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SUMMARY WITH CRITICAL APPRAISAL

Palivizumab for Infection Prevention in Inuit Infants: A Review of the Clinical Effectiveness and Cost-Effectiveness

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Abbreviations

RSV	Respiratory syncytial virus

Context and Policy Issues

Respiratory syncytial virus (RSV) can cause respiratory illness in persons of all ages and it is the leading cause of lower respiratory tract illness in children.[1,2] The virus infects almost all children prior to 2 years of age during annual epidemics which, in Northern Hemisphere locations, occur seasonally between October to May. It can cause bronchiolitis and pneumonia and is estimated to be responsible for 3.4 million hospital admissions and approximately 200,000 deaths internationally in young children.[3] Data suggest that the rates of hospitalization of children with RSV related illness in northern and Arctic communities in Canada are amongst the highest rates globally.[4-6] Inuit children living in circumpolar regions have higher hospital admission rates for respiratory illness compared to those living in more southern areas.[7] Several patient characteristics have been identified that carry a higher risk of morbidity and mortality including premature birth, infants with chronic lung disease, hemodynamically significant congenital heart disease, immunocompromised conditions and severe neuromuscular disease.[8]

Palivizumab is a monoclonal antibody against RSV and was approved for use in Canada in 2002. Palivizumab is indicated for the prevention of serious lower respiratory tract disease caused by RSV in pediatric patients at high risk of RSV disease. Some Canadian Arctic and far northern jurisdictions have provided government funding for palivizumab as prophylaxis since 2005.[9] Coverage criteria vary across health jurisdictions and have included such restrictions as premature birth up to 35 weeks gestation or significant cardiac or respiratory conditions.[10] For example, eligible children in Quebec can receive up to 5 monthly doses of palivizumab during the RSV season. The Quebec criteria for palivizumab prophylaxis includes children who are at greatest risk for developing serious respiratory illness due to RSV such as premature infants (<33 weeks of gestation) and children with a chronic respiratory disease or a congenital heart disease.[7] In 2016, criteria in Quebec were modified to include healthy Nunavik children born at term and younger than 3 months of age at the start of the RSV season or born during the RSV season.

Many Inuit infants who live in Northern regions do not have access to hospitals equipped to manage severe RSV illness and air evacuation to tertiary hospitals may be necessary. The appropriate use of palivizumab in Canadian northern and arctic communities has been the subject of debate in the scientific literature and the Canadian media.[1,5,6,9-14]

The purpose of this report is to determine the clinical effectiveness and cost effectiveness of universal versus high-risk palivizumab prophylaxis, and seasonal versus year-round palivizumab in Inuit children up to 4 years of age.

Research Questions

1. What is the clinical effectiveness of universal versus high risk palivizumab prophylaxis for respiratory syncytial virus prevention in Inuit infants?
2. What is the clinical effectiveness of seasonal versus year-round palivizumab prophylaxis for respiratory syncytial virus prevention in Inuit infants?
3. What is the cost- effectiveness of universal versus high risk palivizumab prophylaxis for respiratory syncytial virus prevention in Inuit infants?

4. What is the cost-effectiveness of seasonal (~6months) versus year-round palivizumab prophylaxis for respiratory syncytial virus prevention in Inuit infants?

Key Findings

No relevant literature was identified regarding the comparative clinical effectiveness of universal versus high-risk palivizumab or seasonal versus year-round palivizumab prophylaxis in Inuit children up to 4 years of age. Additionally, no relevant literature was identified regarding the comparative cost effectiveness of universal versus high-risk palivizumab or seasonal versus year-round palivizumab prophylaxis in Inuit children up to 4 years of age.

