**Peer Review File**

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**Reviewer A**

The role of population screening for COPD is still under investigation.

This observational study addressed accuracy of two screening tools for diagnosis of COPD. Strengths of the study include the use of two tools, and applicability as part of health checks.

Major comments:

Physical examination centers:
It is not clear from the methods as to how patients are recruited to the physical examination centers (e.g. all people in the local region, or only those referred by their primary care practitioners). The selection of patients attending the centers is important, to assess whether these patients are representative of the general population, and whether they are in fact asymptomatic or unscreened previously in relation to COPD.
Reply: We have added a description of how people choose the medical examination center (see "Introduction, Paragraph 2, Line 2-5"). All individuals who have not been diagnosed with COPD and have never undergone COPD screening and come to the medical examination center can voluntarily participate in this study (see "Methods, Participants, Line 1-4").

Accuracy:
The AUC results and likelihood ratios were relatively modest, with not a very high accuracy overall. The authors should comment as to whether they feel these two questionnaires are indeed accurate enough to use in population health and clinical practice.
Reply: We have added some comments (see "Discussion, Paragraph 4, Line 8-14").

Applicability:
This study focused on one center. The applicability to other centres and other countries is not certain from this study.
Reply: This study focused on only one center. We have described its limitations and would like to have further assessment in larger multi-centre studies in more countries in the future. (see "Discussion, Paragraph 6, Line 1-5")

Excluded participants:
A number of participants were excluded due to not meeting criteria or incomplete data. The authors should comment about whether these excluded participants were different in demographics from the included participants.
Reply: We have added some description about it (see "Results, Participants characteristics, Line 4-6").

**Reviewer B**

The current manuscript describes the administration of two questionnaires for screening COPD in a Chinese PEC (Physical Examination Center). I read an anonymous manuscript without mention of the Hospital where the study was performed. Screening for COPD among subjects is not recommended for a number of reasons: lacking of accurate test to detect early COPD; the best treatment for early COPD is to stop smoking anyway, people with few or no symptoms may not be willing to do this, it is not known if medicines for COPD are effective in people with mild symptoms [UK National Screening Committee, see at https://view-health-screening-recommendations.service.gov.uk/copd/]. Moreover, there is evidence that identifying COPD in people with symptoms is cost effective. Nevertheless, new original researches on COPD screening reporting convincing results are required to improve the knowledge on this issue.
The Authors claimed the originality of their study is the first administration in a Chinese PEC of COPD screening questionnaire, but it seems a little bit feeble as a real strength point for an original study. The questionnaires were administered during the COVID-19 pandemic phase, this it was to be considered as a possible selection bias. Until late 2022, the Chinese government response included a zero-COVID strategy, which aims to eliminate transmission of the virus within the country [ Normile, Dennis (19 November 2021). "'Zero COVID' is getting harder—but China is sticking with it". Science. 374 (6570): 924]. Particularly, it was reported that infection rates increased in 2022, and on 3 April of that year, China reported 13,146 new cases of COVID-19 in the past 24 hours, which was the highest single-day total of new cases since the height of the 2020 outbreak ["China reports 13,000 Covid cases, most since end of Wuhan's first wave". France 24. 4 March 2022]. I wonder if these facts may have influenced the generalizability of this study's results. Nevertheless, the total number of screening participants is quite small, making it another factor of poor representativeness of the recruited population sample. I've also some concerns about the choice to use the Area Under the ROC Curve (AUC) as a valid measure of the performance of a screening test [Katz DL. Fundamentals of Screening: The Art and Science of Looking for Trouble. In: Clinical Epidemiology & Evidence-Based Medicine: Fundamental Principles of Clinical Reasoning, SAGE Ed. Chapter DOI:https://doi.org/10.4135/9781452232638). In fact, the performance of screening tests in distinguishing affected from unaffected individuals is best assessed in terms of the detection rate (DR) (or sensitivity) for a given false-positive rate (FPR) (sometimes given as its complement, specificity). Given an AUC, DRs for specified FPRs or FPRs for specified DRs depend on the means and the standard deviations of the screening test within affected and unaffected individuals. Not surprisingly, the current study shows that the standard deviation is wider in COPD individuals than in unaffected individuals, perhaps because of the added variance of being affected on top of the usual population variance (mean±SD COPD-PS scores 4.88±2.09 vs. 3.17±1.80, and mean±SD COPD-SQ scores 19.68±7.41 vs. 12.79±6.00, respectively COPD subjects vs. non-affected subjects).
Reply: 1) The impact of COVID-19 on this study is very small. This study was conducted in September 2021 to December 2022 in one physical examination center in Shantou, Guangdong, China. Shantou has not been much affected by COVID-19 because of the country's well-established segregation policy. At the end of 2022, the city's resident population in Shantou city was 6,641,900. A total of only 327 cases (0.0049) of Covid were cumulatively diagnosed in the

whole Shantou city during the study period of 487 days (See at https://www.sy72.com/covid19/covid401_2022921.html). We added some descriptions in discussion (see "Discussion, Paragraph 4, Line 1-6").

