

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Factors associated with symptoms of attention deficit hyperactivity disorder among medical students in Cameroon: a web-based cross-sectional study
AUTHORS	Njuwa, Karl; Simo, Larissa Pone; Ntani, Limnyuy Loweh; Forchin, Azumesi Nguni; Parviel, Chirsir; Frank Leonel, Tianyi Tianyi; Bernard, Nsah; Agbor, Ndip

VERSION 1 – REVIEW

REVIEWER	Yigizie Yeshaw University of Gondar, Ethiopia
REVIEW RETURNED	04-Mar-2019

GENERAL COMMENTS	some of the references are not up-to-date. you used snow ball sampling method which is non probability method. so it is difficult to generalize the finding.
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REVIEWER	Desmond AROKE Fontem District Hospital, Fontem, Cameroon
REVIEW RETURNED	15-Mar-2019

GENERAL COMMENTS	<ol style="list-style-type: none"> 1) The authors carried out a cross sectional study in a field of importance but which is almost always neglected in clinical practice in most developing countries. The study is relevant, timely and provides baseline data for further research. 2) The abstract should provide a summary of the methods used to achieve results...A summary of study procedure and diagnostic tool should be included in the abstract. 3) Still in the abstract...the conclusion should read ADHD symptoms not ADHD 4) Authors used the 6 item Adult ADHD Self-Report Scale (ASRS v1.1) to evaluate symptoms of ADHD which is based on the DSM IV criteria. It would have been better to use the updated Adult ADHD Self-Report Screening Scale for DSM V (ASRS 5). 5) More details could be provided on the screening tool such as its specificity and sensitivity. 6) Likewise, more details should be provided in the methodology section on how severe depression and anxiety were diagnosed 7) A separate “ethical consideration” sub-section should be included in the methodology section. Ethical concerns should be addressed here in details 8) Discussion; In addition to comparing study findings to previous studies it will even be more important and meaningful to discuss potential causes and implications of study findings. 9) In table 1, full meaning of “n” should be added to other listed footnotes.
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REVIEWER	Stewart Ndutard Ngasa Royal Oldham Hospital, United Kingdom
REVIEW RETURNED	05-May-2019

GENERAL COMMENTS	<p>Page 2: Please revise the sentence: Attention Deficit/Hyperactivity Disorder (ADHD) is a chronic disease which is very costly and is associated with poor productivity... Costly in the sentence is quite vague. Not sure what kind of 'cost' is referred to here.</p> <p>Page 6: LPS translated the questionnaire from English to French. It seems LPS is the initials of one of the authors. Not sure why the authors explicitly mention her as the translator. Also its not clear if this is the name of an individual or an application. I would advice authors say we translated the questionnaire from English to French except they have a good reason for being specific.</p> <p>Page 8: Under statistical analysis, the authors made mention of qualitative data being summerised as counts and percentages. Not sure if the study actually collected any qualitative data. Authors might want to define what they mean by qualitative study.</p> <p>Page 8: The Shapiro-Wilk's test and Histogram were used to assess for normality of continuous variables. What adjustments methods were used for variables which did not show a normal distribution. Except authors are saying continuous variables demonstrated a normal distribution if some of variables not normalised, then method of analysis used will falsify the results obtained.</p>
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REVIEWER	Mohamed F. Jalloh Centers for Disease Control and Prevention, Division of Global Health Protection
REVIEW RETURNED	23-May-2019

