

Peer Review File

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Reviewer A

Comment 1: Suggest changing the title. "limitation" is more appropriate than "problem."

Reply 1: Thanks for the reviewer's kind advice. The new title has been changed into "Chronic Cough - the Limitation and Advances in Assessment Techniques". (See title)

Comment 2: Add a pictorial or tabular list of all the cough assessment tools reviewed. It helps the reader to grasp the entire content.

Reply 2: We have made figure 1 to briefly present the outline of this review.

Comment 3: I think it is unnecessary to add the explanation about the subheads on page 4, line 70, and page 6, line 127 because the text included them. (natural cough thresholds - "cough if you need to," "try not to cough").

Reply 3: We have deleted these descriptions. (See page 5, line 65 and page 9, line 165).

Comment 4: On page 10, line 220, you need to check the new version of the Cough Hypersensitivity Questionnaire. The current version of the CHQ consists of 23 items evaluating cough-associated laryngeal sensations and triggers. A recent study showed good internal consistency (Cronbach's $\alpha = 0.90$). The response scale is binary (yes/no). The total number of questions was 23, consisting of cough-related sensations (7) and cough triggers (16). (Sinha A, Lee KK, Rafferty GF, Yousaf N, Pavord ID, Galloway J, et al. Predictors of objective cough frequency in pulmonary sarcoidosis. *Eur Respir J*. 2016;47:1461–1471)

Reply 4: We have added these data. (See page 13, line 259-268)

Comment 5: On page 11, change the second subhead like the first, not a question.

Reply 5: We have made changes in the manuscript. (See page 14, line 305)

Reviewer B

This study reviewed the currently available tools for subjectively and objectively measuring both cough sensitivity and severity. It has mentioned the updated Assessment Techniques which is practical. However, there are several aspects should be clarified clearly (e.g. associations among parameters, antitussive drug development challenge tests). Here are my suggestions:

Comment 1: In section of Mechanical challenge tests (MCF), if there any data supporting

- 1) the role of MCF in chronic refractory cough?
- 2) the correlation between MCF and parameter of cough sensitivity/ severity (C2/C5/cough frequency/LCQ/VAS)?
- 3) the ability to distinguish CC from healthy?

Reply 1: We thank for these kind suggestions but the data about MCF are limited and we could not find any further detailed data.

Comment 2: In Line 83-85, I suggest to add the data of relationship between C2/C5 and cough frequency.

Reply 2: We have added the data. (See page 5, line 80)

Comment 3: In Line 89-90, it would be puzzled to consider Emax can reflect the inhibitory control system which refers to the central mechanism, please rephrase the sentence “Emax, implies the presence.....maximum possible coughs”.

Reply 3: We have rephased this sentence. (See page 5, line 84-85)

Comment 4: In Line 95 of antitussive drug development challenge tests, please extend the content including ATP, IFN- γ , distilled water.

Reply 4: We have added the suggested information to page 6, line 91.

Comment 5: I suggest to move the part of Arnold nerve reflex as well as laryngeal sensitivity to Peripheral cough sensitivity.

Reply 5: We have made changes (See page 6-8, line 97-139)

Comment 6: In section of Voluntary cough suppression test, I wonder if you can add more details of CST (e.g. mechanism, process,) and its difference from antitussive drug development challenge tests mentioned above.

Reply 6: We have already tried most thoroughly describing the mechanism and process of CST but the difference between CST and cough challenge test has been further explained in page 9, line 178-180.

Comment 7: In Line 224, is there any subsequent data for validation of CHQ?

Reply 7: Sorry for the missing data. The data of new version of CHQ has been added in page 13, line 259-268.

Comment 8: In Line 247, please add the content between utc and parameter of cough sensitivity/ severity (C2/C5/cough frequency/LCQ/VAS)?

Reply 8: We have added the data we could find currently. (See page 14, line 295-304)

Comment 9: In section of Objective measurement of cough frequency (Line 258-283), it is confusing to understand the definition and difference among cough sounds, cough epochs, cough bouts, the time spent coughing which also be associated with the algorithm of cough counts. I suggest to

1) quote figure 1&2 in A. Kelsall et al study (A. Kelsall, 2008), to show different methods for quantifying cough sound recordings as well as typical cough sound waveform.

2) clarify which algorithm is most widely used in clinical.

Reply 9.1: We have quoted figure 1&2 as suggested. (See page 15, line 315-320)

Reply 9.2: We already mentioned that most of the current studies utilized the individual explosive cough sound as the cough counting unit. (See page 16, line 332-334)

Comment 10: In Table2, please add the association between cough severity and cough sensitivity/ frequency in column of Validity.

Reply 10: We have added all the data we could get to Table 2 now.

Comment 11: In Table3, please

1) rephrase the validity of CCIQ and COAT

2) add the associate between Patients Reported Outcomes and cough sensitivity/frequency in column of Validity.

Reply 11: Due to the limited validity data, we could not get more detail about the relationships between most QoL questionnaires and cough sensitivity/frequency. So, we only made minor changes in Table 3.

Comment 12: The title is confusing, I suggest to change it into “Chronic Cough - the Advances in Assessment Techniques”.

Reply 12: The new title has been changed into “Chronic Cough - the Limitation and Advances in Assessment Techniques”.

Reviewer C

This is a nice comprehensive review of current cough evaluation tools. It reads very well, but I have some suggestions.

Comment 1: A number of cough questionnaires were listed, but the listing looks confusing. Some are considered as the international standards in clinical studies, but others were utilized rarely or just locally. I suggest the authors add expert comments on how they recommend to use those questionnaires, based on their construct validity or purpose (for example, research or practice).

Reply 1: Thanks for the reviewer’s professional suggestions. We have added the necessary information into text where appropriate.

Comment 2: According to the ERS cough guidelines 2020, cough severity numerical rating scale (0-10) was recommended for use in clinics. I wonder why it was not mentioned in this manuscript.

Reply 2: We have added NRS to the text. (See page 21, line 455-468)

Comment 3: Please check the content about CHQ. It is a 23-item questionnaire, and the correlations with LCQ and cough severity VAS were reported recently (Won HK, et al. Cough-Related Laryngeal Sensations and Triggers in Adults with Chronic Cough: Symptom Profile and Impact. Allergy Asthma Immunol Res. 2019 Sep;11(5):622-631).

Reply 3: We have updated the content of CHQ. (See page 13, line 259-268)

Comment 4: Line 256: The section was not limited to cough severity. The subtitle should be revised as "How to assess cough as an outcome?".

Reply 4: We have rephased this subtitle as "Assessing cough as an outcome". (See page 14, line 305)

Comment 5: Line 404: It might be worth mentioning the importance of providing anchors in cough severity VAS or NRS.

Reply 5: We have added this on page 21, line 457.

Comment 6: Line 510: Cough frequency monitors are not yet practical.

Reply 6: We have corrected the mistake. (See page 25, line 566)

Comment 7: Line 384-401: Some recent papers are missing. For example, Gabaldón-Figueira JC, et al. ERJ Open Res. 2022 May 16;8(2):00001-2022.

Reply 7: We have added the missing paper. (See page 20, line 449-451)

Comment 8: CET and COAT: Both questionnaires do not appear to be specific to cough severity or QoL. Their classification in Table 2 and 3 needs to be reviewed.

Reply 8: We have renamed Table 2&3 and made the classification more accurate.

Comment 9: Titles of Table 2 and 3 should be better if revised as "Content and validity of questionnaires to scale cough severity...". The table content is not limited to strength. Some of the questionnaires are not commonly used.

Reply 9: We have renamed Table 2&3.