# 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)	Epidemiology of Diabetes Mellitus in Pakistan: A Systematic
	Review Protocol
AUTHORS	Hasan, Syed Umar; Siddiqui, M. A. Rehman

### **VERSION 1 – REVIEW**

REVIEWER	Paudel, Grish
	Manmohan Memorial Institute of Health Sciences, Department of
	Public Health
REVIEW RETURNED	19-Sep-2023
GENERAL COMMENTS	Overall, I find the manuscript to be well-written, with the authors demonstrating a commendable level of clarity and coherence in presenting their research. The abstract and body sections, including the Introduction, Methods, and Discussion, have been articulated effectively.
	However, I believe there are some aspects that need attention to enhance the clarity and readability of the protocol paper for a broader audience:
	factor of DM will be assessed, however, no objectives have been outlined aiming to assess the risk factors within the objective section.
	b. Please replace the term "other databases" (Page Number-2, Line Number-25) with the name of the database that you intend to search for the literature.
	c. Please state the full form of acronyms such as NGSP and DCCT (Page Number-8, Line Number-9) during their first use. d. Authors have mentioned that they will use the Newcastle- Ottawa Scale (NOS) tool for quality assessment (Page Number-9)
	Line Number-50). Why this tool? I'm sure there are others! Please provide the rationale for using this tool.
	e. On Page Number-7, Line Number-47, studies with a sample size of less than 500 will be excluded. Please provide the rationale for this cut-off value. Moreover, what if most studies have a sample size less than 500?
	f. A similar review paper was published in 2019 (Akhtar S, Nasir JA, Abbas T, Sarwar A. Diabetes in Pakistan: A systematic review and meta-analysis. Pak J Med Sci. 2019 Jul-Aug;35(4):1173-1178. doi: 10.12669/pjms.35.4.194.). How does this proposed review differ from the review study published in 2019? What new

strengthen the rationale of this review.

knowledge or evidence does this review generate in the existing literature? This should be outlined in the introduction section to

g. In the reference lists, reference numbers 1, 6, 20, 21, and 23 are not listed appropriately. Authors are required to revise those references adhering to the journal's reference guidelines.
I want to emphasize that these are minor suggestions aimed at improving the manuscript's accessibility to a wider readership. The core content and structure of the paper are strong and well- organized.
In conclusion, I recommend that the authors consider the aforementioned points and make the necessary revisions to enhance the clarity and readability of their protocol paper. I believe that addressing these minor issues will significantly contribute to the overall quality of the manuscript.
Thank you.

REVIEWER	Riaz, Muhammad
	Qatar University, Public Health
REVIEW RETURNED	19-Dec-2023

GENERAL COMMENTS	General remarks:
	This manuscript entitles "Epidemiology of Diabetes Mellitus in
	Pakistan: A Systematic Review Protocol". This is an important
	topic from the public health perspective. The protocol is prepared
	for conducting a systematic review and meta-analysis (SR&MA) on
	the published studies in Pakistan to report the pooled prevalence,
	risk factors, and disparities between rural and urban populations.
	This research work is important as it is coming from a developing
	country (Pakistan), where the public health services are
	depressing. The manuscript is well-written, but some changes are
	required at various places in the manuscript to make it concise. My
	major concern is that a SR&MA on similar topic is already
	conducted in Pakistan and the authors do not explain, why there is
	a need for another SR&MA.
	I would like to recommend the manuscript for publication, if the
	author provide an adequate explanation for the need to conduct
	another SR&MA with reference to the previously conducted one
	["Diabetes in Pakistan": Akhtar S et al, 2019]. This could be added
	in the last paragraph of introduction section. In addition, I would
	like to suggest further changes as below:
	1. Abstract
	Introduction
	- The text "considering its epidemiological context" is not very clear
	and it may be extra wording as the author states: "prevalence of
	DM, risk factors, and disparities between rural and urban
	populations". Please state clearly, if there are any other
	epidemiological investigations.
	Methods and analysis
	- "employing WHO or ADA criteria", not clear, criteria of what?
	- or Urdu Tbelleve, there will be hardly any paper in Urdu
	language and if any exist, they may not be of decent quality.
	- I am not sure, why other designs such as case-control if exist are
	NOL Stated here.
	- will pool prevalence estimates, will the author require to pool
	it should be clearly stated
	2 Introduction
	2. "Introduction "this number amplified to approximately 33 million in 2021 (5)". It
	would have been better to see what the prevalence is
	שטמוט המאב שבבה שבונבו נט שבב שוומנ נווב אובימובווטב וש.

