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Keywords:	Prevalence, Multimorbidity, Cross-Sectional Studies, Population Surveys, Brazil

Prevalence and patterns of multimorbidity and associated determinants: a cross-sectional study

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ABSTRACT

Objectives: To estimate the prevalence of multimorbidity and to identify factors associated with it in the adult population from the metropolitan region of Manaus.

Design: Cross-sectional population-based study.

Setting: Interviews conducted between May and August of 2015 in eight cities that compose the metropolitan region of Manaus, Amazonas, Brazil.

Participants: 4000 adults aged ≥18 years

Primary outcome measures: Multimorbidity, measured by the occurrence of ≥2 and ≥3 chronic diseases, was the primary outcome. The associated factors were investigated by calculating the prevalence ratio (PR) obtained by Poisson regression, with robust adjustment of the variance in a hierarchical model. A factor analysis was conducted to investigate multimorbidity clusters.

Results: Half of the interviewees were women. The presence of a chronic disease was reported by 57.2% (95% CI 56.6% to 59.7%) of the interviewees, and the mean morbidity was 1.2 (1.1-1.2); 29% (95% CI 27.6% to 30.5%) reported ≥2 morbidities, and 15% (95% CI 14.1% to 16.4%) reported ≥3 chronic conditions. Back pain was reported by one-third of the interviewees. Multimorbidity was higher in women PR = 1.7 (95% CI 1.5 to 1.8), the elderly, PR = 5.7 (95% CI 4.5 to 7.1) and individuals with worse health perception, PR = 3.7 (95% CI 2.7-5.0). Associated factors also included undergoing medical consultations, hospitalization in the last year, suffering from dengue in the last year and using a reference health service. Factor analysis revealed a pattern of multimorbidity in women, including cardiometabolic, musculoskeletal, respiratory, psychosomatic and cancer diseases. In men, an association was identified in two groups: the first included musculoskeletal, respiratory and psychosomatic diseases, and the second included cardiometabolic diseases.

Conclusion: Multimorbidity was frequent in the metropolitan region of Manaus. It occurred more in women, in the elderly and in those with worse health perception.

Keywords: Prevalence, Multimorbidity, Cross-Sectional Studies, Population Surveys, Brazil.

Strengths and limitations of this study:

This is the first study on the prevalence of multimorbidity in adults from the metropolitan region of Manaus, Amazonas state, Brazil, using data from a population-based survey.

More than half of the adults from this region reported a chronic disease, and approximately 3 out of 10 interviewees reported ≥2 morbidities.

This research increases the knowledge about the epidemiologic factors associated with multimorbidity.

The measurement method of the outcome, self-report, is subject to errors and influenced by memory bias.

BACKGROUND

Multimorbidity is the occurrence of different chronic clinical conditions in an individual, without a single condition being considered the main cause.[1 2] It is operationally defined as the occurrence of two or more chronic diseases.[3-5] In recent decades, population ageing, lifestyle changes, improved socio-economic conditions, and increased diagnostic ability of health services have contributed to a significant rise in the population that survives serious diseases, causing an accumulation of health problems in specific population groups. This situation has contributed to the increased prevalence of multimorbidity.[6-8]

The multimorbidity frequency varies according to the evaluated diseases, the age of the population, the individual's socioeconomic and demographic level, and the individual's health condition. The rising prevalence of multimorbidity has resulted in higher costs to health services.[9-12] The costs associated with multimorbidity can reach 75% of total health expenditures, which includes physician consultation, hospitalization, odontological care, medication and rehabilitation.[13]

In Brazil, the 2013 National Health Survey (*Pesquisa Nacional de Saúde*), including 64 308 individuals over 18 years old, has identified that the prevalence of multimorbidity was 26-29% in the southern region and 14-19% in the northern region.[14] The differences found suggest heterogeneity in economic development and greater use of health services. The systematic review conducted in 2016 included 27 studies and showed the southern region presented the highest increase of physical visit, while there was a reduction in the northern region.[15] These differences show the need for regional studies to expand our knowledge about multimorbidity at the local level.

