



RESEARCH ARTICLE

REVISED The network structure of depressive symptomatology in Peruvian adults with arterial hypertension [version 3; peer review: 2 approved]

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Abstract

Background: Globally, arterial hypertension (AH) has increased by 90% over the last four decades, and has increased by 1.6% in Peru over the previous four years. Scientific evidence indicates the prevalence of depressive symptoms in patients with AH and its importance in the comprehensive evaluation of the adult for adherence to clinical treatment. Previous studies carried out in the Peruvian population with AH mostly report the prevalence and associations, but do not indicate which depressive symptoms are more relevant in patients with AH. This study involved a network analysis of depressive symptomatology in Peruvian patients with AH using network estimation. Network analysis is used in this study for analysis, control, and monitoring purposes.

Method: A representative cross-sectional study at the national level, using secondary data from 2019 Demographic and Family Health Survey (ENDES) was performed. The sample used included men and women of age over 17 years diagnosed with AH and was able to respond to Patient Health Questionnaire-9 (PHQ-9).

Results: The symptoms of depressive mood (bridging force and centrality) and energy fatigue or loss (bridge centrality) play an essential role in the network structure, as does the feeling of uselessness in terms of closeness and intermediation.

Conclusion: The study highlighted the symptoms related to depressive mood and energy fatigue or loss as bridging symptoms, which could trigger a depressive episode in patients diagnosed with AH. The results will contribute to developing personalized treatments

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aimed at patients with specific depressive symptoms who have also been diagnosed with AH. The study analysis presents statistical coefficients of effect size ($\leq 0,1$ = small; $> 0,1$ to $< 0,5$ = moderate; $\geq 0,5$ = large) to determine network connections.

Keywords

Hypertension, Depression, Mental Health, Health Surveys, Peru

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REVISED Amendments from Version 2

The reviewer had a concern about our study not being similar to those reported by McWilliams *et al.* and this was clarified and responded to in the discussion section as suggested by the reviewer.

"The results agree with the network study by McWilliams *et al.*²⁸ in a sample of patients with chronic pain, which reported 4 symptoms with the highest centrality, where depressed mood and fatigue or loss of tiredness had the highest values. However, the authors indicate the relevance of two other symptoms, for example, loss of interest and concentration difficulties. These last two symptoms were not found in our study and a probable explanation is due to the type of population. The authors indicate that people who experience chronic pain are also less able to devote their attention to other activities or simply lose interest since it is difficult for them to concentrate while in pain²⁸. For this reason, in patients with chronic pain, it is even more likely to find more central symptoms due to the persistent pain that generates discomfort, compared to patients with HA who do not present this type of chronic pain".

Any further responses from the reviewers can be found at the end of the article

Introduction

Diagnoses of arterial hypertension (AH) among other chronic non-communicable diseases are common¹. It necessarily requires a change of lifestyle that favors the adherence to pharmacological and psychological treatments, to reduce the development of cardiovascular diseases or psychological problems which complicate the patient's health condition. An international study based on various surveys and reviews from 200 countries indicated that AH cases worldwide have increased by 90% over the last four decades, with issues mostly identified in low- and middle-income countries². In Peru, the prevalence of AH has increased in recent years: 2016 (8.6%), 2017 (8.7%), 2018 (9.5%) and 2019 (10.2%)³. This increase is due to a rise in the population of older people and various lifestyle factors (such as food, for instance, saturated fatty acids, salt sugar, and so on, minimal physical activity, alcohol consumption, among others)³. Systematic review research conducted by Li *et al.*,⁴ described how common depression is among people with a diagnosis of AH.

Likewise, there is evidence that patients suffering from AH have a higher frequency of presenting emotional disorders, mainly depressive symptoms (40%), anxiety (56%), or stress (20%)⁵, which interferes with their clinical treatment, leading to poor prognosis (not following the doctor's instructions regarding medicines, minimal personal care) and preventing the acquisition of desirable behaviors to improve their quality of life⁵. A recent study in the Peruvian population indicated that depressive symptoms are most likely to occur in the first year of diagnosis of hypertension⁶. On the other hand, although in chronic disease the development of emotional disorders is likely, there is evidence that emotional disorders contribute to the development of chronic diseases, for example, a study concluded that the greater the depressive symptoms and anxiety, the greater the probability. The fact that the person is diagnosed with AH 5 years later than⁷ and, on the other hand, a greater number of prescribed

medications, is considered a risk factor in the development of depressive symptoms in patients with AH⁸.

Several studies have indicated that clinical interventions should primarily focus on depression in patients with AH^{5,7} since its prevalence is between 3% and 23.7% in the Peruvian adult population^{5,9}, while international studies report between 4% and 38%^{5,10}. Patients diagnose with AH normally experience negative emotions because they have to consume the drugs prescribed for the treatment for the rest of their lives or a very long period, these emotions are more powerful in situations where their condition is severe, and may generate feelings of loss of control or fear of failure, thus making it more likely that those with AH condition can develop some emotional disturbances¹¹. These emotions are also related to the economic expenses involved in treatment (especially in low and middle-income countries) and the decrease in social interaction with friends or family¹. In this sense, research reveals that health professionals should pay greater attention to negative emotions that occur in patients with AH⁵ since their evaluation and intervention are important in adherence to clinical treatment. Previous studies carried out in Peru in patients with AH mostly report the prevalence and its association with depressive symptoms^{5,6,9}, but they do not indicate which depressive symptom is more relevant or important in patients with AH, which would be appropriate to know this nature. One approach to solving this question is network analysis. This type of analysis makes it possible to analyze how individual behaviors or symptoms are associated with each other and, in turn, how they reinforce and interact. That is, the symptoms and their interaction with other symptoms are the main problem and individual identities, which are not explained by a common latent disorder or cause, mostly explained by the classical medical model¹². In this sense, network analysis is relevant to understand and explain psychopathological phenomena, which would allow focusing clinical interventions on specific central symptoms to prevent others, for example, to investigate which depressive symptoms are more important in Peruvian patients diagnosed with AH. Ignoring negative emotions may result in physical disorders¹³. These are likely to decrease adherence to treatments where psychological support is needed, especially the ones associated with risky behaviors such as alcohol consumption^{5,14}.

