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)	Exposure to persistent organic pollutants and thyroid cancer risk: a study protocol of systematic review and meta-analysis
AUTHORS	Zhang, Yuxue; Liu, YuPeng; Miao, SuSheng; Liu, Xiaodong; Ma, ShuMei; Qu, ZhangYi

VERSION 1 – REVIEW

REVIEWER REVIEW RETURNED	Fiore, M University of Catania 30-Mar-2021
GENERAL COMMENTS	This is an interesting and clearly written protocol for a systematic review which aims to synthesize the evidence for the health effects of POPs on the risk of thyroid cancer.
REVIEWER REVIEW RETURNED	Gorini, Francesca National Research Council 17-Apr-2021

OFNEDAL COMMENTO	
GENERAL COMMENTS	In this study protocol the authors described the background and
	methodology of a systematic review and meta-analysis aimed at
	summarizing the existing evidence on the relationship between
	exposure to persistent organic pollutants and the risk of thyroid
	cancer. Overall, the manuscript is well written and the analyses
	planned for the meta-analysis clear and complete. My minor
	revisions are listed below in order of appearance:
	Line 15. Please provide the full name of RR.
	Line 29. Please amend the typo in "pattern".
	Lines 31-32. Please rephrase the incidence in an appropriate way.
	Line 42. Consider replacing "that" with "which".
	Line 53. I suggest writing "bioaccumulation" before
	"biomagnification".
	Line 59. Reference 18 is out of context as it focused on the
	associations between thyroid cancer and exposure to two
	chemicals, namely bisphenols and phthalates, which are not
	persistent organic pollutants.
	Line 68. Consider changing "aims" to "aim".
	Lines 127-128. Consider inserting a full stop after "literatures";
	therefore, delete "and".
	Lines 139. "Reference list of relevant reviews, editorials, and
	letters" is already present on line 138.
	Line 147. Extracted data should also include information on the
	subtype of thyroid cancer and pathophysiological characteristics of
	the subjects, if available.
	Line 178. "maximal" or "maximum"?
	Line 180. "POP, not "POPs".

Ī	Line 182. "type", not "types".
	Line 200. "adjust", not "adjusted".
	Line 229. "study", not "studies".

VERSION 1 – AUTHOR RESPONSE

Reviewer: #1

Dr. M Fiore, University of Catania

Comments to the Author:

This is an interesting and clearly written protocol for a systematic review which aims to synthesize the evidence for the health effects of POPs on the risk of thyroid cancer.

Reply: We are very grateful for your kind comments and for your appreciation to our work in this study.

Reviewer: #2

Dr. Francesca Gorini, National Research Council

Comments to the Author:

In this study protocol the authors described the background and methodology of a systematic review and meta-analysis aimed at summarizing the existing evidence on the relationship between exposure to persistent organic pollutants and the risk of thyroid cancer. Overall, the manuscript is well written and the analyses planned for the meta-analysis clear and complete. My minor revisions are listed below in order of appearance:

Reply: Thank you very much for your great patience and for your consideration. We have carefully considered all of your comments and accordingly implemented your suggestions, which did help us to improve the quality and clarity of this manuscript.

Line 15. Please provide the full name of RR.

Reply: Thank you for your suggestion. As you suggested, we have provided the full name of confounding RR as confounding risk ratio in the revised manuscript. (see Line 15 on Page 2 in the Main Document - marked copy)

Line 29. Please amend the typo in "pattern".

Reply: Thank you very much for your suggestion. We have corrected this typo of "patter" with "pattern" in the above-mentioned sentence. (see Line 29 on Page 3 in the Main Document - marked copy)

Lines 31-32. Please rephrase the incidence in an appropriate way.

Reply: Thank you very much for your careful review. We have rephrased the incidence with "incident cases" in the above-mentioned sentence, as follows: "In China, the estimated incident cases of thyroid cancer reached 221,093 in 2020, accounting for about 38% of all annually diagnosed thyroid cancer cases". (see **Lines 31-33 on Page** in the Main Document - marked copy)

Line 42. Consider replacing "that" with "which".

Reply: Thank you for your suggestion. We have replaced "that" with "which" in the above-mentioned sentence. (see **Line 43 on Page 3** in the Main Document - marked copy)

Line 53. I suggest writing "bioaccumulation" before "biomagnification".

Reply: Thank you very much for your careful review. We have rewritten the above-mentioned sentence according to your kind suggestions. (see **Line 54 on Page 4** in the Main Document - marked copy)

Line 59. Reference 18 is out of context as it focused on the associations between thyroid cancer and exposure to two chemicals, namely bisphenols and phthalates, which are not persistent organic pollutants.

Reply: Thank you very much for your kind comments. We have deleted this reference (#18) in the revised manuscript. (see **Line 61 on Page 4** in the Main Document - marked copy)

Line 68. Consider changing "aims" to "aim".

Reply: Thank you very much for your suggestion. We have corrected "aims" with "aim" in the abovementioned sentence. (see **Line 70 on Page 4** in the Main Document - marked copy)

Lines 127-128. Consider inserting a full stop after "literatures"; therefore, delete "and".

Reply: Thank you very much for your kind suggestions. We have rewritten the above-mentioned sentences. (see **Lines 130-131 on Page 7** in the Main Document - marked copy)

Lines 139. "Reference list of relevant reviews, editorials, and letters" is already present on line 138.

Reply: Thank you for your suggestion. We apologize for our carelessness. As you suggested, we have deleted this sentence in the revised manuscript. (see **Line 142 on Page 7** in the Main Document - marked copy)

Line 147. Extracted data should also include information on the subtype of thyroid cancer and pathophysiological characteristics of the subjects, if available.

Reply: We are very grateful for your suggestions. As you suggested, we have added this information in the section of "3.4. Data extraction and data items" in the revised manuscript. (see Lines 156-157 on Page 8 in the Main Document - marked copy)

Line 178. "maximal" or "maximum"?

Reply: Thank you very much for your kind suggestion. We have corrected "maximal" with "maximum" in the above-mentioned sentence. (see **Lines 182-183 on Page 9** in the Main Document - marked copy)

Line 180. "POP, not "POPs".

Reply: Thank you for your suggestion. We have corrected "POPs" with "POP" in the above-mentioned sentence. (see **Line 184 on Page 9** in the Main Document - marked copy)

Line 182. "type", not "types".

Reply: Thank you for your suggestion. We have corrected "types" with "type" in the above-mentioned sentence. (see **Line 186 on Page 9** in the Main Document - marked copy)

Line 200. "adjust", not "adjusted".

Reply: Thank you very much for your suggestion. We have corrected "adjusted" with "adjust" in the above-mentioned sentence. (see **Line 204 on Page 10** in the Main Document - marked copy)

Line 229. "study", not "studies".

Reply: Thank you for your suggestion. We have corrected "studies" with "study" in the above-mentioned sentence. (see **Line 233 on Page 11** in the Main Document - marked copy)

Thanks again for your great patience and considerate suggestions.

The excellent and considerate suggestions and comments from all of the reviewers really did help us to improve the quality and clarity of this manuscript. However, there may remain some deficiencies. Please tell us directly if it needs further corrections, we will be very grateful and appreciate it, and try our best to revise this manuscript until it is qualified for publication in your honourable journal.

VERSION 2 - REVIEW

REVIEWER	Gorini, Francesca
	National Research Council
REVIEW RETURNED	03-Jul-2021

GENERAL COMMENTS	The authors addressed my previous comments and the
	manuscript is suitable for publication in the current form.