GENERAL COMMENTS	<p>Symptoms of attention deficit hyperactivity disorder among medical students in Cameroon: a web-based survey bmjopen-2019-029602</p> <p>Paper review</p> <p>GENERAL FEEDBACK</p> <p>The authors have submitted a well written paper that addresses an important area of clinical importance and implications for mental health screening for ADHD among medical students in Cameroon. The comparability of the findings to another study in sub-Sahara Africa point to potentially high burden of ADHD among medical students on the continent. A strength of the study is the use an already validated scale. However, this is also a limitation because in the current study the authors did not perform any analysis to see how the classification model for ADHD performed in their study. Also, the authors failed to conduct Confirmatory Factor Analysis to assess the goodness of fit of the tool -- important because while the scale has been validated elsewhere it has not been previously validated for use in any population of Cameroonians.</p> <p>ABSTRACT</p>
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	<ul style="list-style-type: none"> - No need to calculate and report p-values for difference in gender among respondents from the convenience sample - Symptom prevalence should be followed by ...”in our non-representative sample” - Use of R squared (or pseudo R squared) not necessary – this is mostly no longer recommended as it is not a good indicator for evaluating variability explained in a logistic model - Need to exercise caution by saying that “ADHD MAY be prevalent mental disorder...” - ADHD is not a disease but a mental disorder (this may have been translation issues from French?) <p>METHODS</p> <ul style="list-style-type: none"> - The assumptions in the sample size calculations presented are for probability sampling, however non-probability sampling was used in this study - Efforts should have been made to stratify the sample by medical school to ensure more diverse representation of medical students in the sample - Looking at the table it appears that forward selection might have been used by the authors but backward elimination reported - Authors need to generate ROC curve and assess the area-under-the curve (AUC) - Authors need to conduct Confirmatory Factor Analysis and assess model goodness of fit <p>RESULTS</p> <ul style="list-style-type: none"> - Better to show IQR for age - How does your sample compare to the distribution of medical student population across the different schools? This is important to mention because of the use of non-probability sampling - Authors need to generate a post-estimation ROC curve and assess AUC in order to determine discrimination of cases (those with ADHD symptom) versus non-cases in the fitted model - Report on construct validity of 6-items from the ASRS - No need to report R-squared; more important to report AUC for the classification model - Did you perform interaction analysis to see if there was any interactions in the variables associated with the outcome? If not, this should also be considered <p>DISCUSSION</p> <ul style="list-style-type: none"> - The authors need to exercise greater caution in how the findings are interpreted. For instance, the sample obtained was not random or representative of the population of student medical students in Cameroon. - Important limitations are not acknowledge including use of convenience sample, which likely biased the estimation of prevalence in the sample; use of a scale never validated in Cameroon without any analysis to determine construct validity.
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VERSION 1 – AUTHOR RESPONSE

Reviewer #1

Comment: some of the references are not up-to-date. you used snow ball sampling method which is non probability method. so it is difficult to generalize the finding.

Response 1: Thank you. We have updated the references. The study design does not permit us to use a randomised sampling because this was practically impossible to implement. However, we collected data in strata to ensure that all the classes in every school are equally represented to the best of our ability. This limitation has been highlighted in the strength and limitation of our study.

Reviewer #2

Comment 1: The authors carried out a cross sectional study in a field of importance but which is almost always neglected in clinical practice in most developing countries. The study is relevant, timely and provides baseline data for further research.

Response 1: Thank you.

Comment 2: The abstract should provide a summary of the methods used to achieve results...A summary of study procedure and diagnostic tool should be included in the abstract.

Response 2: Thank you. We were respecting the BMJ Open author submission guidelines: https://bmjopen.bmj.com/pages/authors/#submission_guidelines

Comment 3: Still in the abstract...the conclusion should read ADHD symptoms not ADHD

Response 3: Thank you. We have corrected accordingly.

Comment 4: Authors used the 6 item Adult ADHD Self-Report Scale (ASRS v1.1) to evaluate symptoms of ADHD which is based on the DSM IV criteria. It would have been better to use the updated Adult ADHD Self-Report Screening Scale for DSM V (ASRS 5).

Response 4: The authors agree with the reviewer. This is a limitation. We used the ASRS v1.1 to improve the comparability of study of our finding with previous studies.

Comment 5: More details could be provided on the screening tool such as its specificity and sensitivity.