Therefore, the research aimed to explore the network dynamics of depressive symptomatology in Peruvian adults with arterial hypertension from a network analysis approach, which allows a broad understanding of the interactions and the bridges force or centrality between the depressive symptoms and the study population.

Methods

A secondary cross-sectional study was conducted based on data from ENDES 2019, which is a national representative survey that collects information on chronic non-communicable diseases and gives access to diagnostic and treatment services in Peru. ENDES design includes a two-stage random sampling technique, differentiated for rural and urban areas. In rural areas, the primary sampling units were groups of 500–2000 individuals and the secondary sampling units were the households

within each of these groups. On the other hand, in urban areas, the sampling units consisted of blocks or groups of blocks with more than 2,000 individuals and an average of 140 households. The secondary sampling units were the same as in rural settings where we have 36,760 sampled households, 34971 persons aged 15 and older who were surveyed with the Health questionnaire. Details of data sampling, processing, and collection are contained in the [ENDES technical report](#) produced by the National Institute of Statistics and Data Processing (INEI).

Our sample included men and women over the age of 17 diagnosed with AH. The diagnostic criteria for AH were those with systolic blood pressure greater than and/or equal to 140 mmHg and/or diastolic blood pressure greater than and/or equal to 90 mmHg¹⁵, and had completed the Patient Health Questionnaire (PHQ-9)¹⁶. Exclusion criteria were those who did not meet the diagnostic criteria for hypertension or did not report any blood pressure measurements, or omitted any PHQ-9 questions. This allows evaluation of each of the nine DSM-IV depression criteria. PHQ-9 has four response options (0 = nothing at all, 1 = several days, 2 = more than half of days, and 3 = almost every day) and assesses the presence of depressive symptomatology in the last two weeks, the overall response score is in the range of 0 to 27.

Sample

A total of 2915 participants were included in this study, of whom 1106 (37.94%) were male, and 1809 (63.06%) were female. The mean age was 57.9 years (standard deviation: 16.9), with 1456 (49.88%) being older adults (55 years old and over). Of these, 1144 (39.24%) had completed primary education, 844 (28.95%) secondary, 637 (21.75%) higher and 290 (9.94%) did not answer. Regarding the participants' native language, 2106 (72.24%) indicated Spanish, 688 (23.6%) Quechua, and 121 (4.16%) a different native language.

Data analysis

For the analysis of the data, the graph package version 1.6.5¹⁷ was used in the statistical software R version 4.0.3, which allows estimation of a Gaussian chart model (GGM) of a regularized partial correlation network to model the interaction between the components of PHQ-9 as autonomous entities, which are represented as circles, called "nodes". Nodes are connected by lines, called "edges." Edges in GGM can be understood as conditional dependency relationships between elements. If two items are connected to the resulting network, they are dependent after all other items are adjusted. This analysis presents statistical coefficients of effect size ($\leq 0,1$ = small; $> 0,1$ to $< 0,5$ = moderate; $\geq 0,5$ = large) to determine network connections. The precision of the edge weights was estimated to provide greater stability to the results, with a precision of 95% of the confidence intervals through Bootstrapping of 5000 samples around each edge in the network¹⁶. Also considered were the most commonly used centrality indices in psychological networks: strength, closeness, betweenness¹⁸.

Ethical considerations

The investigation did not require the approval of an ethics committee because it only involved the analysis of secondary

data obtained from a public and open-source, which does not require the identification of the participants and maintains the anonymity of the participants.

Results

In [Table 1](#), the mean scores for each item of the PHQ-9 are shown¹⁹. This shows that people with arterial hypertension have a higher level of "Depressed mood". The item also reports that there is a more significant measure of force in terms of other depressive symptoms. Another essential item on the web was Tired or little energy. The elements of lower centrality were "Moving/restless" and "Appetite change". [Table 2](#) shows all the PHQ-9 items weight partial correlation matrix.

[Figure 1](#) shows the network chart of PHQ-9 in Peruvian adults with arterial hypertension, where most of the elements are positively associated with a total of 36 possible edges, in which the highest magnitude associations are found with "Moving/ restless" (PH8) and "Suicidal thoughts" (PH9). Also highlighted are the relationships between "Moving/ restless" (PH8) "Interest loss" (PH1) and "Depressed mood" (PH2), and the connection of "Feelings of worthlessness" (PH6) and "Trouble concentrating" (PH7). Other measures of centrality have highlighted greater closeness (1.57) and brokering (1.12) in reagent 6. [Figure 2](#) shows the PHQ-9 network estimated border weight confidence intervals.

Regarding the accuracy of network connection magnitudes calculated by Bootstrap analysis, the analysis indicates that there is high precision with the dependent intervals of the evaluated network.

Discussion

This research aimed to explore the dynamics of depression symptoms in adults having Pulmonary arterial hypertension (PAH). This study is the first to use network analysis for PHQ-9 in the Latin American region such as Peru, although several kinds of research have considered network analysis for psychopathological symptoms which may be up to 13 items. Several network training on depression symptoms has been evaluated using diverse clinical samples such as chronic pain, depression, bipolar disorder, cancer, but it had been assumed that

Table 1. Mean and power centrality of items of PHQ-9.

