PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Contextual and individual inequalities of multimorbidity in Brazilian adults: a cross-sectional national-based study
AUTHORS	Nunes, BP; Chiavegatto Filho, Alexandre; Pati, Sanghamitra; Teixeira, Doralice; Flores, Thaynã; Camargo-Figuera, Fabio Alberto; Munhoz, Tiago; Thume, Elaine; Facchini, Luiz; Batista, Sandro Rogerio

VERSION 1 - REVIEW

REVIEWER	José Almirall Université de Sherbrooke, Canada.
REVIEW RETURNED	31-Jan-2017

GENERAL COMMENTS	This is a timely article that brings new information about the increasing health problem of multiple chronic diseases in Brazil. To my knowledge, this is the first nationwide study on this subject in that country. Based on data from the Brazilian National Health Survey, with a sample representative of people living in permanent housing, the study is backed by solid data collection. Due to the characteristics of this study, its results may contribute “to design interventions/public policies” (page 14, line 265), and hence its importance. However, I am concerned with some paradoxical results that might convey a misleading message. Previous publications have consistently reported that socioeconomic status (SES) is negatively associated with the prevalence of multimorbidity, regardless of whether SES is measured through education, income, occupation, or area-based deprivation. I am aware of only one study in which the contrary was reported. It was a study in which self-reported multimorbidity was associated with slightly higher household income per head in China (Wang, Wang et al. 2014). The authors of that study recognized that the finding seemed a paradox; they provided some plausible explanations and concluded that further work was necessary to clarify this. In the present study, the occurrence of multimorbidity was higher among those who had less schooling, as expected. However, paradoxically, individuals living in states with low levels of education had less multimorbidity than those living in states with high educational level. On the other hand, there was no relationship between multimorbidity frequency and asset ownership. Furthermore, the adjusted models showed that subjects in the second and third wealthiest quintiles had greater odds of multimorbidity. These findings are at variance with those reported by the same authors in a study in a Southern Brazilian city in which, as expected, multimorbidity was greater among subjects from lower socioeconomic classes (Nunes, Camargo-Figuera et al. 2016). I think that the authors should make more efforts (that might include

	data analysis) to try to explain the unexpected results. For example, just to give an idea, without demanding the authors to do it, the same nationwide analyses made in this study could be applied to the sample split in two groups; one group with the states included in the North and Northeast regions that show the poorest health indicators and concentrate subjects with low income and low education, an another group with the states found in the center-west, southeast, and south regions where the SES of the population is higher. If this study might contribute to designing interventions/public policies, I think that it is necessary to say that there are results that need to be clarified with further work. Particular aspects Introduction Page 4, line 67, it says "…multiple disease is more frequent in adults with less schooling and the elderly." I suggest adding lower socioeconomic status. Results Table 4. COPD is one of the morbidities in the Table. However, it is not among the morbidities listed in the Methods section. Schizophrenia and Obsessive Compulsive Disorder are not among the variables excluded for evaluation of the models (page 6, lines124-125) and they are not in the Table. Discussion Page 12, lines 218-219: in my opinion, the sentence "The Southern states presented more income and schooling which tend to increase the burden of multimorbidity as observed in the results presented here" conveys a misleading message. The results of the study showed that more income and schooling increased the frequency of finding or diagnosing self-reported multimorbidity at state-level analyses, but not the burden of multimorbidity. The burden of multimorbidity represents the suffering and limitations imposed by the varying degrees of severity of the concomitant conditions, diagnosed or not, affecting an individual. The number of self-reported diagnoses is frequently used as a proxy of disease burden but it does not inform about disease severity and limitations. Page 12, line 223-224, it says "Older adults show more exposure to events, including unhealthy ones…" Please, explain the events, including unhealthy events, and provide a reference. Page 12, lines 233-234, "Having private health plans was associated with multimorbidity and its factors…role of health plans as a socioeconomic indicator…" If having private health plans is accepted as a socioeconomic indicator, it should be discussed that the association with multimorbidity in this study is not the expected one. We know from the Results section that Cardiometabolic and Respiratory/mental/muscle-skeletal factors were greater when state-level education and income were lower. These results were not discussed. The absence of an association between multimorbidity and wealth