Response 5: Thank you we have updated this section of the methods. The data collection section now reads: *“Using a pre-established Google Form, we collected data on: sociodemographic data (age [in years], gender, name of school, academic level, number and types of social media accounts), past history (diagnosis of ADHD, family history of ADHD, learning disability, chronic disease, current illness, histories of head injury, snoring, recreational drug use, severe depression, anxiety) and the six-item Adult ADHD Self-Report Scale (ASRS) v1.1 Screener [14,15]. The diagnosis of severe depression and anxiety was based on a self-reported physician and/or specialist’s diagnosis of the condition. The 6-*

items adult ASRS v1.1 screener is based on the 18-item DSM-IV ADHD symptom criteria and assesses symptoms of ADHD that occurred in the last six-months. Each of the six-items constitutes of responses of “never”, “rarely”, “sometimes”, “often” or “very often”. Each question has a threshold level which is used to screen a participant’s symptoms as either related to ADHD or not. A participant’s symptoms were considered to be consistent with ADHD if their response to at least four of the questions correspond to the threshold level for the question. The ASS-v1.1 has been reported to have moderate sensitivity, excellent specificity, and excellent accuracy of 68.7%, 99.5% and 97.9% in the general population, respectively.”

Comment 6: Likewise, more details should be provided in the methodology section on how severe depression and anxiety were diagnosed

Response 6: Thank you. Please, see our response to the previous comment.

Comment 7: A separate “ethical consideration” sub-section should be included in the methodology section. Ethical concerns should be addressed here in details

Response 7: Thank you. We have included a subsection under the methods to elaborated on the ethical considerations.

Comment 8: Discussion; In addition to comparing study findings to previous studies it will even be more important and meaningful to discuss potential causes and implications of study findings.

Response 8: The authors are not sure they understand the reviewer’s request but we believe have provided a balance discussion of our findings.

Comment 9: In table 1, full meaning of “n” should be added to other listed footnotes

Response 9: Thank you. We have implemented.

Reviewer #3

Comment 1:

Page 2: Please revise the sentence: Attention Deficit/Hyperactivity Disorder (ADHD) is a chronic disease which is very costly and is associated with poor productivity... Costly in the sentence is quite vague. Not sure what kind of 'cost' is referred to here.

Response 1: Thank you. The words “very costly” have been removed from the sentence.

Comment 2: Page 6: LPS translated the questionnaire from English to French. It seems LPS is the initials of one of the authors. Not sure why the authors explicitly mention her as the translator. Also its

not clear if this is the name of an individual or an application. I would advice authors say we translated the questionnaire from English to French except they have a good reason for being specific.

Response 2: Thank you. We agree with the reviewer's suggestion. This sentence now reads: "*The questionnaire was translated from English to French to improved comprehension for French-speaking students.*"

Comment 3: Page 8: Under statistical analysis, the authors made mention of qualitative data being summerised as counts and percentages. Not sure if the study actually collected any qualitative data. Authors might want to define what they mean by qualitative study.

Response 3: Thank you. We collected qualitative variables (also called categorical variables) such as "gender" (Male/Female) and "Family history of ADHD" (Yes/No). We did not mentioned "qualitative study", as mentioned by the reviewer, which is different from qualitative variable (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5506151/>). However, this has been changed to "categorical variables" to avoid any confusions.

Comment 4: Page 8: The Shapiro-Wilk's test and Histogram were used to assess for normality of continuous variables. What adjustments methods were used for variables which did not show a normal distribution. Except authors are saying continuous variables demonstrated a normal distribution if some of variables not normalised, then method of analysis used will falsify the results obtained.

Response 4: Thank you for your comment. Only the variable "Number of hours spent on social media per day" was dichotomised at the median due to the presence of significant outliers. Mild skewed distributions were not transformed to normal distributions, as normality is not an assumption of logistic regression analysis as opposed to linear regression (<https://pdfs.semanticscholar.org/3305/2b1d2363aee3ad290612109dcea0aed2a89e.pdf>).

Reviewer #5

Abstract

Comment 1: No need to calculate and report p-values for difference in gender among respondents from the convenience sample

Response 1: Thank you. We have deleted. We used the snowballing and not a convenient sampling technique, and we used all means possible to get participants from the respective schools to responding to the questionnaire while respecting the participant's autonomy to participate.