Depression symptoms (PHQ-9)	Mean (ME)	Strength
PH1. Interest loss	0,63	-0,60
PH2. Depressed mood	0,77	1,93
PH3. Trouble sleeping	0,63	-0,25
PH4. Tired or little energy	0,55	0,96
PH5. Appetite change	0,44	-1,06
PH6. Feelings of worthlessness	0,38	0,06
PH7. Trouble concentrating	0,40	0,27
PH8. Moving slowly/restless	0,23	-1,37
PH9. Suicidal thoughts	0,29	-0,47

Table 2. Weight matrix of PHQ-9 items.

Network									
Variable	PH1	PH2	PH3	PH4	PH5	PH6	PH7	PH8	PH9
PH1	0.000	0.318	0.095	0.170	0.101	0.082	0.088	0.000	0.000
PH2	0.318	0.000	0.209	0.193	0.081	0.042	0.081	0.071	0.082
PH3	0.095	0.209	0.000	0.152	0.152	0.059	0.100	0.067	0.000
PH4	0.170	0.193	0.152	0.000	0.122	0.142	0.104	0.038	0.046
PH5	0.101	0.081	0.152	0.122	0.000	0.141	0.062	0.051	0.033
PH6	0.082	0.042	0.059	0.142	0.141	0.000	0.261	0.000	0.141
PH7	0.088	0.081	0.100	0.104	0.062	0.261	0.000	0.084	0.112
PH8	0.000	0.071	0.067	0.038	0.051	0.000	0.084	0.000	0.396
PH9	0.000	0.082	0.000	0.046	0.033	0.141	0.112	0.396	0.000

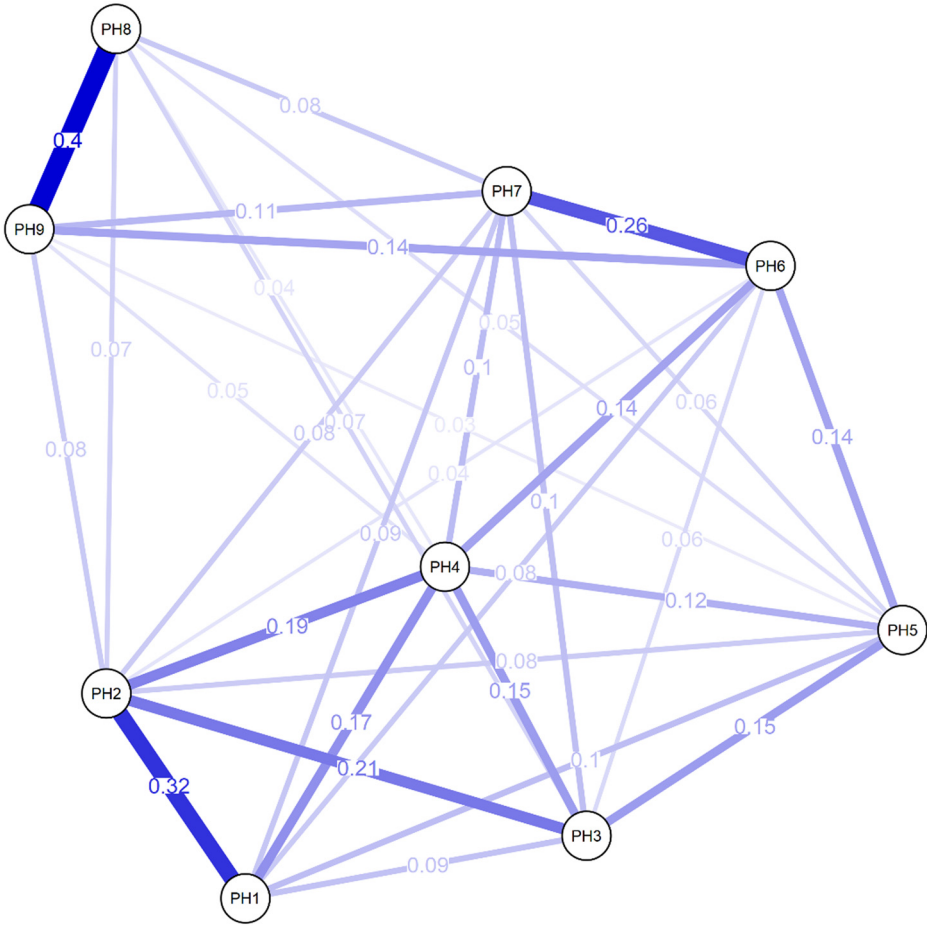


Figure 1. Network analysis of PHQ-9.