	quintiles was not discussed. A possible explanation to the state level paradoxical association with multimorbidity was discussed in only three lines (page 13, lines 246-248) and was attributed to not fully adjusted models. This discussion should be expanded. References Nunes, B. P., F. A. Camargo-Figuera, M. Guttier, P. D. de Oliveira, T. N. Munhoz, A. Matijasevich, A. D. Bertoldi, F. C. Wehrmeister, M. P. Silveira, E. Thume and L. A. Facchini (2016). "Multimorbidity in adults from a southern Brazilian city: occurrence and patterns." Int J Public Health. Wang, H., J. Wang, S. Wong, M. Wong, F. Li, P. Wang, Z. Zhou, C. Zhu, S. M. Griffiths and S. W. Mercer (2014). "Epidemiology of multimorbidity in China and implications for the healthcare system: cross-sectional survey among 162,464 community household residents in southern China." BMC Med 12(1): 188.

REVIEWER	Clara Dismuke US Department of Veterans Affairs United States
REVIEW RETURNED	24-Feb-2017

GENERAL COMMENTS	Well written and interesting study. I would love to know more about those who live in the Amazon region relative to other Brazilians.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
José Almirall
Université de Sherbrooke, Canada.
Please state any competing interests or state ‘None declared’: None declared
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Please leave your comments for the authors below This is a timely article that brings new information about the increasing health problem of multiple chronic diseases in Brazil. To my knowledge, this is the first nationwide study on this subject in that country. Based on data from the Brazilian National Health Survey, with a sample representative of people living in permanent housing, the study is backed by solid data collection.

Response to the reviewer comment: Thank you for the comment. Since our article’s submission (January 6, 2017), a Brazilian multimorbidity paper using the same database was published in February 9, 2017 (http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0171813). This is possible due to public availability of PNS microdata. We include the paper on the references and stated in the introduction the differences regarding our manuscript.

Due to the characteristics of this study, its results may contribute “to design interventions/public policies” (page 14, line 265), and hence its importance. However, I am concerned with some paradoxical results that might convey a misleading message.
Previous publications have consistently reported that socioeconomic status (SES) is negatively associated with the prevalence of multimorbidity, regardless of whether SES is measured through education, income, occupation, or area-based deprivation. I am aware of only one study in which the contrary was reported. It was a study in which self-reported multimorbidity was associated with slightly

higher household income per head in China (Wang, Wang et al. 2014). The authors of that study recognized that the finding seemed a paradox; they provided some plausible explanations and concluded that further work was necessary to clarify this.
In the present study, the occurrence of multimorbidity was higher among those who had less schooling, as expected. However, paradoxically, individuals living in states with low levels of education had less multimorbidity than those living in states with high educational level. On the other hand, there was no relationship between multimorbidity frequency and asset ownership. Furthermore, the adjusted models showed that subjects in the second and third wealthiest quintiles had greater odds of multimorbidity.
These findings are at variance with those reported by the same authors in a study in a Southern Brazilian city in which, as expected, multimorbidity was greater among subjects from lower socioeconomic classes (Nunes, Camargo-Figuera et al. 2016). I think that the authors should make more efforts (that might include data analysis) to try to explain the unexpected results. For example, just to give an idea, without demanding the authors to do it, the same nationwide analyses made in this study could be applied to the sample split in two groups; one group with the states included in the North and Northeast regions that show the poorest health indicators and concentrate subjects with low income and low education, an another group with the states found in the center-west, southeast, and south regions where the SES of the population is higher.
If this study might contribute to designing interventions/public policies, I think that it is necessary to say that there are results that need to be clarified with further work.

Response to the reviewer comment: Thank you for the comment. We performed more detailed analysis to account the suggestions. More arguments were included in the discussion section.

Particular aspects

Introduction
Page 4, line 67, it says "…multiple disease is more frequent in adults with less schooling and the elderly." I suggest adding lower socioeconomic status.

Response to the reviewer comment: Thank you for the comment. We changed the sentence as suggested.

Results
Table 4. COPD is one of the morbidities in the Table. However, it is not among the morbidities listed in the Methods section.
Schizophrenia and Obsessive Compulsive Disorder are not among the variables excluded for evaluation of the models (page 6, lines124-125) and they are not in the Table.

Response to the reviewer comment: Thank you for the comment. For factor analysis, we encompassed some diseases to better model fit. We corrected the paragraph in methods section.