The present research estimated the prevalence of and identified the factors associated with multimorbidity in the adult population of the metropolitan region of Manaus, the most populated region and largest economic cluster in northern Brazil.

METHODS

Study design

This is a cross-sectional population-based study in the metropolitan region of Manaus, composed by the capital of Amazonas, Manaus, and seven surrounding cities.

Multimorbidity was considered a primary outcome, which was categorized as ≥2 or ≥3 chronic diseases. The present analysis is part of a larger study, which aimed to study the use of health services and inputs in the region from May to August 2015.[16]

Participants and study size

We calculated the sample size as 4,000 adults ≥18 years old to be interviewed, who were selected by probabilistic complex sampling—by cluster and stratified by sex and age—in three stages (census track, household and individual).[16] We assume an estimated 50% prevalence of use of health services, considering a CI of 95%, accuracy of 2% and a design effect value of 1.5.[17] We added 10% to compensate for possible losses and refusals.

Variables and data collection

The primary outcome was self-reported multimorbidity, defined as two or more affirmative answers to any of the following questions: "Have any doctors ever diagnosed you with [...]?" [1] hypertension, [2] diabetes, [3] high cholesterol, [4] heart disease (heart attack, angina, heart failure or other), [5] stroke, [6] asthma or asthmatic bronchitis, [7] arthritis or rheumatism, [8] depression, [9] pulmonary disease (pulmonary emphysema, chronic bronchitis or chronic obstructive pulmonary disease), [10] cancer, or [11] chronic kidney disease, and [12] "Do you have any chronic spinal problems, such as chronic back or neck pain, low back pain, sciatic pain, vertebral or disc problems?"

The independent variables were sex; age; marital status; self-reported skin colour; education; social class;[18] occupation; private health insurance (yes, no); self-perception of health status; place of attendance (capital, countryside); using a reference health service, that is, use of the same healthcare professional for attendance (yes, no); physician visit in the last 12 months (yes, no); hospitalization in the last year (yes, no); malaria in the last 12 months (yes, no); dengue in the last 12 months (yes, no); and types of services one usually seeks when in need of medical care (primary, secondary, or tertiary).

Interviewers with experience in conducting home interviews collected the data on a mobile electronic device (Samsung® Galaxy Tab3 SM-T110). Interview records were transmitted over the Internet and stored using Survey To Go software (Dooblo Ltd., Israel).

Statistical analyses

Statistical analyses were carried out in Stata v. 14.2. In all calculations, the complex sampling design was weighted by incorporating sample weights (*svy* command).

Descriptive statistics were initially obtained through prevalence calculation. The respective confidence intervals and P values of difference were calculated by Pearson's chi-square between sociodemographic characteristics and multimorbidity. The prevalence of the most common diseases stratified by sex, age group and multimorbidity was also calculated. At this stage, morbidities with a prevalence of <5% were excluded.

Bivariate analyses were performed between all independent and dependent variables to calculate prevalence ratios (PRs) and 95% confidence intervals (CIs). To identify the factors associated with multimorbidity, PRs were adjusted using Poisson regression with robust variance adjustment.[19-21]

A hierarchical model consisting of three blocks was constructed of the most distal to the most proximal determinants of multimorbidity: (1) demographic variables (sex, age, race, marital status); (2) socioeconomic variables (economic, education classification, occupation); and (3) health variables (private health insurance, health status, demand for the same health service, physician visit, hospitalization, dengue, malaria and type of service usually used). The variables from the first block were kept for the next stage if they presented a p-value ≤0.05. Multicollinearity among the independent variables was discarded by assessing the variance inflation factors.[22]