Objectives: "Specifically, the review aims to". I think, first should be
aims and then objectives: The main aim of the study is to conduct
a systematic review and meta-analysis and write a comprehensive
report on the enidemiology of diabetes. Then state the objectives
as listed in the paper
as instead in the paper.
- At the end of the introduction, a more rational case can be made
for the need to conduct another SR&MA investigating
epidemiology of diabetes in Pakistan with reference to the existing
one ["Diabetes in Pakistan": Akhtar S et al. 2019].
3 Methods
Study Design: "This protocol for systematic review is written as
-Study Design. This protocol for systematic review is written as
Preferred Reporting Items for Systematic Reviews and Meta-
Analyses extension for protocol paper (PRISMA-P) (17). This
systematic review will follow the Preferred Reporting Items for
Systematic Reviews and Meta-Analyses (PRISMA) guidelines
(18)" There is a repetition of text 1 suggest rephrasing it
Inclusion criteria "Urdu language" I den't think there will be any
- inclusion chienal Ordullanguage, i don t think, there will be any
study in Urdu published in a proper peer review journal.
-"Studies with a sample size less than 500 will be excluded" If the
author can have a large number of studies, then it might be ok to
exclude. If the number of studies is small, then I would suggest
including studies with small sample sizes. I suggest reducing the
cut-off to 300 at least
outon to sou at least.
- outcome, percentage or proportion it is better to say proportion
expressed as percentage.
- outcome: "Additionally, if available, the review will explore the
prevalence of diabetes across various subgroups based on age,
gender, and geographical location (e.g., provinces, urban vs.
rural)" this can be deleted from here and add/leave it in the
analysis section
Soarch stratogy: "A comprohonsive search stratogy will be
- Search strategy. A comprehensive search strategy will be
developed to identify relevant studies. I think the protocol should
have a clearly stated final search strategy.
<ul> <li>I suggest, the search strategy should be in MeSH terms with</li> </ul>
Boolean operators in text and then the actual search strategy with
appropriate Boolean operators AND/OR added in the supplement.
- Data extraction:
- "Confounders" all factors stated may not be confounders. I don't
- comounders, an lactors stated may not be comounders, r don't
unink uie terri comounders is appropriate to use nere.
- Prevalence data: prevalence rates delete "rates"
-Methodological details: study design?
- Quality assessment: It is just to mention NOS is good to use, if
the aim is to report a comprehensive epidemiology of diabetes. For
investigating prevalence only. "Joanna Briggs Institute critical
appraisal checklist for studies reporting prevalence data" could be
hottar to use
Dete enclusion
Data analysis:
-it is not clear, how meta-analysis will be conducted to pool the
prevalences together. I think, they will have to transform the
prevalence to an appropriate scale to be pooled.
-Analysis for identifying temporal trends in DM is not added.
-If the authors are conducting meta-analysis for the effect
estimates of risk factors, they need to mention what measure of
estimates of the lactors, they need to mention what measure of
association such as one ratios (OKS) will be extracted/calculated
for each of the variables (risk factors) and pooled using a meta-
analysis. A detailed statistical analysis needs to be added for this.
4. Discussion
- The discussion reads to me like a discussion for reporting the
actual SR&MA already conducted. I think, it could be written in the
sense that it is a protocol for conducting SR&MA

"Comparing the prevalence rates reported in this review with
previous estimates can offer insights into the temporal trends of
DM in Pakistan (25, 26)". I suggest, conducting a meta-analysis on
data extracted from all included studies to report the temporal
trends DM. I don't think, it will identify proper temporal trends if it is
based on the results comparison of this study with the results of
previously conducted meta-analysis.

## **VERSION 1 – AUTHOR RESPONSE**

Reviewer: 1 Dr. Grish Paudel, Manmohan Memorial Institute of Health Sciences

Comments to the Author:

-Overall, I find the manuscript to be well-written, with the authors demonstrating a commendable level of clarity and coherence in presenting their research. The abstract and body sections, including the Introduction, Methods, and Discussion, have been articulated effectively.

Authors' reply: Thank you for the appreciation of our manuscript.

However, I believe there are some aspects that need attention to enhance the clarity and readability of the protocol paper for a broader audience:

a. In Page Number-2, Line Number-17, it is stated that the risk factor of DM will be assessed, however, no objectives have been outlined aiming to assess the risk factors within the objective section.

