Cost-Effectiveness of Nirsevimab and Abrysvo for Preventing Respiratory Syncytial Virus Disease in Infants Across Canada

Samara Bugden[1], Shweta Mital[2], Hai Van Nguyen[1]

[1]School of Pharmacy, Memorial University of Newfoundland, St. John's [2]College of Pharmacy, University of Manitoba, Winnipeg

Introduction

- Respiratory syncytial virus (RSV) infects virtually all children before the age of two[1], and RSV is the primary cause of lower respiratory tract infections in children under five[2].
- Infants in Canada's remote northern Inuit communities experience RSV hospitalization rates 2-17 times that of southern Canada[3-5]. Hospitalizing these infants involves expensive medical evacuations.

Fig 1: Northern regions of Canada
Wilson A, Levkoe CZ, Andrée P, Skinner K, Spring A, Wesche S, et al. Strengthening Sustainable Northern Food Systems: Federal Policy Constraints and Potential Opportunities. ARCTIC. 2020 Sep 28;73(3):292–311.

Table 1: Regional Disparities in RSV Hospitalizations

Region	Hospitalization Rate (/1000 infants)[3-5]	Cost to Transport for Hospitalization ($)[6]
Southern Canada	8.3	0
Northwest Territories	15.8	8070.30
Nunavut	60.2	20,484.91
Nunavik	58.1	6529.59

- For 20 years, palivizumab has been the only preventive defense against RSV disease. It must be administered monthly, costing up to $10,000 to protect a single infant for one RSV season[7].
- Due to its expense, palivizumab is only given to high-risk infants[8]:
  - Young infants born very prematurely
  - Infants with congenital heart disease (CHD)
  - Infants with chronic lung disease of prematurity (CLD)
- New prophylactics are now available:
  - RSVpreF vaccine (Abrysvo®, by Pfizer) for pregnant women, which confers immunity through transplacental antibody transfer.
  - Nirsevimab, a long-acting monoclonal antibody that offers protection for an entire season following a single dose.
- Canadian pricing and coverage decisions for these prophylactics are pending, but they will offer a cheaper, more easily administered alternative to palivizumab.
- This opens the potential to expand preventive care beyond only the highest-risk infants, but questions must first be answered:
  - Could universal administration of either prophylactic to all infants across Canada be cost-effective?
  - If not, which infants should receive prophylaxis?
  - Which prophylactic is more cost-effective?
- A thorough analysis of these questions will consider infant comorbidities, level of prematurity, and the differences seen in both hospitalization rates and resource use across different Canadian regions. **No published study has fully incorporated these factors in a cost-effectiveness analysis for these prophylactics in Canada.** As such, the optimal strategy for RSV prevention in infants across Canada is still unknown.
- In this study, we conducted a cost-effectiveness analysis of nirsevimab and Abrysvo® through a range of strategies, with differentiation for prematurity and comorbidity, across southern Canada and three northern Canadian regions: the Northwest Territories, Nunavut, and Nunavik, Quebec.

Methods

- **Target Population**
  - Canadian infants under one year, divided into:
    - Monthly birth cohorts, to capture seasonal risk variation
      - (Infants who are younger during the RSV season are more at risk of serious illness.)
    - Geographical region:
      - Southern Canada, Northwest Territories, Nunavut, Nunavik QC
    - Comorbidity
      - CHD, CLD
    - Level of prematurity
      - Greater than 37 weeks of gestational age (wGA) or full term, 33-37 wGA, less than 33 wGA

- **Model Structure**
  - Decision tree, developed using TreeAge Pro 2024. R1.1
  - Followed infants from birth to one year
  - Tracked medically-attended infections, including:
    - Hospitalizations
    - Intensive care unit (ICU) admissions
    - Outpatient visits (emergency room and primary care)

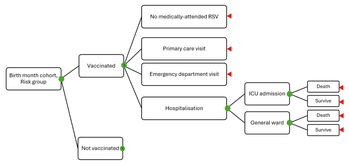

Fig 2: Decision tree

- **Immunization Strategies**
  1. Palivizumab to high-risk infants **(PVZ)**
  2. Nirsevimab to high-risk infants **(NIRS HR)**
  3. Nirsevimab to high-risk and medium-risk infants **(NIRS HR+MR)**
  4. Nirsevimab to all infants under six months at the start of the RSV season **(NIRS <6)**
  5. Nirsevimab to all infants under twelve months **(NIRS ALL)**
  6. Abrysvo® to pregnant women with in-season due dates **(ABR SEASONAL)**
  7. Abrysvo® to all pregnant women **(ABR ALL)**
  8. Abrysvo® to women with in-season due dates, plus nirsevimab to high-risk and medium-risk infants **(ABR SEASONAL + NIRS)**
  9. Abrysvo® to all women, plus nirsevimab to high-risk and medium-risk infants **(ABR ALL + NIRS)**

