

BMJ Open

Multimorbidity in Brazilian adults: magnitude, patterns, individual and state-level inequalities

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2017-015885
Article Type:	Research
Date Submitted by the Author:	06-Jan-2017
Complete List of Authors:	Nunes, BP; Universidade Federal de Pelotas, Department of Nursing Chiavegatto Filho, Alexandre; Harvard School of Public Health, Society, Human Development and Health; Faculdade de Saúde Pública da Universidade de São Paulo, Departamento de Epidemiologia Pati, Sanghamitra; Public Health Foundation of India, Indian Institute of Public Health Bhubaneswar; Sanghamitra Pati, Teixeira, Doralice; Secretaria Municipal da Saúde de São Paulo, São Paulo, Brasil Flores, Thaynã; Federal University of Pelotas, Postgraduate Program of Epidemiology Camargo-Figuera, Fabio; Universidad Industrial de Santander, School of Nursing Munhoz, Tiago; Universidade Federal de Pelotas, Postgraduate Programme in Epidemiology Thume, Elaine; Universidade Federal de Pelotas, Department of Nursing/Postgraduate Program of Nursing Facchini, Luiz; Universidad Federal de Pelotas, Departamento de Medicina Social Batista, Sandro Rogerio; Federal University of Goias, Department of Internal Medicine of Medical School
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Public health
Keywords:	Comorbidity, Multimorbidity, Chronic disease, Statistical disease clustering, Multilevel Analysis

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4 **Title page**

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6 **Title:** Multimorbidity in Brazilian adults: magnitude, patterns, individual and state-level
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8 inequalities

9
10 **Authors:** Bruno P Nunes¹; Alexandre DP Chiavegatto-Filho²; Sanghamitra Pati³; Doralice S
11 Cruz Teixeira⁴; Thaynã R Flores⁵; Fabio A Camargo-Figuera⁶; Tiago N Munhoz⁵; Elaine
12 Thumé⁷; Luiz A Facchini^{5,7}; Sandro R Batista Rodrigues⁸

13
14
15
16 1 – Department of Nursing, Federal University of Pelotas, Brazil

17
18 2 – Department of Epidemiology, School of Public Health, University of São Paulo,
19 São Paulo, Brazil

20
21 3 – Indian Institute of Public, Health, Bhubaneswar, Public Health Foundation of
22 India, Bhubaneswar, Odisha, India

23
24 4 – Municipal Health Department of São Paulo, São Paulo, Brasil.

25
26 5 – Postgraduate Program in Epidemiology, Federal University of Pelotas, Pelotas,
27 Brazil

28
29 6 – School of Nursing, Universidad Industrial de Santander, Bucaramanga, Colombia.

30
31 7 – Postgraduate Program in Nursing, Federal University of Pelotas, Pelotas, Brazil

32
33 8 – Faculty of Medicine, Federal University of Goiás, Goiânia, Brazil

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41
42 **Correspondence to:** Bruno P Nunes, Department of Nursing, Federal University of Pelotas,
43
44 Gomes Carneiro, 1, Phone: +5553 3284-3820, Pelotas-RS, Brazil. Email:
45
46 nunesbp@gmail.com

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49 **Key-words:** Comorbidity; Multimorbidity; Chronic disease; Statistical disease clustering;
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52 Multilevel Analysis.

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55 **Word count:** 2678

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4 25 **Abstract**
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7 26 **Objectives:** Multimorbidity is a public health problem worldwide. In Low and Middle
8
9 27 Income Countries (LMIC), such as Brazil, the problem is made worse by greater individual
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11 28 and contextual inequalities. However, little information is available about the topic.
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14 29 **Methods:** A national-based cross-sectional study was carried out in 2013 with Brazilian
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16 30 adults. Multimorbidity was evaluated by a list of 22 physical and mental morbidities (based
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18 31 on self-reported medical diagnosis and Patient Health Questionnaire 9 for depression). The
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20 32 outcome was analyzed taking ≥ 2 and ≥ 3 diseases as cut-off points. Factor analysis (FA) was
21
22 33 used to identify disease patterns and multilevel models were used to test association with
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24 34 individual and contextual variables.
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28 35 **Results:** The sample was comprised of 60,202 individuals. Multimorbidity frequency was
29
30 36 22.2% (CI95% 21.5; 22.9) for ≥ 2 morbidities and 10.2% (CI95% 9.7; 10.7) for ≥ 3
31
32 37 morbidities. In the multilevel adjusted models, females, older people, those living with a
33
34 38 partner and having less schooling presented more multiple diseases. No linear association was
35
36 39 found according to asset ownership but greater outcome frequency was found in individuals
37
38 40 with mid-range asset ownership quintiles. Living in states with higher levels of education and
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40 41 wealthier states was associated with greater multimorbidity. Two patterns of morbidities
41
42 42 (cardiometabolic problems and Respiratory/mental/muscle-skeletal disorders) explained 92%
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44 43 of total variance. The relationship of disease patterns with individual and contextual variables
45
46 44 was similar to the multimorbidity cut-off associations.
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51 45 **Conclusions:** In Brazil, at least 19 million adults had multimorbidity. Frequency is similar to
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53 46 that found in other LMIC. Contextual and individual social inequalities were observed.
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4 47 **Strengths and limitations of this study**
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- 7 48 • Comprehensive information about multimorbidity is still scarce in Low and Middle
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9 49 Income countries, especially in Brazil
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11 50 • As far as we are aware, this is among the first information about multimorbidity
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13 51 occurrence, patterns, individual and contextual factors in a sample representative of
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15 52 the whole of Brazil
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17 53 • Multimorbidity is a challenge to the Brazilian health system due to its high frequency
18
19 54 (two in every ten adults had ≥ 2 diseases and one in every ten had ≥ 3 diseases,
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21 55 representing at least 19 million Brazilians) and the interplay of individual and
22
23 56 contextual characteristics associated with the problem.
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25 57 • Except for depression, other morbidities were evaluated by self-reporting and we are
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27 58 not able to evaluate the contextual determinants at neighborhood level
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59 **Introduction**

60 Multimorbidity is a current and worldwide public health problem mainly due to its high
61 frequency (>60% in adults) and its association with negative outcomes [1-4]. Most evidence
62 is from High Income Countries [4] but results from Low and Middle Income Countries
63 (LMIC) are also available and increasing in the literature [5-8], including epidemiological
64 information about multimorbidity in Brazilian cities [9-11].

65 Similar to international evidence, multimorbidity in Brazil is greater in females and increases
66 according to age. Socioeconomic inequalities are also observed mainly related to educational
67 differences whereas multiple disease is more frequent in adults with less schooling and the
68 elderly[10, 11].

69 However, as far as we are aware, Brazilian evidence on multimorbidity for the entire country
70 is not available. Brazil is the 5th most populous country in the world with more than 200
71 million people. Furthermore, it is marked by historic social inequalities in different health
72 aspects comprising the occurrence of chronic diseases including both physical and mental
73 disorders [12-14]. Understanding the occurrence and patterns of multimorbidity in the whole
74 country can be relevant for Brazilian Unified Health System management of the challenges
75 resulting from the rapid demographic and epidemiological transitions that have occurred in
76 recent years. Additionally, identifying and comprehending the contextual and individual
77 differences surrounding multimorbidity occurrence helps policy-makers to prioritize and
78 promote health actions and interventions related to multimorbidity management.

79 Thus, the aim of this study was to evaluate the frequency and patterns of multimorbidity in
80 Brazilian adults, as well to measure their association with individual and contextual factors.

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4 81 **Methods**
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7 82 This was a cross-sectional study using population-based data from the Brazilian National
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9 83 Health Survey (*Pesquisa Nacional de Saúde - PNS*) carried out in Brazil in 2013. The survey
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11 84 was conducted by *Instituto Brasileiro de Geografia e Estatística (IBGE)* and the Ministry of
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13 85 Health. The sample is representative of people living in permanent housing, located in urban
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15 86 or rural areas, covering the country's five major geographical regions, its 26 states and
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17 87 Federal District.

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21 88 Sampling was done in three stages, the first being the selection of census tracts, followed by
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23 89 households and, finally, individuals aged 18 or over. More details about the sampling process
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25 90 can be found elsewhere[15, 16].
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29 91 Multimorbidity was evaluated by using a list of all 22 self-reported morbidities available in
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31 92 the study, 21 of which were based on self-reported medical diagnosis, while depression was
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33 93 based on the Patient Health Questionnaire-9(PHQ-9)[17]. The question applied to measure
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35 94 each disease based on self-reported medical diagnosis was: "*Has any physician already*
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37 95 *diagnosed you as having [each disease]?*". The following morbidities were included: High
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39 96 Blood Pressure - HBP; Spinal column problem; Hypercholesterolemia; Depression; Diabetes;
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41 97 Arthritis/rheumatism; Asthma/wheezy bronchitis; Work-related muscle-skeletal disorders;
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43 98 Cancer; Other heart disease; Stroke; Kidney problem; Heart attack; Heart failure; Bronchitis;
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45 99 Angina; Emphysema; Other lung disease; Bipolar disorder; Other mental disease;
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49 100 Schizophrenia; and Obsessive Compulsive Disorder (OCD). Multimorbidity was evaluated by
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51 101 two cut-off points as per the literature[4, 18]: ≥ 2 and ≥ 3 morbidities. Women who had HBP or
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53 102 diabetes only during pregnancy were considered as not having these diseases.
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4 103 Independent variables were sex (male; female), age (continuous), Skin color (white; black;
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6 104 and brown - Asian-Brazilian and indigenous were not shown because they represented less
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8 105 than 1.6% of the sample), marital status (without partner; with partner), schooling in years (0:
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10 106 No schooling; 1-8: incomplete primary school; 8-11: complete primary school and incomplete
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12 107 secondary school; ≥12: complete secondary school up to complete higher education), asset
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14 108 ownership in quintiles (based on ownership of bathroom, car, motorcycle, refrigerator,
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16 109 washing machine, DVD player, TV, landline telephone, microcomputer and microwave
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18 110 oven), private health plan (no; yes), geographical area (urban; rural); state-level education in
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20 111 terciles – proportion of literacy rate obtained from IBGE, 2010 and state-level income in
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22 112 terciles (nominal income per capita - average monthly value - in permanent private housing
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24 113 obtained from IBGE, 2010).

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29 114 Statistical analyses were performed using Stata 12.1 software and the *svy* command was used,
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31 115 which takes into consideration sample weights. Sample weights were defined for the primary
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33 116 sampling units, households and all inhabitants, as well as for the selected inhabitant.

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36 117 Complete information about PNS sample weights and sampling process have been published
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38 118 elsewhere [15, 16]. The results from the sample were expanded for the Brazilian population.

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41 119 Descriptive analysis was based on the calculation of prevalence and its respective confidence
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43 120 intervals. Factor analysis (FA) was performed to identify patterns of morbidities[19]. This
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45 121 analysis was based on tetrachoric correlation, this being more appropriate than Pearson's
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47 122 correlation for dichotomous variables [20]. Before FA analysis, Kaiser-Meyer-Olkin (KMO)
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49 123 and Bartlett sphericity tests were used to evaluate the applicability of this approach. After the
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51 124 first evaluation of the model, some variables were excluded (bronchitis, emphysema, other
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53 125 lung disease, other mental disease and other heart disease) in order to obtain a better model
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55 126 fit. Oblique (oblimin or promax) rotation was performed. In order to establish the number of
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4 127 components to be retained, we used Cattell graphics, Kaiser criteria (eigenvalue>1) and
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6 128 minimum explained variance (>10% for each component). Variables with loadings ≥ 0.3
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8 129 were kept [21]. Through factorial analysis, we obtained the predicted scores of morbidities
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10 130 (factors).

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13 131 Multilevel models were performed to account for state-level variance, with the individuals as
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15 132 the first level and the state of residence as the second level. First, the models were initially
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17 133 adjusted without inclusion of the independent variables (null model) to test the initial variance
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19 134 attributable to the state accounting for approximately 1% ($p < 0.05$) of variance for the four
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21 135 analyses (Multimorbidity ≥ 2 ; Multimorbidity ≥ 3 , factor 1 and factor 2). Then, we performed a
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23 136 logistic regression model for multimorbidity (≥ 2 and ≥ 3 morbidities) and linear regression
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25 137 models to evaluate the association of factors (patterns) of diseases and independent variables.
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27 138 We included sex, age, skin color, marital status, schooling in years, private health plan,
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29 139 geographical area, state-level education and income in these models.
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140 Results

141 The sample was comprised of 60,202 adults. The most frequent diseases were High Blood
142 Pressure (22.3%) and Spinal column problem (19.0%). Angina, emphysema, other lung
143 disease, bipolar disorder, other mental disease, schizophrenia and Obsessive Compulsive
144 Disorder (OCD) were present in less than 1% of the sample. Lung disease problems showed,
145 on average, longer duration of disease. Greater comorbidities were observed for individuals
146 with health problems (heart attack; heart failure and angina). The mean range of comorbidities
147 was from 2.3 to 4.5 diseases (Table 1).

148 Females comprised 55.1% of the sample and mean age was 43.7 years (SD=17.0), ranging
149 from 18 to 101. Most individuals reported white skin color (47.8%) followed by brown
150 (41.7%). Almost two thirds lived with a partner. Out of the total sample, 45.2% had ≥ 12 years
151 of schooling and 13.9% had zero schooling. Less than one third had a private health plan and
152 13.5% lived in rural areas (Table 2). The mean average proportion of literacy rate at the state-
153 level was 7.3%, ranging from 3.3% to 22.5%. The average monthly value of nominal income
154 per capita was R\$ 1,069 (approximately US\$ 644 in 2010).

155 The occurrence of multimorbidity was 22.2% (CI95% 21.5; 22.9) for ≥ 2 morbidities and
156 10.2% (CI95% 9.7; 10.7) for ≥ 3 morbidities. Irrespective of cut-off point, multimorbidity was
157 higher in females, older people, individuals reporting white skin color, who lived with a
158 partner, had less schooling, had a private health plan and living in urban areas. At state-level,
159 multimorbidity was more frequent in states with higher education levels and wealthier states
160 (Table 2).

161 In the adjusted multilevel models, females had 1.86 (CI95% 1.78; 1.95) and 1.97 (CI95%
162 1.85; 2.10) more odds of multimorbidity than males, for ≥ 2 and ≥ 3 morbidities, respectively.

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4 163 In all cases, every additional year of age increased by 1.06 times the odds of multiples
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6 164 diseases. Self-reported skin color was not associated with multimorbidity in the adjusted
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9 165 models. On average, living with a partner increased by 1.15 times the odds of the outcome.
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11 166 Compared to individuals with ≥ 12 years of schooling, adults with 1-8 years of schooling had
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13 167 more odds of multimorbidity (OR 1.40 - CI95% 1.32; 1.49, for ≥ 2 diseases and OR 1.58
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15 168 CI95% 1.45; 1.72, for ≥ 3 morbidities). In general, adults in the second and third wealthiest
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17 169 quintiles had greater odds of multimorbidity. Individuals with private health plans and who
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19 170 lived in urban areas had greater odds of multiple diseases. Individuals who lived in states with
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21 171 low and middle education levels had less multimorbidity compared to states with high
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23 172 education levels. With regard to income at state-level, the higher multimorbidity difference
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25 173 was demonstrated simply by comparing low with high income states (Table 3).

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29 174 In the FA analysis, the KMO coefficient was 0.84. Two patterns of morbidities explained
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31 175 92% of total variance, after rotation. The two components identified were: (1)
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33 176 cardiometabolic problems (High Blood Pressure, heart attack, angina, heart failure, stroke,
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35 177 hypercholesterolemia, diabetes and arthritis/rheumatism); (2) Respiratory/mental/muscle-
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37 178 skeletal disorders (arthritis/rheumatism, spinal column problem, asthma/wheezy bronchitis,
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39 179 COPD, work-related muscle-skeletal disorders, depression, bipolar disorder and kidney
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41 180 problem) (Table4).

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45 181 The adjusted multilevel analyses of the two factors are presented in Table 5. Overall, the
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47 182 results were similar to those observed in Table 3. Females, older people, those with less
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49 183 schooling, those with intermediate asset ownership quintiles and who had private health plans
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51 184 showed more burden of factors. People who lived in rural geographical areas showed less
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53 185 burden of the cardiometabolic factor. Individuals with partners presented less burden of the
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55 186 Respiratory/mental/muscle-skeletal factor compared to individuals who did not have a
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4 187 partner. Cardiometabolic and Respiratory/mental/muscle-skeletal factors were greater when
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6 188 state-level education and income were lower.
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For peer review only