Authors' reply: This has been corrected.

b. Please replace the term "other databases" (Page Number-2, Line Number-25) with the name of the database that you intend to search for the literature.

Authors' reply: Thank you for your comment. We have now added the names of all the databases in the abstract as follows:

" ...... applied to databases like PubMed, Scopus, Cochrane, PakMediNet, and CINAHL from inception......."

c. Please state the full form of acronyms such as NGSP and DCCT (Page Number-8, Line Number-9) during their first use.

Authors' reply: We have now added the full forms of the acronyms as follows:

".....using a method that is National Glycohemoglobin Standardization Program (NGSP) certified and standardized to the Diabetes Control and Complications Trial (DCCT) assay."

d. Authors have mentioned that they will use the Newcastle-Ottawa Scale (NOS) tool for quality assessment (Page Number-9, Line Number-50). Why this tool? I'm sure there are others! Please provide the rationale for using this tool.

Authors' reply: Thank you for pointing this out, the authors have reconsidered the choice of quality assessment tool and will now be using "Joanna Briggs Institute (JBI) critical appraisal checklist for studies reporting prevalence data". This has been updated in the manuscript. JBI checklist can help in assessing the quality of individual studies and identify potential biases or limitations in the research. This, in turn, contributes to the overall validity and reliability of your meta-analysis results.

e. On Page Number-7, Line Number-47, studies with a sample size of less than 500 will be excluded. Please provide the rationale for this cut-off value. Moreover, what if most studies have a sample size less than 500?

Authors' reply: A small sample size in a prevalence study can yield imprecise estimates with wider confidence intervals, compromising the accuracy and reliability of prevalence rates. It may introduce sampling bias, hindering the representation of diverse population characteristics and potentially skewing findings. Small sample sizes also increase the instability of estimates, making prevalence rates susceptible to substantial fluctuations, and they pose challenges in generalizing findings to the broader population, limiting the study's overall validity and applicability. More importantly, it is crucial to note that in the research community there is no consensus on what exactly defines a small sample size as there are several factors that comes into play. Nonetheless, since diabetes is a prevalent disease a small sample size may produce instability of estimate. Moreover, a preliminary literature review suggested that most of the studies have a sample size of more than 500 A.

A. Serdar, C. C., Cihan, M., Yücel, D., & Serdar, M. A. (2021). Sample size, power and effect size revisited: simplified and practical approaches in pre-clinical, clinical and laboratory studies. Biochemia medica, 31(1), 010502.

f. A similar review paper was published in 2019 (Akhtar S, Nasir JA, Abbas T, Sarwar A. Diabetes in Pakistan: A systematic review and meta-analysis. Pak J Med Sci. 2019 Jul-Aug;35(4):1173-1178. doi: 10.12669/pjms.35.4.194.). How does this proposed review differ from the review study published in 2019? What new knowledge or evidence does this review generate in the existing literature? This should be outlined in the introduction section to strengthen the rationale of this review.

Authors' reply: Thank you for the comment, there are several points that will make our meta-analysis better,

1. The previously published study by Akhtar 2019, did not include several studies with large sample size such as Mahar 2010A (n = 19211) and Aamir 2019B (n = 18856).

2. One of the studies included in Akhtar 2019, Shera 2007C, is actually an amalgamation of four other previously published studies by the same author (Shera D-G)

3. The study by Akhtar 2019, only assessed the prevalence of diabetes and prediabetes, while the current study aims to find a longitudinal trend of change in the prevalence of diabetes over time by grouping studies conducted in a particular time period in a designated group as explained in the methodology section of the protocol paper. Additionally, the current study also aims to assess the prevalence of diabetes and pre-diabetes based on gender (males vs females), location (urban vs rural) and provincial level.

All of this has already been mentioned under the subsection of introduction, named objectives. References:

A. Mahar PS, Awan MZ, Manzar N, Memon MS. Prevalence of type-II diabetes mellitus and diabetic retinopathy: the Gaddap study. J Coll Physicians Surg Pak. 2010;20(8):528-32.

B. Aamir AH, UI-Haq Z, Mahar SA, Qureshi FM, Ahmad I, Jawa A, et al. Diabetes Prevalence Survey of Pakistan (DPS-PAK): prevalence of type 2 diabetes mellitus and prediabetes using HbA1c: a population-based survey from Pakistan. BMJ Open. 2019;9(2):e025300.