  - High-risk infants:
    - Those born <33 wGA AND <6 months at season start
    - Those with CLD or CHD
  - Medium-risk infants:
    - Those born <37 wGA AND <6 months at season start

- **Cost-Effectiveness Analysis**
  - Costs: 2024 Canadian dollars
  - Effectiveness: quality-adjusted life years (QALYs)
  - One-way sensitivity analyses on all parameters
  - Two-way sensitivity analysis to vary the prices of nirsevimab and Abrysvo® in tandem ($50 - $1000)
  - Probabilistic sensitivity analyses: all parameters varied simultaneously over 1000 Monte-Carlo simulations

Results

- In southern Canada, it is most cost-effective to directly replace palivizumab with nirsevimab given to high-risk infants only.
- In contrast, at least some level of expanded coverage with nirsevimab is more cost-effective in each northern region, and in Nunavut, universal administration is most cost-effective.

Table 2: Base case results

Strategy	Cost* ($)	Effectiveness (QALY)	ICER ($/QALY)
SOUTH			
NIRS HR	**150,270**	**999.208**	
NO INTERVENTION	154,410	999.185	Dominated
NIRS HR + MR	165,910	999.243	445,161
ABR SEASONAL	*214,400*	*999.321*	*623,159*
ABR SEASONAL + NIRS	236,960	999.363	584,168
ABR ALL	293,730	999.457	611,878
ABR ALL + NIRS	*319,860*	*999.489*	*821,536*
PVZ	340,560	999.202	Dominated
NIRS <6	479,090	999.685	812,806
NIRS ALL	513,390	999.723	894,419
NORTHWEST TERRITORIES			
NIRS HR + MR	**364,050**	**999.187**	
NIRS HR	366,880	999.147	Dominated
ABR SEASONAL + NIRS	385,020	999.322	156,042
ABR SEASONAL	388,940	999.271	Dominated
NO INTERVENTION	392,730	999.117	Dominated
ABR ALL	*437,360*	*999.416*	*555,497*
ABR ALL + NIRS	443,620	999.454	442,253
NIRS <6	562,380	999.681	573,555
PVZ	564,410	999.139	Dominated
NIRS ALL	591,890	999.701	743,857
NUNAVUT			
NIRS ALL	**1,206,440**	**999.562**	
NIRS <6	1,214,250	999.514	Dominated
ABR ALL + NIRS	1,410,740	999.240	Dominated
ABR SEASONAL + NIRS	1,543,040	999.065	Dominated
ABR ALL	1,550,540	999.162	Dominated
ABR SEASONAL	1,737,170	998.982	Dominated
NIRS HR + MR	1,888,200	998.847	Dominated
NIRS HR	2,027,950	998.774	Dominated
NO INTERVENTION	2,208,240	998.697	Dominated
PVZ	2,278,350	998.750	Dominated
NUNAVIK			
NIRS <6	**828,860**	**999.521**	
ABR ALL + NIRS	833,640	999.250	Dominated
NIRS ALL	842,940	999.568	296,329
ABR SEASONAL + NIRS	858,370	999.077	Dominated
ABR ALL	902,570	999.174	Dominated
ABR SEASONAL	960,480	998.976	Dominated
NIRS HR + MR	1,006,760	998.863	Dominated
NIRS HR	1,075,970	998.792	Dominated
NO INTERVENTION	1,190,930	998.717	Dominated
PVZ	1,302,540	998.768	Dominated

- Given the uncertainty of the prices for nirsevimab and Abrysvo®, the two-way sensitivity analysis on their prices can be used to identify the optimal strategy for each region at multiple price points.

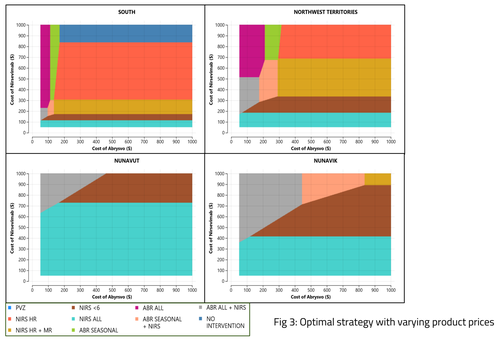

Fig 3: Optimal strategy with varying product prices

- Varying all parameters simultaneously through probabilistic sensitivity analysis produces the following cost-effectiveness acceptability curves:

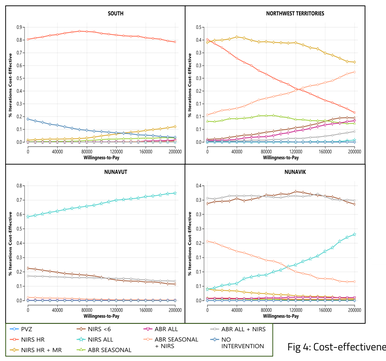

Fig 4: Cost-effectiveness acceptability curves

Discussion

- The model identified a different optimal strategy for every region, highlighting the importance of incorporating regional health inequities into this cost-effectiveness analysis.
- For universal nirsevimab administration to be cost-effective nation-wide, the price per dose would need to be under $112.
- In general, nirsevimab strategies are more cost-effective than Abrysvo® strategies.
- If uptake of nirsevimab is low, Abrysvo®-nirsevimab combination strategies become more cost-effective. For example, if uptake of nirsevimab is less than 78% in Nunavik, it becomes more cost-effective to administer Abrysvo® to all women and top up protection with nirsevimab to high-risk and medium-risk infants than to administer nirsevimab to all infants under six months.
- If supply of nirsevimab is limited, Abrysvo®-nirsevimab combination strategies are a potential cost-effective alternative.

- Strengths
  - The is the first study to incorporate the effects of prematurity, comorbidities, and regional risk differentiation into one analysis.
  - This is the first study to evaluate the cost-effectiveness of seasonal Abrysvo® administration strategies.

- Limitations
  - No long-term sequelae or healthcare resource use/QALY loss beyond the acute infection were included.
  - Equal outpatient rates were assumed between all regions without evidence to support the contrary.
  - The model structure divided outpatient and inpatient pathways and did not account for the realistic possibility of patients using both. This may make our results more conservative.
  - Other risk groups, such as immunocompromised children or children with Down syndrome or cystic fibrosis, were not considered in this analysis.

- A note on product uptake:
  - Results in the northern regions were sensitive to variations in product uptake for both nirsevimab and Abrysvo®.
  - Real world uptake of these products is still unknown.
  - The impact of these products will be dependent on their careful and sensitive integration into practice, which will require collaboration with healthcare workers and the Inuit communities in these regions.

References

1.Glezen WP, Taber LH, Frank AL, Kasel JA. Risk of primary infection and reinfection with respiratory syncytial virus. Am J Dis Child 1960. 1986 Jun;140(6):543–6.

2.Li Y, Wang X, Blau DM, Caballero MT, Feikin DR, Gill CJ, et al. Global, regional, and national disease burden estimates of acute lower respiratory infections due to respiratory syncytial virus in children younger than 5 years in 2019: a systematic analysis. The Lancet. 2022 May;399(10340):2047–64.

3.Buchan SA, Chung H, To T, Daneman N, Guttmann A, Kwong JC, et al. Estimating the Incidence of First RSV Hospitalization in Children Born in Ontario, Canada. J Pediatr Infect Dis Soc. 2023 Jul 31;12(7):421–30.

4.Banerji A, Panzov V, Young M, Robinson J, Lee B, Moraes T, et al. Hospital admissions for lower respiratory tract infections among infants in the Canadian Arctic: a cohort study. CMAJ Open. 2016 Oct 18;4(4):E615–22.

5.Gilca R, Billard MN, Zafack J, Papenburg J, Boucher FD, Charest H, et al. Effectiveness of palivizumab immunoprophylaxis to prevent respiratory syncytial virus hospitalizations in healthy full-term <6-month-old infants from the circumpolar region of Nunavik, Quebec, Canada. Prev Med Rep. 2020 Dec;20:101180.

6.Banerji A, Ng K, Moraes TJ, Panzov V, Robinson J, Lee BE. Cost-effectiveness of palivizumab compared to no prophylaxis in term infants residing in the Canadian Arctic. CMAJ Open. 2016 Oct 18;4(4):E623–33.

7.Provinces spent $43M on preemie drug experts say can be made for a fraction of the cost. CBC News [Internet]. 2017 Apr 6 [cited 2024 Jul 7]; Available from: https://www.cbc.ca/news/health/rsv-drug-synagis-palivizumab-premature-infants-abbvie-provinces-health-care-1.4056823

8.National Advisory Committee on Immunization. Recommended use of palivizumab to reduce complications of respiratory syncytial virus infection in infants. Ottawa: Public Health Agency of Canada = Agence de la santé publique du Canada; 2022.