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4 189 **Discussion**

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7 190 Multimorbidity frequency in Brazil is considerable; one in every five Brazilian adults had two
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9 191 or more morbidities and one in every ten had three or more morbidities. Individual and state-
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11 192 level inequalities suggest the complexity of factors and their relationship with multimorbidity
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13 193 occurrence. To our knowledge, this is the first representative Brazilian study to consider
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15 194 individual and contextual factors associated with multimorbidity and its clusters.
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19 195 The study's national representativeness enables us to extrapolate frequencies for the whole
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21 196 Brazilian adult population. Considering 190,755,799 million adults in the most recent
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23 197 Brazilian population census (2010), we are able to infer that approximately 42.7 and 19.5
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25 198 million Brazilian adults had two or more and three or more diseases, respectively. These
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27 199 results bring important challenges for the health system which will need to be more
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29 200 comprehensive in order to deal with the complexity of multimorbidity. Some of the issues are
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31 201 related to need to include multimorbidity in guidelines on reporting these problems to health
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33 202 professionals, as well as giving more emphasis to multimorbidity on health-related university
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35 203 curricula.
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39 204 Relative comparisons with Western countries reveal similar occurrence of two or more
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41 205 diseases in Spain[22] (20.0%; CI95%: 18.8-21.2) and almost ten percentage points less than
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43 206 in Scotland [23] (31.1%, 25 or more years) and Canada[24] (30.9%; CI95% 29.5 – 32.4).In
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45 207 low and middle income countries (LMIC), estimates from countries (China, Ghana, India,
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47 208 Mexico, Russia, and South Africa) included in the WHO Study on global AGEing and adult
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49 209 health (SAGE) Wave-1 (2007/10), found 21.9% (CI95%: 20.9; 22.9) of multimorbidity
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51 210 occurrence (≥ 2 diseases from a list from eight morbidities)[5]. This occurrence varied from
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53 211 20.3% in China to 34.7% in Russia. In the present analysis, we used more diseases to
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4 212 construct multimorbidity (22 against eight in SAGE study). Even so, the prevalence found
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6 213 was, virtually, equal to these other LMIC countries, except for Russia.
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9 214 In Brazil, our occurrence findings were lower than frequencies found in a Southern Brazilian
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11 215 city (29.1%; CI95%: 27.1; 31.1 for ≥ 2 morbidities, and 14.3 %; CI95%: 12.8; 15.8 for ≥ 3
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13 216 morbidities) despite the higher number of morbidities included in this study [10]. The
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15 217 difference observed may be attributed to socioeconomic characteristics of Brazilian states.
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17 218 The Southern states presented more income and schooling which tend to increase the burden
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19 219 of multimorbidity as observed in the results presented here.
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23 220 In terms of socio-demographic characteristics, females and older adults presented more
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25 221 multimorbidity as found in previous Brazilian [10, 11] and international studies [25, 26].
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27 222 Women tend to use health services more and to live longer than males, these being factors
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29 223 which explain part of the higher frequency in this group. Older adults show more exposure to
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31 224 events, including unhealthy ones, that contribute to chronic disease incidence. In the same
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33 225 way, individuals who had partners had higher multimorbidity.
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37 226 Regarding socioeconomic variables, our results follow the pattern found in overall analysis of
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39 227 LMIC included in the SAGE study. Multimorbidity was not associated with wealth quintiles
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41 228 but presented association with education [5]. In the present analysis, the middle wealth
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43 229 quintile strata and their clusters present more multimorbidity whilst showing a negative dose-
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45 230 response relationship with education. These results may be explained by a strong relationship
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47 231 between educational attainment and all aspects of healthier life including those mainly related
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49 232 to better awareness of chronic disease risk factors [27, 28].
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53 233 Having private health plans was associated with multimorbidity and its factors. This may be
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55 234 explained by role of health plans as a socioeconomic indicator but, even more so, by the
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4 235 relationship with self-reported diagnosis (used here to construct the outcome). Individuals
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6 236 with health plans tend to use health services more frequently regardless the presence of
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8 237 chronic conditions[29, 30] thus affording more diagnosis.
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11 238 Individuals who lived in urban areas presented more multiple diseases. This was similar to
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13 239 results found in the adult population in South Africa [31] and Catalonia (Spain)[32]. In spite
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15 240 of little Brazilian evidence on the topic, as well as the social, cultural and environment
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17 241 differences between rural-urban residents, people from rural areas had more difficulty in
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19 242 accessing health services in Brazil [33]which may explain partially the differences between
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21 243 rural and urban residents in our results of the occurrence of self-reported medical diagnosis of
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23 244 multiple diseases.
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27 245 The state-level differences observed reveal a paradoxical association. Instead of individual
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29 246 inequalities are pro-rich, state-level differences are pro-poor. These results might be explained
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31 247 by demographic differences between states in Brazil which may not be fully adjusted with
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33 248 individual demographic variables included in the analysis. Low income and low education in
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35 249 Brazilian states are concentrated in North and Northeast regions and show the poorest health-
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37 250 related indicators[12].
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41 251 The two factors (cardiometabolic and respiratory/mental/muscle-skeletal) found have some
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43 252 similarity to recent evidence [34, 35] mainly related to cardiometabolic patterns. The
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45 253 respiratory/mental/muscle-skeletal data found was similar to results found in a worldwide
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47 254 study of people aged 50 or over [36]. The majority of studies, especially with adult
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49 255 populations, found two or three patterns of diseases. These combinations of diseases suggest
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51 256 possible causal relationship between diseases or their risk factors [19]. The cardiometabolic
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53 257 pattern showed a more well know relationship between diseases. On the other hand, the
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4 258 relationship between respiratory, mental and muscle-skeletal disorders is less understood. The
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6 259 concomitant occurrence of these diseases is well described [37] but understanding the
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9 260 biological plausibility of causal relationships will be a challenge for new studies. As a first
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11 261 step, more detailed and specific information about onset of diseases will be needed. At the
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13 262 same time, the use of approaches related to network analysis can be useful for a better
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15 263 understanding of causal relationships [38]. Even so, the results presented here may contribute
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17 264 to the inclusion of recommendations in Brazilian clinical guidelines about the relationship
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19 265 with chronic conditions, as well as to designing interventions/public policies considering the
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21 266 presence of multiple diseases in the same individual.
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25 267 Some limitations of the study should be addressed. With the exception of depression, all the
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27 268 other morbidities were evaluated by self-reporting. This may provide a misclassification bias
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29 269 even though self-reported diagnosis is considered an adequate and common source of
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31 270 information used in population-based studies on multimorbidity [4, 39, 40]. Nevertheless, the
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33 271 lack of adequate information about diagnosis, including longitudinal information, limits the
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35 272 causal inference related to concomitant diseases expressed in factorial analysis. Furthermore,
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37 273 we are not able to evaluate the contextual determinants at neighborhood level which may
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39 274 produce more complete associations with state-level differences.
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43 275 The absolute and relative number of Brazilian individuals with multimorbidity was high.
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45 276 Addressing the complexity of multiple disease management for at least 19 million people will
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47 277 be a challenge for the health system. The clusters of diseases identified might contribute to
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49 278 strategies for the prevention and clinical care of these diseases. State-level and individual
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51 279 inequalities increase the problem reinforcing the need of a wide lens to organize health
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53 280 services and to decrease the inequities among the Brazilian population.
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4 281 **Author contributions**

5
6 282 BPN designed the article, obtained and analyzes the data, drafted the first version and revised
7
8 283 the manuscript. ADPCF and FACF analyzed the data, and drafted and revised the manuscript.
9
10 284 SP, DS, TRF, TNM, ET and LAF drafted and revised the manuscript. SBR designed the
11
12 285 article, drafted and revised the manuscript. All authors approved the final version of the
13
14 286 manuscript.

15 287 **Funding:** There are no funding related to the production of the paper. The Brazilian Ministry
16
17 288 of Health financed the PNS survey. The funder of the survey played no role in the study
18
19 289 design; collection, analysis, and interpretation of data; writing of the report; or the decision to
20
21 290 submit the article for publication.

22 291 **Conflict of interest:** All authors have no potential conflicts.

23
24 292 **Data sharing statement:** All PNS data are available from the Brazilian Institute of
25
26 293 Geography and Statistics website, located here:
27 294 http://www.ibge.gov.br/home/estatistica/populacao/pns/2013/default_microdados.shtm.

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401 **Tables and figures**

402 Table 1. Individual prevalence, duration and number of comorbidities for each morbidity
 403 evaluated. Brazil, 2013.

Morbidities	Individual prevalence		Duration of disease	Number of comorbidities
	%	(95%CI)	Mean (median; Q25-Q75)	Mean (median; Q25-Q75)
High Blood Pressure	22.3	21.7 - 23.0	13.1 (9; 3-18)	2.3 (2; 1-3)
Spinal column problem	19.0	18.3 - 19.7	14.7 (10; 4-21)	2.3 (2; 1-3)
Hypercholesterolemia	8.4	8.0 - 8.8	6.9 (3; 1-9)	2.3 (2; 1-3)
Arthritis/rheumatism	6.7	6.4 - 7.1	14.6 (10; 3-20)	3.0 (3; 2-4)
Diabetes	6.5	6.2 - 6.9	11.3 (6; 2-15)	2.9 (3; 2-4)
Asthma/wheezy bronchitis	4.4	4.1 - 4.8	25.1 (23; 13-35)	2.4 (2; 1-3)
Depression	4.2	3.9 - 4.5	-	2.9 (3; 2-4)
Work-related muscle-skeletal disorders	2.5	2.2 - 2.8	7.5 (5; 2-11)	2.5 (2; 1-3)
Cancer	1.9	1.7 - 2.2	8.5 (6; 2-13)	2.8 (2; 2-4)
Another heart disease	1.9	1.6 - 2.1	13.9 (9; 3-20)	3.1 (3; 2-4)
Stroke	1.6	1.4 - 1.8	10.2 (6; 2-13)	3.4 (3; 2-5)
Kidney problem	1.5	1.3 - 1.7	13.5 (9; 3-20)	3.2 (3; 2-4)
Heart attack	1.3	1.2 - 1.5	12.4 (7; 2-18)	4.0 (4; 3-5)
Heart failure	1.2	1.1 - 1.4	13.2 (8; 4-19)	4.0 (4; 2-5)
Bronchitis	1.0	0.8 - 1.1	23.2 (20; 9-32)	3.3 (3; 2-5)
Angina	0.8	0.7 - 0.9	15.5 (11; 5-21)	4.5 (4; 3-6)
Emphysema	0.5	0.4 - 0.6	14.9 (9; 3-18)	3.7 (3; 2-5)
Another lung disease	0.5	0.4 - 0.6	16.2 (12; 5-24)	2.8 (2; 1-4)
Bipolar disorder	0.4	0.3 - 0.5	11.3 (8; 4-16)	3.1 (3; 2-4)
Another mental disease	0.3	0.2 - 0.4	2.8 (2; 1-4)	2.5 (2; 1-3)
Schizophrenia	0.2	0.2 - 0.3	19.7 (19; 8-26)	2.7 (3; 2-3)
Obsessive Compulsive Disorder (OCD)	0.2	0.1 - 0.2	14.5 (12; 6-21)	3.4 (3; 2-4)

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406 Table 2. Description of the sample and multimorbidity frequency. Brazil, 2013.

Variables	n	%	Multimorbidity			
			%	≥2 95%CI	%	≥3 95%CI
Sex						
Male	25,920	44.9	17.5	16.6; 18.3	7.2	6.6; 7.8
Female	34,282	55.1	26.1	25.2; 27.0	12.6	12.0; 13.3
Age (in years)						
18 to 29	14,321	24.3	4.9	4.2; 5.6	1.2	0.9; 1.5
30 to 39	14,269	21.0	10.6	9.6; 11.5	2.8	2.3; 3.3
40 to 49	11,405	18.8	20.8	19.5; 22.1	7.8	7.0; 8.6
50 to 59	9,030	16.8	32.9	31.2; 34.6	15.5	14.3; 16.8
60 to 69	6,238	10.8	46.3	44.1; 48.6	24.7	22.8; 26.6
70 to 79	3,441	5.7	52.2	49.2; 55.2	30.9	28.0; 33.9
80 or more	1,498	2.6	52.8	48.6; 57.0	30.6	26.5; 34.7
Skin color*						
White	24,106	47.8	24.3	23.3; 25.4	11.6	10.8; 12.3
Black	5,631	9.2	22.2	20.2; 24.2	10.3	8.9; 11.6
Brown	29,512	41.7	19.8	18.9; 20.6	8.6	8.1; 9.2
Marital status						
Without partner	25,680	38.4	20.6	19.7; 21.5	9.9	9.3; 10.6
With partner	34,522	61.6	23.2	22.4; 24.1	10.4	9.7; 11.0
Schooling (in years)						
0	9,434	13.9	33.2	31.4; 35.0	16.3	14.9; 17.7
1-8	14,649	25.7	30.0	28.6; 31.4	16.1	14.9; 17.2
8-11	9,215	15.3	17.9	16.5; 19.3	7.5	6.5; 8.4
≥12	26,904	45.2	15.8	15.0; 16.7	5.9	5.4; 6.5
Asset ownership (in quintiles)						
1° (High)	10,153	22.3	22.0	20.5; 23.6	9.3	8.3; 10.4
2°	11,531	22.4	22.3	21.0; 23.6	10.5	9.5; 11.5
3°	11,621	19.5	23.1	21.8; 24.4	10.6	9.7; 11.5
4°	14,380	21.0	22.2	20.9; 23.5	10.6	9.7; 11.6
5° (Low)	12,517	14.7	21.3	19.9; 22.7	9.9	8.9; 10.9
Private health plan						
No	43,834	69.4	21.1	20.3; 21.9	9.8	9.3; 10.4
Yes	16,368	30.6	24.8	23.5; 26.1	11.0	10.1; 12.0
Geographical area						
Urban	49,245	86.5	22.8	22.0; 23.5	10.5	10.0; 11.1
Rural	10,957	13.5	18.6	17.2; 20.0	8.0	7.1; 8.8
State-level education						
High	22,382	37.2	24.7	23.7; 25.7	11.7	10.9; 12.4
Middle	19,515	32.4	20.1	18.6; 21.7	9.3	8.3; 10.4

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4	Low	18,305	30.4	19.0	18.0; 20.1	8.0	7.3; 8.6
5	State-level income						
6							
7	High	21,683	36.0	24.6	23.6; 25.7	11.6	10.8; 12.3
8	Middle	18,087	30.0	21.8	20.2; 23.3	10.5	9.5; 11.6
9	Low	20,432	33.9	18.2	17.2; 19.2	7.5	6.9; 8.1
10	Total	60,202	100.0	22.2	21.5; 22.9	10.2	9.7; 10.7
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407 Table 3. Adjusted multilevel models of multimorbidity with independent variables. Brazil, 2013.

Variables	Multimorbidity (≥2)						Multimorbidity (≥3)					
	Model 1		Model 2		Model 3		Model 1		Model 2		Model 3	
	OR	CI95%	OR	CI95%	OR	CI95%	OR	CI95%	OR	CI95%	OR	CI95%
Sex (ref: male)												
Female	1.84	1.76; 1.94	1.85	1.77; 1.94	1.85	1.77; 1.94	1.95	1.83; 2.08	1.95	1.83; 2.08	1.95	1.83; 2.09
Age (in years)	1.06	1.06; 1.06	1.06	1.06; 1.06	1.06	1.06; 1.06	1.06	1.06; 1.06	1.06	1.06; 1.06	1.06	1.06; 1.06
Skin color* (ref: White)												
Black	1.07	0.99; 1.16	1.08	0.99; 1.17	1.08	0.99; 1.17	1.09	0.98; 1.21	1.09	0.98; 1.21	1.09	0.98; 1.21
Brown	1.01	0.96; 1.06	1.01	0.96; 1.07	1.01	0.96; 1.07	0.97	0.91; 1.04	0.97	0.91; 1.04	0.97	0.91; 1.04
Marital status (ref: Without partner)												
With partner	1.13	1.08; 1.18	1.13	1.08; 1.19	1.13	1.08; 1.19	1.17	1.09; 1.24	1.17	1.09; 1.24	1.17	1.09; 1.24
Schooling (in years) # (ref: ≥12)												
8-11	1.19	1.11; 1.28	1.19	1.10; 1.28	1.19	1.10; 1.28	1.22	1.10; 1.35	1.22	1.10; 1.35	1.22	1.10; 1.35
1-8	1.41	1.33; 1.51	1.41	1.33; 1.50	1.41	1.33; 1.50	1.57	1.44; 1.71	1.57	1.44; 1.71	1.57	1.44; 1.71
0	1.34	1.24; 1.44	1.34	1.24; 1.44	1.34	1.24; 1.44	1.41	1.27; 1.56	1.41	1.28; 1.56	1.41	1.28; 1.56
Asset ownership (in quintiles) (ref: High)												
2°	1.12	1.04; 1.20	1.12	1.04; 1.20	1.12	1.04; 1.20	1.15	1.04; 1.28	1.15	1.04; 1.28	1.15	1.04; 1.28
3°	1.21	1.12; 1.31	1.21	1.12; 1.31	1.21	1.12; 1.31	1.19	1.07; 1.33	1.19	1.07; 1.33	1.19	1.07; 1.33
4°	1.05	0.96; 1.14	1.05	0.97; 1.14	1.05	0.97; 1.14	1.09	0.98; 1.22	1.10	0.98; 1.23	1.10	0.98; 1.23
5° (Low)	0.91	0.83; 1.00	0.92	0.84; 1.01	0.92	0.84; 1.01	0.95	0.84; 1.08	0.95	0.84; 1.08	0.95	0.84; 1.08
Private health plan (ref: no)												
Yes	1.15	1.08; 1.21	1.15	1.08; 1.20	1.15	1.08; 1.20	1.09	1.01; 1.18	1.09	1.01; 1.18	1.09	1.01; 1.18
Geographical area (ref: urban)												
Rural	0.86	0.80; 0.92	0.86	0.80; 0.92	0.86	0.80; 0.92	0.78	0.71; 0.86	0.78	0.71; 0.86	0.78	0.71; 0.86
State-level education (ref: High)												
Middle			0.82	0.71; 0.94					0.76	0.64; 0.90		
Low			0.83	0.72; 0.96					0.76	0.64; 0.90		
State-level income (ref: High)												
Middle					0.89	0.77; 1.04					0.88	0.73; 1.05
Low					0.82	0.71; 0.95					0.75	0.63; 0.89

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409 Table 4. Factor analysis. Brazil, 2013.

Morbidities	Factor 1	Factor 2
High Blood Pressure	0.77	
Heart attack	0.79	
Angina	0.68	
Heart failure	0.69	
Stroke	0.58	
Hypercholesterolemia	0.57	
Diabetes	0.62	
Arthritis/rheumatism	0.30	0.37
Spinal column problem		0.45
Asthma/wheezy bronchitis		0.57
COPD		0.63
Work-related muscle-skeletal disorders		0.45
Depression		0.46
Bipolar disorder		0.46
Kidney problem		0.31
Cancer	-	-
Eigenvalor	4.46	1.11
Explained variance %*	0.73 (0.69)	0.18 (0.47)
KMO		0.84

*Before oblique rotation (after oblique rotation)

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411 Table 5. Adjusted multilevel models of patterns of diseases (factors) with independent variables. Brazil, 2013.

Variables	Factor 1 (Cardiometabolic)						Factor 2 (Respiratory/mental/ muscle-skeletal)						
	Model 1		Model 2		Model 3		Model 1		Model 2		Model 3		
	β	CI95%	β	CI95%	β	CI95%	β	CI95%	β	CI95%	β	CI95%	
Sex (ref: male)													
Female	.024	.022; .026	.024	.022; .026	.024	.022; .026	.038	.036; .040	.038	.036; .040	.038	.036; .040	
Age (in years)	.004	.004; .004	.004	.004; .004	.004	.004; .004	.001	.001; .001	.001	.001; .001	.001	.001; .001	
Skin color* (ref: White)													
Black	.007	-.003; .010	.007	.003; .010	.007	.003; .010	-.009	-.013; -.005	-.009	-.013; -.005	-.009	-.013; -.005	
Brown	.001	-.001; .004	.002	-.001; .004	.002	-.001; .004	-.004	-.006; -.001	-.004	-.006; -.001	-.004	-.006; -.001	
Marital status (ref: Without partner)													
With partner	.000	-.002; .002	.000	-.002; .002	.000	-.002; .002	-.005	-.007; -.002	-.005	-.007; -.003	-.005	-.007; -.003	
Schooling (in years)[#] (ref: ≥ 12)													
8-11	.013	.010; .016	.013	.010; .016	.013	.010; .016	.004	.001; .008	.005	.002; .008	.005	.002; .008	
1-8	.021	.018; .023	.021	.018; .023	.021	.018; .023	.011	.008; .014	.011	.008; .014	.011	.008; .014	
0	.014	.010; .017	.014	.010; .017	.014	.010; .017	.001	-.003; .004	.001	-.003; .005	.001	-.003; .005	
Asset ownership (in quintiles) (ref: High)													
2°	.007	.004; .010	.007	.004; .010	.007	.004; .010	.005	.001; .008	.005	.001; .008	.005	.001; .008	
3°	.009	.006; .013	.009	.006; .013	.009	.006; .013	.010	.006; .014	.010	.006; .014	.010	.006; .014	
4°	.006	.002; .009	.006	.002; .009	.006	.002; .009	.004	.000; .008	.004	.000; .008	.004	.000; .008	
5° (Low)	-.003	-.007; .001	-.003	-.007; .001	-.003	-.007; .001	.001	-.004; .005	.001	-.004; .005	.001	-.004; .005	
Private health plan (ref: no)													
Yes	.006	.004; .009	.006	.004; .009	.006	.004; .009	.007	.005; .010	.007	.005; .010	.007	.005; .010	
Geographical area (ref: urban)													
Rural	-.008	-.011; -.005	-.008	-.011; -.005	-.008	-.011; -.005	-.002	-.005; .002	-.002	-.005; .002	-.002	-.005; .002	
State-level education (ref: High)													
Middle			-.010	-.016; -.004					-.016	-.027; -.005			
Low			-.008	-.015; -.002					-.018	-.029; -.006			
State-level income (ref: High)													
Middle					-.006	-.012; .001					-.011	-.022; .001	
Low					-.009	-.016; -.003					-.017	-.028; -.006	