C. Shera, A. S., Jawad, F., & Maqsood, A. (2007). Prevalence of diabetes in Pakistan. Diabetes research and clinical practice, 76(2), 219–222.

D. Shera AS, Basit A, Fawwad A, Hakeem R, Ahmedani MY, Hydrie MZ, et al. Pakistan National Diabetes Survey: prevalence of glucose intolerance and associated factors in the Punjab Province of Pakistan. Prim Care Diabetes. 2010;4(2):79-83.

E. Shera AS, Rafique G, Khwaja IA, Ara J, Baqai S, King H. Pakistan national diabetes survey: prevalence of glucose intolerance and associated factors in Shikarpur, Sindh Province. Diabet Med. 1995;12(12):1116-21.

F. Shera AS, Rafique G, Khwaja IA, Baqai S, Khan IA, King H. Pakistan National Diabetes Survey prevalence of glucose intolerance and associated factors in North West at Frontier Province (NWFP) of Pakistan. J Pak Med Assoc. 1999;49(9):206-11.

G. Shera AS, Rafique G, Khawaja IA, Baqai S, King H. Pakistan National Diabetes Survey: prevalence of glucose intolerance and associated factors in Baluchistan province. Diabetes Res Clin Pract. 1999;44(1):49-58

g. In the reference lists, reference numbers 1, 6, 20, 21, and 23 are not listed appropriately. Authors are required to revise those references adhering to the journal's reference guidelines. Authors' reply: Thank you for your comment. We have now revised the references and highlighted them in the manuscript. Additionally we noticed that one reference (number 20) was repeated, so we have deleted that.

Reviewer: 2 Dr. Muhammad Riaz, Qatar University

Comments to the Author:

General remarks:

This manuscript entitles "Epidemiology of Diabetes Mellitus in Pakistan: A Systematic Review Protocol". This is an important topic from the public health perspective. The protocol is prepared for conducting a systematic review and meta-analysis (SR&MA) on the published studies in Pakistan to report the pooled prevalence, risk factors, and disparities between rural and urban populations. This research work is important as it is coming from a developing country (Pakistan), where the public health services are depressing. The manuscript is well-written, but some changes are required at various places in the manuscript to make it concise.

Authors' reply: Thank you for the appreciation of our manuscript.

My major concern is that a SR&MA on similar topic is already conducted in Pakistan and the authors do not explain, why there is a need for another SR&MA.

I would like to recommend the manuscript for publication, if the author provide an adequate explanation for the need to conduct another SR&MA with reference to the previously conducted one ["Diabetes in Pakistan": Akhtar S et al, 2019]. This could be added in the last paragraph of introduction section.

Authors' reply: Thank you for the comment, there are several things that will make the meta-analysis that we are performing better,

1. The previously published study by Akhtar 2019, did not include several studies with large sample size such as Mahar 2010A (n = 19211) and Aamir 2019B (n = 18856).

2. One of the studies included in Akhtar 2019, Shera 2007C, is actually an amalgamation of four other previously published studies by the same author (Shera D-G)

3. The study by Akhtar 2019, only assessed the prevalence of diabetes and prediabetes, while the current study aims to find a longitudinal trend of change in the prevalence of diabetes over time, additionally, the current study also aims to assess the prevalence of diabetes and pre-diabetes in males, and females as well as in urban and rural population separately. Lastly, our study also aims to assess the prevalence of diabetes on provincial level.

All of this has already been mentioned under the subsection of introduction, named objectives. References:

A. Mahar PS, Awan MZ, Manzar N, Memon MS. Prevalence of type-II diabetes mellitus and diabetic retinopathy: the Gaddap study. J Coll Physicians Surg Pak. 2010;20(8):528-32.

B. Aamir AH, UI-Haq Z, Mahar SA, Qureshi FM, Ahmad I, Jawa A, et al. Diabetes Prevalence Survey of Pakistan (DPS-PAK): prevalence of type 2 diabetes mellitus and prediabetes using HbA1c: a population-based survey from Pakistan. BMJ Open. 2019;9(2):e025300.

C. Shera, A. S., Jawad, F., & Maqsood, A. (2007). Prevalence of diabetes in Pakistan. Diabetes research and clinical practice, 76(2), 219–222.

D. Shera AS, Basit A, Fawwad A, Hakeem R, Ahmedani MY, Hydrie MZ, et al. Pakistan National Diabetes Survey: prevalence of glucose intolerance and associated factors in the Punjab Province of Pakistan. Prim Care Diabetes. 2010;4(2):79-83.