2) 198 screening participants is quite small. We consider this to be one of the limitations of this study and include it in the "Discussion, Paragraph 6". The aim of this study is assessing the feasibility and effectiveness of two questionnaires in a Chinese physical examination center. For this purpose, the sample size is adequate. The sample size was estimated with reference to the following formula: $n = [(Z\alpha/22 \times \pi \times (1 - \pi)]/E2$. The prevalence rate of people aged ≥40 years in China is 13.7%. If the error is allowed to be no more than 5%, $\pi$=13.7%, E=5%, and $Z\alpha/2$=1.96 at the 95% confidence level, then a total of at least 181 study participants would be needed.

3) We added the false-positive rate (FPR) result and discuss it in the article. (see "Methods, Data analysis, line 13", "Result, Performance of COPD-PS and COPD-SD, line 16 and Table 3", and "Discussion, Paragraph 4, Line 8-14")

**Reviewer C**

This study assesses the diagnostic yield of two validated COPD screening tools in a Chinese physical examination centre. This work was done previously in China on a larger population (Ref 14, n=1023). Hence the results achieved here basically confirm the value of the two COPD questionnaires tested, yielding very similar diagnostic cut-offs. Hence the authors should highlight that their results validate the previous study's results.

Reply: We have highlighted it in discussion (see "Discussion, Paragraph 5, Line 1-3")

In the Introduction section, on page 4, the authors describe the programme of health checks in China. Is there an agreed age cut-off for these health screening services?

Reply: These health screening services do not have an agreed age cut-off.

In their conclusions at the end of the manuscript, the authors recommend the use of cut-off values for COPD-PS and COPD-QS of 4 and 15 respectively in Chinese PECs. However, looking at Figure 4, the ROC curves are quite shallow with unclear inflection points. Furthermore, the total number of individuals included in this study is small (n=198). Hence the conclusion given above is not fully justified. The authors may instead compare their results to the previous Chinese study's results on a larger population of 1023 individuals suggesting cut-offs of 4 and 16 respectively for these COPD questionnaires (Ref 14).

Reply: We have added the comparison of previous Chinese study and this study in discussion (see "Discussion, Paragraph 5, Line 1-11")

Figures 1, 2 and 3 are redundant and may be removed, as the numbers showing FEV1/FVC <0.7 and those given for GOLD1-4 are very small, and their description in the results section suffices. The remaining three tables and the figure showing ROC curves are important and should be kept.

Reply: We have moved it from article.

The manuscript's English needs significant improvement, and there are a few other minor points to consider:
Reply: We embellish the language of the article and revised the article according to the following suggestions.

Please give age range instead of standard deviation for age.
Reply: We have removed the standard deviation of age and retained the age range.

In the conclusions given in the abstract, the first sentence may be re-written as 'Applying the COPD-PS and COPD-SQ in Chinese PECs is feasible, workable, cost-effective and effective. The next sentence should conclude as 'improve the quality of life and prognosis of participants remains to be studied.'
Reply: We have re-written as above. (see in "Abstract, Conclusions")
Changes in the text: Applying the COPD-PS and COPD-SQ in Chinese PECs is feasible, cost-effective and effective. COPD-PS and COPD-SQ can facilitate the early diagnosis of COPD, and improve the quality of life of participants remains to be studied.

Key words should be written in alphabetical order.
Reply: We have re-written as above. (see in "Abstract, Conclusions")

In 'Key findings', please re-write the first sentence as 'COPD population Screener (COPD-PS) and COPD Screening Questionnaire (COPD-SQ) are both feasible and effective...'
Reply: We have re-written as above. (see "Highlight box, Key findings")

The authors used the term 'pulmonary function test' throughout the manuscript. It should be changed to 'spirometry' as that is what was performed to confirm the diagnosis of COPD.
Reply: We have re-written as above.

The last sentence on page 4 should be re-written as 'A diagnosis of COPD based on spirometry helped in assessing the diagnostic value of the two screening tools and their optimal cut-offs.'
Reply: We have re-written as above. (see "Introduction, Paragraph 3, second last sentence")
Changes in the text: A diagnosis of COPD based on spirometry helped in assessing the diagnostic value of the two screening tools and their optimal cutoff values.

Please change the ending of the last sentence to 'and requires spirometry for confirmation (18).'
Reply: We have re-written as above. (see "Method, Screening questionnaires, line 7-8)

On page 6, in the 1st para, please add the name and location of the manufacturer of MicroLoop spirometer.
Reply: We have added the name and location of the manufacturer of MicroLoop spirometer. (see "Method, Spirometry, line 1-3)
Changes in the text: All participants underwent spirometry with bronchodilator response (MicroLoop Spiro USB spirometer, Micro, England) for free as per the European Respiratory Society standards.