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STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	5
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	-
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6
Bias	9	Describe any efforts to address potential sources of bias	6
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5-6
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	6-7
		(b) Describe any methods used to examine subgroups and interactions	-
		(c) Explain how missing data were addressed	-
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	6
		(e) Describe any sensitivity analyses	-

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(b) Give reasons for non-participation at each stage	-
		(c) Consider use of a flow diagram	-
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8
		(b) Indicate number of participants with missing data for each variable of interest	-
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	-
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	-
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	-
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	8
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8-9
		(b) Report category boundaries when continuous variables were categorized	8-9
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	-
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14
Generalisability	21	Discuss the generalisability (external validity) of the study results	14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

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

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2017-015885.R1
Article Type:	Research
Date Submitted by the Author:	07-Apr-2017
Complete List of Authors:	Nunes, BP; Universidade Federal de Pelotas, Department of Nursing Chiavegatto Filho, Alexandre; Harvard School of Public Health, Society, Human Development and Health; Faculdade de Saúde Pública da Universidade de São Paulo, Departamento de Epidemiologia Pati, Sanghamitra; Public Health Foundation of India, Indian Institute of Public Health Bhubaneswar; Sanghamitra Pati, Teixeira, Doralice; Secretaria Municipal da Saúde de São Paulo, São Paulo, Brasil Flores, Thaynã; Federal University of Pelotas, Postgraduate Program of Epidemiology Camargo-Figuera, Fabio Alberto; Universidad Industrial de Santander, School of Nursing Munhoz, Tiago; Universidade Federal de Pelotas, Postgraduate Programme in Epidemiology Thume, Elaine; Universidade Federal de Pelotas, Department of Nursing/Postgraduate Program of Nursing Facchini, Luiz; Universidad Federal de Pelotas, Departamento de Medicina Social Batista, Sandro Rogerio; Federal University of Goias, Department of Internal Medicine of Medical School
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Public health
Keywords:	Comorbidity, Multimorbidity, Chronic disease, Statistical disease clustering, Multilevel Analysis

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4 **Title page**

5
6 **Title:** Contextual and individual inequalities of multimorbidity in Brazilian adults: a cross-
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8 sectional national-based study

9
10 **Authors:** Bruno P Nunes¹; Alexandre DP Chiavegatto-Filho²; Sanghamitra Pati³; Doralice S
11 Cruz Teixeira⁴; Thaynã R Flores⁵; Fabio A Camargo-Figuera⁶; Tiago N Munhoz⁵; Elaine
12 Thumé⁷; Luiz A Facchini^{5,7}; Sandro R Batista Rodrigues⁸

13
14
15
16 1 – Department of Nursing, Federal University of Pelotas, Brazil

17
18 2 – Department of Epidemiology, School of Public Health, University of São Paulo,
19 São Paulo, Brazil

20
21 3 – Indian Institute of Public, Health, Bhubaneswar, Public Health Foundation of
22 India, Bhubaneswar, Odisha, India

23
24 4 – Municipal Health Department of São Paulo, São Paulo, Brasil.

25
26 5 – Postgraduate Program in Epidemiology, Federal University of Pelotas, Pelotas,
27 Brazil

28
29 6 – School of Nursing, Universidad Industrial de Santander, Bucaramanga, Colombia.

30
31 7 – Postgraduate Program in Nursing, Federal University of Pelotas, Pelotas, Brazil

32
33 8 – Faculty of Medicine, Federal University of Goiás, Goiânia, Brazil

34
35
36
37
38
39
40
41
42 **Correspondence to:** Bruno P Nunes, Department of Nursing, Federal University of Pelotas,
43
44 Gomes Carneiro, 1, Phone: +5553 3284-3820, Pelotas-RS, Brazil. Email:
45
46 nunesbp@gmail.com

47
48
49 **Key-words:** Comorbidity; Multimorbidity; Chronic disease; Statistical disease clustering;
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52 Multilevel Analysis.

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55 **Word count:** 3094

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4 25 **Abstract**

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7 26 **Objectives:** The study aims to evaluate the magnitude of multimorbidity in Brazilian adults,
8
9 27 as well to measure their association with individual and contextual factors stratified by
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11 28 Brazilian states and regions.

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14 29 **Methods:** A national-based cross-sectional study was carried out in 2013 with Brazilian
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16 30 adults. Multimorbidity was evaluated by a list of 22 physical and mental morbidities (based
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18 31 on self-reported medical diagnosis and Patient Health Questionnaire 9 for depression). The
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20 32 outcome was analyzed taking ≥ 2 and ≥ 3 diseases as cut-off points. Factor analysis (FA) was
21
22 33 used to identify disease patterns and multilevel models were used to test association with
23
24 34 individual and contextual variables.

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27
28 35 **Results:** The sample was comprised of 60,202 individuals. Multimorbidity frequency was
29
30 36 22.2% (CI95% 21.5; 22.9) for ≥ 2 morbidities and 10.2% (CI95% 9.7; 10.7) for ≥ 3
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32 37 morbidities. In the multilevel adjusted models, females, older people, those living with a
33
34 38 partner and having less schooling presented more multiple diseases. No linear association was
35
36 39 found according to asset ownership but greater outcome frequency was found in individuals
37
38 40 with mid-range asset ownership quintiles. Living in states with higher levels of education and
39
40 41 wealthier states was associated with greater multimorbidity. Two patterns of morbidities
41
42 42 (cardiometabolic problems and Respiratory/mental/muscle-skeletal disorders) explained 92%
43
44 43 of total variance. The relationship of disease patterns with individual and contextual variables
45
46 44 was similar to the overall multimorbidity, with differences among Brazilian regions.

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51 45 **Conclusions:** In Brazil, at least 19 million adults had multimorbidity. Frequency is similar to
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53 46 that found in other LMIC. Contextual and individual social inequalities were observed.
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4 47 **Strengths and limitations of this study**
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- 7 48 • Comprehensive information about multimorbidity is still scarce in Brazil
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9 49 • As far as we are aware, this is among the first information about multimorbidity
10 assessment of individual and contextual factors in a sample representative of the
11 whole of Brazil
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16 52 • Multimorbidity is a challenge to the Brazilian health system due to its high frequency
17 (two in every ten adults had ≥ 2 diseases and one in every ten had ≥ 3 diseases,
18 representing at least 19 million Brazilians) and the interplay of individual and
19 contextual characteristics associated with the problem. Differences within the country
20 were observed.
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27 57 • Except for depression, other morbidities were evaluated by self-reporting and we are
28 not able to evaluate the contextual determinants at neighborhood level
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59 **Introduction**

60 Multimorbidity is a current and worldwide public health problem mainly due to its high
61 frequency (>60% in adults) and its association with negative outcomes [1-4]. Most evidence
62 is from High Income Countries [4] but results from Low and Middle Income Countries
63 (LMIC) are also available and increasing in the literature [5-8], including epidemiological
64 information about multimorbidity in Brazilian cities [9-11].

65 Similar to international evidence, multimorbidity in Brazil is greater in females and increases
66 according to age. Socioeconomic inequalities are also observed mainly related to educational
67 differences whereas multiple disease is more frequent in adults and elderly with less
68 schooling and lower socioeconomic status adults and elderly [10 11].

69 However, as far as we are aware, Brazilian evidence on multimorbidity for the entire country
70 is scarce. Only recently, a paper evaluating epidemiology of multimorbidity in Brazil was
71 published [12]. The authors found a 24.2% (95% CI 23.5–24.9) prevalence rate of
72 multimorbidity [12] and correlates were similar to Brazilian located previous studies ([10
73 11].

74 Brazil is the 5th most populous country in the world with more than 200 million people.
75 Furthermore, it is marked by historic social inequalities in different health aspects comprising
76 the occurrence of chronic diseases including both physical and mental disorders [13-15].

77 Understanding the occurrence and patterns of multimorbidity in the whole country can be
78 relevant for Brazilian Unified Health System management of the challenges resulting from the
79 rapid demographic and epidemiological transitions that have occurred in recent years.

80 Additionally, identifying and comprehending the contextual and individual differences

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4 81 surrounding multimorbidity occurrence helps policy-makers to prioritize and promote health
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6 82 actions and interventions related to multimorbidity management.
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9 83 Thus, the aim of this study was to evaluate the frequency and patterns of multimorbidity in
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11 84 Brazilian adults, as well to measure their association with individual and contextual factors
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14 85 stratified by Brazilian states and regions.
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60**86 Methods**

87 This was a cross-sectional study using population-based data from the Brazilian National
88 Health Survey (*Pesquisa Nacional de Saúde - PNS*) carried out in Brazil in 2013. The survey
89 was conducted by *Instituto Brasileiro de Geografia e Estatística (IBGE)* and the Ministry of
90 Health. The sample is representative of people living in permanent housing, located in urban
91 or rural areas, covering the country's five major geographical regions, its 26 states and
92 Federal District.

93 Sampling was done in three stages, the first being the selection of census tracts, followed by
94 households and, finally, individuals aged 18 or over. More details about the sampling process
95 can be found elsewhere[16 17].

96 Multimorbidity was evaluated by using a list of all 22 self-reported morbidities available in
97 the study, 21 of which were based on self-reported medical diagnosis, while depression was
98 based on the Patient Health Questionnaire-9(PHQ-9)[18]. The question applied to measure
99 each disease based on self-reported medical diagnosis was: "*Has any physician already*
100 *diagnosed you as having [each disease]?*". The following morbidities were included: High
101 Blood Pressure - HBP; Spinal column problem; Hypercholesterolemia; Depression; Diabetes;
102 Arthritis/rheumatism; Asthma/wheezy bronchitis; Work-related muscle-skeletal disorders;
103 Cancer; Other heart disease; Stroke; Kidney problem; Heart attack; Heart failure; Bronchitis;
104 Angina; Emphysema; Other lung disease; Bipolar disorder; Other mental disease;
105 Schizophrenia; and Obsessive Compulsive Disorder (OCD). Multimorbidity was evaluated by
106 two cut-off points as per the literature[4 19]: ≥ 2 and ≥ 3 morbidities. Women who had HBP or
107 diabetes only during pregnancy were considered as not having these diseases.

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4 108 Independent variables were sex (male; female), age (continuous), skin color (white; black;
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6 109 and brown - Asian-Brazilian and indigenous were not shown because they represented less
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8 110 than 1.6% of the sample), marital status (without partner; with partner), schooling in years (0:
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10 111 No schooling; 1-8: incomplete primary school; 8-11: complete primary school and incomplete
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12 112 secondary school; ≥12: complete secondary school up to complete higher education), wealth
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14 113 index in quintiles (based on ownership of bathroom, car, motorcycle, refrigerator, washing
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16 114 machine, DVD player, TV, landline telephone, microcomputer and microwave oven), private
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18 115 health plan (no; yes), geographical area (urban; rural); state-level education in terciles –
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20 116 proportion of literacy rate obtained from IBGE, 2010 and state-level income in terciles
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22 117 (nominal income per capita - average monthly value - in permanent private housing obtained
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24 118 from IBGE, 2010).

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29 119 Statistical analyses were performed using Stata 12.1 software and the *svy* command was used,
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31 120 which takes into consideration sample weights. Sample weights were defined for the primary
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33 121 sampling units, households and all inhabitants, as well as for the selected inhabitant.

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36 122 Complete information about PNS sample weights and sampling process have been published
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38 123 elsewhere [16 17]. The results from the sample were expanded for the Brazilian population.

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41 124 Descriptive analysis was based on the calculation of prevalence and its respective confidence
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43 125 intervals. Factor analysis (FA) was performed to identify patterns of morbidities[20]. This
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45 126 analysis was based on tetrachoric correlation, this being more appropriate than Pearson's
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47 127 correlation for dichotomous variables [21]. Before FA analysis, Kaiser-Meyer-Olkin (KMO)
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49 128 and Bartlett sphericity tests were used to evaluate the applicability of this approach. After the
50
51 129 first evaluation of the model, some variables were encompassed (bronchitis, emphysema and
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53 130 other lung disease to other respiratory problems - COPD) and others excluded (schizophrenia,
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55 131 Obsessive Compulsive Disorder, another mental disease and another heart disease) in order to
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4 132 obtain a better model fit regarding KMO and Bartlett sphericity tests. Oblique (oblimin or
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6 133 promax) rotation was performed. In order to establish the number of components to be
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8 134 retained, we used Cattell graphics, Kaiser criteria (eigenvalue>1) and minimum explained
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10 135 variance (>10% for each component). Variables with loadings ≥ 0.3 were kept [22]. Through
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12 136 factorial analysis, we obtained the predicted scores of morbidities (factors).

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16 137 Multilevel models were performed to account for state-level variance, with the individuals as
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18 138 the first level and the state of residence as the second level. First, the models were initially
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20 139 adjusted without inclusion of the independent variables (null model) to test the initial variance
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22 140 attributable to the state accounting for approximately 1% ($p < 0.05$) of variance for the four
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24 141 analyses (Multimorbidity ≥ 2 ; Multimorbidity ≥ 3 , factor 1 and factor 2). Then, we performed a
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26 142 logistic regression model for multimorbidity (≥ 2 and ≥ 3 morbidities) and linear regression
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28 143 models to evaluate the association of factors (patterns) of diseases and independent variables.
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30 144 We included sex, age, skin color, marital status, schooling in years, private health plan,
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32 145 geographical area, state-level education and income in these models. Stratified region-level
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34 146 analyzes were performed to better understanding disparities among states.

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39 147 The study was approved by the National Research Ethics Commission on July 8, 2013, under
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41 148 No. 10853812.7.0000.0008. All respondents signed a free and informed consent statement
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43 149 form prior to data collection
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4 150 **Results**

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7 151 The sample was comprised of 60,202 adults. The most frequent diseases were High Blood
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9 152 Pressure (22.3%) and Spinal column problem (19.0%). Angina, emphysema, other lung
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11 153 disease, bipolar disorder, other mental disease, schizophrenia and Obsessive Compulsive
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13 154 Disorder (OCD) were present in less than 1% of the sample. Lung disease problems showed,
14
15 155 on average, longer duration of disease. Greater comorbidities were observed for individuals
16
17 156 with health problems (heart attack; heart failure and angina). The mean range of comorbidities
18
19 157 was from 2.3 to 4.5 diseases (Supplementary table 1).

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23 158 Females comprised 55.1% of the sample and mean age was 43.7 years (SD=17.0), ranging
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25 159 from 18 to 101. Most individuals reported white skin color (47.8%) followed by brown
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27 160 (41.7%). Almost two thirds lived with a partner. Out of the total sample, 45.2% had ≥ 12 years
28
29 161 of schooling and 13.9% had zero schooling. Less than one third had a private health plan and
30
31 162 13.5% lived in rural areas (Table 1). The mean average proportion of literacy rate at the state-
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33 163 level was 7.3%, ranging from 3.3% to 22.5%. The average monthly value of nominal income
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35 164 per capita was R\$ 1,069 (approximately US\$ 644 in 2010).