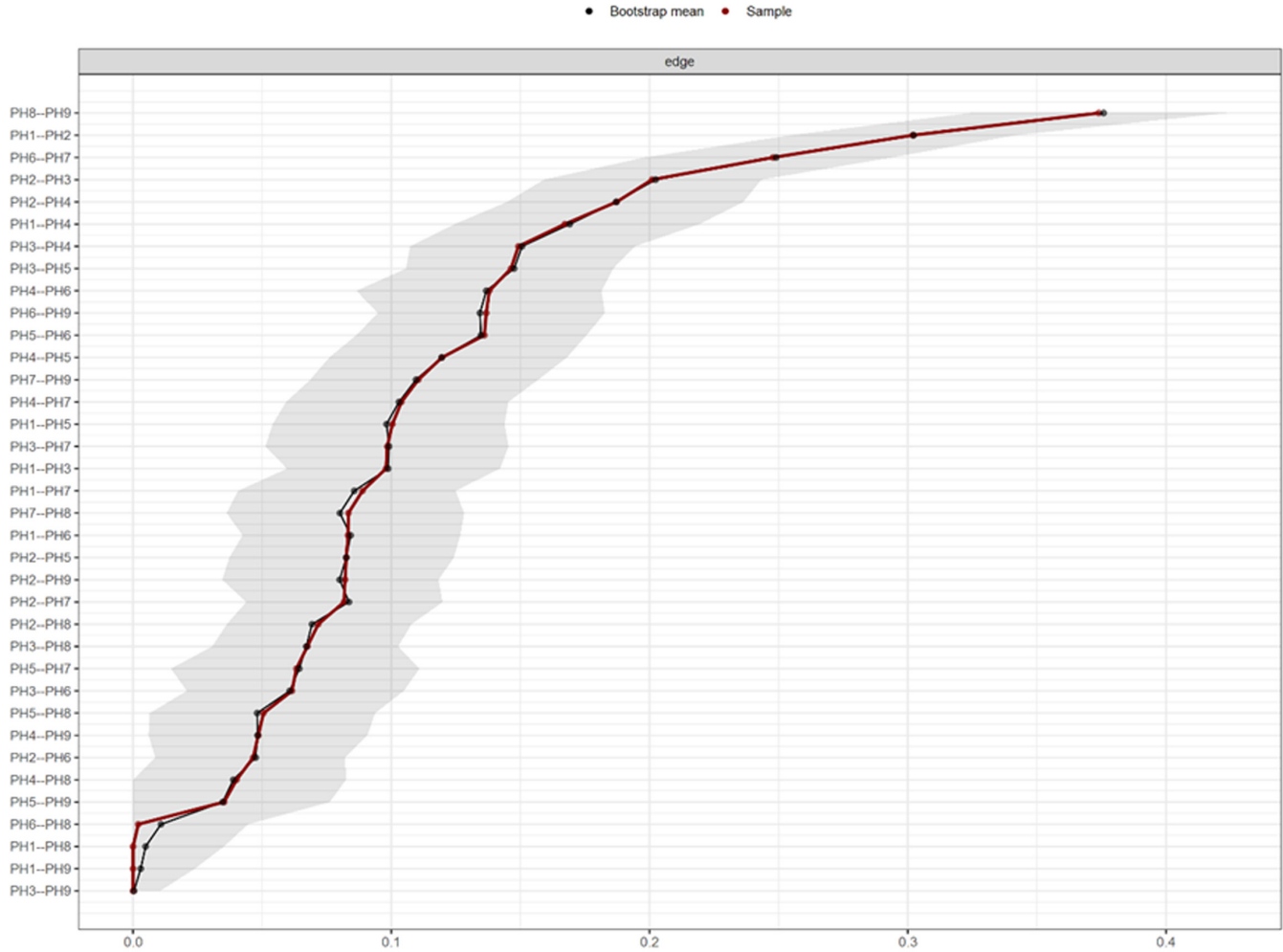


Figure 2. PHQ-9 network estimated border weight confidence intervals.

network analysis has not been performed on Spanish-speaking individuals with AH²⁰.

Bringmann *et al.*¹⁸ suggested the utilization of these measures with substantial care thus postulating 3 ways forward. The first is employing a novel centrality measure, the second was to employ and enhance the measures of importance that have been explicitly established for the statistical models which are utilized for the psychological network. The last is leaving the entire idea of centrality entirely behind. Lately, numerous investigators have similarly raised reservations concerning the utilization of centrality indices in psychological networks²¹⁻²⁴. The first limitation is that centrality indices were initially established for social networks which vary from psychological networks in imperative ways. Secondly, centrality indices particularly closeness and betweenness centrality have been demonstrated to be unbalanced in few cross-sectional and temporal networks^{23,25}. The third is that little study has been conducted on the predictive power of centrality indices²⁶. The researchers concluded that clinicians

may perhaps employ extremely central symptoms of cross-sectional networks but merely treating the utmost frequently conveyed symptoms would perhaps exert better²⁷.

Therefore, the importance of identifying the deduced components such as chronic pain, depression, bipolar, disorder, and cancer with a greater focus on evaluating would make it possible to strengthen clinical effectiveness for future interventions in patients diagnosed with AH. This would be considered only to highlight the strength of the node as the main centeredness index due to its stability¹⁶. In this sense, the results revealed that the elements with the most centrality are the items of “depressive mood” and “fatigue or energy loss”, this indication may suggest that these symptoms are probably more prevalent in adults diagnosed with AH. The results are consistent with the McWilliams *et al.*'s²⁸ network studies in a sample of patients with chronic pain, which indicated the importance of such symptoms. Other longitudinal network studies have also reinforced the centrality of the “depressed state” symptom^{26,29}.

Furthermore, a recent systematic study of psychopathological networks¹⁸ also reported transversal and longitudinal studies of depressive and anxious symptomatology, where the depressive mood symptom has greater network centrality. Therefore, health professionals may consider these symptoms as being in a negative emotional mood, they can also be indicators for resistance to clinical treatment³⁰.

The results agree with the network study by McWilliams *et al.*²⁸ in a sample of patients with chronic pain, which reported 4 symptoms with the highest centrality, where depressed mood and fatigue or loss of tiredness had the highest values. However, the authors indicate the relevance of two other symptoms, for example, loss of interest and concentration difficulties. These last two symptoms were not found in our study and a probable explanation is due to the type of population. The authors indicate that people who experience chronic pain are also less able to devote their attention to other activities or simply lose interest since it is difficult for them to concentrate while in pain²⁸. For this reason, in patients with chronic pain, it is even more likely to find more central symptoms due to the persistent pain that generates discomfort, compared to patients with HA who do not present this type of chronic pain.

These findings are similar to previous PHQ-9 network studies in cancer patients³¹, which indicate a greater centrality in reagent 4 (energy loss), which may suggest an indirect relationship of this symptom in people with an irreversible chronic disease.

Conclusions

In conclusion, the most central reagents in the network (2 and 4) with the most connections report a moderate relationship and are relatively close to the system. These network findings suggest possible routes of greater concentration and dynamism in the process of depressive symptomatology that at a higher level and prevalence, it is more likely to activate the interactive development of the various symptoms of PHQ-9, which may even lead to a depressive episode. Those reagents could have a more significant influence on the components with greater online covariance such as “Psychomotor issues,” “suicidal ideation,” and “anhedonia.” Therefore, the findings of this study will contribute to developing personalized treatments

aimed at patients with specific depressive symptoms who have also been diagnosed with AH.

