

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Predicting sleep disordered breathing in outpatients with suspected OSA
AUTHORS	Cowan, Douglas; Allardice, Gwen; MacFarlane, Duncan; Ramsay, Darren; Ambler, Heather; Banham, Stephen; Livingston, Eric; Carlin, Christopher

VERSION 1 - REVIEW

REVIEWER	Dimitar Sajkov Australian Respiratory and Sleep Medicine Institute Flinders Medical Centre
REVIEW RETURNED	27-Dec-2013

GENERAL COMMENTS	Can the authors justify the use of AHI cut points of 5 and 15 in the study? A third cut point of $AHI \geq 30$ for severe OSAS would be more clinically relevant. This may require inclusion of additional subjects and re-analysis of the data. ROC curves for the three groups ($AHI < 5$, ≥ 15 and ≥ 30) can be shown on one figure in different colours.
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REVIEWER	Chol Shin Department of Sleep and Critical Care Medicine, Korea University Ansan Hospital, South Korea
REVIEW RETURNED	27-Dec-2013

GENERAL COMMENTS	Major comments: <ol style="list-style-type: none">1. The aim of the present study was to evaluate whether previously reported questionnaires are useful in a sleep service-referred population for prediction of OSA. The authors compared the sensitivity, specificity and predictive values among the three questionnaires and concluded that both STOP and STOP-BANG are useful for the prediction of OSA with a maximum accuracy of 72% and 79% when predicted $AHI \geq 5$ and $AHI \geq 15$, respectively. Given the subjects who visit sleep clinics due to SDB usually have moderate-severe degree of sleep apnea, however, low sensitivity, specificity, predicted value and accuracy for an $AHI \geq 15$ makes the usefulness of the questionnaire for prediction of OSA to be limited.
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	<p>2. Does it have better sensitivity, specificity or accuracy than other questionnaires for the prediction of OSA? The authors should compare the questionnaires with those which have been already used in sleep clinics for the prediction of OSA (e.g., SACS).</p> <p>3. From the results of multivariate logistic regression analysis authors found that neck circumference and witnessed apneas are independent predictors of SDB, but such variables are already known to be a component for the prediction of OSA. Thus, the novelty of the findings appears to be limited.</p> <p>Minor comments:</p> <p>1. It is needed to be checked whether reference style in the manuscript is suitable for the BMJ Open style.</p>
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REVIEWER	Robin Smith Ninewells Hospital dundee UK
REVIEW RETURNED	06-Jan-2014

GENERAL COMMENTS	<p>Interesting study which contributes to the debate on the utility of patient questionnaires in predicting outcome of investigations of patients with suspected sleep apnoea. Statistics appear appropriate and the data is well presented. Further discussion on how STOP-BANG could be utilised in primary care as a guide to referral would be helpful. Also more discussion on how the questionnaire might be used for the more important issue of predicting treatment outcome would strengthen the paper and help guide future research on this. The grammar is clumsy in places and the manuscript would benefit from "tidying up" in this respect.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer Name Dimitar Sajkov
Institution and Country Australian Respiratory and Sleep Medicine Institute
Flinders Medical Centre
Bedford Park, Adelaide, South Australia 5042
AUSTRALIA
Please state any competing interests or state 'None declared': None declared

1) Can the authors justify the use of AHI cut points of 5 and 15 in the study? A third cut point of $AHI \geq 30$ for severe OSAS would be more clinically relevant. This may require inclusion of additional subjects and re-analysis of the data.

The aim of this project was to evaluate predictors of sleep disordered breathing. We selected the AHI cut points of ≥ 5 and ≥ 15 to identify those (based on the AASM OSA task force guideline (1)) who have OSA, and those for whom treatment with CPAP therapy would be indicated. Whilst there is value in differentiating moderate (AHI 15-30) and severe (>30) OSA in studies such as those evaluating treatment outcomes or co-morbidities, the differentiation between moderate and severe OSA is unlikely to be usefully predicted by any questionnaire or clinical parameter, and does not have a direct clinical application (i.e. it does not currently influence management – anyone with symptoms and $AHI \geq 15$ would be considered for CPAP therapy). We do not believe that re-analysing our data to include an AHI cutpoint >30 would shed further light on our research questions for this study.