In the data analysis section, please mention whether the Student t-test was one- or two-tailed.
Reply: We have mentioned it in the “statistical analysis” section. (see “Method, Statistical Analysis, line 6)
Changes in the text: Data with a normal distribution are presented as mean and standard deviation (SD), and were compared with the Student t-test (two-tailed).

Page 6, last line - please remove 'of 255 participants'
Reply: We have removed 'of 255 participants'.
Changes in the text: A total of 255 participants completed the questionnaires, and data from 198 (77.65%) participants were included for analysis.

The sub-section of 'Screening questionnaires and Pulmonary function tests' is wordy and difficult to follow. It needs to be simplified and re-written.
Reply: We have re-written. (see “Results, Screening questionnaires and Spirometry”)

In the 'Performance of COPD-PS and COPD-SQ, the authors mention the statistics for a previously reported COPD-PS score of >5. This needs to be referenced.
Reply: We have added the reference of it. (see “Results, Performance of COPD-PS and COPD-SQ”)

Page 9, 1st para, last sentence - please re-write as 'Routine use of COPD-PS and COPD-SQ may even promote risk avoidance among non-COPD individuals.'
Reply: We have revised as above. (see “Discussion, last Paragraph 4, last sentence”)

Page 9, 2nd para, 3rd sentence - please re-write as 'Questionnaire-based screening is recommended in asymptomatic individuals in China according to the...'
Reply: This sentence has been mentioned in the “Introduction” section and was deleted because the discussion section was too length.

Page 9, last sentence - please re-write as 'One patient with COPD GOLD4 had higher COPD-PS and COPD-SQ scores than the corresponding mean scores of GOLD3 patients for these questionnaires.'
Reply: We have re-written as above (see “Discussion, paragraph 4, line 6-8”).

The authors could write a few sentences as to which of these screening tools (COPD-PS and COPD-SQ) would be easier, more cost-effective, and less time consuming to use in the Chinese PECs setting.
Reply: We have added in discussion (see “Discussion, last paragraph, line 3-6”).

The authors should include the names of the hospital and the affiliated institution in their revision, as I feel anonymity was relevant only for this review.
Reply: This article includes the names of the hospital and the affiliated institution in the non-anonymous version.

**Reviewer D**

The authors report on two COPD-PS and COPD-SQ questionnaires to predict the risk of COPD. These questionnaires were for the first time used in a hospital setting. After adjustment of the cut-off values, the questionnaires were proven to be easily applicable and effective in the prediction of the COPD diagnosis. The findings are important as they help improve the screening of COPD in a reliable and cost-effective way. I have some questions/comments to the authors:

1. Did both sexes benefit equally from the surveys?
Reply: We have added the Gender Disparity. (see "table 4; Method, Data analysis, Last sentence; Results, Performance of COPD-PS and COPD-SD, Last three sentences; Discussion, Paragraph 4, last two sentences")

2. Could you please provide a more detailed description of how the pulmonary tests were conducted? E.g. were bronchodilators used where needed to exclude asthmatic components?
Reply: We have added the description of pulmonary tests (spirometry) (see "Methods, Spirometry, line 3-4).

3. Were there any significant differences in baseline characteristics between COPD and non-COPD participants in tables 1 and 2 (e.g. non-COPD participants seem to be heavier according to BMI than the COPD ones)? If yes, please provide p values.
Reply: Unfortunately, we did not collect specific BMI values from the participants, who simply checked off answers that were just a BMI range but not a specific number.

4. Figures 2 and 3: could you please provide which results are significant (indicating them e.g. with an asterisk) compared to control?
Reply: One of reviewers suggested deleting the figure 1-3 directly, so we have deleted them and did not make other modifications.

5. Figure 2: please correct the legend of the x axis from COPD4 to GOLD4, so that it is consistent with other descriptions.
Reply: The same as above. One of reviewers suggested deleting the figure 1-3 directly, so we have deleted them and did not make other modifications.

6. Discussion, page 8: "Our study suggested that this approach is feasible with xx% participants completed the questionnaires". -> could you please specify xx%?
Reply: We have removed this sentence from the article.

7. In the table: "Quality assessment criteria for survey research reports" the items are reported on wrong pages/lines. As an example, the authors report on "research tools" or "sample

selection" on page 5, lines beyond 140, whereas (at least in the pdf version I got) line 140 is the last line on page 5. Please check the whole table for the correctness.

Reply: Because the reviewer received an anonymous version of the article, which is not provide by the authors and had some information removed, resulting in a change in the number of lines. We estimate that the anonymous version has approximately 24 fewer lines than the non-anonymous version.