However, the research has the following limitations; for example, the study is cross-sectional, which does not allow inference of whether a given node is caused or caused by another node to which it is connected, considering that they are non-directed networks. Another point is the selected small sample of a national survey, which also does not allow for generalization of the results to other patients with physical disorders. Another limitation is that the sample did not exclude people with other serious diseases that are usually associated with high blood pressure, and which could also be related to the appearance of depressive manifestations (for example stroke or chronic kidney disease).

Data availability

Underlying data

Zenodo: ENDES2019 Dataset with interpretation on depressive symptomatology in Peruvian adults with HTA. <http://doi.org/10.5281/zenodo.4384035>¹⁹.

This project contains the following underlying data:

- ENDES2019 Dataset With Code Interpretation.xlsx

Data are available under the terms of the [Creative Commons Attribution 4.0 International license \(CC-BY 4.0\)](#).

Consent

All informed consent was obtained for experimentation with human subjects. All the participation was utterly consensual, unspecified, and voluntary.

Author contributions

Cristian Antony Ramos-Vera: Conceptualization, Formal Analysis, Methodology, Validation, Visualization, Writing-Original Draft Preparation; **Jonatan Banos-Chaparro:** Data Curation, Investigation, Formal Analysis, Writing-Original Draft Preparation; **Roseline Oluwaseun Ogundokun:** Resource, Methodology, Supervision, Writing-Review, and Editing

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Rahul Shidhaye 

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Thank you for your response.

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 2

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Rahul Shidhaye 

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Thank you so much for your responses. In my understanding the findings of this study are not similar to those reported by McWilliams et al., who have reported that in addition to the depressed mood and tiredness/low energy, two other symptoms - loss of interest and trouble concentrating also have high centrality. This study reports higher centrality only for tiredness/low energy and depressed mood. Please clearly mention this in the discussion.

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 18 Nov 2021

Roseline Ogundokun, Landmark University Omu Aran, Omu Aran, Nigeria

The results agree with the network study by McWilliams et al. [28] in a sample of patients with chronic pain, which reported 4 symptoms with the highest centrality, where depressed mood and fatigue or loss of tiredness had the highest values. However, the authors indicate the relevance of two other symptoms, for example, loss of interest and concentration difficulties. These last two symptoms were not found in our study and a probable explanation is due to the type of population. The authors indicate that people who experience chronic pain are also less able to devote their attention to other activities or simply lose interest since it is difficult for them to concentrate while in pain [28]. For this reason, in patients with chronic pain, it is even more likely to find more central symptoms due to the persistent pain that generates discomfort, compared to patients with HA who do not present this type of chronic pain.

Competing Interests: No competing interests are disclosed in this article.

Author Response 10 Mar 2022

Roseline Ogundokun, Landmark University Omu Aran, Omu Aran, Nigeria

This is the response to your concern and it has been added in the discussion section as suggested by you.

"The results agree with the network study by McWilliams et al. [28] in a sample of patients with chronic pain, which reported 4 symptoms with the highest centrality, where depressed mood and fatigue or loss of tiredness had the highest values. However, the authors indicate the relevance of two other symptoms, for example, loss of interest and concentration difficulties. These last two symptoms were not found in our study and a probable explanation is due to the type of population. The authors indicate that people who experience chronic pain are also less able to devote their attention to other activities or simply lose interest since it is difficult for them to concentrate while in pain [28]. For this reason, in patients with chronic pain, it is even more likely to find more central symptoms due to the persistent pain that generates discomfort, compared to patients with HA who do not present this type of chronic pain".

Competing Interests: No competing interests were disclosed.

Reviewer Report 09 April 2021

<https://doi.org/10.5256/f1000research.55636.r82482>

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Santiago Stucchi-Portocarrero 

Hospital Víctor Larco Herrera, Universidad Peruana Cayetano Heredia, Magdalena del Mar, Peru

I think that "over the age of 17" is not very clear. Maybe it would be better "18 years and older". The authors still mentioned "Pulmonary arterial hypertension (PAH)" in the discussion, although it is not mentioned in the rest of the article.

Finally, I still believe that the authors should better explain how the results of the study can lead to personalized treatments.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Clinical psychiatry, suicide, psychopharmacology, history of psychiatry

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

Reviewer Report 01 March 2021

<https://doi.org/10.5256/f1000research.30303.r78628>

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Rahul Shidhaye 

Pravara Institute of Medical Sciences, Loni, India

Rachana Parikh

PATH, New Delhi, Delhi, India

In this paper, Cristian Ramos-Vera and colleagues present the findings of network analysis of symptoms of depression in adults with arterial hypertension in Peru. This is a secondary data analysis of a nationally representative survey: ENDES 2019. Very few studies have applied network analysis in the field of mood disorders, especially for co-morbid depression¹. This is quite a unique study for which we would like to congratulate the authors. However, there are some issues related to methodology, presentation of results, and discussion of limitations which need to be addressed by the authors.

[Abstract](#)

1. Background: The first word should be edited to “Globally, arterial hypertension...” instead of “Global arterial hypertension...”. The salience of depression as a comorbidity among people with arterial hypertension needs to be highlighted. Please mention the rationale for using network analysis.
2. Methods: The authors need to clarify the sample included in the study, particularly that: 1) it is a sub-sample (people with arterial hypertension) from the ENDES 2019 dataset, 2) clarify if only those who had ‘complete PHQ-9 questionnaires’ were included.
3. Results: The authors have used terms such as bridging force/ bridge centrality, closeness, and intermediation in the abstract, which are different from the corresponding terms in the manuscript. The authors need to use uniform and standard terminology throughout the paper. These results need to also include the corresponding coefficients for the results.
4. Conclusion: The conclusion reads like results. The interpretation of the results and its implications should be included.