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39 165 The occurrence of multimorbidity was 22.2% (CI95% 21.5; 22.9) for ≥ 2 morbidities and
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41 166 10.2% (CI95% 9.7; 10.7) for ≥ 3 morbidities. Irrespective of cut-off point, multimorbidity was
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43 167 higher in females, older people, individuals reporting white skin color, who lived with a
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45 168 partner, had less schooling, had a private health plan and living in urban areas. At state-level,
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47 169 multimorbidity was more frequent in states with higher education levels and wealthier states
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49 170 (Table 1). States in the South of Brazil showed the highest occurrence of multimorbidity
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51 171 (Supplementary figure 1),
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4 172 In the adjusted multilevel models, females had 1.86 (CI95% 1.78; 1.95) and 1.97(CI95%
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6 173 1.85; 2.10) more odds of multimorbidity than males, for ≥ 2 and ≥ 3 morbidities, respectively.
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8 174 In all cases, every additional year of age increased by 1.06 times the odds of multiples
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10 175 diseases. Self-reported skin color was not associated with multimorbidity in the adjusted
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12 176 models. On average, living with a partner increased by 1.15 times the odds of the outcome.
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14 177 Compared to individuals with ≥ 12 years of schooling, adults with 1-8 years of schooling had
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16 178 more odds of multimorbidity (OR 1.40 - CI95% 1.32; 1.49, for ≥ 2 diseases and OR 1.58
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18 179 CI95% 1.45; 1.72, for ≥ 3 morbidities). In general, adults in the second and third wealthiest
19
20 180 quintiles had greater odds of multimorbidity. Individuals with private health plans and who
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22 181 lived in urban areas had greater odds of multiple diseases. Individuals who lived in states with
23
24 182 low and middle education levels had less multimorbidity compared to states with high
25
26 183 education levels. With regard to income at state-level, the higher multimorbidity difference
27
28 184 was demonstrated simply by comparing low with high income states (Table 2). The
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30 185 associations stratified by region revealed a similar pattern to the whole Brazil, except to
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32 186 Central Western region in relation to lack of association of overall multimorbidity and private
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34 187 health plan, geographical area (observed to Southeastern region too) and schooling (no dose-
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36 188 response relationship) (Table 3).
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42 189 In the FA analysis, the KMO coefficient was 0.84. Two patterns of morbidities explained
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44 190 92% of total variance, after rotation. The two components identified were: (1)
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46 191 cardiometabolic problems (High Blood Pressure, heart attack, angina, heart failure, stroke,
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48 192 hypercholesterolemia, diabetes and arthritis/rheumatism); (2) Respiratory/mental/muscle-
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50 193 skeletal disorders (arthritis/rheumatism, spinal column problem, asthma/wheezy bronchitis,
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52 194 COPD, work-related muscle-skeletal disorders, depression, bipolar disorder and kidney
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54 195 problem) (Supplementary table 2).
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4 196 The adjusted multilevel analyses of the two factors are presented in Table 4. Overall, the
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6 197 results were similar to those observed in Table 2. Females, older people, those with less
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8 198 schooling, those with intermediate asset ownership quintiles and who had private health plans
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10 199 showed more burden of factors. People who lived in rural geographical areas showed less
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12 200 burden of the cardiometabolic factor. Individuals with partners presented less burden of the
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14 201 Respiratory/mental/muscle-skeletal factor compared to individuals who did not have a
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16 202 partner. Cardiometabolic and Respiratory/mental/muscle-skeletal factors were greater when
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18 203 state-level education and income were lower. The cardiometabolic factor presented similar
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20 204 associations as overall multimorbidity to stratified analysis. As for the Respiratory/mental/
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22 205 muscle-skeletal factor did not show association with schooling in all regions (except to
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24 206 Northern) (Table 5).
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4 208 **Discussion**
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7 209 Multimorbidity frequency in Brazil is considerable; one in every five Brazilian adults had two
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9 210 or more morbidities and one in every ten had three or more morbidities. Individual and state-
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11 211 level inequalities suggest the complexity of factors and their relationship with multimorbidity
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13 212 occurrence. To our knowledge, this is the first representative Brazilian study to consider
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15 213 individual and contextual factors associated with multimorbidity and its clusters.
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19 214 The study's national representativeness enables us to extrapolate frequencies for the whole
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21 215 Brazilian adult population. Considering 190,755,799 million adults in the most recent
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23 216 Brazilian population census (2010), we are able to infer that approximately 42.7 and 19.5
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25 217 million Brazilian adults had two or more and three or more diseases, respectively. These
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27 218 results bring important challenges for the health system which will need to be more
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29 219 comprehensive in order to deal with the complexity of multimorbidity. Some of the issues are
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31 220 related to need to include multimorbidity in guidelines on reporting these problems to health
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33 221 professionals, as well as giving more emphasis to multimorbidity on health-related university
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35 222 curricula.
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39 223 Relative comparisons with Western countries reveal similar occurrence of two or more
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41 224 diseases in Spain [23] (20.0%; CI95%: 18.8-21.2) and almost ten percentage points less than
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43 225 in Scotland [24] (31.1%, 25 or more years) and Canada[25] (30.9%; CI95% 29.5 – 32.4).In
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45 226 low and middle income countries (LMIC), estimates from countries (China, Ghana, India,
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47 227 Mexico, Russia, and South Africa) included in the WHO Study on global AGEing and adult
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49 228 health (SAGE) Wave-1 (2007/10), found 21.9% (CI95%: 20.9; 22.9) of multimorbidity
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51 229 occurrence (≥ 2 diseases from a list from eight morbidities)[5]. This occurrence varied from
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53 230 20.3% in China to 34.7% in Russia. In the present analysis, we used more diseases to
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4 231 construct multimorbidity (22 against eight in SAGE study). Even so, the prevalence found
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6 232 was, virtually, equal to these other LMIC countries, except for Russia.
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9 233 In Brazil, our occurrence findings were slightly lower than the result found in a paper with
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11 234 same database (-2 pp). This is explained by the differences among diseases selected to
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13 235 measure multimorbidity and present an urgent call to more uniform multimorbidity
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15 236 operationalization. Comparing with located Brazilian results, the prevalences presented here
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17 237 were lower than frequencies found in a Southern Brazilian city (29.1%; CI95%: 27.1; 31.1 for
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19 238 ≥ 2 morbidities, and 14.3 %; CI95%: 12.8; 15.8 for ≥ 3 morbidities) despite the higher number
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21 239 of morbidities included in this study [10]. The difference observed may be attributed to
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23 240 socioeconomic characteristics of Brazilian states. The Southern states presented more income
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25 241 and schooling which tend to increase the occurrence of multimorbidity as observed in the
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27 242 results presented here.
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32 243 In terms of socio-demographic characteristics, females and older adults presented more
33
34 244 multimorbidity in all Brazilian regions as found in previous Brazilian [10 11] and
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36 245 international studies [26 27]. Women tend to use health services more and to live longer than
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38 246 males, these being factors which explain part of the higher frequency in this group. Survivors
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40 247 older adults tend to be exposed to more physiological damages in lifetime that contribute to
41
42 248 chronic disease incidence [28]. In the same way, individuals who had partners had higher
43
44 249 multimorbidity except to Central Western residents. The association between marital status
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46 250 should be more understanding through studies which include cultural assessment and its
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48 251 impact on chronic diseases development and diagnosis. One explanation is related to the fact
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50 252 that individuals with partner tend to use more health services increasing the probability of
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52 253 medical diagnosis [29].
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4 254 Regarding socioeconomic variables, our results follow the pattern found in overall analysis of
5
6 255 a worldwide study [27] and LMIC included in the SAGE study. Multimorbidity and its factors
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8 256 was not associated with wealth quintiles but presented association with education [5]
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10
11 257 regardless Brazilian regions. In the present analysis, the middle wealth quintile strata and their
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13 258 clusters present more multimorbidity whilst showing a negative dose-response relationship
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15 259 with education. These results may be explained by a strong relationship between educational
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17 260 attainment and all aspects of healthier life including those mainly related to better awareness
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19 261 of chronic disease risk factors [30 31]. Education level seems to be a more adequate
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21 262 socioeconomic indicator to evaluate multimorbidity inequalities due to its worldwide
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23 263 association with poor health outcomes and longevity, and the persistent effect overtime [30].
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25 264 Except for the early effect of childhood health status on education [32 33], chronic diseases in
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27 265 adult life tend to increase the risk of poverty (wealth index) [34] but the effect on education
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29 266 tend to be less relevant since education is usually achieved is early life
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33 267 Having private health plans was associated with multimorbidity and its factors, except to
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35 268 Central Western and Southern. This may be explained, by the relationship with self-reported
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37 269 diagnosis (a fundamental characteristic of the outcome). Individuals with health plans tend to
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39 270 use health services more frequently regardless the presence of chronic conditions[35 36] thus
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41 271 affording more diagnosis.
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45 272 Individuals who lived in urban areas presented more multiple diseases. This was similar to
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47 273 results found in the adult population in South Africa [37] and Catalonia (Spain)[38]. In spite
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49 274 of little Brazilian evidence on the topic, as well as the social, cultural and environment
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51 275 differences between rural-urban residents, people from rural areas had more difficulty in
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53 276 accessing health services in Brazil [39] which may explain partially the differences between
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4 277 rural and urban residents in our results of the occurrence of self-reported medical diagnosis of
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6 278 multiple diseases.
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9 279 The state-level differences observed reveal a paradoxical association. Instead of individual
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11 280 inequalities are pro-rich, state-level differences are pro-poor. These results might be explained
12
13 281 by demographic differences between states in Brazil which may not be fully adjusted with
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15 282 individual demographic variables included in the analysis. Low income and low education in
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17 283 Brazilian states are concentrated in North and Northeast regions and show the poorest health-
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19 284 related indicators[13]. The states further south (*Rio Grande do Sul* - 27.2% and *Santa*
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21 285 *Catarina* - 27.1%) present greater multimorbidity frequencies.
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25 286 The two factors (cardiometabolic and respiratory/mental/muscle-skeletal) found have some
26
27 287 similarity to recent evidence [40 41] mainly related to cardiometabolic patterns. The
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29 288 respiratory/mental/muscle-skeletal data found was similar to results found in a worldwide
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31 289 study of people aged 50 or over [42]. The majority of studies, especially with adult
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33 290 populations, found two or three patterns of diseases. These combinations of diseases suggest
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35 291 possible causal relationship between diseases or their risk factors [20]. The cardiometabolic
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37 292 pattern showed a more well know relationship between diseases. On the other hand, the
38
39 293 relationship between respiratory, mental and muscle-skeletal disorders is less understood. The
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41 294 concomitant occurrence of these diseases is well described [43] but understanding the
42
43 295 biological plausibility of causal relationships will be a challenge for new studies. As a first
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45 296 step, more detailed and specific information about onset of diseases will be needed. At the
46
47 297 same time, the use of approaches related to network analysis can be useful for a better
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49 298 understanding of causal relationships [44]. Even so, the results presented here may contribute
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51 299 to the inclusion of recommendations in Brazilian clinical guidelines about the relationship
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4 300 with chronic conditions, as well as to designing interventions/public policies considering the
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6 301 presence of multiple diseases in the same individual.
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9 302 Some limitations of the study should be addressed. With the exception of depression, all the
10
11 303 other morbidities were evaluated by self-reporting. This may provide a misclassification bias
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13 304 even though self-reported diagnosis is considered an adequate and common source of
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15 305 information used in population-based studies on multimorbidity [4 45 46]. Nevertheless, the
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17 306 lack of adequate information about diagnosis, including longitudinal information, limits the
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19 307 causal inference related to concomitant diseases expressed in factorial analysis. Furthermore,
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21 308 we are not able to evaluate the contextual determinants at neighborhood level which may
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23 309 produce more complete associations with state-level differences.
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27 310 The absolute and relative number of Brazilian individuals with multimorbidity was high.
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29 311 Addressing the complexity of multiple disease management for at least 19 million people will
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31 312 be a challenge for the health system. The clusters of diseases identified might contribute to
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33 313 strategies for the prevention and clinical care of these diseases. State-level and individual
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35 314 inequalities increase the problem reinforcing the need of a wide lens to organize health
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37 315 services and to decrease the inequities among the Brazilian population.
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4 316 **Author contributions**

5
6 317 BPN designed the article, obtained and analyzes the data, drafted the first version and revised
7
8 318 the manuscript. ADPCF and FACF analyzed the data, and drafted and revised the manuscript.
9
10 319 SP, DS, TRF, TNM, ET and LAF drafted and revised the manuscript. SBR designed the
11
12 320 article, drafted and revised the manuscript. All authors approved the final version of the
13
14 321 manuscript.

15 322 **Funding:** There are no funding related to the production of the paper. The Brazilian Ministry
16
17 323 of Health financed the PNS survey. The funder of the survey played no role in the study
18
19 324 design; collection, analysis, and interpretation of data; writing of the report; or the decision to
20
21 325 submit the article for publication.

22 326 **Conflict of interest:** All authors have no potential conflicts.

23
24 327 **Data sharing statement:** All PNS data are available from the Brazilian Institute of
25
26 328 Geography and Statistics website, located here:
27
28 329 http://www.ibge.gov.br/home/estatistica/populacao/pns/2013/default_microdados.shtm.

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475 **Tables and figures**

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

Variables	n	%	Multimorbidity			
			%	≥2 95%CI	%	≥3 95%CI
Sex						
Male	25,920	44.9	17.5	16.6; 18.3	7.2	6.6; 7.8
Female	34,282	55.1	26.1	25.2; 27.0	12.6	12.0; 13.3
Age (in years)						
18 to 29	14,321	24.3	4.9	4.2; 5.6	1.2	0.9; 1.5
30 to 39	14,269	21.0	10.6	9.6; 11.5	2.8	2.3; 3.3
40 to 49	11,405	18.8	20.8	19.5; 22.1	7.8	7.0; 8.6
50 to 59	9,030	16.8	32.9	31.2; 34.6	15.5	14.3; 16.8
60 to 69	6,238	10.8	46.3	44.1; 48.6	24.7	22.8; 26.6
70 to 79	3,441	5.7	52.2	49.2; 55.2	30.9	28.0; 33.9
80 or more	1,498	2.6	52.8	48.6; 57.0	30.6	26.5; 34.7
Skin color*						
White	24,106	47.8	24.3	23.3; 25.4	11.6	10.8; 12.3
Black	5,631	9.2	22.2	20.2; 24.2	10.3	8.9; 11.6
Brown	29,512	41.7	19.8	18.9; 20.6	8.6	8.1; 9.2
Marital status						
Without partner	25,680	38.4	20.6	19.7; 21.5	9.9	9.3; 10.6
With partner	34,522	61.6	23.2	22.4; 24.1	10.4	9.7; 11.0
Schooling (in years)						
0	9,434	13.9	33.2	31.4; 35.0	16.3	14.9; 17.7
1-8	14,649	25.7	30.0	28.6; 31.4	16.1	14.9; 17.2
8-11	9,215	15.3	17.9	16.5; 19.3	7.5	6.5; 8.4
≥12	26,904	45.2	15.8	15.0; 16.7	5.9	5.4; 6.5
Wealth index (in quintiles)						
1° (High)	10,153	22.3	22.0	20.5; 23.6	9.3	8.3; 10.4
2°	11,531	22.4	22.3	21.0; 23.6	10.5	9.5; 11.5
3°	11,621	19.5	23.1	21.8; 24.4	10.6	9.7; 11.5
4°	14,380	21.0	22.2	20.9; 23.5	10.6	9.7; 11.6
5° (Low)	12,517	14.7	21.3	19.9; 22.7	9.9	8.9; 10.9
Private health plan						
No	43,834	69.4	21.1	20.3; 21.9	9.8	9.3; 10.4
Yes	16,368	30.6	24.8	23.5; 26.1	11.0	10.1; 12.0
Geographical area						
Urban	49,245	86.5	22.8	22.0; 23.5	10.5	10.0; 11.1
Rural	10,957	13.5	18.6	17.2; 20.0	8.0	7.1; 8.8
State-level education						

High	22,382	37.2	24.7	23.7; 25.7	11.7	10.9; 12.4
Middle	19,515	32.4	20.1	18.6; 21.7	9.3	8.3; 10.4
Low	18,305	30.4	19.0	18.0; 20.1	8.0	7.3; 8.6
State-level income						
High	21,683	36.0	24.6	23.6; 25.7	11.6	10.8; 12.3
Middle	18,087	30.0	21.8	20.2; 23.3	10.5	9.5; 11.6
Low	20,432	33.9	18.2	17.2; 19.2	7.5	6.9; 8.1
Total	60,202	100.0	22.2	21.5; 22.9	10.2	9.7; 10.7

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477 Table 2. Adjusted multilevel models of multimorbidity with independent variables. Brazil, 2013.

Variables	Multimorbidity (≥2)						Multimorbidity (≥3)					
	Model 1		Model 2		Model 3		Model 1		Model 2		Model 3	
	OR	CI95%	OR	CI95%	OR	CI95%	OR	CI95%	OR	CI95%	OR	CI95%
Sex (ref: male)												
Female	1.84	1.76; 1.94	1.85	1.77; 1.94	1.85	1.77; 1.94	1.95	1.83; 2.08	1.95	1.83; 2.08	1.95	1.83; 2.09
Age (in years)	1.06	1.06; 1.06	1.06	1.06; 1.06	1.06	1.06; 1.06	1.06	1.06; 1.06	1.06	1.06; 1.06	1.06	1.06; 1.06
Skin color* (ref: White)												
Black	1.07	0.99; 1.16	1.08	0.99; 1.17	1.08	0.99; 1.17	1.09	0.98; 1.21	1.09	0.98; 1.21	1.09	0.98; 1.21
Brown	1.01	0.96; 1.06	1.01	0.96; 1.07	1.01	0.96; 1.07	0.97	0.91; 1.04	0.97	0.91; 1.04	0.97	0.91; 1.04
Marital status (ref: Without partner)												
With partner	1.13	1.08; 1.18	1.13	1.08; 1.19	1.13	1.08; 1.19	1.17	1.09; 1.24	1.17	1.09; 1.24	1.17	1.09; 1.24
Schooling (in years) # (ref: ≥12)												
8-11	1.19	1.11; 1.28	1.19	1.10; 1.28	1.19	1.10; 1.28	1.22	1.10; 1.35	1.22	1.10; 1.35	1.22	1.10; 1.35
1-8	1.41	1.33; 1.51	1.41	1.33; 1.50	1.41	1.33; 1.50	1.57	1.44; 1.71	1.57	1.44; 1.71	1.57	1.44; 1.71
0	1.34	1.24; 1.44	1.34	1.24; 1.44	1.34	1.24; 1.44	1.41	1.27; 1.56	1.41	1.28; 1.56	1.41	1.28; 1.56
Wealth index (in quintiles) (ref: High)												
2°	1.12	1.04; 1.20	1.12	1.04; 1.20	1.12	1.04; 1.20	1.15	1.04; 1.28	1.15	1.04; 1.28	1.15	1.04; 1.28
3°	1.21	1.12; 1.31	1.21	1.12; 1.31	1.21	1.12; 1.31	1.19	1.07; 1.33	1.19	1.07; 1.33	1.19	1.07; 1.33
4°	1.05	0.96; 1.14	1.05	0.97; 1.14	1.05	0.97; 1.14	1.09	0.98; 1.22	1.10	0.98; 1.23	1.10	0.98; 1.23
5° (Low)	0.91	0.83; 1.00	0.92	0.84; 1.01	0.92	0.84; 1.01	0.95	0.84; 1.08	0.95	0.84; 1.08	0.95	0.84; 1.08
Private health plan (ref: no)												
Yes	1.15	1.08; 1.21	1.15	1.08; 1.20	1.15	1.08; 1.20	1.09	1.01; 1.18	1.09	1.01; 1.18	1.09	1.01; 1.18
Geographical area (ref: urban)												
Rural	0.86	0.80; 0.92	0.86	0.80; 0.92	0.86	0.80; 0.92	0.78	0.71; 0.86	0.78	0.71; 0.86	0.78	0.71; 0.86
State-level education (ref: High)												
Middle			0.82	0.71; 0.94					0.76	0.64; 0.90		
Low			0.83	0.72; 0.96					0.76	0.64; 0.90		
State-level income (ref: High)												
Middle					0.89	0.77; 1.04					0.88	0.73; 1.05
Low					0.82	0.71; 0.95					0.75	0.63; 0.89

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479 Table 3. Adjusted multilevel models of multimorbidity with independent variables stratified by region. Brazil, 2013.

Variables	Northern region		Northeastern region		Central Western region		Southeastern region		Southern region	
	MM (≥2)	MM (≥3)	MM (≥2)	MM (≥3)	MM (≥2)	MM (≥3)	MM (≥2)	MM (≥3)	MM (≥2)	MM (≥3)
	OR	OR	OR	OR	OR	OR	OR	OR	OR	OR
	CI95%	CI95%	CI95%	CI95%	CI95%	CI95%	CI95%	CI95%	CI95%	CI95%
Sex (ref: male)										
Female	1.81	2.06	1.96	2.08	2.22	2.37	1.62	1.61	1.84	2.04
	1.62; 2.02	1.75; 2.43	1.8; 2.14	1.84; 2.36	1.94; 2.54	1.97; 2.86	1.48; 1.78	1.43; 1.82	1.63; 2.08	1.73; 2.39
Age (in years)	1.05	1.06	1.06	1.06	1.07	1.07	1.05	1.05	1.06	1.06
	1.05; 1.06	1.05; 1.06	1.06; 1.06	1.06; 1.06	1.06; 1.07	1.06; 1.07	1.05; 1.06	1.05; 1.06	1.05; 1.06	1.06; 1.07
Marital status (ref: Without partner)										
With partner	1.13	1.17	1.16	1.23	1.00	0.93	1.15	1.22	1.16	1.19
	1.02; 1.27	1; 1.38	1.07; 1.27	1.09; 1.39	0.87; 1.14	0.78; 1.11	1.05; 1.26	1.08; 1.38	1.02; 1.32	1.01; 1.4
Skin color* (ref: White)										
Black	1.01	1.06	1.12	1.14	0.94	0.89	1.11	1.15	1.00	0.98
	0.82; 1.23	0.79; 1.42	0.97; 1.3	0.94; 1.39	0.74; 1.21	0.63; 1.26	0.96; 1.29	0.95; 1.4	0.76; 1.31	0.7; 1.38
Brown	0.92	0.92	0.96	0.93	1.13	1.14	1.07	1.02	1.08	0.88
	0.81; 1.04	0.76; 1.1	0.87; 1.05	0.81; 1.05	0.98; 1.29	0.95; 1.36	0.97; 1.18	0.89; 1.16	0.91; 1.27	0.71; 1.09
Schooling (in years) # (ref: more educated)										
III	1.17	1.12	1.10	0.95	1.16	1.32	1.35	1.47	1.12	1.27
	0.99; 1.39	0.86; 1.47	0.95; 1.28	0.76; 1.18	0.94; 1.42	0.99; 1.75	1.18; 1.55	1.22; 1.78	0.94; 1.35	0.99; 1.62
II	1.23	1.36	1.33	1.35	1.33	1.32	1.65	1.89	1.43	1.73
	1.05; 1.44	1.08; 1.71	1.18; 1.51	1.14; 1.6	1.11; 1.59	1.03; 1.68	1.46; 1.86	1.61; 2.22	1.22; 1.68	1.41; 2.13
I (less educated)	1.32	1.48	1.38	1.36	1.17	1.25	1.43	1.40	1.19	1.46
	1.12; 1.55	1.16; 1.88	1.21; 1.58	1.13; 1.65	0.94; 1.46	0.94; 1.68	1.22; 1.67	1.14; 1.71	0.97; 1.47	1.12; 1.89
Wealth index (in quintiles) (ref: High)										
2°	1.03	0.92	1.07	1.21	1.29	1.17	1.03	1.09	1.22	1.25
	0.83; 1.29	0.67; 1.27	0.91; 1.26	0.96; 1.52	1.05; 1.58	0.89; 1.55	0.90; 1.18	0.91; 1.3	1.04; 1.44	1.00; 1.57
3°	1.21	0.98	1.26	1.40	1.19	1.10	1.02	1.05	1.42	1.33
	0.98; 1.51	0.71; 1.34	1.07; 1.48	1.11; 1.76	0.95; 1.48	0.82; 1.48	0.89; 1.18	0.87; 1.27	1.18; 1.7	1.05; 1.69
4°	0.90	0.82	1.07	1.22	1.13	1.18	0.96	0.98	1.34	1.30
	0.72; 1.12	0.60; 1.11	0.91; 1.26	0.97; 1.53	0.9; 1.42	0.88; 1.59	0.82; 1.12	0.79; 1.20	1.09; 1.66	1.00; 1.7
5° (Low)	0.80	0.74	0.93	0.97	1.05	1.16	0.94	1.13	0.92	0.85
	0.64; 1.01	0.53; 1.03	0.78; 1.12	0.76; 1.25	0.80; 1.36	0.83; 1.62	0.77; 1.14	0.88; 1.45	0.71; 1.20	0.61; 1.19

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Private health plan (ref: no)

Yes	1.15	1.29	1.23	1.22	1.15	1.16	1.12	1.05	1.10	0.91
	0.98; 1.35	1.02; 1.61	1.09; 1.39	1.04; 1.44	0.99; 1.34	0.95; 1.41	1.01; 1.24	0.92; 1.2	0.96; 1.25	0.77; 1.09

Geographical area (ref: urban)

Rural	0.89	0.76	0.84	0.75	0.91	0.85	0.88	0.82	0.82	0.83
	0.77; 1.03	0.61; 0.94	0.75; 0.94	0.64; 0.88	0.75; 1.11	0.65; 1.11	0.76; 1.02	0.67; 1.00	0.68; 0.97	0.67; 1.04

480 Note: MM = Multimorbidity

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483 Table 4. Adjusted multilevel models of patterns of diseases (factors) with independent variables. Brazil, 2013.