To analyse whether the diseases grouped in patterns, an exploratory factor analysis was conducted by the principal component method, stratified by sex.[23 24] This technique allowed us to identify the tendency of coexisting diseases and to select a set of variables with potentially common causal factors, such as interaction between diseases and/or their treatments and/or common risk factors, which were interpreted as multimorbidity patterns. The tetrachoric correlation coefficient was used in the analysis because it is better than Pearson's correlation coefficient for dichotomous outcomes.[25] The suitability of the sampling was evaluated by the Kaiser-Meyer-Olkin test (KMO), which was considered adequate if the index was ≥0.70, and the Bartlett sphericity test, which was considered adequate if its p-value was ≤0.05.[23 26] To establish the number of factors to be maintained, Cattell's graphic (Cattell's scree plot) was used, which represents the eigenvalues of the correlation matrix in descending order. The factor number extracted corresponds to the eigenvalue that produces the inflection point in the curve (eigenvalue> 1) and explains the minimum variance (>10% for each component). Variables were defined as being associated

with a factor if they presented loads ≥0.30 [23] (the closer to 1, the greater the association). Oblique rotation (promax) was performed to allow for better interpretation of the factor analysis.[23]

RESULTS

Participant characteristics

Table 1 shows the characteristics of the participants and the prevalence of multimorbidity. The sample was composed of 4001 adults and had a response rate of 76%. Women constituted over half of the sample. About one-half of the interviewees were between 25 and 44 years old, and 81% were black, brown or indigenous. The predominant social stratum was the lower middle class (57%), and about one-third of the participants were students or housewives. More than half reported good health (54%), and the majority had had a physician visit in the last year (76%). In the last 12 months, 7% reported dengue and 6% reported malaria. One-half of respondents reported seeking a tertiary health service when they needed care (47%).

Prevalence of multimorbidity

The prevalence of at least one chronic disease was 57% (95% CI 56.6-59.7%), with a mean of 1.2 ± 1.5 diseases. The prevalence of ≥2 chronic conditions was 29% (95% CI 27.6-30.5%) and ≥3 chronic diseases was 15% (95% CI 14.1-16.4%).Higher prevalence was observed in women, in widowers, in individuals with lower education, in retired individuals, in individuals who had the worst perceptions of health and in those who visited a doctor and were hospitalized in the last year (Table 1). The prevalence of any chronic disease and of multimorbidity increased with age (mean 0.5 ± 0.8 in the 18-24-year-old group and 2.5 ± 1.9 in those 60 years or above). In the previous year, dengue was reported by 44% of those who had two or more chronic conditions.

Back pain was the most reported health problem in both women and men (Table 2). When coexisting diseases were stratified by sex, age, and multimorbidity, diabetes (94%) was the most prevalent disease in young women aged 18-34 years who reported ≥2 morbidities, while in men, it was arthritis (89%). In the age group of 35-59 years, heart

Table 1. Characteristics of participants and prevalence of multimorbidity (%), Manaus metropolitan region, Brazil, 2015 (n= 4001)*

