Author's response to reviews

Title: Systematic Review of Clinical Practice Guidelines in the Diagnosis and Management of Thyroid Nodules and Cancer

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Dear Chief Editors and Reviewers of the *BMC Medicine*,

We sincerely appreciate your review and interest in our manuscript entitled "Systematic Review of Clinical Practice Guidelines in the Diagnosis and Management of Thyroid Nodules and Cancer". According to the comments of the editors and the reviewers, we have revised the manuscript and made corrections as the followings. We hope that the revised manuscript will now be suitable for publication in your journal.

Sincerely Yours,

Tsai-Wei Huang and Ka-Wai Tam

**Reviewer #1**

This manuscript provides a review of clinical practice guidelines (CPGs) related to the diagnosis and management of thyroid nodules and cancer. The idea of the review is important and timely. However, I do have some major comments.

1. The major comment relates to inconsistency throughout the manuscript on what is being evaluated. In the Abstract and Results, the evaluation of all 6 AGREE-II domains are listed and the evaluation relates to >50% score in all 6 AGREE-II domains. However, the Methods, in the first paragraph under “Guideline quality assessment” describe evaluation of 6 of the 8 “Rigour in Development” elements although how these 6 were chosen is not clear. Further, there is no separate description of the Rigour scores – it looks like 6/10 CPGs scored > 50% in the Rigour domain.

**Response:** Thank you for your comments. We assessed the guidelines according to the rules of AGREE-II instrument. Because the previous description on “Guideline quality assessment” was unclear, we revised the words as follows: “Four investigators (K.W. Tam, T.W. Huang, J.H. Lai, and M.Y. Wu) independently appraised all the selected guidelines by using the AGREE-II instrument.” AGREE-II consists of 23
key items organized into 6 domains: (1) “scope and purpose,” (2) “stakeholder involvement,” (3) “rigor of development,” (4) “clarity and presentation,” (5) “applicability,” and (6) “editorial independence.” Each domain captured a separate dimension of the guideline quality with a 7-point scale (from 7 (strongly agree) down to 1 (strongly disagree)). For each reviewer, AGREE-II scores were calculated as a percentage by using the sum of the 7-point scale and the maximum possible score (range 0% to 100%). Item scores were discussed by the four reviewers, and large scoring discrepancies (defined as ≤ 3 points difference in the score assigned by the appraisers to the same item) were resolved by consensus. We considered satisfactory any guideline that scored at least 50% in all 6 domains, as defined by AGREE-II.

Upon completing the 23 items, each reviewer provided the overall assessments of the guideline. We compared the mean values of each of the 6 domain scores and the overall scores obtained by the 4 reviewers to evaluate the possible risk of bias and the recommendation for future use, for each CPG they appraised.”

2. Eligibility criteria are not clear. One inclusion criterion was “developed on behalf of a national or international medical specialty”. I am not clear why this should be an eligibility criterion. I believe that non-English articles were excluded but this is not stated within eligibility. Further, the definition of a CPG is not clearly stated. Shouldn’t older CPGs be excluded (i.e. > 5 years) since they should no longer be used?

Response: Thank you for your comments. We deleted the words “developed on behalf of a national or international medical specialty”. We added “have published in English” as our inclusion criteria. We didn’t limit our search according to the published date. However, when more than one set of guidelines was produced by the same professional body, only the most recently issued was considered.

3. It looks like only one person screened but this is not clear. There is no mention of agreement in terms of inclusion/exclusion or in abstraction of AGREE-II elements.

Response: Thank you for your comments. In our study, two reviewers searched for relevant studies, we provided the details in the paragraph. Besides, we added the words “Item scores were discussed by the four reviewers, and large scoring discrepancies (defined as ≤ 3 points difference in the score assigned by the appraisers to the same item) were resolved by consensus.” to clarify the methods of guideline quality assessment.

4. I disagree with one of the final recommendations from the authors. The authors suggest that clinicians should be more concerned about the “applicability” domain.
Rather, I believe that clinicians should really focus on “rigour” since that is what the CPG recommendations should hinge upon. Applicability elements such as costs, barriers at the local institution and tools for implementation can also be handled by individual sites if they are missing from the CPG.

**Response:** We agree with the reviewer comment. Therefore, we revised our sentence as “Although the AGREE-II instrument provides 6 independent scores for 6 corresponding aspects of the guidelines, we believe that clinicians would be more concerned about the “rigor of development”. However, the quality of “applicability” domain also plays a critical role in implementation of the guideline.…”

**Reviewer #2**

This is a well written and carefully presented analysis of the most important guidelines on thyroid nodules and thyroid cancer. The manuscript is well written and the data is presented in an orderly fashion. My only critique is that I don't understand the importance or presentation of the data in Table 3. This should either be removed or the relevance explained more clearly and the data presented in an easier way to understand.

**Response:** Thank you for your comment. In Table 3, we provided the full names of each guideline, and added the description of all the 23 items of the AGREE-II instrument on a 7-point scale to clarify the methodological quality assessment of each guideline.