Variables	Factor 1 (Cardiometabolic)						Factor 2 (Respiratory/mental/ muscle-skeletal)						
	Model 1		Model 2		Model 3		Model 1		Model 2		Model 3		
	β	CI95%	β	CI95%	β	CI95%	β	CI95%	β	CI95%	β	CI95%	
Sex (ref: male)													
Female	.024	.022; .026	.024	.022; .026	.024	.022; .026	.038	.036; .040	.038	.036; .040	.038	.036; .040	
Age (in years)	.004	.004; .004	.004	.004; .004	.004	.004; .004	.001	.001; .001	.001	.001; .001	.001	.001; .001	
Skin color* (ref: White)													
Black	.007	.003; .010	.007	.003; .010	.007	.003; .010	-.009	-.013; -.005	-.009	-.013; -.005	-.009	-.013; -.005	
Brown	.001	-.001; .004	.002	-.001; .004	.002	-.001; .004	-.004	-.006; -.001	-.004	-.006; -.001	-.004	-.006; -.001	
Marital status (ref: Without partner)													
With partner	.000	-.002; .002	.000	-.002; .002	.000	-.002; .002	-.005	-.007; -.002	-.005	-.007; -.003	-.005	-.007; -.003	
Schooling (in years)[#] (ref: ≥12)													
8-11	.013	.010; .016	.013	.010; .016	.013	.010; .016	.004	.001; .008	.005	.002; .008	.005	.002; .008	
1-8	.021	.018; .023	.021	.018; .023	.021	.018; .023	.011	.008; .014	.011	.008; .014	.011	.008; .014	
0	.014	.010; .017	.014	.010; .017	.014	.010; .017	.001	-.003; .004	.001	-.003; .005	.001	-.003; .005	
Wealth index (in quintiles) (ref: High)													
2°	.007	.004; .010	.007	.004; .010	.007	.004; .010	.005	.001; .008	.005	.001; .008	.005	.001; .008	
3°	.009	.006; .013	.009	.006; .013	.009	.006; .013	.010	.006; .014	.010	.006; .014	.010	.006; .014	
4°	.006	.002; .009	.006	.002; .009	.006	.002; .009	.004	.000; .008	.004	.000; .008	.004	.000; .008	
5° (Low)	-.003	-.007; .001	-.003	-.007; .001	-.003	-.007; .001	.001	-.004; .005	.001	-.004; .005	.001	-.004; .005	
Private health plan (ref: no)													
Yes	.006	.004; .009	.006	.004; .009	.006	.004; .009	.007	.005; .010	.007	.005; .010	.007	.005; .010	
Geographical area (ref: urban)													
Rural	-.008	-.011; -.005	-.008	-.011; -.005	-.008	-.011; -.005	-.002	-.005; .002	-.002	-.005; .002	-.002	-.005; .002	
State-level education (ref: High)													
Middle			-.010	-.016; -.004					-.016	-.027; -.005			
Low			-.008	-.015; -.002					-.018	-.029; -.006			
State-level income (ref: High)													
Middle					-.006	-.012; .001					-.011	-.022; .001	
Low					-.009	-.016; -.003					-.017	-.028; -.006	

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486 Table 5. Adjusted multilevel models of multimorbidity factors with independent variables stratified by region. Brazil, 2013.

Variables	Northern region		Northeastern region		Central Western region		Southeastern region		Southern region	
	Factor 1	Factor 2	Factor 1	Factor 2	Factor 1	Factor 2	Factor 1	Factor 2	Factor 1	Factor 2
	β	β	β	β	β	β	β	β	β	β
	CI95%	CI95%	CI95%	CI95%	CI95%	CI95%	CI95%	CI95%	CI95%	CI95%
Sex (ref: male)										
Female	0.022	0.023	0.027	0.030	0.029	0.050	0.020	0.041	0.023	0.061
	0.018; 0.026	0.019; 0.027	0.023; 0.03	0.027; 0.034	0.023; 0.034	0.044; 0.056	0.015; 0.024	0.036; 0.045	0.017; 0.03	0.053; 0.069
Age (in years)	0.003	0.001	0.004	0.001	0.004	0.001	0.004	0.001	0.004	0.002
	0.003; 0.003	0.001; 0.001	0.003; 0.004	0.001; 0.001	0.004; 0.004	0.001; 0.002	0.004; 0.004	0.001; 0.001	0.004; 0.004	0.001; 0.002
Marital status (ref: Without partner)										
With partner	0.001	-0.002	0.000	-0.002	-0.007	-0.013	0.001	-0.005	0.002	-0.010
	-0.003; 0.005	-0.006; 0.003	-0.003; 0.004	-0.005; 0.002	-0.013; -0.002	-0.02; -0.007	-0.003; 0.005	-0.010; 0.000	-0.004; 0.009	-0.018; -0.002
Skin color* (ref: White)										
Black	0.005	-0.007	0.007	-0.003	-0.001	-0.021	0.008	-0.011	0.013	-0.018
	-0.002; 0.013	-0.015; 0.001	0.001; 0.013	-0.01; 0.003	-0.011; 0.009	-0.033; -0.01	0.001; 0.016	-0.02; -0.003	-0.001; 0.026	-0.036; 0.000
Brown	-0.002	-0.007	-0.001	-0.003	0.004	-0.003	0.004	-0.002	0.005	0.004
	-0.007; 0.002	-0.012; -0.002	-0.005; 0.003	-0.008; 0.001	-0.001; 0.01	-0.010; 0.004	-0.001; 0.009	-0.008; 0.003	-0.003; 0.014	-0.007; 0.015
Schooling (in years) # (ref: more educated)										
III	0.006	0.007	0.011	0.000	0.012	-0.001	0.016	0.007	0.019	0.010
	0.000; 0.011	0.001; 0.013	0.006; 0.017	-0.006; 0.006	0.004; 0.02	-0.011; 0.008	0.010; 0.023	0.000; 0.014	0.01; 0.028	-0.002; 0.021
II	0.009	0.005	0.015	0.006	0.016	-0.001	0.029	0.019	0.037	0.020
	0.003; 0.014	-0.001; 0.011	0.010; 0.020	0.001; 0.012	0.009; 0.024	-0.01; 0.008	0.023; 0.035	0.013; 0.026	0.028; 0.046	0.009; 0.031
I (less educated)	0.014	0.008	0.010	0.002	0.015	-0.009	0.022	-0.002	0.016	-0.005
	0.008; 0.02	0.001; 0.014	0.004; 0.015	-0.004; 0.008	0.005; 0.025	-0.021; 0.002	0.014; 0.03	-0.011; 0.007	0.004; 0.027	-0.02; 0.01
Wealth index (in quintiles) (ref: High)										
2°	0.005	0.005	0.005	0.002	0.008	0.004	0.004	-0.003	0.011	0.017
	-0.003; 0.013	-0.004; 0.013	-0.002; 0.011	-0.005; 0.009	-0.001; 0.016	-0.005; 0.014	-0.002; 0.011	-0.01; 0.004	0.003; 0.002	0.007; 0.028
3°	0.009	0.004	0.012	0.010	0.002	0.002	0.004	0.002	0.012	0.027
	0.001; 0.017	-0.004; 0.013	0.005; 0.018	0.003; 0.017	-0.007; 0.011	-0.008; 0.013	-0.003; 0.011	-0.005; 0.01	0.003; 0.021	0.015; 0.039

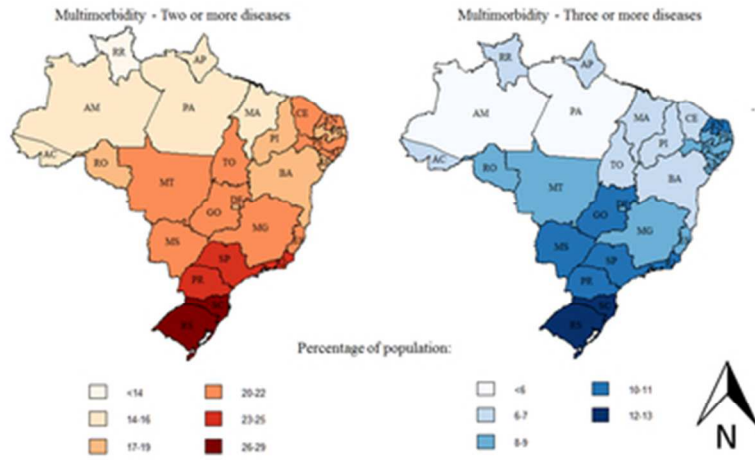
4°	0.004	-0.001	0.005	0.004	0.005	0.005	0.003	-0.007	0.009	0.019
	-0.004; 0.011	-0.01; 0.007	-0.002; 0.011	-0.003; 0.011	-0.005; 0.014	-0.006; 0.016	-0.004; 0.011	-0.015; 0.001	-0.002; 0.02	0.005; 0.033
5° (Low)	-0.004	-0.009	-0.001	0.004	0.001	0.004	-0.006	-0.004	-0.012	0.012
	-0.012; 0.004	-0.017; 0.000	-0.009; 0.006	-0.003; 0.012	-0.010; 0.012	-0.008; 0.017	-0.015; 0.004	-0.015; 0.006	-0.026; 0.002	-0.006; 0.029
Private health plan (ref: no)										
Yes	0.009	0.009	0.010	0.008	0.007	0.009	0.002	0.008	0.005	0.001
	0.003; 0.015	0.003; 0.016	0.006; 0.015	0.003; 0.013	0.000; 0.013	0.001; 0.016	-0.003; 0.006	0.002; 0.013	-0.002; 0.012	-0.008; 0.01
Geographical area (ref: urban)										
Rural	-0.007	0.004	-0.008	-0.006	-0.009	-0.001	-0.007	-0.010	-0.008	0.009
	-0.012; -0.002	-0.002; 0.009	-0.013; -0.004	-0.011; -0.001	-0.018; -0.001	-0.01; 0.009	-0.014; 0.000	-0.018; -0.001	-0.017; 0.002	-0.003; 0.021

487 Note: Factor 1: cardiometabolic; factor 2: (Respiratory/mental/ muscle-skeletal)

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

Morbidities	Individual prevalence		Duration of disease	Number of comorbidities
	%	(95%CI)	Mean (median; Q25-Q75)	Mean (median; Q25-Q75)
High Blood Pressure	22.3	21.7 - 23.0	13.1 (9; 3-18)	2.3 (2; 1-3)
Spinal column problem	19.0	18.3 - 19.7	14.7 (10; 4-21)	2.3 (2; 1-3)
Hypercholesterolemia	8.4	8.0 - 8.8	6.9 (3; 1-9)	2.3 (2; 1-3)
Arthritis/rheumatism	6.7	6.4 - 7.1	14.6 (10; 3-20)	3.0 (3; 2-4)
Diabetes	6.5	6.2 - 6.9	11.3 (6; 2-15)	2.9 (3; 2-4)
Asthma/wheezy bronchitis	4.4	4.1 - 4.8	25.1 (23; 13-35)	2.4 (2; 1-3)
Depression	4.2	3.9 - 4.5	-	2.9 (3; 2-4)
Work-related muscle-skeletal disorders	2.5	2.2 - 2.8	7.5 (5; 2-11)	2.5 (2; 1-3)
Cancer	1.9	1.7 - 2.2	8.5 (6; 2-13)	2.8 (2; 2-4)
Another heart disease	1.9	1.6 - 2.1	13.9 (9; 3-20)	3.1 (3; 2-4)
Stroke	1.6	1.4 - 1.8	10.2 (6; 2-13)	3.4 (3; 2-5)
Kidney problem	1.5	1.3 - 1.7	13.5 (9; 3-20)	3.2 (3; 2-4)
Heart attack	1.3	1.2 - 1.5	12.4 (7; 2-18)	4.0 (4; 3-5)
Heart failure	1.2	1.1 - 1.4	13.2 (8; 4-19)	4.0 (4; 2-5)
Bronchitis	1.0	0.8 - 1.1	23.2 (20; 9-32)	3.3 (3; 2-5)
Angina	0.8	0.7 - 0.9	15.5 (11; 5-21)	4.5 (4; 3-6)
Emphysema	0.5	0.4 - 0.6	14.9 (9; 3-18)	3.7 (3; 2-5)
Another lung disease	0.5	0.4 - 0.6	16.2 (12; 5-24)	2.8 (2; 1-4)
Bipolar disorder	0.4	0.3 - 0.5	11.3 (8; 4-16)	3.1 (3; 2-4)
Another mental disease	0.3	0.2 - 0.4	2.8 (2; 1-4)	2.5 (2; 1-3)
Schizophrenia	0.2	0.2 - 0.3	19.7 (19; 8-26)	2.7 (3; 2-3)
Obsessive Compulsive Disorder (OCD)	0.2	0.1 - 0.2	14.5 (12; 6-21)	3.4 (3; 2-4)



Multimorbidity frequency by Brazilian states. Brazil, 2013

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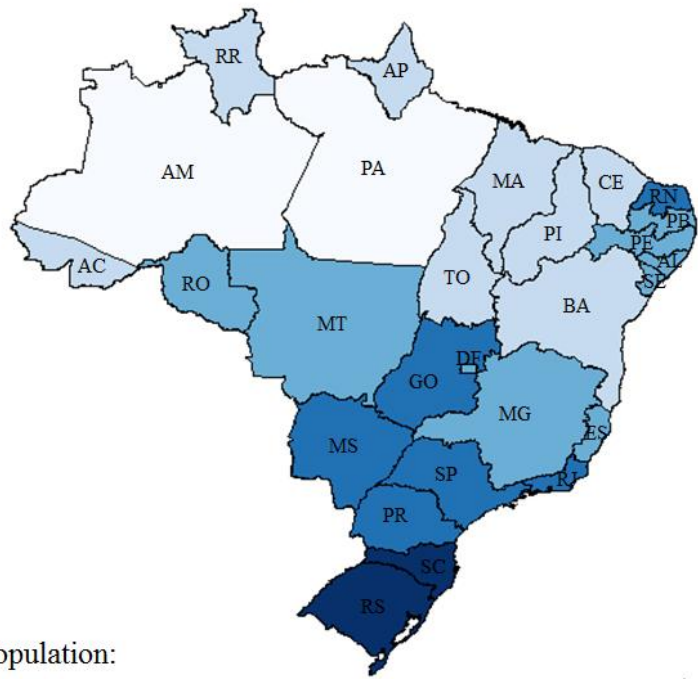
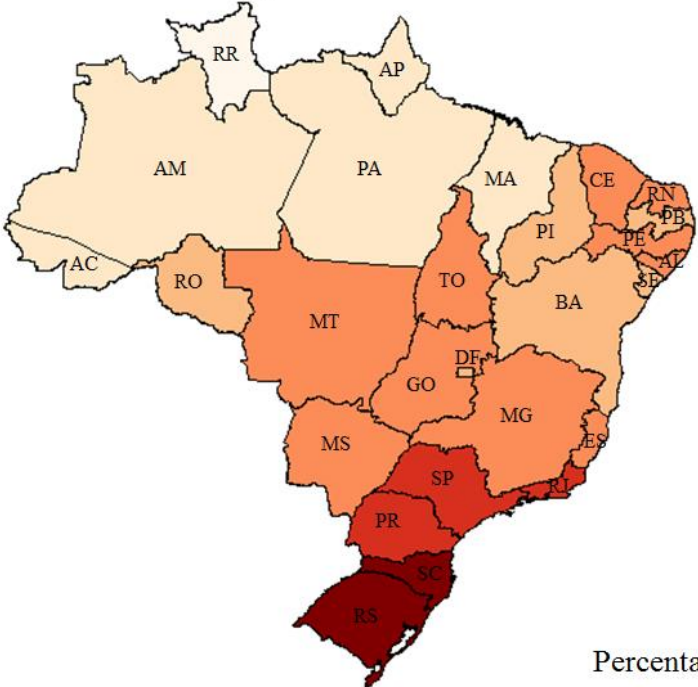
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Multimorbidity - Two or more diseases

Multimorbidity - Three or more diseases



Percentage of population:



Supplementary table 2. Factor analysis. Brazil, 2013.