Methods

Literature Search Methods

A limited literature search was conducted by an information specialist on key resources including PubMed, the Cochrane Library, the University of York Centre for Reviews and Dissemination (CRD) databases, the websites of Canadian and major international health technology agencies, as well as a focused Internet search. The search strategy was comprised of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were Palivizumab and respiratory syncytial virus and Inuit infants. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. A narrower search was also limited to English language documents published between January 1, 2009 and November 20, 2019. A second broader search was also limited to English language documents published between January 1, 2014 and November 20, 2019.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Q1-4: Infants living in the Arctic or Northern communities or who are Inuit or First Nations aged 0 to 4 years
Intervention	Q1,3: Universal Palivizumab (brand name: Synagis) administration Q2,4: Palivizumab administered during RSV season/ 6 months
Comparator	Q1,3: Palivizumab administered only to high risk infants; No prophylaxis Q2,4: Palivizumab administered year round
Outcomes	Q1: Clinical effectiveness: number of hospital admissions, number of medical evacuations/transfers, incidence respiratory infection (e.g. respiratory syncytial virus [RSV] infection, bronchiolitis), morbidity Q2: Cost-effectiveness
Study Designs	Health technology assessments, systematic reviews, meta-analyses, economic evaluations, randomized controlled trials, non-randomized studies

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1, they were duplicate publications, or were published before 2009. Studies in non-aboriginal populations were excluded but studies were accepted for inclusion if a majority of the study population were Inuit or First Nations.

Summary of Evidence

Quantity of Research Available

A total of 362 citations were identified in the literature search. Following screening of titles and abstracts, 335 citations were excluded and 27 potentially relevant reports from the electronic search were retrieved for full-text review. Two potentially relevant publications were retrieved from the grey literature search for full text review. Of these potentially relevant articles all were excluded for various reasons; no publications met the inclusion criteria and therefore none were included in this report. Appendix 1 presents the PRISMA[15] flowchart of the study selection.

Limitations

This report is limited by the timeframe used for literature searches (from 2009 onwards) and by restricting the search to English language articles.

Conclusions and Implications for Decision or Policy Making

No relevant literature was identified regarding the comparative clinical effectiveness of universal versus high-risk palivizumab or seasonal versus year-round palivizumab prophylaxis in Inuit children up to 4 years of age. Additionally, no relevant literature was identified regarding the comparative cost effectiveness of universal versus high-risk palivizumab or seasonal versus year-round palivizumab prophylaxis in Inuit children up to 4 years of age. Therefore, no conclusions regarding relative clinical effectiveness and cost effectiveness can be provided.

Two reports that were evaluated for inclusion in this review assessed the clinical effectiveness[7] and cost-effectiveness[9] of palivizumab in infants residing in Canadian far north or Arctic communities, but did not address the comparisons of interest. Glica et al. evaluated the impact of palivizumab prophylaxis policies in Nunavik infants.[7] Banerji et al. compared the cost effectiveness of palivizumab prophylaxis relative to no prophylaxis in term infants residing in the Canadian arctic.[9] These reports did not address the comparisons of interest and hence did not satisfy the inclusion criteria for this current report and were not critically appraised or included in the summary of findings. However, as these reports may provide some relevant analyses, they are mentioned briefly here.

Gilca et al. (2018) attempted to evaluate the impact of the extension of palivizumab prophylaxis criteria on Nunavik Inuit infants <3 months of age born at term, since the reason for broadening the criteria in 2016 was based upon expert opinion and not based on empirical evidence.[7]

Gilca et al. reported that their analysis of data following the first year of implementing the broader prophylaxis criteria was inconclusive and that a longer observation period was required to evaluate the impact of palivizumab prophylaxis in Nunavik.[7] Banerji et al.

reported that there is great variability in incremental cost effectiveness ratios for palivizumab prophylaxis compared to no prophylaxis across several regions of the Canadian arctic.[9]

Further research using well-designed studies is needed to provide evidence to evaluate the comparative clinical and cost-effectiveness in Inuit populations with respect to seasonal versus year-round administration and with respect to universal versus high risk prophylaxis.

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Appendix 1: Selection of Included Studies