Introduction

1. The authors need to describe how common is depression among people with a diagnosis of arterial hypertension in this section.
2. The appropriate abbreviation for Arterial Hypertension would be AHT or AH. It is not clear why HTA is used.
3. Referring to the sentence - “This increase is due to... such as food” - the type of food needs to be included to suggest poor eating habits.
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4. Referring to the sentence - “There is also evidence that patients with HTA have a higher incidence of emotional disorders” - please include how much higher and include appropriate reference.
5. In the same sentence “... mainly depressive symptomatology (anxiety or stress)” - the use of parenthesis is confusing. Perhaps the authors mean “...depressive symptomatology, anxiety and stress”.
6. The sentence “Ignoring negative emotions may result in physical disorders.” - This requires appropriate citation and some further explanation.
7. The rationale for undertaking network analysis and the need to explore network dynamics for symptoms of depression in individuals with hypertension needs to be clearly explained.
8. In the last paragraph of the introduction, the terms used are ‘interactions’ and ‘bridges of connections,’ which are different than the terms used in the abstract earlier and the methods section later (refer to comment # 3 in the section on abstract). As this is a new field, it is important to clearly define the key terms preferably using a box.

Methods

1. Brief information about ENDES dataset, including the disorders screened/diagnosed for the

sample, particularly how mental health problems were screened/diagnosed need to be described. Please provide the reference for this study as well.

2. The sentence describing the sampling, "On the other hand, in urban areas... with the Health questionnaire" is confusing. Perhaps a full stop was meant to be included before "from 36,760 sampled households,".
3. The authors might have missed to add "did not" in the sentence, "Exclusion criteria were those who (did not) meet the diagnostic criteria for hypertension, or did not report any blood pressure measurements, or who omitted any PHQ-9 questions."
4. Please provide the flow chart for sample selection. It is particularly important to provide the details regarding the differences between those included and excluded in the analysis. The details related to socio-demographic indicators, severity of hypertension and PHQ-9 scores should at least be included.
5. Missing data should be reported, and especially how it was handled should be described, along with how this is likely to influence the results, if at all.
6. The commonly used term to describe the connection between nodes is 'edges.'¹ It is not clear why the authors have used the term 'border.'
7. Bringmann et al. have used the terms degree and strength centrality, betweenness and closeness centrality to describe centrality indices. Authors have cited this paper (reference # 12)². Please clarify why the terms force, proximity, and intermediation are used by the authors while they cite the above-mentioned paper.

Results

1. For a network with 9 nodes, the possible number of edges is $(n*(n-1))/2$, i.e., $(9*8)/2=36$. Not clear why it is mentioned '32 possible edges.'
2. It is desirable to have a table which includes PHQ-9 scores for the sample, mean with standard deviation, and proportion of sample that is moderately/severely depressed. This could be disaggregated by age, sex, hypertension, socio-economic status and other independent variables.
3. Please provide partial correlation matrix for all PHQ-9 items.
4. The findings related to only strength centrality are presented in table 1. Please also include the findings pertaining to betweenness and closeness centrality.
5. Please clarify the meaning of negative sign in strength column.
6. Please consider presenting the findings separately for those without depression and those with depression (PHQ-9>5). Similarly present the findings disaggregated by sex and severity of depression.
7. Please explain non-inclusion of socio-demographic factors and hypertension in the network

analysis. Factors others than the symptoms of depression are included in the analysis to see how they influence each other.

8. Is it possible to present predictability analysis as suggested by Contreras et al.¹

Discussion and Conclusion

1. Greater centrality for PHQ-6 needs to be further discussed. PHQ-8 and PHQ-9 are clinically very significant but have low centrality measures. This also needs to be discussed.
2. It will be good to discuss the findings related to various centrality indices in detail.
3. The discussion could benefit from including more critical analysis of how their findings differ from other studies and the implications, therefore. For e.g., McWilliams et al (ref 15 in the paper) found that in addition to the depressed mood and tiredness/low energy, two other symptoms - loss of interest and trouble concentrating also have high centrality, which is in contrast with the authors findings. The discussion could explore potential reasons for this and implications.
4. The first paragraph of conclusion appears to fit better with the discussion section.
5. The authors should elaborate and include reference for the statement, "Those reagents could have a more significant influence on the components with greater online covariance such as "Psychomotor issues," "suicidal ideation," and "anhedonia."
6. Referring to sentence, "Therefore, the results will contribute to... have also been diagnosed with HTA." This statement needs to re-phrased for better readability.
7. There are several issues related to use to centrality indices and are discussed in detail by Bringmann et al. They have recommended to use these measures with considerable care. Authors need to include a paragraph to discuss this and highlight the limitation of using centrality indices.
8. It will be desirable to provide R Script as an appendix. This will ensure the reproducibility of the results.

References

1. Contreras A, Nieto I, Valiente C, Espinosa R, et al.: The Study of Psychopathology from the Network Analysis Perspective: A Systematic Review. *Psychother Psychosom.* 2019; **88** (2): 71-83 [PubMed Abstract](#) | [Publisher Full Text](#)
2. Bringmann LF, Elmer T, Epskamp S, Krause RW, et al.: What do centrality measures measure in psychological networks?. *J Abnorm Psychol.* 2019; **128** (8): 892-903 [PubMed Abstract](#) | [Publisher Full Text](#)

Is the work clearly and accurately presented and does it cite the current literature?

Partly

Is the study design appropriate and is the work technically sound?

Partly

Are sufficient details of methods and analysis provided to allow replication by others?