Variable	% (n)	Any chronic disease % (95% CI)	P value	Mean number of chronic health problems (95% CI)	Multimorbidity % (95% CI)			
					≥2	P value	≥3	P value
Overall		57.2 (55.6 to 58.7)		1.17 (1.1 to 1.2)	29.0 (27.6 to 30.5)		15.2 (14.1 to 16.4)	
Sex			<0.001			<0.001		<0.001
Male	47.2 (1,888)	52.1 (49.8 to 54.0)		0.9 (0.8 to 0.9)	21.5 (19.7 to 23.4)		9.3 (8.1 to 10.7)	
Female	52.7 (2,113)	61.8 (59.7 to 63.8)		1.39 (1.3 to 1.4)	35.8 (33.8 to 37.8)		20.5 (18.8 to 22.3)	
Age (years)			<0.001			<0.001		<0.001
18 to 24	20.8 (838)	37.0 (33.8 to 40.3)		0.5 (0.4 to 0.5)	9.8 (7.9 to 12.0)		3.5 (2.5 to 5.0)	
25 to 34	28.7 (1,152)	49.6 (46.7 to 52.5)		0.8 (0.7 to 0.8)	18.6 (16.4 to 20.9)		6.9 (5.6 to 8.5)	
35 to 44	21.1 (843)	61.0 (57.6 to 64.2)		1.1 (1.0 to 1.2)	30.0 (27.0 to 33.2)		12.7 (10.6 to 15.1)	
45 to 59	19.3 (772)	71.4 (68.0 to 74.4)		1.7 (1.6 to 1.8)	46.6 (13.1 to 50.2)		28.1 (25.1 to 31.4)	
≥60	9.9 (396)	86.1 (82.3 to 89.2)		2.5 (2.3 to 2.7)	63.5 (58.6 to 68.1)		44.4 (39.6 to 49.3)	
Marital status			<0.001			<0.001		<0.001
Single	54.2 (2,173)	51.5 (49.3 to 53.5)		0.9 (0.8 to 0.9)	20.8 (19.1 to 22.6)		10.3 (8.8 to 11.3)	
Married	35.2 (1,409)	62.0 (59.4 to 64.5)		1.3 (1.2 to 1.4)	35.3 (32.9 to 37.9)		19.6 (17.6 to 21.8)	
Separated/Divorced	6.5 (260)	65.6 (59.6 to 71.2)		1.5 (1.3 to 1.7)	42.6 (36.8 to 48.7)		19.9 (15.5 to 25.2)	
Widower	4.0 (159)	79.3 (72.3 to 84.9)		2.2 (1.9 to 92.5	63.1 (55.3 to 70.2)		39.9 (32.5 to 47.7)	
Skin colour			<0.001			0.0021		0.0016
White/yellow	19.3 (774)	51.7 (48.2 to 55.2)		1.1 (1.0 to 1.2)	27.1 (24.1 to 30.4)		15.7 (13.3 to 18.5)	
Black/brown/ indigenous	80.5 (3,227)	58.5 (56.8 to 60.2)		1.2 (1.1 to 1.2)	29.5 (27.9 to 31.1)		15.1 (13.9 to 16.4)	
Schooling level			<0.001			<0.001		<0.001
High education or above	3.9 (158)	57.1 (49.3 to 64.6)		1.2(1.0 to 1.5)	32.6(25.7 to 40.4)		16.1 (11.7 to 23.7)	
High school	47.5 (1,903)	51.0 (48.8 to 53.3)		0.9 (0.8 to 1.0)	22.5 (20.7 to 24.5)		9.0 (7.8 to 10.4)	
Middle school	16.2 (649)	50.0 (46.2 to 53.8)		0.9 (0.8 to 1.0)	21.1 (18.2 to 24.4)		10.7 (0.8 to 13.3)	
Elementary school or less	32.2 (1,291)	69.9 (67.4 to 72.4)	<0.001	1.7 (1.6 to 1.8)	42.1 (39.5 to 44.8)		26.5 (24.1 to 28.9)	
Economic classification†						<0.001		<0.001
A - B	15.7 (629)	51.2 (47.2 to 55.1)		0.9 (0.8 to 1.1)	24.6 (21.4 to 28.2)		11.1 (8.8 to 13-8)	
C	57.1 (2,285)	55.5 (53.4 to 57.5)		1.0 (1.0 to 1.1)	26.1 (24.3 to 27.9)		13.2 (11.9 to 14.7)	
D - E	27.2 (1,087)	64.3 (61.4 to 67.2)		1.5 (1.4 to 1.6)	37.7 (34.9 to 40.7)		21.8 (19.4 to 24.3)	
Occupation			<0.001			<0.001		<0.001