Morbidities	Factor 1	Factor 2
High Blood Pressure	0.77	
Heart attack	0.79	
Angina	0.68	
Heart failure	0.69	
Stroke	0.58	
Hypercholesterolemia	0.57	
Diabetes	0.62	
Arthritis/rheumatism	0.30	0.37
Spinal column problem		0.45
Asthma/wheezy bronchitis		0.57
COPD		0.63
Work-related muscle-skeletal disorders		0.45
Depression		0.46
Bipolar disorder		0.46
Kidney problem		0.31
Cancer	-	-
Eigenvalor	4.46	1.11
Explained variance %*	0.73 (0.69)	0.18 (0.47)
KMO		0.84

*Before oblique rotation (after oblique rotation)

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	5
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	-
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6
Bias	9	Describe any efforts to address potential sources of bias	6
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5-6
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	6-7
		(b) Describe any methods used to examine subgroups and interactions	-
		(c) Explain how missing data were addressed	-
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	6
		(e) Describe any sensitivity analyses	-

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(b) Give reasons for non-participation at each stage	-
		(c) Consider use of a flow diagram	-
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8
		(b) Indicate number of participants with missing data for each variable of interest	-
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	-
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	-
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	-
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	8
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8-9
		(b) Report category boundaries when continuous variables were categorized	8-9
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	-
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14
Generalisability	21	Discuss the generalisability (external validity) of the study results	14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

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

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2017-015885.R2
Article Type:	Research
Date Submitted by the Author:	23-Apr-2017
Complete List of Authors:	Nunes, BP; Universidade Federal de Pelotas, Department of Nursing Chiavegatto Filho, Alexandre; Harvard School of Public Health, Society, Human Development and Health; Faculdade de Saúde Pública da Universidade de São Paulo, Departamento de Epidemiologia Pati, Sanghamitra; Public Health Foundation of India, Indian Institute of Public Health Bhubaneswar; Sanghamitra Pati, Teixeira, Doralice; Secretaria Municipal da Saúde de São Paulo, São Paulo, Brasil Flores, Thaynã; Federal University of Pelotas, Postgraduate Program of Epidemiology Camargo-Figuera, Fabio Alberto; Universidad Industrial de Santander, School of Nursing Munhoz, Tiago; Universidade Federal de Pelotas, Postgraduate Programme in Epidemiology Thume, Elaine; Universidade Federal de Pelotas, Department of Nursing/Postgraduate Program of Nursing Facchini, Luiz; Universidad Federal de Pelotas, Departamento de Medicina Social Batista, Sandro Rogerio; Federal University of Goias, Department of Internal Medicine of Medical School
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Public health
Keywords:	Comorbidity, Multimorbidity, Chronic disease, Statistical disease clustering, Multilevel Analysis

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1
2
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4 **Title page**

5
6 **Title:** Contextual and individual inequalities of multimorbidity in Brazilian adults: a cross-
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8 sectional national-based study

9
10 **Authors:** Bruno P Nunes¹; Alexandre DP Chiavegatto-Filho²; Sanghamitra Pati³; Doralice S
11 Cruz Teixeira⁴; Thaynã R Flores⁵; Fabio A Camargo-Figuera⁶; Tiago N Munhoz⁵; Elaine
12 Thumé⁷; Luiz A Facchini^{5,7}; Sandro R Rodrigues Batista⁸

13
14
15
16 1 – Department of Nursing, Federal University of Pelotas, Brazil

17
18 2 – Department of Epidemiology, School of Public Health, University of São Paulo,
19 São Paulo, Brazil

20
21 3 – Indian Institute of Public, Health, Bhubaneswar, Public Health Foundation of
22 India, Bhubaneswar, Odisha, India

23
24 4 – Municipal Health Department of São Paulo, São Paulo, Brasil.

25
26 5 – Postgraduate Program in Epidemiology, Federal University of Pelotas, Pelotas,
27 Brazil

28
29 6 – School of Nursing, Universidad Industrial de Santander, Bucaramanga, Colombia.

30
31 7 – Postgraduate Program in Nursing, Federal University of Pelotas, Pelotas, Brazil

32
33 8 – Faculty of Medicine, Federal University of Goiás, Goiânia, Brazil

34
35
36
37
38
39
40
41
42 **Correspondence to:** Bruno P Nunes, Department of Nursing, Federal University of Pelotas,
43
44 Gomes Carneiro, 1, Phone: +5553 3284-3820, Pelotas-RS, Brazil. Email:
45
46 nunesbp@gmail.com

47
48
49 **Key-words:** Comorbidity; Multimorbidity; Chronic disease; Statistical disease clustering;
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51
52 Multilevel Analysis.

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55 **Word count:** 3137

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4 25 **Abstract**
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7 **Objectives:** The study aims to evaluate the magnitude of multimorbidity in Brazilian adults,
8
9 as well to measure their association with individual and contextual factors stratified by
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11 Brazilian states and regions.
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14 **Methods:** A national-based cross-sectional study was carried out in 2013 with Brazilian
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16 adults. Multimorbidity was evaluated by a list of 22 physical and mental morbidities (based
17
18 on self-reported medical diagnosis and Patient Health Questionnaire 9 for depression). The
19
20 outcome was analyzed taking ≥ 2 and ≥ 3 diseases as cut-off points. Factor analysis (FA) was
21
22 used to identify disease patterns and multilevel models were used to test association with
23
24 individual and contextual variables.
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28 **Results:** The sample was comprised of 60,202 individuals. Multimorbidity frequency was
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30 22.2% (CI95% 21.5; 22.9) for ≥ 2 morbidities and 10.2% (CI95% 9.7; 10.7) for ≥ 3
31
32 morbidities. In the multilevel adjusted models, females, older people, those living with a
33
34 partner and having less schooling presented more multiple diseases. No linear association was
35
36 found according to wealth index but greater outcome frequency was found in individuals with
37
38 mid-range wealth index. Living in states with higher levels of education and wealthier states
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40 was associated with greater multimorbidity. Two patterns of morbidities (cardiometabolic
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42 problems and Respiratory/mental/muscle-skeletal disorders) explained 92% of total variance.
43
44 The relationship of disease patterns with individual and contextual variables was similar to
45
46 the overall multimorbidity, with differences among Brazilian regions.
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51 **Conclusions:** In Brazil, at least 19 million adults had multimorbidity. Frequency is similar to
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53 that found in other LMIC. Contextual and individual social inequalities were observed.
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4 47 **Strengths and limitations of this study**
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- 7 48 • Comprehensive information about multimorbidity is still scarce in Brazil
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9 49 • As far as we are aware, this is among the first information about multimorbidity
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11 assessment of individual and contextual factors in a sample representative of the
12
13 whole of Brazil
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15 52 • Multimorbidity is a challenge to the Brazilian health system due to its high frequency
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17 (two in every ten adults had ≥ 2 diseases and one in every ten had ≥ 3 diseases,
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19 representing at least 19 million Brazilians) and the interplay of individual and
20
21 contextual characteristics associated with the problem. Differences within the country
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23 were observed.
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25 56 • Except for depression, other morbidities were evaluated by self-reporting and we are
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27 not able to evaluate the contextual determinants at neighborhood level
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59 **Introduction**

60 Multimorbidity is a current and worldwide public health problem mainly due to its high
61 frequency (>60% in adults) and its association with negative outcomes [1-4]. Most evidence
62 is from High Income Countries [4] but results from Low and Middle Income Countries
63 (LMIC) are also available and increasing in the literature [5-8], including epidemiological
64 information about multimorbidity in Brazilian cities [9-11].

65 Similar to international evidence, multimorbidity in Brazil is greater in females and increases
66 according to age. Socioeconomic inequalities are also observed mainly related to educational
67 differences whereas multiple disease is more frequent in adults and elderly with less
68 schooling and lower socioeconomic status [10 11].

69 However, as far as we are aware, Brazilian evidence on multimorbidity for the entire country
70 is scarce. Only recently, a paper evaluating epidemiology of multimorbidity in Brazil was
71 published [12]. The authors found a 24.2% (95% CI 23.5–24.9) prevalence rate of
72 multimorbidity [12] and correlates were similar to Brazilian located previous studies ([10
73 11].

74 Brazil is the 5th most populous country in the world with more than 200 million people.
75 Furthermore, it is marked by historic social inequalities in different health aspects comprising
76 the occurrence of chronic diseases including both physical and mental disorders [13-15].

77 Understanding the occurrence and patterns of multimorbidity in the whole country can be
78 relevant for Brazilian Unified Health System management of the challenges resulting from the
79 rapid demographic and epidemiological transitions that have occurred in recent years.

80 Additionally, identifying and comprehending the contextual and individual differences

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4 81 surrounding multimorbidity occurrence helps policy-makers to prioritize and promote health
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6 82 actions and interventions related to multimorbidity management.
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9 83 Thus, the aim of this study was to evaluate the frequency and patterns of multimorbidity in
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11 84 Brazilian adults, as well to measure their association with individual and contextual factors
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14 85 stratified by Brazilian states and regions.
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86 **Methods**

87 This was a cross-sectional study using population-based data from the Brazilian National
88 Health Survey (*Pesquisa Nacional de Saúde - PNS*) carried out in Brazil in 2013. The survey
89 was conducted by *Instituto Brasileiro de Geografia e Estatística (IBGE)* and the Ministry of
90 Health. The sample is representative of people living in permanent housing, located in urban
91 or rural areas, covering the country's five major geographical regions, its 26 states and
92 Federal District.

93 Sampling was done in three stages, the first being the selection of census tracts, followed by
94 households and, finally, individuals aged 18 or over. More details about the sampling process
95 can be found elsewhere[16 17].

96 Multimorbidity was evaluated by using a list of all 22 self-reported morbidities available in
97 the study, 21 of which were based on self-reported medical diagnosis, while depression was
98 based on the Patient Health Questionnaire-9(PHQ-9)[18]. The question applied to measure
99 each disease based on self-reported medical diagnosis was: "*Has any physician already*
100 *diagnosed you as having [each disease]?*". The following morbidities were included: High
101 Blood Pressure - HBP; Spinal column problem; Hypercholesterolemia; Depression; Diabetes;
102 Arthritis/rheumatism; Asthma/wheezy bronchitis; Work-related muscle-skeletal disorders;
103 Cancer; Other heart disease; Stroke; Kidney problem; Heart attack; Heart failure; Bronchitis;
104 Angina; Emphysema; Other lung disease; Bipolar disorder; Other mental disease;
105 Schizophrenia; and Obsessive Compulsive Disorder (OCD). Multimorbidity was evaluated by
106 two cut-off points as per the literature[4 19]: ≥ 2 and ≥ 3 morbidities. Women who had HBP or
107 diabetes only during pregnancy were considered as not having these diseases.

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4 108 Independent variables were sex (male; female), age (continuous), skin color (white; black;
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6 109 and brown - Asian-Brazilian and indigenous were not shown because they represented less
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8 110 than 1.6% of the sample), marital status (without partner; with partner), schooling in years (0:
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10 111 No schooling; 1-8: incomplete primary school; 8-11: complete primary school and incomplete
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12 112 secondary school; ≥12: complete secondary school up to complete higher education), wealth
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14 113 index in quintiles (based on ownership of bathroom, car, motorcycle, refrigerator, washing
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16 114 machine, DVD player, TV, landline telephone, microcomputer and microwave oven), private
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18 115 health plan (no; yes), geographical area (urban; rural); state-level education in terciles –
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20 116 proportion of literacy rate obtained from IBGE, 2010 and state-level income in terciles
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22 117 (nominal income per capita - average monthly value - in permanent private housing obtained
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24 118 from IBGE, 2010).

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29 119 Statistical analyses were performed using Stata 12.1 software and the *svy* command was used,
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31 120 which takes into consideration sample weights. Sample weights were defined for the primary
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33 121 sampling units, households and all inhabitants, as well as for the selected inhabitant.

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36 122 Complete information about PNS sample weights and sampling process have been published
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38 123 elsewhere [16 17]. The results from the sample were expanded for the Brazilian population.

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41 124 Descriptive analysis was based on the calculation of prevalence and its respective confidence
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43 125 intervals. Factor analysis (FA) was performed to identify patterns of morbidities[20]. This
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45 126 analysis was based on tetrachoric correlation, this being more appropriate than Pearson's
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47 127 correlation for dichotomous variables [21]. Before FA analysis, Kaiser-Meyer-Olkin (KMO)
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49 128 and Bartlett sphericity tests were used to evaluate the applicability of this approach. After the
50
51 129 first evaluation of the model, some variables were encompassed (bronchitis, emphysema and
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53 130 other lung disease to other respiratory problems - COPD) and others excluded (schizophrenia,
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55 131 Obsessive Compulsive Disorder, another mental disease and another heart disease) in order to
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4 132 obtain a better model fit regarding KMO and Bartlett sphericity tests. Oblique (oblimin or
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6 133 promax) rotation was performed. In order to establish the number of components to be
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8 134 retained, we used Cattell graphics, Kaiser criteria (eigenvalue>1) and minimum explained
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10 135 variance (>10% for each component). Variables with loadings ≥ 0.3 were kept [22]. Through
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12 136 factorial analysis, we obtained the predicted scores of morbidities (factors).

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16 137 Multilevel models were performed to account for state-level variance, with the individuals as
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18 138 the first level and the state of residence as the second level. First, the models were initially
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20 139 adjusted without inclusion of the independent variables (null model) to test the initial variance
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22 140 attributable to the state accounting for approximately 1% ($p < 0.05$) of variance for the four
23
24 141 analyses (Multimorbidity ≥ 2 ; Multimorbidity ≥ 3 , factor 1 and factor 2). Then, we performed a
25
26 142 logistic regression model for multimorbidity (≥ 2 and ≥ 3 morbidities) and linear regression
27
28 143 models to evaluate the association of factors (patterns) of diseases and independent variables.
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30 144 We included sex, age, skin color, marital status, schooling in years, private health plan,
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32 145 geographical area, state-level education and income in these models. Stratified region-level
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34 146 analyzes were performed to better understanding disparities among states.

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39 147 The study was approved by the National Research Ethics Commission on July 8, 2013, under
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41 148 No. 10853812.7.0000.0008. All respondents signed a free and informed consent statement
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43 149 form prior to data collection
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4 150 **Results**

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7 151 The sample was comprised of 60,202 adults. The most frequent diseases were High Blood
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9 152 Pressure (22.3%) and Spinal column problem (19.0%). Angina, emphysema, other lung
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11 153 disease, bipolar disorder, other mental disease, schizophrenia and Obsessive Compulsive
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13 154 Disorder (OCD) were present in less than 1% of the sample. Lung disease problems showed,
14
15 155 on average, longer duration of disease. Greater comorbidities were observed for individuals
16
17 156 with health problems (heart attack; heart failure and angina). The mean range of comorbidities
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19 157 was from 2.3 to 4.5 diseases (Supplementary table 1).

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23 158 Females comprised 55.1% of the sample and mean age was 43.7 years (SD=17.0), ranging
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25 159 from 18 to 101. Most individuals reported white skin color (47.8%) followed by brown
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27 160 (41.7%). Almost two thirds lived with a partner. Out of the total sample, 45.2% had ≥ 12 years
28
29 161 of schooling and 13.9% had zero schooling. Less than one third had a private health plan and
30
31 162 13.5% lived in rural areas (Table 1). The mean average proportion of literacy rate at the state-
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33 163 level was 7.3%, ranging from 3.3% to 22.5%. The average monthly value of nominal income
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35 164 per capita was R\$ 1,069 (approximately US\$ 644 in 2010).

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39 165 The occurrence of multimorbidity was 22.2% (CI95% 21.5; 22.9) for ≥ 2 morbidities and
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41 166 10.2% (CI95% 9.7; 10.7) for ≥ 3 morbidities. Irrespective of cut-off point, multimorbidity was
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43 167 higher in females, older people, individuals reporting white skin color, who lived with a
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45 168 partner, had less schooling, had a private health plan and living in urban areas. At state-level,
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47 169 multimorbidity was more frequent in states with higher education levels and wealthier states
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49 170 (Table 1). States in the South of Brazil showed the highest occurrence of multimorbidity
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51 171 (Supplementary figure 1),
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4 172 In the adjusted multilevel models, females had 1.86 (CI95% 1.78; 1.95) and 1.97(CI95%
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6 173 1.85; 2.10) more odds of multimorbidity than males, for ≥ 2 and ≥ 3 morbidities, respectively.
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8 174 In all cases, every additional year of age increased by 1.06 times the odds of multiples
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10 175 diseases. Self-reported skin color was not associated with multimorbidity in the adjusted
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12 176 models. On average, living with a partner increased by 1.15 times the odds of the outcome.
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14 177 Compared to individuals with ≥ 12 years of schooling, adults with 1-8 years of schooling had
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16 178 more odds of multimorbidity (OR 1.40 - CI95% 1.32; 1.49, for ≥ 2 diseases and OR 1.58
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18 179 CI95% 1.45; 1.72, for ≥ 3 morbidities). In general, adults in the second and third wealthiest
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20 180 quintiles had greater odds of multimorbidity. Individuals with private health plans and who
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22 181 lived in urban areas had greater odds of multiple diseases. Individuals who lived in states with
23
24 182 low and middle education levels had less multimorbidity compared to states with high
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26 183 education levels. With regard to income at state-level, the higher multimorbidity difference
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28 184 was demonstrated simply by comparing low with high income states (Table 2). The
29
30 185 associations stratified by region revealed a similar pattern to the whole Brazil, except to
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32 186 Central Western region in relation to lack of association of overall multimorbidity and private
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34 187 health plan, geographical area (observed to Southeastern region too) and schooling (no dose-
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36 188 response relationship) (Table 3).
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42 189 In the FA analysis, the KMO coefficient was 0.84. Two patterns of morbidities explained
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44 190 92% of total variance, after rotation. The two components identified were: (1)
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46 191 cardiometabolic problems (High Blood Pressure, heart attack, angina, heart failure, stroke,
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48 192 hypercholesterolemia, diabetes and arthritis/rheumatism); (2) Respiratory/mental/muscle-
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50 193 skeletal disorders (arthritis/rheumatism, spinal column problem, asthma/wheezy bronchitis,
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52 194 COPD, work-related muscle-skeletal disorders, depression, bipolar disorder and kidney
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54 195 problem) (Supplementary table 2).
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4 196 The adjusted multilevel analyses of the two factors are presented in Table 4. Overall, the
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6 197 results were similar to those observed in Table 2. Females, older people, those with less
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8 198 schooling, those with intermediate asset ownership quintiles and who had private health plans
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10 199 showed more burden of factors. People who lived in rural geographical areas showed less
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12 200 burden of the cardiometabolic factor. Individuals with partners presented less burden of the
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14 201 Respiratory/mental/muscle-skeletal factor compared to individuals who did not have a
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16 202 partner. Cardiometabolic and Respiratory/mental/muscle-skeletal factors were greater when
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18 203 state-level education and income were lower. The cardiometabolic factor presented similar
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20 204 associations as overall multimorbidity to stratified analysis. As for the Respiratory/mental/
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22 205 muscle-skeletal factor did not show association with schooling in all regions (except to
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24 206 Northern) (Table 5).
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4 208 **Discussion**
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7 209 Multimorbidity frequency in Brazil is considerable; one in every five Brazilian adults had two
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9 210 or more morbidities and one in every ten had three or more morbidities. Individual and state-
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11 211 level inequalities suggest the complexity of factors and their relationship with multimorbidity
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13 212 occurrence. To our knowledge, this is the first representative Brazilian study to consider
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15 213 individual and contextual factors associated with multimorbidity and its clusters.
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19 214 The study's national representativeness enables us to extrapolate frequencies for the whole
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21 215 Brazilian adult population. Considering 190,755,799 million adults in the most recent
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23 216 Brazilian population census (2010), we are able to infer that approximately 42.7 and 19.5
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25 217 million Brazilian adults had two or more and three or more diseases, respectively. These
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27 218 results bring important challenges for the health system which will need to be more
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29 219 comprehensive in order to deal with the complexity of multimorbidity. Some of the issues are
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31 220 related to need to include multimorbidity in guidelines on reporting these problems to health
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33 221 professionals, as well as giving more emphasis to multimorbidity on health-related university
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35 222 curricula.
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39 223 Relative comparisons with Western countries reveal similar occurrence of two or more
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41 224 diseases in Spain [23] (20.0%; CI95%: 18.8-21.2) and almost ten percentage points less than
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43 225 in Scotland [24] (31.1%, 25 or more years) and Canada[25] (30.9%; CI95% 29.5 – 32.4).In
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45 226 low and middle income countries (LMIC), estimates from countries (China, Ghana, India,
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47 227 Mexico, Russia, and South Africa) included in the WHO Study on global AGEing and adult
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49 228 health (SAGE) Wave-1 (2007/10), found 21.9% (CI95%: 20.9; 22.9) of multimorbidity
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51 229 occurrence (≥ 2 diseases from a list from eight morbidities)[5]. This occurrence varied from
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53 230 20.3% in China to 34.7% in Russia. In the present analysis, we used more diseases to
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4 231 construct multimorbidity (22 against eight in SAGE study). Even so, the prevalence found
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6 232 was, virtually, equal to these other LMIC countries, except for Russia.
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9 233 In Brazil, our occurrence findings were slightly lower than the result found in a paper with
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11 234 same database (-2 pp). Furthermore, the authors found three clusters which differ of our
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13 235 results (n=2) despite the resemblance of diseases grouping[12]. These variations are explained
14
15 236 by the differences among diseases selected to measure multimorbidity and analysis steps to
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17 237 obtain the clusters. The standardization of multimorbidity operationalization is an urgent call
18
19 238 to avoid loss of consistency in the development of the area [4]. Comparing with
20
21 239 geographically located Brazilian results, our prevalence were lower than frequencies found
22
23 240 in a Southern Brazilian city (29.1%; CI95%: 27.1; 31.1 for ≥ 2 morbidities, and 14.3 %;
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25 241 CI95%: 12.8; 15.8 for ≥ 3 morbidities) despite the higher number of morbidities included in
26
27 242 this study [10]. The difference observed may be attributed to socioeconomic characteristics of
28
29 243 Brazilian states. The states further South presented more development, wealth (both income
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31 244 and schooling) and higher life expectancy compared to other states [13] which tend to
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33 245 increase the occurrence of multimorbidity at contextual level.
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38 246 In terms of socio-demographic characteristics, females and older adults presented more
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40 247 multimorbidity in all Brazilian regions as found in previous Brazilian [10 11] and
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42 248 international studies [26 27]. Women tend to use health services more and to live longer than
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44 249 males, these being factors which explain part of the higher frequency in this group. Survivors
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46 250 older adults tend to be exposed to more physiological damages in lifetime that contribute to
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48 251 chronic disease incidence [28]. In the same way, individuals who had partners had higher
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50 252 multimorbidity except to Central Western residents. The association between marital status
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52 253 should be more understanding through studies which include cultural assessment and its
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54 254 impact on chronic diseases development and diagnosis. One explanation is related to the fact
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4 255 that individuals with partner tend to use more health services increasing the probability of
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6 256 medical diagnosis [29].
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9 257 Regarding socioeconomic variables at individual level, our results follow the pattern found in
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11 258 overall analysis of a worldwide study [27] and LMIC included in the SAGE study.
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13 259 Multimorbidity and its factors was not associated with wealth quintiles but presented
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15 260 association with education [5] regardless Brazilian regions. In the present analysis, the middle
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17 261 wealth quintile strata and their clusters present more multimorbidity whilst showing a
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19 262 negative dose-response relationship with education. These results may be explained by a
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21 263 strong relationship between educational attainment and all aspects of healthier life including
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23 264 those mainly related to better awareness of chronic disease risk factors [30 31]. Education
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25 265 level seems to be a more adequate socioeconomic indicator to evaluate multimorbidity
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27 266 inequalities due to its worldwide association with poor health outcomes and longevity, and the
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29 267 persistent effect overtime [30]. Except for the early effect of childhood health status on
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31 268 education [32 33], chronic diseases in adult life tend to increase the risk of poverty (wealth
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33 269 index) [34] but the effect on education tend to be less relevant since education is usually
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35 270 achieved is early life
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40 271 Having private health plans was associated with multimorbidity and its factors, except to
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42 272 Central Western and Southern. This may be explained, by the relationship with self-reported
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44 273 diagnosis (a fundamental characteristic of the outcome). Individuals with health plans tend to
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46 274 use health services more frequently regardless the presence of chronic conditions[35 36] thus
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48 275 affording more diagnosis.
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52 276 Individuals who lived in urban areas presented more multiple diseases. This was similar to
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54 277 results found in the adult population in South Africa [37] and Catalonia (Spain)[38]. In spite
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4 278 of little Brazilian evidence on the topic, as well as the social, cultural and environment
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6 279 differences between rural-urban residents, people from rural areas had more difficulty in
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8 280 accessing health services in Brazil [39] which may explain partially the differences between
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10 281 rural and urban residents in our results of the occurrence of self-reported medical diagnosis of
11
12 282 multiple diseases.

