions becoming available.

Health policy on who should receive approved and efficacious medicines such as palivizumab is often guided by cost-effectiveness analyses, which consider the financial

cost of an intervention against cost savings from reduced illness and the value of improved health to the patient. This is typically accomplished via a cost-utility analysis, which involves dividing the cost of an intervention by the expected health benefit (often expressed as the cost of gaining 1 year of perfect health or quality-adjusted life year [QALY]) or a death prevented by administering the intervention. QALYs measure the disease burden on both quality and quantity of life. In this type of analysis, death is expressed as zero utility, while full health is defined as a utility of 1.0. To put this into context, a general population of children aged 6–11 years had an average utility score of 0.95,[65] while for children of a similar age (7, 12 years) with mild or severe asthma symptoms, scores of 0.79 and 0.28, respectively, have been reported.[66] Health utility values are used to convert life years gained into QALYs. Therefore, 2 years at a utility of 0.5 is equal to 1 year at a utility of 1.0 which is equal to 1 QALY. The basic concepts invoked in cost-utility analyses are universal, but health care costs incurred for RSV illness are country dependent. Interventions can be more effective and less costly (very desirable) or more costly and less effective (undesirable); however, most new treatments increase both costs and QALY's.[67] If the cost per unit of health gained for an intervention is below a certain number of dollars set by the decision makers based on how much they are willing to pay, the intervention will likely be approved as being cost-effective. In Canada, the level that is set for approval of an intervention as being cost-effective for reimbursement in the publicly funded health care system is typically stated as $50,000 *per* unit of health gained, though this can sometimes be higher.[68] Thresholds in the United States and Europe for new drugs and interventions to be considered cost-effective and thereby eligible for funding by the health care system (e.g., the United Kingdom's National Health Service) or public health insurance (e.g., U.S. Medicare/Medicaid) are commonly quoted as USD$50,000 and €30–€50,000 *per* QALY, respectively.[69–72] Reimbursement policies for private insurance tend to be broader than the public equivalent, pursuant to the level of coverage paid for, and will also consider the costs versus benefits of medications.