Discussion
Page 12, lines 218-219: in my opinion, the sentence "The Southern states presented more income and schooling which tend to increase the burden of multimorbidity as observed in the results presented here" conveys a misleading message. The results of the study showed that more income and schooling increased the frequency of finding or diagnosing self-reported multimorbidity at state-level analyses, but not the burden of multimorbidity. The burden of multimorbidity represents the suffering and limitations imposed by the varying degrees of severity of the concomitant conditions,

diagnosed or not, affecting an individual. The number of self-reported diagnoses is frequently used as a proxy of disease burden but it does not inform about disease severity and limitations.

Response to the reviewer comment: Thank you for the comment. We agree and corrected the sentence.

Page 12, line 223-224, it says “Older adults show more exposure to events, including unhealthy ones…” Please, explain the events, including unhealthy events, and provide a reference.

Response to the reviewer comment: Thank you for the comment. We provided a misleading message. Our arguments were to be related to more lifetime exposed to multimorbidity risk factors. We corrected the sentence and provided a reference.

Page 12, lines 233-234, “Having private health plans was associated with multimorbidity and its factors…role of health plans as a socioeconomic indicator…” If having private health plans is accepted as a socioeconomic indicator, it should be discussed that the association with multimorbidity in this study is not the expected one.

Response to the reviewer comment: Thank you for the comment. Theoretically this association would be expected because those who have private health plan may have more access to health services. Those who have more access will have a higher prevalence of multimorbidity. The explanation of health plan as socioeconomic indicator was excluded.

We know from the Results section that Cardiometabolic and Respiratory/mental/muscle-skeletal factors were greater when state-level education and income were lower. These results were not discussed.

Response to the reviewer comment: Many thanks for the comment. These results follow the same pattern of overall multimorbidity. It is included in the discussion section.

The absence of an association between multimorbidity and wealth quintiles was not discussed. A possible explanation to the state level paradoxical association with multimorbidity was discussed in only three lines (page 13, lines 246-248) and was attributed to not fully adjusted models. This discussion should be expanded.

Response to the reviewer comment: Thank you for the comment. The explanation was increased through more detailed concerns about role of education and wealth index.

References

Nunes, B. P., F. A. Camargo-Figuera, M. Guttier, P. D. de Oliveira, T. N. Munhoz, A. Matijasevich, A. D. Bertoldi, F. C. Wehrmeister, M. P. Silveira, E. Thume and L. A. Facchini (2016). "Multimorbidity in adults from a southern Brazilian city: occurrence and patterns." Int J Public Health.

Wang, H., J. Wang, S. Wong, M. Wong, F. Li, P. Wang, Z. Zhou, C. Zhu, S. M. Griffiths and S. W. Mercer (2014). "Epidemiology of multimorbidity in China and implications for the healthcare system: cross-sectional survey among 162,464 community household residents in southern China." BMC Med 12(1): 188.

Reviewer: 2

Clara Dismuke

US Department of Veterans Affairs, United States Please state any competing interests or state ‘None

declared': none declared

Please leave your comments for the authors below Well written and interesting study. I would love to know more about those who live in the Amazon region relative to other Brazilians.

Response to the reviewer comment: Thank you for the comment. An additional figure was included with the requested analyzes showing that Amazon region presented lower multimorbidity frequency compared to other Brazilian states.

VERSION 2 – REVIEW

REVIEWER	José Almirall Université de Sherbrooke, Canada.
REVIEW RETURNED	18-Apr-2017

GENERAL COMMENTS	Reviewer: José Almirall Manuscript (new title): Contextual and individual inequalities of multimorbidity in Brazilian adults: a cross-sectional national-based study. I think that the manuscript has greatly improved from its first version. However, I would like to make the authors aware of a few issues. Abstract: in lines 39 and 40, the authors still use the names "asset ownership" and "ownership quintiles" which they have substituted by "wealth index" and "wealth quintiles" in the article. Introduction: in lines 67 and 68 the word "elderly" is used twice in the same sentence. Discussion: Lines 240-242: the sentence "The Southern states presented more income and schooling which tend to increase the occurrence of multimorbidity as observed in the results presented here" was modified. However, I think that it is still confusing. The sentence, which refers only to the Southern states, should stop after "multimorbidity", because the expression "as observed in the results presented here" can be interpreted as the general results of the study, and it is a contradiction with other results. It is shown in the results of this study and is discussed in lines 258 to 262 the negative relationship between education and health. The authors even propose education level "as a more adequate socioeconomic indicator to evaluate multimorbidity." The unexpected observation in the Southern states that schooling tends to increase the occurrence of multimorbidity is at variance with other results in this study and with other published studies. The newly introduced reference 12 of a recent paper analyzing the same Brazilian database is briefly discussed in lines 233-234. The authors of that study (reference 12) also performed a factor analysis that was not discussed in this paper.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1
José Almirall
Université de Sherbrooke, Canada.
Please state any competing interests or state 'None declared': None declared
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Please leave your comments for the authors below