Partly

If applicable, is the statistical analysis and its interpretation appropriate?

Partly

Are all the source data underlying the results available to ensure full reproducibility?

Partly

Are the conclusions drawn adequately supported by the results?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Rahul Shidhaye: Epidemiology, public mental health, depression, health services research Rachana Parikh: Global Mental Health, Adolescent Health, Epidemiology, Health Systems research.

We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however we have significant reservations, as outlined above.

Author Response 22 Mar 2021

Roseline Ogundokun, Landmark University Omu Aran, Omu Aran, Nigeria

Title. The authors describe the population studied as "Peruvian adults". However, the sample used included 17-year-olds, and in Peru only those over 18 are considered adults.

Response: It was stated in the article that more than 17years of age which means from 18years and above

Introduction. "HTA" is the acronym for *hipertensión arterial* (arterial hypertension in Spanish); it is not applicable in an article published in English. On the other hand, the relationship between depression and arterial hypertension is described; however, it is necessary to analyze other possibilities. For example, depression and chronic anxiety are considered risk factors for the development of high blood pressure, and emotional disturbances might be the adverse effect of some antihypertensive medications.

Response: The comment has been attended to.

Methods. It should be mentioned that there is a validation of PHQ-9 for the Peruvian population, which was done precisely from ENDES 2019 1 Also, there is an obvious error in the following sentence: "Exclusion criteria were those who met the diagnostic criteria for hypertension."

Response: The comment has been attended to.

Discussion. The authors mentioned that “this research aimed to explore the dynamics of depression symptoms in adults having Pulmonary arterial hypertension (PAH).” However, in the rest of the article only arterial hypertension is mentioned, without further specification.

Response: The comment has been attended to.

Conclusions. It should be mentioned, as a limitation, that the sample did not exclude people with other serious diseases that are usually associated with high blood pressure, and which could also be related to the appearance of depressive manifestations (for example: stroke or chronic kidney disease). Finally, it is not clear how the results of the study can lead to personalized treatments; this part should be better explained by the authors.

Response: The comment has been attended to.

Competing Interests: No competing interests were disclosed.

Reviewer Report 12 February 2021

<https://doi.org/10.5256/f1000research.30303.r78631>

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Santiago Stucchi-Portocarrero 

Hospital Víctor Larco Herrera, Universidad Peruana Cayetano Heredia, Magdalena del Mar, Peru

Title. The authors describe the population studied as “Peruvian adults”. However, the sample used included 17 year olds, and in Peru only those over 18 are considered adults.

Introduction. “HTA” is the acronym for *hipertensión arterial* (arterial hypertension in Spanish); it is not applicable in an article published in English. On the other hand, the relationship between depression and arterial hypertension is described; however, it is necessary to analyze other possibilities. For example, depression and chronic anxiety are considered risk factors for the development of high blood pressure, and emotional disturbances might be the adverse effect of some antihypertensive medications.

Methods. It should be mentioned that there is a validation of PHQ-9 for the Peruvian population, which was done precisely from ENDES 2019 ¹ Also, there is an obvious error in the following sentence: “Exclusion criteria were those who met the diagnostic criteria for hypertension.”
Discussion. The authors mentioned that “this research aimed to explore the dynamics of

depression symptoms in adults having Pulmonary arterial hypertension (PAH).” However, in the rest of the article only arterial hypertension is mentioned, without further specification.

Conclusions. It should be mentioned, as a limitation, that the sample did not exclude people with other serious diseases that are usually associated with high blood pressure, and which could also be related to the appearance of depressive manifestations (for example: stroke or chronic kidney disease). Finally, it is not clear how the results of the study can lead to personalized treatments; this part should be better explained by the authors.

References

1. Villarreal-Zegarra D, Copez-Lonzoy A, Bernabé-Ortiz A, Melendez-Torres GJ, et al.: Valid group comparisons can be made with the Patient Health Questionnaire (PHQ-9): A measurement invariance study across groups by demographic characteristics. *PLoS One*. 2019; **14** (9): e0221717
[PubMed Abstract](#) | [Publisher Full Text](#)

Is the work clearly and accurately presented and does it cite the current literature?

Partly

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

I cannot comment. A qualified statistician is required.

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Clinical psychiatry, suicide, psychopharmacology, history of psychiatry.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 22 Mar 2021

Roseline Ogunokun, Landmark University Omu Aran, Omu Aran, Nigeria

Abstract

Background: The first word should be edited to “Globally, arterial hypertension...” instead of

“Global arterial hypertension...”. The salience of depression as a comorbidity among people with arterial hypertension needs to be highlighted. Please mention the rationale for using network analysis.

Response: The comment has been attended to

Methods: The authors need to clarify the sample included in the study, particularly that: it is a sub-sample (people with arterial hypertension) from the ENDES 2019 dataset.

Response: This has been discussed in the article

clarify if only those who had ‘complete PHQ-9 questionnaires’ were included.

Response: This has been discussed in the article

Response: The comment has been attended to

Results: The authors have used terms such as bridging force/ bridge centrality, closeness, and intermediation in the abstract, which are different from the corresponding terms in the manuscript. The authors need to use uniform and standard terminology throughout the paper. These results need to also include the corresponding coefficients for the results.

Response: The comment has been attended to

Conclusion: The conclusion reads like results. The interpretation of the results and its implications should be included.

Response: The comment has been attended to

Introduction

The authors need to describe how common is depression among people with a diagnosis of arterial hypertension in this section.

Response: The comment has been attended to

The appropriate abbreviation for Arterial Hypertension would be AHT or AH. It is not clear why HTA is used.

Response: The comment has been attended to

Referring to the sentence - “This increase is due to... such as food” - the type of food needs to be included to suggest poor eating habits.

Response: The comment has been attended to

Referring to the sentence - “There is also evidence that patients with HTA have a higher incidence of emotional disorders” - please include how much higher and include

appropriate reference.