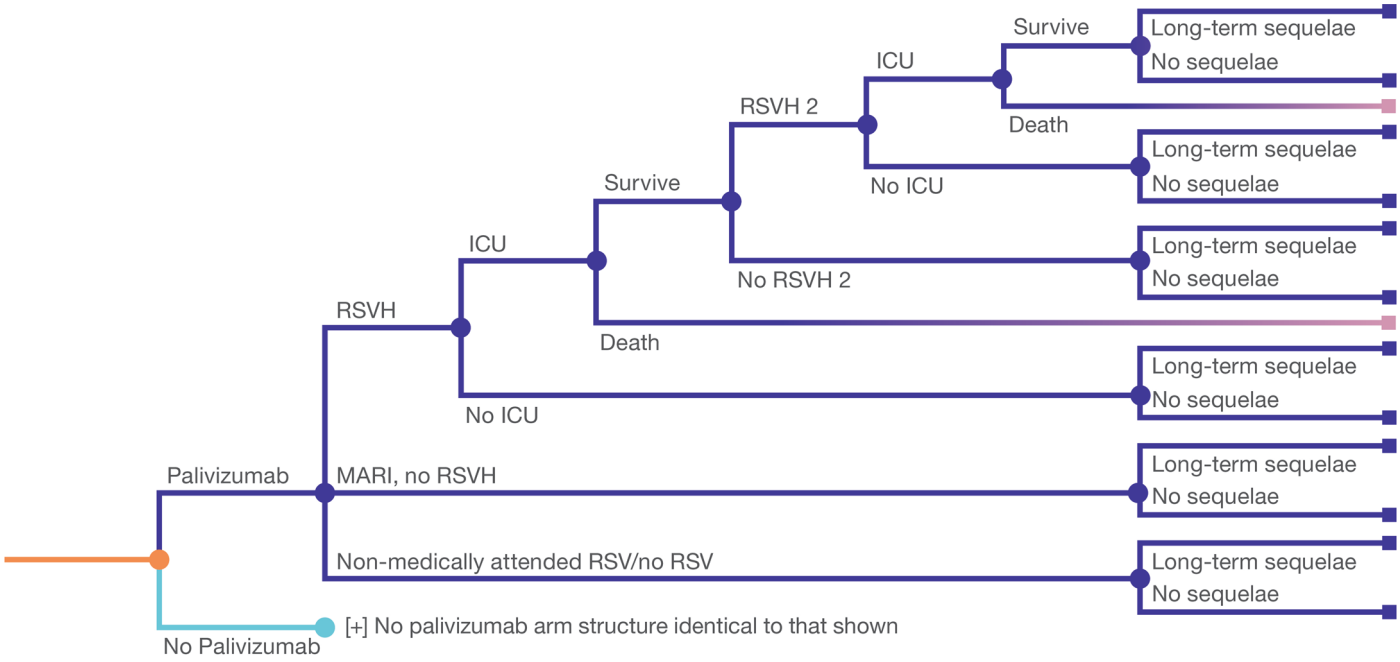
A number of different approaches are available for economic modeling, which can potentially have a considerable differential impact on the calculated cost-effectiveness of an intervention. For palivizumab, "static" models have most often been used,[11,73] whereas for vaccines, it is sometimes preferred to use "dynamic" models, as the latter assumes the impact of the intervention on viral transmission and can better account for waning immunity over time.[74,75] The World Health Organization advises that for a maternal vaccine, the target group (i.e., pregnant women) is not influential for the transmission of RSV, so a static model is also acceptable.[76] Dynamic models have also been found to produce similar results to static ones for RSV monoclonal antibodies because the community impact on RSV transmission by reducing infants' infectivity through passive immunoprophylaxis likely remains limited.[75]

Regardless of the type of model employed, a key consideration is the perspective taken, typically either relating to direct costs to the health service alone (sometimes called the "payer perspective") or a wider assessment including the impact of the disease and intervention on society as a whole (including indirect costs, such as productivity losses from inability to work). A recent systematic review of health economic analyses of palivizumab for infants born 32–35 wGA identified 20 studies published between 1999 and 2020 of which approximately half (9; 45 percent) took a payer perspective alone and half (11; 55 percent) considered the wider societal impact.[11] Inclusion of a broader societal perspective is recognized to provide a more accurate representation of the true impact of an intervention,[77,78] and, it can be argued, is particularly relevant for RSV considering the substantial psychological and pecuniary effects it can have on the parents, caregivers, and families of children with severe infections.[25,26]

New Canadian Economic Analysis of Palivizumab and Future Models

A new Canadian economic analysis of palivizumab use in 32–35 wGA infants that incorporates a societal perspective has recently been developed following a review by experts in RSV and health economics of the latest evidence in RSV and all previously published cost-effectiveness studies of palivizumab in infants born at this gestational age.[11] This new study was similar to previous analyses[73,79] in that it considered criteria such as RSVH, ICU admission, and mortality following RSV infection (Figure 2).[11] However, the cost-utility model also included the impact of MARI, which had not been previously included in a cost analysis of palivizumab use. Moreover, the new analysis directed particular focus on the potential long-term effects following RSV infection in infancy, such as wheezing and asthma, for up to 18 years.[11] Older analyses did not include such long-term effects or limited them to a certain number of years during childhood and adolescence.[73,79] Regarding indirect costs, these included those related to the administration of palivizumab as well as the costs to parents/caregivers of missed work, visiting their children in the hospital, or taking them to the ED/outpatient services.[11] Where possible, the analysis used Canada-specific data and sources, including the effectiveness of palivizumab, the risk of RSVH, and health care resource use for infants who developed severe RSV infection.[80–83] The analysis also incorporated the International Risk Scoring Tool (IRST) [84] and the Canadian Risk Scoring Tool (CRST)[85] to guide prophylaxis for infants most vulnerable to RSVH. The IRST includes three risk factors and ascribes a score out of 56, while the CRST uses seven variables and assigns a score out of 100 (Table 2). For the analysis, infants scored at a moderate- or high-risk of RSVH received prophylaxis.[11]