**Reviewer E**

Major comments:

In the present report, the authors sought to elucidate the feasibility and performance of two chronic obstructive pulmonary disease (COPD) screening questionnaires in a Chinese physical examination center. Among 198 participants, 25 (12.6%) were diagnosed as COPD and the scores of two COPD screening questionnaires (COPD-PS and COPD-SQ) were significantly higher in participants with COPD compared to those without, indicating the usefulness of these two questionnaires to facilitate the diagnosis of COPD. These findings might be potentially intriguing, however, this report has several serious concerns as follows.

1) The greatest problem is that the results of this study have little significance, which extremely lowers its priority. As the authors described, several previous studies have already reported the effectiveness of the COPD-PS and COPD-SQ in the general population in China, and this study seems to be no more than an imitation of previous reports. Applied COPD screening questionnaires (COPD-PS and COPD-SQ) were identical and study design was also similar to previous reports, although study participants were different. Moreover, the sample size (N = 198) was quite smaller than previous studies.

Reply: This study was conducted in a physical examination center, which was consided as the most important place for health checks in China. We added the difference between those individuals attending health checks in PECs and the general population, to indicate that the feasibility and effectiveness of the COPD-PS and COPD-SQ in Chinese PECs should be identified before a full-scale implementation. (see "Introduction, Paragraph 3, Line 11-22")

2) The design of this study was not well-organized. The study endpoints were not described at all in the manuscript. The method of sample size estimation was quite invalid.

Reply: We have added the description of the study endpoints (see "Introduction, Paragraph 3, Second last sentence"). The sample size was estimated with reference to the following formula: $n = [(Z\alpha/22 \times \pi \times (1 - \pi)]/E2$.

3) The manuscript was poorly written and the contents were quite inadequate. In Abstract section, the authors mentioned that "applying the COPD-PS and COPD-SQ in Chinese PECs is cost-effective", however, no data regarding medical fee was shown in the manuscript. The quality of figures was insufficient. The flowchart of the study shown in Figure 1 was difficult to understand. The description of Discussion section was quite redundant and confusing.

Reply: There is no pricing for COPD questionnaire screening in China yet. The cost of

implementing COPD-PS and COPD-SQ is negligible. We provide data on the price of COPD questionnaires and spirometry from one previous study. (Details see "Discussions, Paragraph 2, line 2-10)

Minor points:
1) There were some inconsistent descriptions miss spellings in the manuscript.
Reply: We have read and revised the full manuscript.

**Reviewer F**

The article evaluates the feasibility and effectiveness of two questionnaires, COPD Population Screener (COPD-PS) and COPD Screening Questionnaire (COPD-SQ), for COPD screening in a Chinese physical examination center. It involves participants aged 40 and above, PFTs for diagnosis. The study finds optimal cutoff values for the questionnaires and concludes that they are feasible and effective for early COPD diagnosis in such settings. The findings suggest integrating these questionnaires into health checks for people over 40. After reviewing it, i think that authors made a very interesting job, which robust data and a well-written article. I have identified several potential areas for critique and improvement:

-The study is conducted in a single center with a relatively small and specific population. The generalizability of the findings could be questioned. A larger, more diverse sample across multiple centers would strengthen the results. This is the main limitation of the study and should be better addressed in discussion section.
Reply: This is the main limitation of the study and we have added some discussion about it (see. "Discussions, Last Paragraph, line 1-4)

-There could be more detailed explanations of the methodology, particularly regarding the selection process for participants and the statistical analysis techniques used. This would help in understanding how the study minimizes potential biases and the robustness of the data analysis.
Reply: We have added a description of how people choose the medical examination center (see "Introduction, Paragraph 2, Line 2-5"), and all those who volunteered to participate in the study were participants (see "Methods, Participants, Line 1-3"). Statistical analysis techniques are described in "Methods, Data analysis".

-While the study compares two questionnaires, it does not extensively compare these with existing screening methods. A more comprehensive comparison might provide a clearer understanding of the questionnaires' relative effectiveness.
Reply: We have added these in the "Discussion" (see "Discussion, Paragraph 4, line 14-17")

-The study briefly touches on cost-effectiveness but does not provide a detailed economic analysis. A more thorough economic evaluation would be beneficial, especially for policymakers and healthcare providers considering the implementation of these

questionnaires.
Reply: We have added some data about it (see “Discussion, Paragraph 2, line 2-8”).

-While the study acknowledges some limitations, a more detailed discussion of potential confounding factors, biases, and limitations of the study design would strengthen the credibility of the research.
Reply: We added these to “discussion” (see “Discussion, Paragraph 6, Line 5-10)

- Missing reference should be added and commented in discussion: doi: 10.3390/medicina59071252
Reply: We have added and commented in discussion.