

## PEER REVIEW HISTORY

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### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Does non-invasive ventilation change metabolic markers in children with obstructive sleep apnea? A Systematic Review and Meta-Analysis Study Protocol
<b>AUTHORS</b>	Gerdung, Christopher; Rodriguez-Lopez, Sara; Palkowski, Stefan; Keto-Lambert, Diana; Sebastianski, Meghan; Castro Codesal, Maria

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Gonzalo Labarca Universidad de Concepcion, Chile
<b>REVIEW RETURNED</b>	17-May-2020

<b>GENERAL COMMENTS</b>	<p>I would like to congrats to Dr. Gerdung and colleges for this protocol of systematic review.</p> <p>I have some minor comments:</p> <ol style="list-style-type: none"><li>1. The PICO question in the protocol reads like an overview, rather than an intervention review as it contains a number of outcomes, rather than one package of care.</li><li>2. The author defines "inflammatory markers", without any specification about which markers will be included after the literature search. This definition is relevant in a protocol, in order to avoid inaccurate literature search.</li><li>3. Similar to point (3), for cardiovascular outcomes.</li><li>4. Please, provide details about how to deal with potential inconsistency in results after meta-analysis (high heterogeneity), and provide predefined subgroup analysis</li><li>5. Do you plan to provide a sensitive analysis (example: analysis by NVI adherence, Follow up, others)</li></ol>
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<b>REVIEWER</b>	Cara Bossley King's College Hospital, London United Kingdom
<b>REVIEW RETURNED</b>	06-Jun-2020

<b>GENERAL COMMENTS</b>	<p>This is a description of the study protocol of performing a systematic review of the literature pertaining to the use of a respiratory intervention (NIV) on the metabolic syndrome. The protocol describes an important clinical question. The methodology is as expected for a systematic review and meta-analysis.</p> <p>I think it is appropriate to publish this protocol and am happy with the protocol and research questions.</p> <p>The study dates are stated.</p>
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## VERSION 1 – AUTHOR RESPONSE

Reviewer 1:

- With respect to the PICO question, our preliminary search identified limited literature regarding the impact of NIV on a range of metabolic markers in children. Therefore, we aimed for a broader spectrum of metabolic outcomes. As explained in the protocol, we have classified the outcomes in several categories including markers of systemic inflammation, cardiovascular outcomes, changes in weight/body mass index, lipid profile, liver enzymes, glucose control and markers of insulin resistance, renal function and other metabolic markers. Our expectation is that we will be able to run meta-analysis for some of them and have a more narrative systematic review for the ones with more heterogeneity.

- With respect to the the definitions of "inflammatory markers" and "cardiovascular outcomes" the specific markers are outlined in the supplemental document (Appendix A). We have added a sentence to the "Types of Outcomes" subheading to ensure clarity.

- With respect to the potential inconsistency in results after heterogeneity, we have added the following sentence to the text "Heterogeneity in the pooled data will be minimized, by pooling data based on outcome, as well as the indication for NIV. In the event that pooled data remains heterogeneous within these pooled groups, a narrative description will be included. If the data allows, we will analyze the data with respect to NIV adherence and the length of time wearing NIV."

Reviewer 2:

- Thank you for your comments

## VERSION 2 – REVIEW

<b>REVIEWER</b>	Gonzalo Labarca University of Concepcion
<b>REVIEW RETURNED</b>	05-Jul-2020
<b>GENERAL COMMENTS</b>	I would like to congrats the authors for the effort in this protocol. This version includes my previous comments, thank you