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Title	Cost-effectiveness of palivizumab compared to no prophylaxis in term infants who reside in the Canadian Arctic
Authors	Anna Banerji MPH MD, Kaspar Ng BPharm MD, Theo Morales MD, Vladimir Panzov MD, Joan Robinson MD, Bonita E. Lee MD
Reviewer 1	Dr. Mohsen Sadatsafavi
Institution	Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC
General comments (author response in bold)	This is a peer-review of the manuscript entitled "Economic evaluation of palivizumab prophylaxis to healthy term infants in the Canadian Arctic regions: Simulations based on multi-site lower respiratory tract infection surveillance data". This is a cost-effectiveness analysis of programs of universal prophylactic therapy with palivizumab in term infants among the Inuit Canadians. The analysis also attempts to find which regions in the Canadian Arctic have the highest costs associated with RSV admissions and could benefit from universal prophylaxis with palivizumab. The perspective is that of the third-party payer and costs are reported in 2011 Canadian Dollars. The effectiveness outcome is hospital admissions prevented (HAP). The authors also discuss the Number Needed to Treat (NNT). This is a topical question and tackles an important source of burden for Canadian underserved populations. The strength of the study is the use of real world data on the prospective surveillance of lower respiratory tract infections in the target areas. It appears the method of costing the drug administration and hospital admission is rigorous. However, the study suffers from major problems in terms of following principles of cost-effectiveness analysis and its reporting. Major comments are provided below. It seems the authors need to go back to the drawing board and re-perform the analysis by adhering to the guidelines and best practice standards in economic evaluations. Similarly, the manuscript should be significantly revised to adhere to the reporting standards and guidelines in the field. Major comments: 1. The authors need to critically evaluate the structure of the manuscript against standards of reporting economic evaluations. Over the years the standards have been consolidated, and the exporting standards are not much different, in terms of rigor, than the standards of reporting RCTs. One suggestion is that the authors consult the CHEERS checklist as a guide for presentation of their analysis. Husereau, D. et al., 2013. Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement. BMC medicine, 11, p.80. **Have used this to guide us** Given the scattered information it is difficult to understand what has been done. On the contrary, tables 3 and 4, which represent the main analysis, are largely understandable and show the analysis has been done with some rigor (albeit the analysis does not fully conform to principles – see below). It is unfortunate that the presentation has not helped explain the logic and methodology behind the analysis. The authors need to clearly describe the details of their model. The setting and comparators (models 1 and 2) could both be described much earlier in the Methods section. It is first mentioned under the Data Analysis section. A proposed outline is **Done** - Settings: population, comparators, perspective - Costs and effectiveness outcomes - A graphical description of the model in terms of decision trees (more detailed and structure than the simple flow chart) **As we did not use probalistic modeling we did not use a decision tree, but added two figures which the editors may feel would be helpful to understand the study** - A dedicated table presenting all input parameters together, with references and some descriptions. **Done** 2- Modern cost-effectiveness analyses should be probabilistic. The present cost-effectiveness analysis is deterministic. This is not much different than reporting a clinical trial with only point estimates of outcomes. Please refer to the relevant best practice standards namely "Briggs, A.H. et al., 2012. Model parameter estimation and uncertainty: a report of the ISPOR-SMDM Modeling Good Research Practices Task Force--6. Value in health: the journal of the International Society for Pharmacoeconomics and Outcomes Research, 15(6), pp.835–842." This is not impossible to achieve. Once all input parameters are identified, the investigators need to assign appropriate probability distributions representing the level of uncertainty, and then perform Monte Carlo simulation (re-analysis with random draws from the input; easy to do in excel or specialist software for economic evaluations). **On discussion with our co-authors we have decided to express the comparison using incremental cost per hospital admission avoided. We recognize the importance of probablistic analysis, however inputs are based on actual data rather than estimates, narrowing the range and the data findins are so strong tha the rane of inputs should not have a big impact. neverless we have acknowledged a lack of probalistic sensitivity analyis in the limitations.**

	Minor comments and suggestions: 3. The abstract is confusing, and seem to have been written in a rush. The confusion starts when it is said that eight scenarios are compared for universal palivizumab prophylaxis, but then only talks about Model A and Model B. It does not help at all that the terms such as NT are not defined. The closing sentences are difficult to understand. **The paper has been extensively rewritten** 4. Background, first paragraph, last sentence: please provide citation. **Done** 5. Data analysis: It is not obvious how the one month of protection is modeled. Again this is about carefully documenting all the assumptions and being transparent in calculations. 6. It will help the reader to understand what exactly the technology is: a drug? injectable? There is currently only one sentence on top of the third paragraph. Might be a good idea to expand. **We have explained that this is a monthly antiobody injection that provides 30 days of protection** 7. Please mention the analytical platform (the software used) somewhere in the methods (again part of reporting standards). **Excel** 8. Page 5, line 11: cost of palivizumab is reported per kg; this does not require weight estimates. Perhaps costs per individual is meant here? Please correct. **Changed to per kg weight of the infant** 9. Page 6, second para: efficacy is not a well-defined epidemiological term. Please provide the relevant scale and outcomes, e.g., a relative risk (RR) of 0.78 for RSV-related hospital admissions. 10. Page 7: The formula at the end of the page is vague. Is there a difference between "untreated admission RV rate" and "untreated RSV admission rate?" '**This has been moved to the table** 11. Interpretation: the first notion of the costs per HAP ($327,000) is in this section. This is the Incremental Cost-Effectiveness Ratio (ICER) which is the main output of an economic evaluation. This should have been the main part of the results section. **We have documented HAP in the results and it is the first part of the discussion** 12. Is Herd Immunity a relevant concern in this evaluation? Given that this is an infectious agent the authors should at least discuss this in the Interpretations. **Herd immunity is not a factor here. Most kids get infected one or twice a year** 13 Please correct the following typos: Page 3, line 30 (NNT calculating does not require costs, rather the number of HAPs). **Relocated** Page 4, line 11: a word (between or from) is missing for the date range. So is another word towards the end of the sentence. **Revised** Page 5, line 6: a word is missing (from hospital finance …?) **Department added** Page 7, line 32: "revised admissions" is a vague term **Removed**