# PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (http://bmjopen.bmj.com/site/about/resources/checklist.pdf) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

### **ARTICLE DETAILS**

TITLE (PROVISIONAL)	Global prevalence of spondyloarthritis in low-and-middle income countries: a systematic review and meta-analysis protocol.
AUTHORS	ALLADO, Edem; MOUSSU, Anthony; Bigna, Jean Joel; HAMROUN, Sabrina; CAMIER, Aurore; CHENUEL, Bruno; HAMROUN, Aghiles

# **VERSION 1 – REVIEW**

REVIEWER	Nelly ZIADE
	Saint-Joseph University, Beirut, Lebanon
REVIEW RETURNED	27-Jun-2020

GENERAL COMMENTS	1- The primary objective of the study should be more precise: it should be either the prevalence of SpA or the HLA-B27. Other objectives should be listed as secondary.  2- The primary objective and the title are not in harmony: the "burden" of SpA (title) is not a synonym to the "prevalence" of SpA (objective).  3- How will the "Middle and Low Income" status be identified?  4- Introduction, line #83:  "distinguishing two main forms of the disease according to its clinical and radiological phenotype: 84 radiographic and non-radiographic forms": this sentence is not very accurate as the
	current trend is to consider these two forms as the same disease 5- Methods, line#126:
	Please explain the definition of adults as age> 15years
	6- Methods, line #131:
	Why case-control studies are not considered?
	7- Methods, line #149:
	8- Why is the search stopping in September 2019 (9 months ago)? 9- The estimated dates for each step of the study should be mentioned.
	mentioned.

REVIEWER	Polina Putrik
	Monash University/Maastricht University
REVIEW RETURNED	27-Jul-2020

GENERAL COMMENTS	This is a protocol for a systematic review to assess the prevalence of SpA in low and middle income countries. This work is important as it provides relevant insights into epidemiology of the disease and eventual treatment gaps. Before proceeding with the work, this reviewer suggests that authors clarify a number of points outlined below.
	Comments for authors: Major:

1) Stolwijk et al, 2015 have performed a review of global prevalence of SpA (ref 24). To my knowledge, this was a review that included among others LMIC countries. Could authors justify the need to search the overlapping databases from inception?
2) Have authors involved a librarian to advise on search strategy and databases? E.g. were African Journals online or African Index Medicus considered? And similarly, any other databases specific to regions with most LMIC?

#### Moderate:

- 3) Why is date of the search limited to 30 September 2019? We are now almost a year from it. I assume authors will update it after the protocol is accepted.
- 4) p.9 line 198 how were cut-offs for I-square defined?

#### Minor:

5) manuscript should be proof-read for English grammar given multiple typos and grammatical errors.

## **VERSION 1 – AUTHOR RESPONSE**

#### Reviewer #1

Reviewer #1, Comment #1: The primary objective of the study should be more precise: it should be either the prevalence of SpA or the HLA-B27. Other objectives should be listed as secondary.

Author response: Thank you very much for highlighting this issue. As suggested, the study objectives have been clarified: SpA prevalence as primary objective, HLAB27 and its association with SpA as secondary objectives (p9 lines 86-93).

Reviewer #1, Comment #2: The primary objective and the title are not in harmony: the "burden" of SpA (title) is not a synonym to the "prevalence" of SpA (objective).

Author response: Thank you for pointing this out. The title has been modified in accordance with the reviewer suggestion: "Global prevalence of spondyloarthritis in low-and-middle income countries: a systematic review and meta-analysis protocol".

Reviewer #1, Comment #3: How will the "Middle and Low Income" status be identified?

Author response: Thank you for this valuable question. We added this sentence in the methodology section of the manuscript (page 6, lines 109-113): "Only participants from LMICs will be included as classified by the World Bank. For the 2020 fiscal year, low-income economies are defined as those with a gross national income (GNI) per capita, calculated using the World Bank Atlas method, of \$1025 or less in 2018; lower-middle-income economies are those with a GNI per capita between \$1026 and \$3995; and upper-middle-income economies are those with a GNI per capita between \$3996 and \$12.375."

Reviewer #1, Comment #4: Introduction, line #83: "distinguishing two main forms of the disease according to its clinical and radiological phenotype: radiographic and non-radiographic forms": this sentence is not very accurate as the current trend is to consider these two forms as the same disease.