Manuscript (new title): Contextual and individual inequalities of multimorbidity in Brazilian adults: a cross-sectional national-based study.

I think that the manuscript has greatly improved from its first version. However, I would like to make the authors aware of a few issues.

Abstract: in lines 39 and 40, the authors still use the names "asset ownership" and "ownership quintiles" which they have substituted by "wealth index" and "wealth quintiles" in the article.

Response to reviewer comment: Thank you for the comment. We changed the terms as suggested.

Introduction: in lines 67 and 68 the word "elderly" is used twice in the same sentence.

Response to reviewer comment: Thank you for the comment. We exclude the repeated words.

Discussion:

Lines 240-242: the sentence "The Southern states presented more income and schooling which tend to increase the occurrence of multimorbidity as observed in the results presented here" was modified. However, I think that it is still confusing. The sentence, which refers only to the Southern states, should stop after "multimorbidity", because the expression "as observed in the results presented here" can be interpreted as the general results of the study, and it is a contradiction with other results. It is shown in the results of this study and is discussed in lines 258 to 262 the negative relationship between education and health. The authors even propose education level "as a more adequate socioeconomic indicator to evaluate multimorbidity." The unexpected observation in the Southern states that schooling tends to increase the occurrence of multimorbidity is at variance with other results in this study and with other published studies.

Response to reviewer comment: Thank you for the comment. We agreed with the reviewer that these arguments should be improved. We exclude part of the sentence as suggested. Furthermore, we tried to highlight in the discussion section that associations with education are different between state and individual-level. At state-level, more education level is related to more development and life expectancy which contribute (among other causes) to more proportion of older adults and multimorbidity. We provided a reference in this sentence.

The newly introduced reference 12 of a recent paper analyzing the same Brazilian database is briefly discussed in lines 233-234. The authors of that study (reference 12) also performed a factor analysis that was not discussed in this paper.

Response to reviewer comment: Thank you for the comment. We included the difference between factor analysis and increased the arguments related to the sentences.

VERSION 3 – REVIEW

REVIEWER	José Almirall Université de Sherbrooke, Canada.
REVIEW RETURNED	25-Apr-2017

GENERAL COMMENTS	I have no more comments. The authors have been receptive to the suggestions intended to enhance the quality of their paper.

Correction: *Contextual and individual inequalities of multimorbidity in Brazilian adults: a cross-sectional national-based study*

Nunes BP, Chiavegatto Filho ADP, Pati S, *et al*. Contextual and individual inequalities of multimorbidity in Brazilian adults: a cross-sectional national-based study. *BMJ Open* 2017;7:e015885. doi: 10.1136/bmjopen-2017-015885.

This article was previously published with some errors.

In table 1 and supplementary table 1, the percentages of the descriptive analyses, no full postestimation of complex sampling are performed resulting in minor discrepancies on decimal places. Absolute numbers are not affected. The issue didn't affect the main results or the conclusions of the paper. The corrected numbers are displayed below.