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15 283 The state-level differences observed reveal a paradoxical association. Instead of individual
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17 284 inequalities are pro-rich, state-level differences are pro-poor. These results might be explained
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19 285 by demographic differences between states in Brazil which may not be fully adjusted with
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21 286 individual demographic variables included in the analysis. Low income and low education in
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23 287 Brazilian states are concentrated in North and Northeast regions and show the poorest health-
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25 288 related indicators[13]. The states further south (*Rio Grande do Sul* - 27.2% and *Santa*
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27 289 *Catarina* - 27.1%) present greater multimorbidity frequencies.

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32 290 The two factors (cardiometabolic and respiratory/mental/muscle-skeletal) found have some
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34 291 similarity to recent evidence [40 41] mainly related to cardiometabolic patterns. The
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36 292 respiratory/mental/muscle-skeletal data found was similar to results found in a worldwide
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38 293 study of people aged 50 or over [42]. The majority of studies, especially with adult
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40 294 populations, found two or three patterns of diseases. These combinations of diseases suggest
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42 295 possible causal relationship between diseases or their risk factors [20]. The cardiometabolic
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44 296 pattern showed a more well know relationship between diseases. On the other hand, the
45
46 297 relationship between respiratory, mental and muscle-skeletal disorders is less understood. The
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48 298 concomitant occurrence of these diseases is well described [43] but understanding the
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50 299 biological plausibility of causal relationships will be a challenge for new studies. As a first
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52 300 step, more detailed and specific information about onset of diseases will be needed. At the
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54 301 same time, the use of approaches related to network analysis can be useful for a better
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4 302 understanding of causal relationships [44]. Even so, the results presented here may contribute
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6 303 to the inclusion of recommendations in Brazilian clinical guidelines about the relationship
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8 304 with chronic conditions, as well as to designing interventions/public policies considering the
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10 305 presence of multiple diseases in the same individual.
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12
13 306 Some limitations of the study should be addressed. With the exception of depression, all the
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15 307 other morbidities were evaluated by self-reporting. This may provide a misclassification bias
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17 308 even though self-reported diagnosis is considered an adequate and common source of
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19 309 information used in population-based studies on multimorbidity [4 45 46]. Nevertheless, the
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21 310 lack of adequate information about diagnosis, including longitudinal information, limits the
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23 311 causal inference related to concomitant diseases expressed in factorial analysis. Furthermore,
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25 312 we are not able to evaluate the contextual determinants at neighborhood level which may
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27 313 produce more complete associations with state-level differences.
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31 314 The absolute and relative number of Brazilian individuals with multimorbidity was high.
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33 315 Addressing the complexity of multiple disease management for at least 19 million people will
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35 316 be a challenge for the health system. The clusters of diseases identified might contribute to
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37 317 strategies for the prevention and clinical care of these diseases. State and individual-level
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39 318 inequalities increase the problem reinforcing the need of a wide lens to organize health
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41 319 services and to decrease the inequities among the Brazilian population.
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4 320 **Author contributions**

5
6 321 BPN designed the article, obtained and analyzes the data, drafted the first version and revised
7
8 322 the manuscript. ADPCF and FACF analyzed the data, and drafted and revised the manuscript.
9
10 323 SP, DS, TRF, TNM, ET and LAF drafted and revised the manuscript. SBR designed the
11
12 324 article, drafted and revised the manuscript. All authors approved the final version of the
13
14 325 manuscript.

15 326 **Funding:** There are no funding related to the production of the paper. The Brazilian Ministry
16
17 327 of Health financed the PNS survey. The funder of the survey played no role in the study
18
19 328 design; collection, analysis, and interpretation of data; writing of the report; or the decision to
20
21 329 submit the article for publication.

22 330 **Conflict of interest:** All authors have no potential conflicts.

23
24 331 **Data sharing statement:** All PNS data are available from the Brazilian Institute of
25
26 332 Geography and Statistics website, located here:
27 333 http://www.ibge.gov.br/home/estatistica/populacao/pns/2013/default_microdados.shtm.

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479 **Tables and figures**

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

Variables	n	%	Multimorbidity			
			%	≥2 95%CI	%	≥3 95%CI
Sex						
Male	25,920	44.9	17.5	16.6; 18.3	7.2	6.6; 7.8
Female	34,282	55.1	26.1	25.2; 27.0	12.6	12.0; 13.3
Age (in years)						
18 to 29	14,321	24.3	4.9	4.2; 5.6	1.2	0.9; 1.5
30 to 39	14,269	21.0	10.6	9.6; 11.5	2.8	2.3; 3.3
40 to 49	11,405	18.8	20.8	19.5; 22.1	7.8	7.0; 8.6
50 to 59	9,030	16.8	32.9	31.2; 34.6	15.5	14.3; 16.8
60 to 69	6,238	10.8	46.3	44.1; 48.6	24.7	22.8; 26.6
70 to 79	3,441	5.7	52.2	49.2; 55.2	30.9	28.0; 33.9
80 or more	1,498	2.6	52.8	48.6; 57.0	30.6	26.5; 34.7
Skin color*						
White	24,106	47.8	24.3	23.3; 25.4	11.6	10.8; 12.3
Black	5,631	9.2	22.2	20.2; 24.2	10.3	8.9; 11.6
Brown	29,512	41.7	19.8	18.9; 20.6	8.6	8.1; 9.2
Marital status						
Without partner	25,680	38.4	20.6	19.7; 21.5	9.9	9.3; 10.6
With partner	34,522	61.6	23.2	22.4; 24.1	10.4	9.7; 11.0
Schooling (in years)						
0	9,434	13.9	33.2	31.4; 35.0	16.3	14.9; 17.7
1-8	14,649	25.7	30.0	28.6; 31.4	16.1	14.9; 17.2
8-11	9,215	15.3	17.9	16.5; 19.3	7.5	6.5; 8.4
≥12	26,904	45.2	15.8	15.0; 16.7	5.9	5.4; 6.5
Wealth index (in quintiles)						
1° (High)	10,153	22.3	22.0	20.5; 23.6	9.3	8.3; 10.4
2°	11,531	22.4	22.3	21.0; 23.6	10.5	9.5; 11.5
3°	11,621	19.5	23.1	21.8; 24.4	10.6	9.7; 11.5
4°	14,380	21.0	22.2	20.9; 23.5	10.6	9.7; 11.6
5° (Low)	12,517	14.7	21.3	19.9; 22.7	9.9	8.9; 10.9
Private health plan						
No	43,834	69.4	21.1	20.3; 21.9	9.8	9.3; 10.4
Yes	16,368	30.6	24.8	23.5; 26.1	11.0	10.1; 12.0
Geographical area						
Urban	49,245	86.5	22.8	22.0; 23.5	10.5	10.0; 11.1
Rural	10,957	13.5	18.6	17.2; 20.0	8.0	7.1; 8.8
State-level education						

High	22,382	37.2	24.7	23.7; 25.7	11.7	10.9; 12.4
Middle	19,515	32.4	20.1	18.6; 21.7	9.3	8.3; 10.4
Low	18,305	30.4	19.0	18.0; 20.1	8.0	7.3; 8.6
State-level income						
High	21,683	36.0	24.6	23.6; 25.7	11.6	10.8; 12.3
Middle	18,087	30.0	21.8	20.2; 23.3	10.5	9.5; 11.6
Low	20,432	33.9	18.2	17.2; 19.2	7.5	6.9; 8.1
Total	60,202	100.0	22.2	21.5; 22.9	10.2	9.7; 10.7

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481 Table 2. Adjusted multilevel models of multimorbidity with independent variables. Brazil, 2013.

Variables	Multimorbidity (≥2)						Multimorbidity (≥3)					
	Model 1		Model 2		Model 3		Model 1		Model 2		Model 3	
	OR	CI95%	OR	CI95%	OR	CI95%	OR	CI95%	OR	CI95%	OR	CI95%
Sex (ref: male)												
Female	1.84	1.76; 1.94	1.85	1.77; 1.94	1.85	1.77; 1.94	1.95	1.83; 2.08	1.95	1.83; 2.08	1.95	1.83; 2.09
Age (in years)	1.06	1.06; 1.06	1.06	1.06; 1.06	1.06	1.06; 1.06	1.06	1.06; 1.06	1.06	1.06; 1.06	1.06	1.06; 1.06
Skin color* (ref: White)												
Black	1.07	0.99; 1.16	1.08	0.99; 1.17	1.08	0.99; 1.17	1.09	0.98; 1.21	1.09	0.98; 1.21	1.09	0.98; 1.21
Brown	1.01	0.96; 1.06	1.01	0.96; 1.07	1.01	0.96; 1.07	0.97	0.91; 1.04	0.97	0.91; 1.04	0.97	0.91; 1.04
Marital status (ref: Without partner)												
With partner	1.13	1.08; 1.18	1.13	1.08; 1.19	1.13	1.08; 1.19	1.17	1.09; 1.24	1.17	1.09; 1.24	1.17	1.09; 1.24
Schooling (in years) # (ref: ≥12)												
8-11	1.19	1.11; 1.28	1.19	1.10; 1.28	1.19	1.10; 1.28	1.22	1.10; 1.35	1.22	1.10; 1.35	1.22	1.10; 1.35
1-8	1.41	1.33; 1.51	1.41	1.33; 1.50	1.41	1.33; 1.50	1.57	1.44; 1.71	1.57	1.44; 1.71	1.57	1.44; 1.71
0	1.34	1.24; 1.44	1.34	1.24; 1.44	1.34	1.24; 1.44	1.41	1.27; 1.56	1.41	1.28; 1.56	1.41	1.28; 1.56
Wealth index (in quintiles) (ref: High)												
2°	1.12	1.04; 1.20	1.12	1.04; 1.20	1.12	1.04; 1.20	1.15	1.04; 1.28	1.15	1.04; 1.28	1.15	1.04; 1.28
3°	1.21	1.12; 1.31	1.21	1.12; 1.31	1.21	1.12; 1.31	1.19	1.07; 1.33	1.19	1.07; 1.33	1.19	1.07; 1.33
4°	1.05	0.96; 1.14	1.05	0.97; 1.14	1.05	0.97; 1.14	1.09	0.98; 1.22	1.10	0.98; 1.23	1.10	0.98; 1.23
5° (Low)	0.91	0.83; 1.00	0.92	0.84; 1.01	0.92	0.84; 1.01	0.95	0.84; 1.08	0.95	0.84; 1.08	0.95	0.84; 1.08
Private health plan (ref: no)												
Yes	1.15	1.08; 1.21	1.15	1.08; 1.20	1.15	1.08; 1.20	1.09	1.01; 1.18	1.09	1.01; 1.18	1.09	1.01; 1.18
Geographical area (ref: urban)												
Rural	0.86	0.80; 0.92	0.86	0.80; 0.92	0.86	0.80; 0.92	0.78	0.71; 0.86	0.78	0.71; 0.86	0.78	0.71; 0.86
State-level education (ref: High)												
Middle			0.82	0.71; 0.94					0.76	0.64; 0.90		
Low			0.83	0.72; 0.96					0.76	0.64; 0.90		
State-level income (ref: High)												
Middle					0.89	0.77; 1.04					0.88	0.73; 1.05
Low					0.82	0.71; 0.95					0.75	0.63; 0.89

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483 Table 3. Adjusted multilevel models of multimorbidity with independent variables stratified by region. Brazil, 2013.

Variables	Northern region		Northeastern region		Central Western region		Southeastern region		Southern region	
	MM (≥2)	MM (≥3)	MM (≥2)	MM (≥3)	MM (≥2)	MM (≥3)	MM (≥2)	MM (≥3)	MM (≥2)	MM (≥3)
	OR	OR	OR	OR	OR	OR	OR	OR	OR	OR
	CI95%	CI95%	CI95%	CI95%	CI95%	CI95%	CI95%	CI95%	CI95%	CI95%
Sex (ref: male)										
Female	1.81	2.06	1.96	2.08	2.22	2.37	1.62	1.61	1.84	2.04
	1.62; 2.02	1.75; 2.43	1.8; 2.14	1.84; 2.36	1.94; 2.54	1.97; 2.86	1.48; 1.78	1.43; 1.82	1.63; 2.08	1.73; 2.39
Age (in years)	1.05	1.06	1.06	1.06	1.07	1.07	1.05	1.05	1.06	1.06
	1.05; 1.06	1.05; 1.06	1.06; 1.06	1.06; 1.06	1.06; 1.07	1.06; 1.07	1.05; 1.06	1.05; 1.06	1.05; 1.06	1.06; 1.07
Marital status (ref: Without partner)										
With partner	1.13	1.17	1.16	1.23	1.00	0.93	1.15	1.22	1.16	1.19
	1.02; 1.27	1; 1.38	1.07; 1.27	1.09; 1.39	0.87; 1.14	0.78; 1.11	1.05; 1.26	1.08; 1.38	1.02; 1.32	1.01; 1.4
Skin color* (ref: White)										
Black	1.01	1.06	1.12	1.14	0.94	0.89	1.11	1.15	1.00	0.98
	0.82; 1.23	0.79; 1.42	0.97; 1.3	0.94; 1.39	0.74; 1.21	0.63; 1.26	0.96; 1.29	0.95; 1.4	0.76; 1.31	0.7; 1.38
Brown	0.92	0.92	0.96	0.93	1.13	1.14	1.07	1.02	1.08	0.88
	0.81; 1.04	0.76; 1.1	0.87; 1.05	0.81; 1.05	0.98; 1.29	0.95; 1.36	0.97; 1.18	0.89; 1.16	0.91; 1.27	0.71; 1.09
Schooling (in years) # (ref: more educated)										
III	1.17	1.12	1.10	0.95	1.16	1.32	1.35	1.47	1.12	1.27
	0.99; 1.39	0.86; 1.47	0.95; 1.28	0.76; 1.18	0.94; 1.42	0.99; 1.75	1.18; 1.55	1.22; 1.78	0.94; 1.35	0.99; 1.62
II	1.23	1.36	1.33	1.35	1.33	1.32	1.65	1.89	1.43	1.73
	1.05; 1.44	1.08; 1.71	1.18; 1.51	1.14; 1.6	1.11; 1.59	1.03; 1.68	1.46; 1.86	1.61; 2.22	1.22; 1.68	1.41; 2.13
I (less educated)	1.32	1.48	1.38	1.36	1.17	1.25	1.43	1.40	1.19	1.46
	1.12; 1.55	1.16; 1.88	1.21; 1.58	1.13; 1.65	0.94; 1.46	0.94; 1.68	1.22; 1.67	1.14; 1.71	0.97; 1.47	1.12; 1.89
Wealth index (in quintiles) (ref: High)										
2°	1.03	0.92	1.07	1.21	1.29	1.17	1.03	1.09	1.22	1.25
	0.83; 1.29	0.67; 1.27	0.91; 1.26	0.96; 1.52	1.05; 1.58	0.89; 1.55	0.90; 1.18	0.91; 1.3	1.04; 1.44	1.00; 1.57
3°	1.21	0.98	1.26	1.40	1.19	1.10	1.02	1.05	1.42	1.33
	0.98; 1.51	0.71; 1.34	1.07; 1.48	1.11; 1.76	0.95; 1.48	0.82; 1.48	0.89; 1.18	0.87; 1.27	1.18; 1.7	1.05; 1.69
4°	0.90	0.82	1.07	1.22	1.13	1.18	0.96	0.98	1.34	1.30
	0.72; 1.12	0.60; 1.11	0.91; 1.26	0.97; 1.53	0.9; 1.42	0.88; 1.59	0.82; 1.12	0.79; 1.20	1.09; 1.66	1.00; 1.7
5° (Low)	0.80	0.74	0.93	0.97	1.05	1.16	0.94	1.13	0.92	0.85
	0.64; 1.01	0.53; 1.03	0.78; 1.12	0.76; 1.25	0.80; 1.36	0.83; 1.62	0.77; 1.14	0.88; 1.45	0.71; 1.20	0.61; 1.19

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Private health plan (ref: no)											
Yes	1.15	1.29	1.23	1.22	1.15	1.16	1.12	1.05	1.10	0.91	
	0.98; 1.35	1.02; 1.61	1.09; 1.39	1.04; 1.44	0.99; 1.34	0.95; 1.41	1.01; 1.24	0.92; 1.2	0.96; 1.25	0.77; 1.09	
Geographical area (ref: urban)											
Rural	0.89	0.76	0.84	0.75	0.91	0.85	0.88	0.82	0.82	0.83	
	0.77; 1.03	0.61; 0.94	0.75; 0.94	0.64; 0.88	0.75; 1.11	0.65; 1.11	0.76; 1.02	0.67; 1.00	0.68; 0.97	0.67; 1.04	

484 Note: MM = Multimorbidity

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487 Table 4. Adjusted multilevel models of patterns of diseases (factors) with independent variables. Brazil, 2013.