We have added the following in paragraph 9 of Discussion: "We chose AHI cut-points of ≥ 5 and ≥ 15 to define significant SDB. This was based on the consensus guideline produced by the Adult Obstructive Sleep Apnea Task Force of the American Academy of Sleep Medicine that states that diagnosis of OSA is based on a cut-point of >15 events/hr or >5 events/hr with relevant symptoms, and that CPAP is indicated for treatment of moderate to severe OSA with ≥ 15 events/hr.(1) Although the cut-point of >30 events/hr is consistent with severe OSA we suggest that this cut-point is less clinically relevant from a diagnostic perspective or from that of determining treatment."

2) ROC curves for the three groups (AHI <5 , ≥ 15 and ≥ 30) can be shown on one figure in different colours.

As noted in point 1, we are not including a 3rd group with AHI >30 . We have replaced Figure 1 Model A and Figure 1 Model B with a single figure including both ROC curves (Model A in blue and Model B in red).

Reviewer Name Chol Shin
Institution and Country Department of Sleep and Critical Care Medicine, Korea University
Ansan Hospital, South Korea
Please state any competing interests or state 'None declared': I have no competing interests.

Major comments:

1. The aim of the present study was to evaluate whether previously reported questionnaires are useful in a sleep service-referred population for prediction of OSA. The authors

compared the sensitivity, specificity and predictive values among the three questionnaires and concluded that both STOP and STOP-BANG are useful for the prediction of OSA with a maximum accuracy of 72% and 79% when predicted AHI ≥ 5 and AHI ≥ 15 , respectively. Given the subjects who visit sleep clinics due to SDB usually have moderate-severe degree of sleep apnea, however, low sensitivity, specificity, predicted value and accuracy for an AHI ≥ 15 makes the usefulness of the questionnaire for prediction of OSA to be limited.

We note the reviewers concerns:

- The prevalence of moderate to severe OSA in sleep clinic referrals depends on referral thresholds from primary care, which is highly variable. With regard to number of patients in this study with different degrees of OSA, 32 patients had AHI < 5 , 41 patients had AHI 5-15 and 56 had AHI > 15 . With this spread, our results are not confounded by the concerns raised in this point.
- Moreover, as shown in Table 3A, accuracies for STOP and STOP-BANG at a cut-point of ≥ 5 events/hr were 77 and 79%, whilst, as shown in Table 3B, the corresponding accuracies for AHI ≥ 15 events/hr were 48 and 56%, respectively. Contrary to the concern raised in this point, we found both STOP and STOP-BANG to have high (not low) sensitivities and negative predictive values (STOP-BANG superior to STOP) for AHI ≥ 15 events/hr, as shown in Table 3B. These results suggest that these questionnaires are useful, at least in ruling out moderate to severe sleep apnoea.
- We hope we have made this clearer by adding the following in paragraph 4 of Discussion: "We suggest that of the two AHI cut-points, ≥ 15 events/hr is the more important, being diagnostic of at least moderate SDB and also an indication for CPAP treatment. At this cut-point, STOP and STOP-BANG performed with high sensitivities and negative predictive values (STOP-BANG superior to STOP) indicating that these questionnaires are more useful in excluding significant SDB. This is further corroborated by the..."

2. Does it have better sensitivity, specificity or accuracy than other questionnaires for the prediction of OSA? The authors should compare the questionnaires with those which have been already used in sleep clinics for the prediction of OSA (e.g., SACS).

This was a prospective observational study and unfortunately the completion of other questionnaires including SACS was not included in the protocol. The SACS questionnaire cannot be completed retrospectively as it includes partner responses; furthermore, patients at our sleep clinics rarely attend with their partner. This question would need to be dealt with in further research prospectively and we have added a comment on this in the revised discussion.

We have added the following to Paragraph 9 of Discussion: "Finally, due to the prospective design of our study, we cannot comment on the relative value of other tools developed for prediction of OSA such as the Sleep Apnea Clinical Score (2) and American Society of Anesthesiologists Checklist. (3) To compare their utility with that of the Berlin, STOP and STOP-BANG questionnaires in the population referred to the sleep service would require a further study."

3. From the results of multivariate logistic regression analysis authors found that neck circumference and witnessed apneas are independent predictors of SDB, but such variables are already known to be a component for the prediction of OSA. Thus, the novelty of the

findings appears to be limited.