Comment 2: Symptom prevalence should be followed by ... "in our non-representative sample"

Response 2: Thank you. We think the sampling methods and further discussion on the representiveness and generalisability of our findings infers this.

Comment 3: Use of R squared (or pseudo R squared) not necessary – this is mostly no longer recommended as it is not a good indicator for evaluating variability explained in a logistic model

Response 3: Thank you. This was included by default as some reviewers still insist on it being included. We agree with the reviewer and have deleted accordingly.

Comment 4: Need to exercise caution by saying that “ADHD MAY be prevalent mental disorder...”

Response 4: Thank you. This section of the conclusion now reads: “*ADHD may be highly prevalent disease among medical students, and is associated with severe depression, anxiety disorders and chronic diseases.*”

Comment 5: ADHD is not a disease but a mental disorder (this may have been translation issues from French?)

Response 5: Thank you. We have replaced disease with mental disorder. This section of the conclusion now reads: “*ADHD may be highly prevalent mental disorder among medical students, and is associated with severe depression, anxiety disorders and chronic diseases.*”

Methods

Comment 1: The assumptions in the sample size calculations presented are for probability sampling, however non-probability sampling was used in this study

Response 1: Thank you. We have deleted the sample size calculations.

Comment 2: Efforts should have been made to stratify the sample by medical school to ensure more diverse representation of medical students in the sample

Response 2: Thank you. If you look at the study procedure and data collection process, you will realise that we made great efforts to ensure that the sample is representative. However, we were careful not to violate the privacy and autonomy of the students to participate in the study. Except there is something the reviewer thinks that the authors were supposed to do that was missed.

Comment 3: Looking at the table it appears that forward selection might have been used by the authors but backward elimination reported

Response 3: Thank you. This is inappropriate. The forward selection methods was conducted. Thank you for pointing that out. However, we reanalysed the data just to be sure of using the maximum likelihood logistic regression method. Variables with p values < 0.2 including key demographic variables like age and gender were considered for inclusion in multivariable logistic regression analysis. The variables were simultaneously added to build the regression model. The statistical analysis sub-section of the methods now reads: “*Multivariable logistic regression analysis was used to identify factors independently associated with ADHD in our study population. The Odd’s ratio (OR) alongside its corresponding 95% CI were used to measure the degree of association between the outcome and independent variables. Only independent variables with a p-value < 0.20 on univariable logistic analysis were included in the multivariable analysis. Variables that were eligible for the multivariable logistic*”

regression analysis were sequentially added to the model starting with: sociodemographic factors (age, gender, institution, number of social media account, and use of recreational drugs), family history of ADHD, and past medical history (history of chronic disease, head injury, anxiety, and severe depression). The contribution of each variable in explaining the total variance in the outcome on multivariable analysis was assessed using the maximum likelihood ratio (LHR) test, and the test for interaction was used to evaluate a possible interaction between history of severe anxiety and depression. The variables “number of social media accounts” was excluded from the final model as it did not significantly improve the model fit. The accuracy or predictive power of the final multivariable model was assessed using the C-statistics. A C-statistics of 0.5, above 0.5 to 0.7, above 0.7 to 0.8 and above 0.8 indicated a poor, fair, good and strong (or excellent) model, respectively [16]. The Cronbach alpha statistic was used to assess reliability of the different items of the Adult ADHD Self-Report Scale (ASRS) v1.1 Screener in screening for ADHD in our study population. The threshold of statistical significance was set at a two-tailed p-value of 0.05.”

Comment 4: Authors need to generate ROC curve and assess the area-under-the curve (AUC)

Response 4: Thank you. The AUROC, accuracy, or discriminatory ability of the model is given by the value of the C-statistic which is 70.3%. Please, see Result/ Factors associated with symptom of ADHD/Paragraph 2.

Comment 5: Authors need to conduct Confirmatory Factor Analysis and assess model goodness of fit

Response 5: Thank you for your comment. We wish to remind the reviewer that our objective is to explore the factors associated with ADHD and not build a predictive model.