FIGURE 2 ■ Decision tree for the new health economic model of palivizumab versus no prophylaxis in Canadian infants born 32–35 wGA.[11]



Abbreviations: ICU = intensive care unit; MARI = medically attended RSV infection (family doctor/emergency room); RSV = respiratory syncytial virus; RSVH = RSV-related hospitalization; wGA = weeks' gestational age.

The new analysis found palivizumab to be highly cost-effective versus no prophylaxis when used in infants assessed at a high and moderate risk of RSVH, as determined by the IRST (incremental cost *per* QALY: $29,789) or CRST ($15,833/QALY).[11] The use of vial sharing, which is common in clinical practice, considerably improved cost-effectiveness (IRST: $22,319/QALY; CRST: $9,231/QALY). Predicated on these results, the Canadian Premature Babies Foundation (CPBF), in collaboration with several national groups, is lobbying decision-makers to update their prophylaxis policies to ensure equitable use of palivizumab across Canada in all moderate- and high-risk infants born 32–35 wGA.[86] Since the analysis focused only on otherwise healthy 32–35 wGA infants, no conclusions regarding the cost-effectiveness of palivizumab in other high-risk groups can be drawn.

The assumptions used in this new analysis and a study comparing different approaches to RSV economic modeling provide a good basis for further economic assessments of palivizumab and the newer preventive interventions (Table 3).[11,75] The assumptions identified as the key drivers of cost-effectiveness in the palivizumab analysis were utility (quality of life) scores, the inclusion of long-term respiratory morbidity, and drug acquisition cost.[11] Key areas where more data are ideally needed to improve the accuracy of economic analyses include better and more recent data on the impact of RSV and, in particular, subsequent respiratory morbidity on the quality of life (utility) of both the children and their families or caregivers. For RSV vaccines, more age-specific data on asymptomatic and symptomatic nonMARI infections in children (to model viral transmission) and on the waning of protection are salient requirements.[75]

Role of Nurses

Nurses play a pivotal role in educating and advising parents and health care providers on RSV prevention. The most important message to communicate is the use of simple hygiene, behavioral and environmental measures (e.g., frequent and proper handwashing and avoiding smoking around the infant and large communal gatherings) that can effectively reduce the risk of infection by RSV (and other pathogens, such as COVID-19). Information on how RSV is transmitted (through sneezing/coughing, contact, etc.) and how long the virus can survive on surfaces (i.e., *an* average of approximately 7 hours on hard surfaces and 30 minutes on the skin[87] should also be provided. This education should occur throughout the year. Materials, such as those provided by the CPBF,[88] are a great resource for nurses to use with parents and health care providers in this regard.

Nurses are also the central figure in educating and informing parents and health care providers on whether their child is eligible or not to receive palivizumab and the reasons behind current decisions, with such conversations due to become more frequent following the advent of the newer monoclonals antibodies and vaccines. Parents struggle to rationalize the concept of

TABLE 2 ■ Risk Factors, Scoring, and RSVH Risk in the IRST and CRST[84,85]

	IRST		CRST	
Risk factors	1. Birth 3 months before to 2 months after season start date 2. Smokers in the household and/or smoking while pregnant 3. Siblings and/or daycare		1. Small (<10th percentile for GA) 2. Male sex 3. Born during the RSV season 4. Family history without eczema 5. Subject or siblings attending daycare 6. >5 individuals in the home including the subject 7. >1 smoker in the household	
Risk group	Risk score	Risk of RSVH	Risk score	Risk of RSVH
High	50–56	9.5%	65–100	18.7%
Moderate + high	≥20–56	6.3%	≥49–100	10.9%
Moderate	20–45	3.3%	49–64	7.1%
Low	0–19	1.0%	0–48	1.7%

Shaded row indicates the combined group used in analysis.[11]

[a]November–January.