Formal job	19.0 (761)	52.7 (49.1 to 56.2)		0.9 (0.8 to 1.0)	22.7 (19.8 to 25.8)		9.2 (7.3 to 11.5)	
Informal job	28.7 (1,149)	55.9 (53.0 to 58.7)		1.0 (1.0 to 1.1)	27.6 (25.1 to 30.3)		12.9 (11.1 to 15.0)	
Retired	7.9 (315)	79.2 (74.3 to 83.3)		2.4 (2.2 to 2.6)	60.5 (55.4 to 65.8)		43.4 (38.0 to 49.0)	
Student/ housewife	29.8 (1,199)	55.0 (52.2 to 57.8)		1.1 (1.1 to 1.2)	29.0 (25.5 to 31.6)		15.8 (13.8 to 18.0)	
Unemployed	14.4 (577)	58.3 (54.2 to 62.3)		1.0 (0.9 to 1.1)	23.1 (19.8 to 26.7)		11.2 (8.9 to 14.1)	
Private health insurance			0.348			0.697		0.616
Yes	13.0 (523)	55.3 (51.0 to 59.5)		1.0 (0.9 to 1.29	28.0 (24.6 to 32.3)		14.5 (11.7 to 17.8)	
No	87.0 (3,478)	57.5 (55.8 to 59.1)		1.2 (1.1 to 1.2)	29.0 (27.6 to 30.7)		15.3 (14.2 to 16.6)	
Health status			<0.001			<0.001		<0.001
Very good	11.9 (471)	30.8 (26.8 to 35.2)		0.4 (0.47 to 0.5)	9.7 (7.3 to 12.7)		3.1 (1.9 to 5.1)	
Good	54.3 (2,175)	50.4 (48.3 to 52.5)		0.8 (0.8 to 0.9)	20.3 (18.7 to 22.0)		7.9 (6.8 to 9.1)	
Fair	27.7 (1,108)	75.1 (72.5 to 77.5)		1.7 (1.6 to 1.8)	45.2 (42.3 to 48.1)		26.0 (23.5 to 28.6)	
Bad	4.8 (193)	88.6 (83.2 to 93.3)		2.6 (2.4 to 2.9)	68.4 (61.6 to 74.6)		50.3 (43.3 to 57.3)	
Very bad	1.3 (54)	81.5 (68.9 to 89.7)		3.6 (3.0 to 4.3)	77.7 (64.8 to 86.9)		70.3 (57.0 to 81.0)	
City			<0.001			<0.001		<0.001
Capital	86.8 (3,479)	58.4 (56.8 to 60.0)		1.2 (1.1 to 1.2)	30.2 (28.7 to 31.7)		15.8 (14.6 to 17.1)	
Countryside	13.1 (522)	49.2 (44.9 to 53.5)		0.9 (0.8 to 1.0)	21.5 (18.2 to 25.3)		11.3 (0.8 to 14.3)	
Health reference			<0.001			<0.001		<0.001
Yes	60.7 (2,434)	62.3 (60.3 to 64.2)		1.3 (1.2 to 1.4)	34.4 (31.5 to 36.3)		18.7 (17.1 to 20.3)	
No	39.2 (1,567)	49.4 (46.9 to 51.9)		0.9 (0.8 to 0.9)	20.8 (18.9 to 22.9)		9.8 (17.2 to 20.3)	
Physician visit			<0.001			<0.001		<0.001
Yes	76.5(3,066)	60.8 (59.0 to 62.5)		1.2 (1.2 to 1.3)	32,1 (30.5 to 33.8)		17.4 (16.1 to 18.8)	
No	23.4(935)	45.5 (42.3 to 48.7)		0.8 (0.7 to 0.9)	18,9 (16.5 to 21.5)		8.2 (6.6 to 10.2)	
Hospitalization			<0.001			<0.001		<0.001
Yes	7.0 (273)	72.9 (67.3 to 77.8)		1.2(1.2 to 1.3)	47 (41.4 to 53.2)		28.1 (23.1 to 33.8)	
No	93.0 (3,728)	56.1 (67.3 to 77.8)		0.8(0.7 to 0.9)	27 (26.3 to 29.2)		14.3 (13.2 to 15.4)	
Dengue			0.002			<0.001		<0.001
Yes	7.0(281)	65.9 (60.1 to 71.2)		1.6 (1.4 to 1.8)	44.2 (38.5 to 50.1)		27.6 (22.7 to 33.1)	
No	93(3.720)	56.5 (54.9 to 58.1)		1.1 (1.0 to 1.1)	27.9 (26.5 to 29.3)		14.3 (13.2 to 15.5)	
Malaria			0.420			0.122		0.014
Yes	5.9(234)	54.6 (48.2 to 60.9)		1.3 (1.1 to 1.5)	33.5 (27.7 to 39.8)		20.8 (16.1 to 26.5)	
No	94(3.767)	57.3 (0.55 to 0.58)		1.1 (1.1 to 1.2)	28.8 (27.3 to 30.2)		14.9 (13.8 to 16.0)	
Medical attention			<0.001			0.0484		0.531
Primary	30.2(1,208)	60.8 (58.0 to 63.5)		1.2 (1.1 to 1.3)	29.9 (27.3 to 32.5)		15.2 (13.3 to 17.3)	
Secondary	14.9(598)	62.3 (58.3 to 66.1)		1.3 (1.2 to 1.5)	33.0 (29.4 to 36.9)		18.9 (15.9 to 22.2)	
Tertiary	47.2(1,886)	54.0 (51.8 to 56.3)		1.1 (1.0 to 1.2)	27.7 (25.7 to 29.8)		14.3 (12.8 to 15.9)	
Others	7.7(309)	52.7 (47.2 to 58.3)		1.0 (0.9 to 1.2)	26.2 (21.6 to 31.4)		14.2 (10.7 to 18.5)	

