PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Intranasal antihistamines and corticosteroids in the treatment of allergic rhinitis: A systematic review and meta-analysis protocol
AUTHORS	Sousa-Pinto, Bernardo; Vieira, Rafael José; Brozek, Jan; Cardoso-Fernandes, António; Lourenço-Silva, Nuno; Ferreira-da-Silva, Renato; Ferreira, André; Gil-Mata, Sara; Bedbrook, Anna; Klimek, L.; Fonseca, Joao A.; Zuberbier, Torsten; Schünemann, Holger; Bousquet, J.

VERSION 1 – REVIEW

REVIEWER	Subha, Sethu Thakachy Universiti Putra Malaysia, Otorhinolaryngology
REVIEW RETURNED	31-Jul-2023

GENERAL COMMENTS	This manuscript needs language editing by a professional and can be considered for publication

REVIEWER	Miligkos, Michael Aglaia Kiriakou Children's Hospital, Allergy and Clinical Immunology
REVIEW RETURNED	24-Aug-2023

GENERAL COMMENTS	Overall, this is a well-written and structured protocol of a systematic review, which will hopefully provide evidence to address important clinical questions regarding optimal symptomatic treatment of allergic rhinitis. Minor comments: 1) Please clarify whether RCTs including both adults and adolescents will be included. In the abstract it is stated that adult patients will be assessed, whereas in the methods the age limit is set at 12 years of age. If adolescents are actually included, how RCTs with overlapping populations (e.g., children and adolescents) will be handled? 2) The aim of this SR is to summarize the existing evidence regarding the efficacy of intranasal medications vs. placebo in patients with AR (no direct comparisons or NMA will be considered at this stage). Therefore, only a qualitative assessment of comparative effectiveness can be made. The following excerpt ("In addition, there is insufficient evidence as to whether effectiveness differences may exist among different intranasal specific medications.") could be modified in order not to confuse the reader about the specific aims of the SR. 3) Apart from gender and age, which other baseline variables will be considered from each included RCT (e.g., concomitant medications or diseases)?

	4) Will publication bias assessment take place? 5) The rationale for the exclusion of cross-over trials is valid. However, the authors should provide the number of excluded cross-over trials in the flowchart (i.e., most cross-over trials could probably be excluded during title/abstract screening and therefore not presented in the list of exluded studies at the "full-text screening box" of the flowchart).

VERSION 1 – AUTHOR RESPONSE

Reviewer Reports:
Reviewer 1:
Dr. Sethu Thakachy Subha, Universiti Putra Malaysia
Comments to the Author:
This manuscript needs language editing by a professional and can be considered for publication.
Both the original version of the manuscript and its revised version (which we are submitting now) have been revised by a native English speaker who is also a co-author of the manuscript (Dr. Anna Bedbrook). She revises all of Prof. Jean Bousquet's papers (around 50 a year) and such a comment is highly surprising. Moreover, the first comment of the second author is "Overall, this is a well-written…"
Reviewer: 2
Dr. Michael Miligkos, University of Thessaly Faculty of Medicine
Comments to the Author:
Overall, this is a well-written and structured protocol of a systematic review, which will hopefully provide evidence to address important clinical questions regarding optimal symptomatic treatment of allergic rhinitis.
Thank you for the note.
Minor comments:
1) Please clarify whether RCTs including both adults and adolescents will be included. In the abstract it is stated that adult patients will be assessed, whereas in the methods the age limit is set at 12 years of age. If adolescents are actually included, how RCTs with overlapping populations (e.g., children and adolescents) will be handled?
Thank you for the question. We will indeed include RCTs assessing adults and adolescents (that is, studies assessing patients ≥12 years old). In allergic rhinitis RCTs, typically adolescents ≥12 years old are assessed alongside adults. We have clarified this issue in the manuscript by replacing "adults" by "patients ≥12 years old" in the abstract and in the "strengths and limitations of this study" (after the abstract) section.
2) The aim of this SR is to summarize the existing evidence regarding the efficacy of intranasal medications vs. placebo in patients with AR (no direct comparisons or NMA will be considered at this stage). Therefore, only a qualitative assessment of comparative effectiveness can be made. The following excerpt ("In addition, there is insufficient evidence as to whether effectiveness differences may exist among different intranasal specific medications.") could be modified in order not to confuse the reader about the specific aims of the SR.
Thank you for the note. As suggested, we have modified the sentence "In addition, there is insufficient evidence as to whether effectiveness differences may exist among different intranasal specific medications", which now reads: "In addition, there is insufficient systematised evidence on the quantitative effectiveness of each specific intranasal medication."
3) Apart from gender and age, which other baseline variables will be considered from each included RCT (e.g., concomitant medications or diseases)?
From each included RCT, we will incorporate information on participants' inclusion and exclusion

criteria (which may indicate, for example, any concomitant disease that patients should or should not have in order to be eligible for study participation). However, beyond age, gender and the outcome variables being assessed, we will not specifically retrieve the distribution of any other baseline variable for each RCT.
4) Will publication bias assessment take place?
Thank you for the note. We will assess publication biases (and, indeed, this is one of the criteria used in the GRADE approach for the assessment of the certainty of evidence), namely by considering whether (i) small and large studies converge on the same effect estimates, (ii) there has been an earlier publication on positive results and (iii) there is any information on registered RCTs without published results. We have added this information to the manuscript, which now reads:
“For the assessment of the possibility of publication biases, we will consider whether (i) small and large studies converge on the same effect estimates, (ii) there has been an earlier publication on positive results and (iii) there is any information on registered RCTs without published results.” (Methods section; risk of bias and certainty assessment subsection).
5) The rationale for the exclusion of cross-over trials is valid. However, the authors should provide the number of excluded cross-over trials in the flowchart (i.e., most cross-over trials could probably be excluded during title/abstract screening and therefore not presented in the list of excluded studies at the "full-text screening box" of the flowchart).
Thank you for the note. We will provide an indication on the number of excluded cross-over trials.

VERSION 2 – REVIEW

REVIEWER	Miligkos, Michael Aglaia Kiriakou Children's Hospital, Allergy and Clinical Immunology
REVIEW RETURNED	21-Sep-2023

GENERAL COMMENTS	None