Author response: Thank you for highlighting this issue. The sentence has been modified in accordance to the comment: "The concept and definition of SpA have evolved significantly over the past thirty years, leading to the current Assessment of Spondyloarthritis International Society (ASAS) classification criteria." (p4, lines 66-67).

Reviewer #1, Comment #5: Methods, line#126: Please explain the definition of adults as age > 15years.

Author response: Thank you for this comment. Fifteen years is commonly used as the cut-off for the definition of young adult in scientific literature, cutting across primary reproductive years.1

Reviewer #1, Comment #6: Methods, line #131: Why case-control studies are not considered?

Author response: Thank you for pointing this out. Because of selection bias, case-control study design is not suitable for SpA prevalence estimation.2 On the other hand, this study design is of great interest for analyzing HLAB27 prevalence and estimating its association with SpA.

Reviewer #1, Comment #7: Methods, line #149:

- a. Why is the search stopping in September 2019 (9 months ago)?
- b. The estimated dates for each step of the study should be mentioned.

Author response: Thank you for this valuable comments. As it has been declared in Prospero registration (CRD42020163898), the literature search dates have been updated in the final version of the manuscript (from inception to 30 April 2020). As suggested, we also added the estimated dates for each step of the study, in the section "review status and expected deadlines" (p10 line 210-213).

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#### Reviewer #2

Reviewer #2, Comment #1: Stolwijk et al, 2015 have performed a review of global prevalence of SpA (ref 24). To my knowledge, this was a review that included among others LMIC countries. Could authors justify the need to search the overlapping databases from inception?

Author response: Thank you for pointing this out. Indeed, Stolwijk et al performed a systematic review and meta-analysis on the global prevalence of SpA. However, they only identified articles issued from Medline and Embase, which are not the most appropriate databases for LMIC literature. Moreover, they decided not to include reports with less than 1000 participants, thus potentially eliminating a substantial number of LMIC data. Finally, Stolwijk et al included a total of 37 studies regarding LMIC, while we were able to include 77 studies in our preliminary searches.

Reviewer #2, Comment #2: Have authors involved a librarian to advise on search strategy and databases? E.g. were African Journals online or African Index Medicus considered? And similarly, any other databases specific to regions with most LMIC?

Author response: Thank you for this valuable comment. In fact, one of the author (JJB) is highly experienced in literature search strategy and systematic review methodology, regarding especially Africa and LMIC databases. As detailed in the manuscript, all relevant records will be identified by

searching EMBASE, PubMed, Global Index Medicus and Web of knowledge. Global Index Medicus and Web of knowledge are two of the most appropriate databases for LMIC.3,4 As a matter of fact, African Index Medicus is included in Global Index Medicus, among other LMIC-related databases.

Reviewer #2, Comment #3: Why is date of the search limited to 30 September 2019? We are now almost a year from it. I assume authors will update it after the protocol is accepted.

Author response: Thank you for pointing this out. The literature search dates have been updated in the manuscript, as mentioned in the response to Reviewer #1, Comment #7.

Reviewer #2, Comment #4: p.9 line 198 – how were cut-offs for I-square defined?

Author response: Thank you for this valuable question. The cut-offs for I-square have been defined, accordingly to the article of Higgins et al.5 In their work about measuring inconsistency in meta-analyses, they have suggested to summarize heterogeneity results as following: low (I2 25-50%), moderate (I2 50-75%), high (I2 >75%).

Reviewer #2, Comment #5: manuscript should be proof-read for English grammar given multiple typos and grammatical errors.

Author response: Thank you for pointing this out. The manuscript has been edited by an English native speaker (PC), as mentioned in the acknowledgement section of the manuscript (p13, line 321).

### **VERSION 2 – REVIEW**

REVIEWER	Nelly Ziade
	Saint-Joseph University, Beirut, Lebanon
REVIEW RETURNED	06-Sep-2020
GENERAL COMMENTS	All the comments have been addressed by the authors.
	I have no further comments.
REVIEWER	Polina Putrik
	Monash University/Maastricht University
REVIEW RETURNED	11-Sep-2020
GENERAL COMMENTS	Authors have addressed the concerns that have been raised.