E. Shera AS, Rafique G, Khwaja IA, Ara J, Baqai S, King H. Pakistan national diabetes survey: prevalence of glucose intolerance and associated factors in Shikarpur, Sindh Province. Diabet Med. 1995;12(12):1116-21.

F. Shera AS, Rafique G, Khwaja IA, Baqai S, Khan IA, King H. Pakistan National Diabetes Survey prevalence of glucose intolerance and associated factors in North West at Frontier Province (NWFP) of Pakistan. J Pak Med Assoc. 1999;49(9):206-11.

G. Shera AS, Rafique G, Khawaja IA, Baqai S, King H. Pakistan National Diabetes Survey: prevalence of glucose intolerance and associated factors in Baluchistan province. Diabetes Res Clin Pract. 1999;44(1):49-58

In addition, I would like to suggest further changes as below:

1. Abstract

Introduction

- The text "considering its epidemiological context" is not very clear and it may be extra wording as the author states: "prevalence of DM, risk factors, and disparities between rural and urban populations". Please state clearly, if there are any other epidemiological investigations. Authors' reply: This has been corrected

Methods and analysis

- "employing WHO or ADA criteria", not clear, criteria of what?

Authors' reply: Thank you for your comment. We want to employ the definition of WHO or ADA for the diagnosis of DM. Therefore, we have changed the sentence in the manuscript accordingly:

" ..... employing WHO or ADA criteria for diagnosis of DM."

- "or Urdu" I believe, there will be hardly any paper in Urdu language and if any exist, they may not be of decent quality.

Authors' reply: Thank you for your comment, we have now removed this from the manuscript.

- I am not sure, why other designs such as case-control if exist are not stated here.

Authors' reply: The systematic review we plan to conduct will only include cross-sectional studies, cohort studies, and population-based surveys. Additionally, case control studies can not be used to assess prevalence or incidence A.

A. Lewallen S, Courtright P. Epidemiology in practice: case-control studies. Community Eye Health. 1998;11(28):57-8. PMID: 17492047; PMCID: PMC1706071.

- "will pool prevalence estimates", will the author require to pool results of the "risk factors" and other subgroups analysis using MA, it should be clearly stated.

Authors' reply: Thank you for pointing this out, this has been corrected.

2. Introduction

- "this number amplified to approximately 33 million in 2021 (5)". It would have been better to see what the prevalence is.'

Authors' Reply: Thank you for your comment. We have now mentioned the exact prevalence: "....... this number amplified to approximately 32,964,500 in 2021."

Objectives: "Specifically, the review aims to". I think, first should be aims and then objectives: The main aim of the study is to conduct a systematic review and meta-analysis and write a comprehensive report on the epidemiology of diabetes. Then state the objectives as listed in the paper.

Authors' reply:

- At the end of the introduction, a more rational case can be made for the need to conduct another SR&MA investigating epidemiology of diabetes in Pakistan with reference to the existing one ["Diabetes in Pakistan": Akhtar S et al, 2019]. Authors' reply: This has been added

### 3. Methods

-Study Design: "This protocol for systematic review is written as Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for protocol paper (PRISMA-P) (17). This systematic review will follow the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (18)". There is a repetition of text, I suggest rephrasing it.

Authors' reply: Thank you for pointing this out, this have been corrected.

- Inclusion criteria "Urdu language", I don't think, there will be any study in Urdu published in a proper peer review journal.

Authors' reply: Thank you for the suggestion. We have now removed this from the manuscript.

-"Studies with a sample size less than 500 will be excluded" If the author can have a large number of studies, then it might be ok to exclude. If the number of studies is small, then I would suggest including studies with small sample sizes. I suggest reducing the cut-off to 300 at least.

Authors' reply: A small sample size in a prevalence study can yield imprecise estimates with wider confidence intervals, compromising the accuracy and reliability of prevalence rates. It may introduce sampling bias, hindering the representation of diverse population characteristics and potentially skewing findings. Moreover, a preliminary literature review suggested that many studies have a sample size of more than 500 A.

A. Serdar, C. C., Cihan, M., Yücel, D., & Serdar, M. A. (2021). Sample size, power and effect size revisited: simplified and practical approaches in pre-clinical, clinical and laboratory studies. Biochemia medica, 31(1), 010502.

- outcome: "percentage or proportion" it is better to say proportion expressed as percentage. Authors' reply: Thank you for the comment. We have made the required change in the manuscript.