Response: The comment has been attended to

In the same sentence "... mainly depressive symptomatology (anxiety or stress)" – the use of parenthesis is confusing. Perhaps the authors mean "...depressive symptomatology, anxiety and stress".

Response: The comment has been attended to

The sentence "Ignoring negative emotions may result in physical disorders." – This requires appropriate citation and some further explanation.

Response: The comment has been attended to

The rationale for undertaking network analysis and the need to explore network dynamics for symptoms of depression in individuals with hypertension needs to be clearly explained.

Response: The comment has been attended to

In the last paragraph of the introduction, the terms used are 'interactions' and 'bridges of connections,' which are different than the terms used in the abstract earlier and the methods section later (refer to comment # 3 in the section on abstract). As this is a new field, it is important to clearly define the key terms preferably using a box.

Response: The comment has been attended to

Methods

Brief information about ENDES dataset, including the disorders screened/diagnosed for the sample, particularly how mental health problems were screened/diagnosed need to be described. Please provide the reference for this study as well.

Response: The comment has been attended to. This has been described in the article and no mental health diagnosis was made. Only those who completed all the PHQ-9 were included.

The sentence describing the sampling, "On the other hand, in urban areas... with the Health questionnaire" is confusing. Perhaps a full stop was meant to be included before "from 36,760 sampled households,".

Response: The comment has been attended to

The authors might have missed to add "did not" in the sentence, "Exclusion criteria were those who (did not) meet the diagnostic criteria for hypertension, or did not report any blood pressure measurements, or who omitted any PHQ-9 questions.

Response: The comment has been attended to

Please provide the flow chart for sample selection. It is particularly important to provide the details regarding the differences between those included and excluded in the analysis. The details related to socio-demographic indicators, severity of hypertension and PHQ-9 scores should at least be included.

Response: This Has Nothing to do with the study objective and reference was already made to the inclusion and exclusion factors

Missing data should be reported, and especially how it was handled should be described, along with how this is likely to influence the results, if at all. The commonly used term to describe the connection between nodes is 'edges.'¹ It is not clear why the authors have used the term 'border.'

Response: The missing data did not influence the results, because they were only not reported in relation to the language and grade of studies, whose variables are not in the network analysis.

Bringmann et al. have used the terms degree and strength centrality, betweenness and closeness centrality to describe centrality indices. Authors have cited this paper (reference # 12)². Please clarify why the terms force, proximity, and intermediation are used by the authors while they cite the above-mentioned paper.

Response: The comment has been attended to

Results

For a network with 9 nodes, the possible number of edges is $(n*(n-1))/2$, i.e., $(9*8)/2=36$. Not clear why it is mentioned '32 possible edges.'

Response: The comment has been attended to. This has been corrected to 36 nodes

It is desirable to have a table which includes PHQ-9 scores for the sample, mean with standard deviation, and proportion of sample that is moderately/severely depressed. This could be disaggregated by age, sex, hypertension, socio-economic status and other independent variables.

Response: The analysis does not have sociodemographic purposes for which it is not considered

Please provide partial correlation matrix for all PHQ-9 items.

Response: This is provided in the article already

The findings related to only strength centrality are presented in table 1. Please also include the findings pertaining to betweenness and closeness centrality.

Response: Reference was made on the use of the only measure that reports greater stability, the others do not allow accurate interpretations, especially with high sample data

Please clarify the meaning of negative sign in strength column.

Response: refers to a negative force

Please consider presenting the findings separately for those without depression and those with depression (PHQ-9>5). Similarly present the findings disaggregated by sex and severity of depression.

Response: The purpose was to evaluate according to the total sample, performing by different categorical variables generates a complexity of different results that do not support the study objective, which, according to the sample size, allows generalizing the symptomatology hypersensitive positivity in priority.

Please explain non-inclusion of socio-demographic factors and hypertension in the network analysis. Factor's others than the symptoms of depression are included in the analysis to see how they influence each other.

Response: The comment has been attended to

Is it possible to present predictability analysis as suggested by Contreras et al.1

Response: This is not possible because it requires Longitudinal Data

Discussion and Conclusion

Greater centrality for PHQ-6 needs to be further discussed. PHQ-8 and PHQ-9 are clinically very significant but have low centrality measures. This also needs to be discussed.

Response: The comment has been attended to.

It will be good to discuss the findings related to various centrality indices in detail.

Response: This was already specified the inclusion of the centrality measures of greatest implication in psychological networks, which must be considered the centrality of force because of its stability.

The discussion could benefit from including more critical analysis of how their findings differ from other studies and the implications, therefore. For e.g., McWilliams et al (ref 15 in the paper) found that in addition to the depressed mood and tiredness/low energy, two other symptoms - loss of interest and trouble concentrating also have high centrality, which is in contrast with the authors findings. The discussion could explore potential reasons for this and implications.

Response: The comment has been attended to.

The first paragraph of conclusion appears to fit better with the discussion section.

Response: The comment has been attended to.

The authors should elaborate and include reference for the statement, "Those reagents could have a more significant influence on the components with greater online covariance such as "Psychomotor issues," "suicidal ideation," and "anhedonia."

Response: The comment has been attended to.

Referring to sentence, "Therefore, the results will contribute to... have also been diagnosed with HTA." This statement needs to be re-phrased for better readability.

Response: The comment has been attended to.

There are several issues related to use of centrality indices and are discussed in detail by Bringmann et al. They have recommended to use these measures with considerable care. Authors need to include a paragraph to discuss this and highlight the limitation of using centrality indices.

Response: This is already explained in the article

It will be desirable to provide R Script as an appendix. This will ensure the reproducibility of the results.

Response: It is not possible because it is part of another study in progress

Competing Interests: No competing interests were disclosed.

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