Variables	Factor 1 (Cardiometabolic)						Factor 2 (Respiratory/mental/ muscle-skeletal)						
	Model 1		Model 2		Model 3		Model 1		Model 2		Model 3		
	β	CI95%	β	CI95%	β	CI95%	β	CI95%	β	CI95%	β	CI95%	
Sex (ref: male)													
Female	.024	.022; .026	.024	.022; .026	.024	.022; .026	.038	.036; .040	.038	.036; .040	.038	.036; .040	
Age (in years)	.004	.004; .004	.004	.004; .004	.004	.004; .004	.001	.001; .001	.001	.001; .001	.001	.001; .001	
Skin color* (ref: White)													
Black	.007	-.003; .010	.007	.003; .010	.007	.003; .010	-.009	-.013; -.005	-.009	-.013; -.005	-.009	-.013; -.005	
Brown	.001	-.001; .004	.002	-.001; .004	.002	-.001; .004	-.004	-.006; -.001	-.004	-.006; -.001	-.004	-.006; -.001	
Marital status (ref: Without partner)													
With partner	.000	-.002; .002	.000	-.002; .002	.000	-.002; .002	-.005	-.007; -.002	-.005	-.007; -.003	-.005	-.007; -.003	
Schooling (in years)[#] (ref: ≥ 12)													
8-11	.013	.010; .016	.013	.010; .016	.013	.010; .016	.004	.001; .008	.005	.002; .008	.005	.002; .008	
1-8	.021	.018; .023	.021	.018; .023	.021	.018; .023	.011	.008; .014	.011	.008; .014	.011	.008; .014	
0	.014	.010; .017	.014	.010; .017	.014	.010; .017	.001	-.003; .004	.001	-.003; .005	.001	-.003; .005	
Wealth index (in quintiles) (ref: High)													
2°	.007	.004; .010	.007	.004; .010	.007	.004; .010	.005	.001; .008	.005	.001; .008	.005	.001; .008	
3°	.009	.006; .013	.009	.006; .013	.009	.006; .013	.010	.006; .014	.010	.006; .014	.010	.006; .014	
4°	.006	.002; .009	.006	.002; .009	.006	.002; .009	.004	.000; .008	.004	.000; .008	.004	.000; .008	
5° (Low)	-.003	-.007; .001	-.003	-.007; .001	-.003	-.007; .001	.001	-.004; .005	.001	-.004; .005	.001	-.004; .005	
Private health plan (ref: no)													
Yes	.006	.004; .009	.006	.004; .009	.006	.004; .009	.007	.005; .010	.007	.005; .010	.007	.005; .010	
Geographical area (ref: urban)													
Rural	-.008	-.011; -.005	-.008	-.011; -.005	-.008	-.011; -.005	-.002	-.005; .002	-.002	-.005; .002	-.002	-.005; .002	
State-level education (ref: High)													
Middle			-.010	-.016; -.004					-.016	-.027; -.005			
Low			-.008	-.015; -.002					-.018	-.029; -.006			
State-level income (ref: High)													
Middle					-.006	-.012; .001					-.011	-.022; .001	
Low					-.009	-.016; -.003					-.017	-.028; -.006	

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490 Table 5. Adjusted multilevel models of multimorbidity factors with independent variables stratified by region. Brazil, 2013.

Variables	Northern region		Northeastern region		Central Western region		Southeastern region		Southern region	
	Factor 1	Factor 2	Factor 1	Factor 2	Factor 1	Factor 2	Factor 1	Factor 2	Factor 1	Factor 2
	β	β	β	β	β	β	β	β	β	β
	CI95%	CI95%	CI95%	CI95%	CI95%	CI95%	CI95%	CI95%	CI95%	CI95%
Sex (ref: male)										
Female	0.022	0.023	0.027	0.030	0.029	0.050	0.020	0.041	0.023	0.061
	0.018; 0.026	0.019; 0.027	0.023; 0.03	0.027; 0.034	0.023; 0.034	0.044; 0.056	0.015; 0.024	0.036; 0.045	0.017; 0.03	0.053; 0.069
Age (in years)	0.003	0.001	0.004	0.001	0.004	0.001	0.004	0.001	0.004	0.002
	0.003; 0.003	0.001; 0.001	0.003; 0.004	0.001; 0.001	0.004; 0.004	0.001; 0.002	0.004; 0.004	0.001; 0.001	0.004; 0.004	0.001; 0.002
Marital status (ref: Without partner)										
With partner	0.001	-0.002	0.000	-0.002	-0.007	-0.013	0.001	-0.005	0.002	-0.010
	-0.003; 0.005	-0.006; 0.003	-0.003; 0.004	-0.005; 0.002	-0.013; -0.002	-0.02; -0.007	-0.003; 0.005	-0.010; 0.000	-0.004; 0.009	-0.018; -0.002
Skin color* (ref: White)										
Black	0.005	-0.007	0.007	-0.003	-0.001	-0.021	0.008	-0.011	0.013	-0.018
	-0.002; 0.013	-0.015; 0.001	0.001; 0.013	-0.01; 0.003	-0.011; 0.009	-0.033; -0.01	0.001; 0.016	-0.02; -0.003	-0.001; 0.026	-0.036; 0.000
Brown	-0.002	-0.007	-0.001	-0.003	0.004	-0.003	0.004	-0.002	0.005	0.004
	-0.007; 0.002	-0.012; -0.002	-0.005; 0.003	-0.008; 0.001	-0.001; 0.01	-0.010; 0.004	-0.001; 0.009	-0.008; 0.003	-0.003; 0.014	-0.007; 0.015
Schooling (in years) # (ref: more educated)										
III	0.006	0.007	0.011	0.000	0.012	-0.001	0.016	0.007	0.019	0.010
	0.000; 0.011	0.001; 0.013	0.006; 0.017	-0.006; 0.006	0.004; 0.02	-0.011; 0.008	0.010; 0.023	0.000; 0.014	0.01; 0.028	-0.002; 0.021
II	0.009	0.005	0.015	0.006	0.016	-0.001	0.029	0.019	0.037	0.020
	0.003; 0.014	-0.001; 0.011	0.010; 0.020	0.001; 0.012	0.009; 0.024	-0.01; 0.008	0.023; 0.035	0.013; 0.026	0.028; 0.046	0.009; 0.031
I (less educated)	0.014	0.008	0.010	0.002	0.015	-0.009	0.022	-0.002	0.016	-0.005
	0.008; 0.02	0.001; 0.014	0.004; 0.015	-0.004; 0.008	0.005; 0.025	-0.021; 0.002	0.014; 0.03	-0.011; 0.007	0.004; 0.027	-0.02; 0.01
Wealth index (in quintiles) (ref: High)										
2°	0.005	0.005	0.005	0.002	0.008	0.004	0.004	-0.003	0.011	0.017
	-0.003; 0.013	-0.004; 0.013	-0.002; 0.011	-0.005; 0.009	-0.001; 0.016	-0.005; 0.014	-0.002; 0.011	-0.01; 0.004	0.003; 0.002	0.007; 0.028
3°	0.009	0.004	0.012	0.010	0.002	0.002	0.004	0.002	0.012	0.027
	0.001; 0.017	-0.004; 0.013	0.005; 0.018	0.003; 0.017	-0.007; 0.011	-0.008; 0.013	-0.003; 0.011	-0.005; 0.01	0.003; 0.021	0.015; 0.039

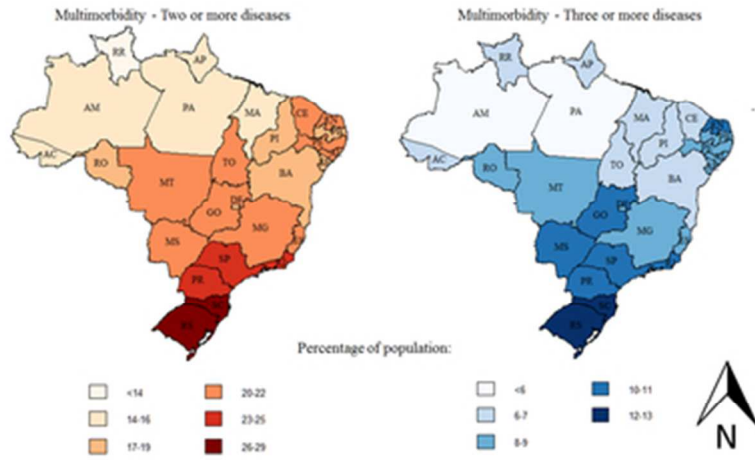
4°	0.004	-0.001	0.005	0.004	0.005	0.005	0.003	-0.007	0.009	0.019
	-0.004; 0.011	-0.01; 0.007	-0.002; 0.011	-0.003; 0.011	-0.005; 0.014	-0.006; 0.016	-0.004; 0.011	-0.015; 0.001	-0.002; 0.02	0.005; 0.033
5° (Low)	-0.004	-0.009	-0.001	0.004	0.001	0.004	-0.006	-0.004	-0.012	0.012
	-0.012; 0.004	-0.017; 0.000	-0.009; 0.006	-0.003; 0.012	-0.010; 0.012	-0.008; 0.017	-0.015; 0.004	-0.015; 0.006	-0.026; 0.002	-0.006; 0.029
Private health plan (ref: no)										
Yes	0.009	0.009	0.010	0.008	0.007	0.009	0.002	0.008	0.005	0.001
	0.003; 0.015	0.003; 0.016	0.006; 0.015	0.003; 0.013	0.000; 0.013	0.001; 0.016	-0.003; 0.006	0.002; 0.013	-0.002; 0.012	-0.008; 0.01
Geographical area (ref: urban)										
Rural	-0.007	0.004	-0.008	-0.006	-0.009	-0.001	-0.007	-0.010	-0.008	0.009
	-0.012; -0.002	-0.002; 0.009	-0.013; -0.004	-0.011; -0.001	-0.018; -0.001	-0.01; 0.009	-0.014; 0.000	-0.018; -0.001	-0.017; 0.002	-0.003; 0.021

491 Note: Factor 1: cardiometabolic; factor 2: (Respiratory/mental/ muscle-skeletal)

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

Morbidities	Individual prevalence		Duration of disease	Number of comorbidities
	%	(95%CI)	Mean (median; Q25-Q75)	Mean (median; Q25-Q75)
High Blood Pressure	22.3	21.7 - 23.0	13.1 (9; 3-18)	2.3 (2; 1-3)
Spinal column problem	19.0	18.3 - 19.7	14.7 (10; 4-21)	2.3 (2; 1-3)
Hypercholesterolemia	8.4	8.0 - 8.8	6.9 (3; 1-9)	2.3 (2; 1-3)
Arthritis/rheumatism	6.7	6.4 - 7.1	14.6 (10; 3-20)	3.0 (3; 2-4)
Diabetes	6.5	6.2 - 6.9	11.3 (6; 2-15)	2.9 (3; 2-4)
Asthma/wheezy bronchitis	4.4	4.1 - 4.8	25.1 (23; 13-35)	2.4 (2; 1-3)
Depression	4.2	3.9 - 4.5	-	2.9 (3; 2-4)
Work-related muscle-skeletal disorders	2.5	2.2 - 2.8	7.5 (5; 2-11)	2.5 (2; 1-3)
Cancer	1.9	1.7 - 2.2	8.5 (6; 2-13)	2.8 (2; 2-4)
Another heart disease	1.9	1.6 - 2.1	13.9 (9; 3-20)	3.1 (3; 2-4)
Stroke	1.6	1.4 - 1.8	10.2 (6; 2-13)	3.4 (3; 2-5)
Kidney problem	1.5	1.3 - 1.7	13.5 (9; 3-20)	3.2 (3; 2-4)
Heart attack	1.3	1.2 - 1.5	12.4 (7; 2-18)	4.0 (4; 3-5)
Heart failure	1.2	1.1 - 1.4	13.2 (8; 4-19)	4.0 (4; 2-5)
Bronchitis	1.0	0.8 - 1.1	23.2 (20; 9-32)	3.3 (3; 2-5)
Angina	0.8	0.7 - 0.9	15.5 (11; 5-21)	4.5 (4; 3-6)
Emphysema	0.5	0.4 - 0.6	14.9 (9; 3-18)	3.7 (3; 2-5)
Another lung disease	0.5	0.4 - 0.6	16.2 (12; 5-24)	2.8 (2; 1-4)
Bipolar disorder	0.4	0.3 - 0.5	11.3 (8; 4-16)	3.1 (3; 2-4)
Another mental disease	0.3	0.2 - 0.4	2.8 (2; 1-4)	2.5 (2; 1-3)
Schizophrenia	0.2	0.2 - 0.3	19.7 (19; 8-26)	2.7 (3; 2-3)
Obsessive Compulsive Disorder (OCD)	0.2	0.1 - 0.2	14.5 (12; 6-21)	3.4 (3; 2-4)



Multimorbidity frequency by Brazilian states. Brazil, 2013

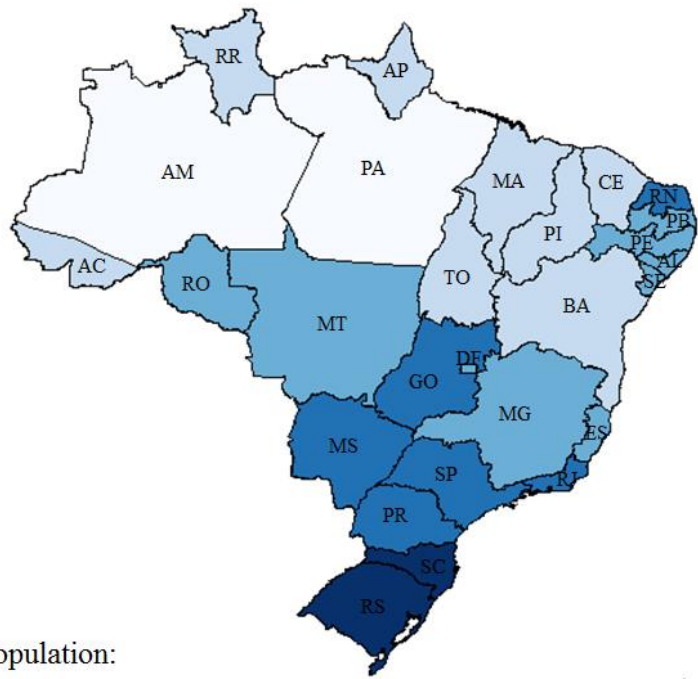
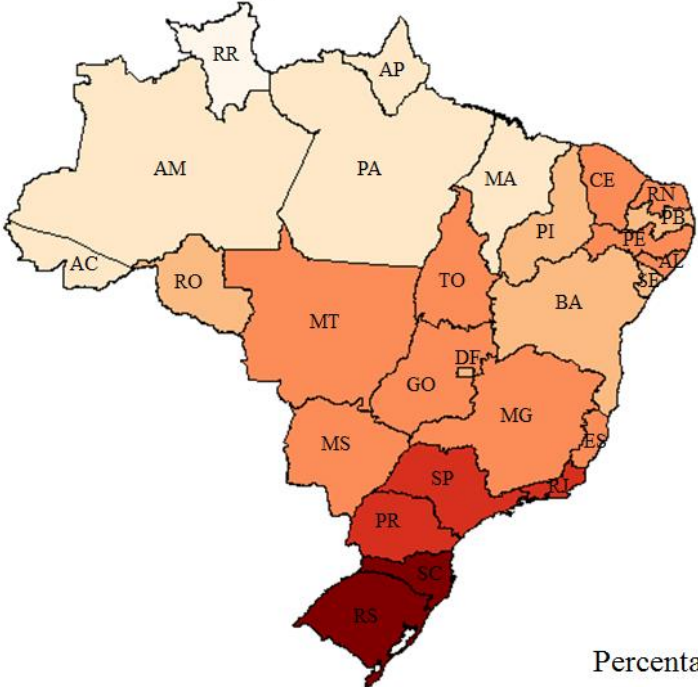
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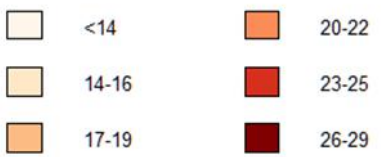
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Multimorbidity - Two or more diseases

Multimorbidity - Three or more diseases



Percentage of population:



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Supplementary table 2. Factor analysis. Brazil, 2013.

Morbidities	Factor 1	Factor 2
High Blood Pressure	0.77	
Heart attack	0.79	
Angina	0.68	
Heart failure	0.69	
Stroke	0.58	
Hypercholesterolemia	0.57	
Diabetes	0.62	
Arthritis/rheumatism	0.30	0.37
Spinal column problem		0.45
Asthma/wheezy bronchitis		0.57
COPD		0.63
Work-related muscle-skeletal disorders		0.45
Depression		0.46
Bipolar disorder		0.46
Kidney problem		0.31
Cancer	-	-
Eigenvalor	4.46	1.11
Explained variance %*	0.73 (0.69)	0.18 (0.47)
KMO		0.84

*Before oblique rotation (after oblique rotation)

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	5
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	-
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6
Bias	9	Describe any efforts to address potential sources of bias	6
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5-6
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	6-7
		(b) Describe any methods used to examine subgroups and interactions	-
		(c) Explain how missing data were addressed	-
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	6
		(e) Describe any sensitivity analyses	-

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(b) Give reasons for non-participation at each stage	-
		(c) Consider use of a flow diagram	-
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8
		(b) Indicate number of participants with missing data for each variable of interest	-
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	-
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	-
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	-
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	8
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8-9
		(b) Report category boundaries when continuous variables were categorized	8-9
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	-
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14
Generalisability	21	Discuss the generalisability (external validity) of the study results	14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.