Table 1 Description of the sample and multimorbidity frequency. Brazil, 2013

Variables	% originally published	% corrected
Sex		
Male	44.9	47.1
Female	55.1	52.9
Age (in years)		
18 to 29	24.3	26.1
30 to 39	21.0	21.6
40 to 49	18.8	18.1
50 to 59	16.8	16.2
60 to 69	10.8	10.2
70 to 79	5.7	5.4
80 or more	2.6	2.5
Skin color*		
White	47.8	47.5
Black	9.2	9.2
Brown	41.7	42.0
Marital status		
Without partner	38.4	38.8
With partner	61.6	61.2
Schooling (in years)		
0	13.9	13.7
1-8	25.7	25.3
8-11	15.3	15.5
≥12	45.2	45.5
Wealth index (in quintiles)		
1º (High)	22.3	22.2
2º	22.4	22.4
3º	19.5	19.5
4º	21.0	21.0
5º (Low)	14.7	14.9
Private health plan		
No	69.4	69.7

Variables	% originally published	% corrected
Yes	30.6	30.3
Geographical area		
Urban	86.5	86.2
Rural	13.5	13.8
State-level education		
High	37.2	37.2
Middle	32.4	32.4
Low	30.4	30.4
State-level income		
High	36.0	36.0
Middle	30.0	30.1
Low	33.9	33.9
Total	100.0	100.0

Supplementary table 1 Individual prevalence, duration and number of comorbidities for each morbidity evaluated. Brazil, 2013

	Individual prevalence originally published		Individual prevalence corrected	
Morbidities	**%**	**(95% CI)**	**%**	**(95% CI)**
High Blood Pressure	22.3	21.7 to 23.0	21.4	20.9 to 22.0
Spinal column problem	19.0	18.3 to 19.7	18.4	17.7 to 19.1
Hypercholesterolemia	8.4	8.0 to 8.8	8.1	7.7 to 8.4
Arthritis/rheumatism	6.7	6.4 to 7.1	6.4	6.1 to 6.8
Diabetes	6.5	6.2 to 6.9	6.2	5.9 to 6.6
Asthma/wheezy bronchitis	4.4	4.1 to 4.8	4.4	4.1 to 4.7
Depression	4.2	3.9 to 4.5	4.1	3.9 to 4.4
Worktorelated muscle-skeletal disorders	2.5	2.2 to 2.8	2.4	2.2 to 2.7
Cancer	1.9	1.7 to 2.2	1.8	1.7 to 2.0
Another heart disease	1.9	1.6 to 2.1	1.8	1.6 to 2.1
Stroke	1.6	1.4 to 1.8	1.5	1.4 to 1.7
Kidney problem	1.5	1.3 to 1.7	1.4	1.3 to 1.6
Heart attack	1.3	1.2 to 1.5	1.2	1.1 to 1.4
Heart failure	1.2	1.1 to 1.4	1.2	1.0 to 1.3
Bronchitis	1.0	0.8 to 1.1	1.0	0.8 to 1.1
Angina	0.8	0.7 to 0.9	0.8	0.7 to 0.9
Emphysema	0.5	0.4 to 0.6	0.4	0.3 to 0.5
Another lung disease	0.5	0.4 to 0.6	0.5	0.4 to 0.6
Bipolar disorder	0.4	0.3 to 0.5	0.4	0.3 to 0.5
Another mental disease	0.3	0.2 to 0.4	0.3	0.2 to 0.4
Schizophrenia	0.2	0.2 to 0.3	0.2	0.2 to 0.3
Obsessive Compulsive Disorder (OCD)	0.2	0.1 to 0.2	0.2	0.1 to 0.2

In reference 17, the last names of the authors were abbreviated. They should read as follows:

Souza-Junior PRB, Freitas MPS, Antonaci GA, *et al*. Sampling design for the National Health Survey, 2013. *Epidemiologia e Serviços de Saúde* 2015;24:207–16.

BMJ Open 2018;**8**:e015885corr1. doi:10.1136/bmjopen-2017-015885corr1

Correction: *Contextual and individual inequalities of multimorbidity in Brazilian adults: a cross-sectional national-based study*

Nunes BP, Chiavegatto Filho ADP, Pati S, *et al*. Contextual and individual inequalities of multimorbidity in Brazilian adults: a cross-sectional national-based study *BMJ Open* 2017;7:e015885. doi: 10.1136/bmjopen-2017-015885.

This article was previously published with an error.

Two conditions used to create multimorbidity were incorrectly explained in the methods section:

1. Hypercholesterolaemia has included individuals presenting the condition for more than 1 year. The information about the time was not described in the original version.
2. Spinal column problem was based on self-reported information from the interviewee. In the original text, the condition was described as a self-reported medical diagnosis.

BMJ Open 2019;**9**:e015885corr2. doi:10.1136/bmjopen-2017-015885corr2