Our primary objective of this study was “to compare utility of Berlin, STOP and STOP-BANG questionnaires for prediction of SDB in a population referred to the sleep clinic for assessment of possible OSA.” As stated in the first paragraph of Discussion “This is the first study to prospectively evaluate the utility of the Berlin, STOP and STOP-BANG questionnaires in prediction of sleep disordered breathing in a population referred to a tertiary sleep service for assessment of possible OSA.” We argue, therefore, that this paper does present novel work that adds to previous research into the prediction of SDB.

We conducted the multivariate LR analysis, not as the primary component but to support the authenticity of our dataset – corroborate it with previous studies to support the validity of our novel observations. That neck circumference and witnessed apnoeas are independent predictors of OSA is of course well established, and we indicate that in paragraph 7 of our revised discussion “This is not a novel finding, but does support the robustness of our data.”

Minor comments:

1. It is needed to be checked whether reference style in the manuscript is suitable for the BMJ Open style.

The reference style is correct.

Reviewer Name Robin Smith
Institution and Country Ninewells Hospital
dundee
UK

Please state any competing interests or state ‘None declared’: None declared

Interesting study which contributes to the debate on the utility of patient questionnaires in predicting outcome of investigations of patients with suspected sleep apnoea. Statistics appear appropriate and the data is well presented.

Further discussion on how STOP-BANG could be utilised in primary care as a guide to referral would be helpful.

Thank you for this suggestion and we have added the following in paragraph 8 of revised discussion: “Ultimately, a predictive tool that can be utilised in primary care is the goal. Our results indicate low specificity of STOP-BANG, and therefore in its current form, if used in primary care to identify patients requiring referral for further assessment, it is likely to result in a significant percentage of patients being referred unnecessarily (false positives). It is hoped that a modified STOP-BANG with improved specificity, while not compromising sensitivity, may be developed that can be used safely in primary care for identification of patients requiring referral to sleep services.”

Also more discussion on how the questionnaire might be used for the more important issue of predicting treatment outcome would strengthen the paper and help guide future research on this.

We have added the following in paragraph 8 of Discussion: “Of utmost importance too is the

prediction of treatment outcome. Non-adherence to CPAP treatment occurs in between 46 and 83%.(4-5) Prediction of poor adherence by STOP-BANG or other similar tools would allow greater attention to interventions to improve adherence in patients more likely to default from treatment. The authors are not aware of any studies investigating this question and future research should explore this important issue.”

The grammar is clumsy in places and the manuscript would benefit from "tidying up" in this respect.

The manuscript has been revised as suggested, as indicated in the marked up version.

References:

1. Epstein LJ, Kristo D, Strollo PJ, Jr., Friedman N, Malhotra A, Patil SP, et al. Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. J Clin Sleep Med. 2009 Jun 15;5(3):263-76.
2. Flemons WW, Whitelaw WA, Brant R, Remmers JE. Likelihood ratios for a sleep apnea clinical prediction rule. Am J Respir Crit Care Med. 1994 Nov;150(5 Pt 1):1279-85.
3. Gross JB, Bachenberg KL, Benumof JL, Caplan RA, Connis RT, Cote CJ, et al. Practice guidelines for the perioperative management of patients with obstructive sleep apnea: a report by the American Society of Anesthesiologists Task Force on Perioperative Management of patients with obstructive sleep apnea. Anesthesiology. 2006 May;104(5):1081-93; quiz 117-8.
4. Weaver TE, Grunstein RR. Adherence to continuous positive airway pressure therapy: the challenge to effective treatment. Proc Am Thorac Soc. 2008 Feb 15;5(2):173-8.
5. Wolkove N, Baltzan M, Kamel H, Dabrusin R, Palayew M. Long-term compliance with continuous positive airway pressure in patients with obstructive sleep apnea. Can Respir J. 2008 Oct;15(7):365-9.

VERSION 2 – REVIEW

REVIEWER	Chol Shin Department of Pulmonary, Sleep, and Critical Care Medicine, Korea University Ansan Hospital
REVIEW RETURNED	24-Feb-2014

GENERAL COMMENTS	The manuscript has been well modified according to the reviewer's comments.
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