* Descriptive statistics using simple frequency and Pearson χ2 test
CI: confidence interval; physician visit, hospitalization, dengue and malaria in last 12 months; † Average household income in 2015: A-B, US$6500-US$1419; C, US$463-US$772; D-E, US$205.

Table 2. Prevalence (%) of most common diseases stratified by sex, age and multimorbidity group, Manaus metropolitan region, Brazil, 2015*

Morbidities	%(n)	Multimorbidity ≥2			Multimorbidity ≥3		
		18-34 % (n)	35-59 % (n)	≥60 % (n)	18-34 % (n)	35-59 % (n)	≥60 % (n)
Women (2,113)							
Spinal column problem†	35.3 (747)	42.6 (135)	75.6 (248)	96.1 (99)	20.1 (64)	53.6 (176)	75.7 (78)
Hypertension	24.4 (516)	62.3 (78)	83.0 (211)	92.0 (126)	32.7 (94)	58.7 (149)	71.6 (98)
Arthritis or rheumatism	19.5 (414)	79.5 (66)	91.6 (197)	94.8 (110)	39.7 (33)	67.7 (146)	79.3 (92)
Hypercholesterolemia	20.1 (425)	79.5 (66)	90.8(217)	97.0 (100)	55.4 (46)	62.4 (149)	82.5 (85)
Diabetes	7.4 (157)	93.7 (15)	90.2 (82)	96.0 (48)	87.4 (14)	76.6 (70)	84.5 (42)
Asthma or asthmatic bronchitis	7.3 (155)	68.5 (50)	85.6 (54)	100.0 (19)	38.3 (28)	73.0 (46)	100.0(19)
Depressive disorder	7.4 (158)	71.0 (44)	91.9 (69)	100.0 (21)	30.6 (19)	73.2 (55)	95.2 (20)
Heart disease ǂ	5.6 (119)	71.8 (23)	98.1 (52)	100.0 (34)	53.0 (17)	86.7 (46)	94.0 (32)
Men (1888)							
Chronic spinal problem†	35.0 (662)	27.5 (77)	49.7 (149)	65.8 (54)	7.1 (20)	21.0 (63)	51.4 (42)
Hypertension	14.4 (271)	77.1 (37)	76.7 (112)	79.5 (61)	35.3 (17)	41.1 (60)	58.6 (45)
Arthritis or rheumatism	9.5 (179)	89.3 (25)	86.8 (80)	84.9 (50)	46.1 (13)	48.9 (45)	64.5 (38)
Hypercholesterolemia	9.0 (171)	57.1 (24)	87.6 (85)	87.6 (28)	33.3 (14)	49.4 (48)	78.2 (25)