Abbreviations: CRST = Canadian Risk Scoring Tool; GA = gestational age; IRST = International Risk Scoring Tool; RSVH = respiratory syncytial virus related hospitalization.

TABLE 3 ■ Ideal Evidence-Based Assumptions to Include (Data Permitting) in Health Economic Aanalyses of Preventive Interventions for RSV Infection[11,75]

Direct assumptions

Drug efficacy and costs

- Efficacy against MARI, RSVH, and long-term respiratory morbidity
- Acquisition costs plus administration

RSVH

Preadmission health care visit (e.g., ED/family doctor)

- Hospital ward admissions
- ICU admissions, including mechanical ventilation, and so forth
- Disutility (negative impact on quality of life)
- Mortality

MARI

- Outpatient visit(s)
- Emergency room visit(s)
- Family doctor/primary care visit, as appropriate
- Disutility (negative impact on quality of life)

Non-MARI symptomatic RSV infections[a]

- For viral transmission in dynamic models of vaccines

Respiratory morbidity (up to 18 years)

- Hospital admissions
- Outpatients' visits
- ED visits
- Family doctor/primary care visits, as appropriate
- ± asthma medications, if available
- Disutility (negative impact on quality of life) over time

Indirect assumptions

Administration of intervention

- Transport
- Missed work, and so forth

RSVH/MARI/respiratory morbidity

- Missed work
- Childcare
- Transport
- Subsistence, and so forth
- Disutility (negative impact on quality of life) to parents/caregivers/families

Loss of earnings following RSV-related mortality over the lifetime time horizon

[a]Non-MARI symptomatic RSV infections: respiratory syncytial virus infections that are symptomatic but do not require any medical attention.

Abbreviations: ED = emergency department; ICU = intensive care unit; MARI = medically attended respiratory syncytial virus infection; RSV = respiratory syncytial virus; RSVH = respiratory syncytial virus-related hospitalization.

cost-effectiveness (appearing to place a cost limit on protecting their child's health) as illustrated by this quote from the CPBF Position Paper: "The idea that decisions around which babies receive potentially lifesaving medicines is based on cost-effectiveness is a hard pill to swallow."[86] It is for this reason that it is valuable for nurses to understand what underpins the funding and reimbursement of these interventions, in addition to receiving regular education and training on effectiveness, safety, dosage, and administration (the latter for passive immunoprophylaxis and childhood vaccines). It is important that parents and health care providers be informed that whatever preventive intervention is employed, none is 100 percent effective. Data available for palivizumab do indicate, however, that prophylaxis may reduce the severity of RSV infection if the child is admitted to the hospital.[89]

If a child does have an RSV infection requiring medical attention, it is important that the short- and longer-term implications are discussed with the parents or caregivers. In the Canadian parents' survey, it was reported that almost one-third (30 percent) of parents reported receiving limited information on RSV following their child's admission to the hospital.[28] Some received no RSV education either in the NICU or from a health care professional following discharge from the hospital. More than half (53 percent) of these parents wished that they had received in-depth information on RSV.[28] It is essential, therefore, that nurses (and other health care

professionals involved in the management of RSV in children) receive regular evidence-based education on RSV to provide them with the skills to converse with and inform families from disparate populations.

CONCLUSION

Economic evaluations of the preventive interventions for RSV are central in determining their use. It is critical that these analyses use the best available evidence and capture the full costs and benefits of the intervention to ensure fair and equitable use. Neonatal and pediatric nurses should be furnished with and understand the key details of these analyses to better inform their discussions with parents, health care providers, and families.

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