- outcome: "Additionally, if available, the review will explore the prevalence of diabetes across various subgroups based on age, gender, and geographical location (e.g., provinces, urban vs. rural)....." this can be deleted from here and add/leave it in the analysis section. Authors' reply: This has been changed in the updated manuscript

- Search strategy: "A comprehensive search strategy will be developed to identify relevant studies." I think the protocol should have a clearly stated final search strategy. - I suggest, the search strategy should be in MeSH terms with Boolean operators in text and then the actual search strategy with appropriate Boolean operators AND/OR added in the supplement.

Authors' reply: Thank you for the comment. We have now added this in supplementary information.

- Data extraction:

- "Confounders", all factors stated may not be confounders, I don't think the term confounders is appropriate to use here.

Authors' reply: This has been corrected.

- Prevalence data: "prevalence rates" delete "rates"

Authors' reply: Thank you for the suggestion. We have made the required change.

-Methodological details: study design? Authors' reply: This has been edited in the manuscript

- Quality assessment: It is just to mention NOS is good to use, if the aim is to report a comprehensive epidemiology of diabetes. For investigating prevalence only, "Joanna Briggs Institute critical appraisal checklist for studies reporting prevalence data" could be better to use.

Authors' reply: Thank you for pointing this out, the authors have reconsidered the choice of quality assessment tool and will now be using "Joanna Briggs Institute critical appraisal checklist for studies reporting prevalence data". This has been updated in the manuscript

Data analysis:

-It is not clear, how meta-analysis will be conducted to pool the prevalences together. I think, they will have to transform the prevalence to an appropriate scale to be pooled.

Authors' reply: Inverse variance-weighted method will be used to conduct the analysis. This has been updated in the manuscript.

-Analysis for identifying temporal trends in DM is not added. Authors' reply: This has been added under the subsection of prevalence synthesis in the manuscript

-If the authors are conducting meta-analysis for the effect estimates of risk factors, they need to mention what measure of association such as odds ratios (ORs) will be extracted/calculated for each of the variables (risk factors) and pooled using a meta-analysis. A detailed statistical analysis needs to be added for this.

Authors' reply: Effect estimates of risk factors will not be analyzed in this systematic review.

4. Discussion

- The discussion reads to me like a discussion for reporting the actual SR&MA already conducted. I think, it could be written in the sense that it is a protocol for conducting SR&MA. Author's reply: This has been corrected

"Comparing the prevalence rates reported in this review with previous estimates can offer insights into the temporal trends of DM in Pakistan (25, 26)". I suggest, conducting a meta-analysis on data extracted from all included studies to report the temporal trends DM. I don't think, it will identify proper temporal trends if it is based on the results comparison of this study with the results of previously conducted meta-analysis.

Authors' reply: This will be done in addition to analyzing temporal trends for DM, using the data extracted from all the included studies.

# **VERSION 2 – REVIEW**

REVIEWER	Riaz, Muhammad Qatar University, Public Health
REVIEW RETURNED	21-Feb-2024

GENERAL COMMENTS	Authors have responded to my comments and revised the paper. I would like to recommend the paper for publication with the following suggestions minor changes.
	clarity.
	"A meta-analysis, if appropriate, will be performed using inverse variance random
	effect model, considering heterogeneity and conducting subgroup and sensitivity analyses"
	I suggest as follow:
	A meta-analysis, will be performed using random effect model with inverse variance weighted method. I-square statistic will be used
	to examine heterogeneity, and subgroups analyses will be
	-Statistical analysis in the main body shall be revised accordingly.

# **VERSION 2 – AUTHOR RESPONSE**

Reviewer: 2

Authors have responded to my comments and revised the paper. I would like to recommend the paper for publication with the following suggestions minor changes.

Authors response: Thank you for taking out time to review the manuscript and thank you for your review.

-In the abstract, the following sentence may be rephrased for clarity.

"A meta-analysis, if appropriate, will be performed using inverse variance random

effect model, considering heterogeneity and conducting subgroup and sensitivity analyses"

I suggest as follow:

A meta-analysis, will be performed using random effect model with inverse variance weighted method. I-square statistic will be used to examine heterogeneity, and subgroups analyses will be performed.

Authors response: Thank you for the comment. This has been updated in the manuscript.

-Statistical analysis in the main body shall be revised accordingly.

Authors response: Thank you for the comment. This has been updated in the manuscript.