Comment 7: Better to show IQR for age

Response 7: Thank you. We have reported the median age and interquartile age for the study participants.

Comment 8: Authors need to generate a post-estimation ROC curve and assess AUC in order to determine discrimination of cases (those with ADHD symptom) versus non-cases in the fitted model

Response 8: Thank you. Please, see our response to our 4th and 5th comment above. Indeed, we did not perform interviews (ideally by a psychiatrist) to confirm the diagnosis of ADHD.

Comment 9: No need to report R-squared; more important to report AUC for the classification model

Response 9: Thank you. Please, see our response above.

Comment 10: Did you perform interaction analysis to see if there was any interactions in the variables associated with the outcome? If not, this should also be considered

Response 10: Thank you. We found no significant interaction between anxiety and depression following the reviewer's comment.

VERSION 2 – REVIEW

REVIEWER	Stewart Ndutard Ngasa Galact Corp Res Grp, General surgery
REVIEW RETURNED	15-Feb-2020

GENERAL COMMENTS	Happy with the changes the authors have made
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REVIEWER	Mohamed Jalloh Centers for Disease Control and Prevention, United States
REVIEW RETURNED	24-Feb-2020

GENERAL COMMENTS	<p>The authors have done a very thorough job of addressing the comments provided by the reviewers. In reviewing their responses, I find them satisfactory overall. My only pending suggestion, as previously recommended also, is that Confirmatory Factor Analysis (CFA) should ideally be conducted because the ASRS has not been validated for use in Cameroon (despite validations elsewhere). CFA is especially useful in this situation because (1) the tool was translated from English to French so meaning may have shifted, which may have affected psychometric attributes of the scale; (2) other researchers planning to use the scale in Cameroon in the future will have evidence regarding the construct validity of the scale in this particular context. Even if the CFA results show poor goodness of fit, the main results and methods of the study will still have substantial public health importance in my opinion. Therefore, I leave the decision on whether or not to ask the authors to conduct CFA to the BMJ Open editorial team.</p> <p>Thanks again for the opportunity to review this important work and for your diligent efforts in addressing the comments provided.</p>
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VERSION 2 – AUTHOR RESPONSE

Reviewers' Comments to Author:

Reviewer: 1

Reviewer Name: Stewart Ndutard Ngasa

Institution and Country: Stepping Hill Mental Institute, Stockport, Manchester, United Kingdom

Please state any competing interests or state 'None declared': None

Happy with the changes the authors have made

Response: Thank you. We are grateful for the reviewer's time and valuable comments.

Reviewer: 2

Reviewer Name: Mohamed Jalloh

Institution and Country: Centers for Disease Control and Prevention, United States

Please state any competing interests or state 'None declared': None declared

The authors have done a very thorough job of addressing the comments provided by the reviewers. In reviewing their responses, I find them satisfactory overall. My only pending suggestion, as previously recommended also, is that Confirmatory Factor Analysis (CFA) should ideally be conducted because the ASRS has not been validated for use in Cameroon (despite validations elsewhere). CFA is especially useful in this situation because (1) the tool was translated from English to French so meaning may have shifted, which may have affected psychometric attributes of the scale; (2) other researchers planning to use the scale in Cameroon in the future will have evidence regarding the construct validity of the scale in this particular context. Even if the CFA results show poor goodness of fit, the main results and methods of the study will still have substantial public health importance in my opinion. Therefore, I leave the decision on whether or not to ask the authors to conduct CFA to the BMJ Open editorial team.

Thanks again for the opportunity to review this important work and for your diligent efforts in addressing the comments provided.

Response: Thank you. We conducted a two-factor CFA according to your comment. We reported measures of goodness of fit. Including the RMSEA, normed chi-squared, and CFI. Please, see the end of the: statistical analysis section; result section; and Figure 1. All changes are highlighted in green.

We are grateful for the reviewer's valuable comments which we must admit have significantly improved our manuscript.