P values of all variables were ≤0.002
* multimorbidity with prevalence ≥5%.
† chronic back pain or neck, low back pain, sciatica, vertebral or disc pain
ǂ heart disease, or heart attack, angina, cardiac insufficiency

diseases (98%), depressive disorders and arthritis (92%) were higher in women with ≥2 morbidities, while in men, hypercholesterolemia was the most common (88%).

Table 3 shows the investigation for factors associated with multimorbidity. After adjustment, multimorbidity (≥2 diseases) was associated with female sex (PR = 1.7, 95% CI 1.5 to 1.8), age between 45 and 59 years (PR = 4.4, 95% CI 3.4 to 5.4) and age ≥60 years (PR = 5.7, 95% CI 4.5 to 7.1). The presence of ≥3 diseases was associated with female sex (PR = 2.2, 95% CI 1.8 to 2.5), age 45-59 years (PR = 7.6, 95% CI 5.2 to 11.1), age ≥60 years (PR = 12.0, 95% CI 8.0 to 17.6), dengue in the last 12 months (PR = 1.3, 95% CI 1.0 to 1.6), and very poor health status (PR = 7.7, 95% CI 4.6 to 12.9). Having ≥3 chronic conditions increased the demand for physician visits, hospitalization in the last

year, and demand for the same health service. Education, income, occupation, and malaria in the last 12 months did not show associations with multimorbidity.

The factor analysis is presented in Table 4. The KMO coefficient was 0.85 for women and 0.78 for men, and the Bartlett sphericity test presented a p-value ≤0.001 for both, suggesting an adequate factor analysis. In women, one multimorbidity pattern (supplemental figure 1) explained 81% of the total variance, including the 12 chronic diseases analysed. In men, two factors were identified (supplemental figure 2). In the first factor, heart diseases, chronic kidney disease, stroke, arthritis or rheumatism, chronic spinal problems, depressive disorders, asthma or bronchitis and lung diseases were the associated chronic diseases, which explained a total of 62% of the variance. In the second, the associated chronic diseases were hypercholesterolemia, hypertension, heart disease, diabetes and arthritis, which explained 56% of the variance.

DISCUSSION

More than half of the adults had some chronic disease. The occurrence of two or more morbidities was reported by more than a quarter of the adults. Four out of twenty-five individuals reported a multimorbidity of three or more. According to the results, it is estimated that over 1 300 000 residents of the metropolitan region of Manaus have a chronic condition, and almost 700 000 have multimorbidity. Female sex, elderly age,

Table 3. Adjusted prevalence ratio (PRs) and 95% CIs for any chronic disease and multimorbidity ≥2 and ≥3, according to sociodemographic and health variables based on hierarchical Poisson regression. Manaus metropolitan region, Brazil, 2015 (n=4001)

Variable	Any chronic disease PR (95% CI)	P value	Multimorbidity PR (95% CI)			
			≥2	P value	≥3	P value
Demographic block†						
Sex						
Male	1.0		1.0		1.0	
Female	1.19 (1.12 to 1.25)	<0.001	1.66 (1.50 to 1.83)	<0.001	2.19 (1.88 to 2.56)	<0.001
Age group						
18 to 24	1.00				1.0	
25 to 34	1.33 (1.19 to 1.48)	<0.001	1.81 (1.42 to 2.30)	<0.001	1.88 (1.24 to 2.84)	0.003
35 to 44	1.63 (1.47 to 1.81)	<0.001	2.85 (2.26 to 3.60)	<0.001	3.40 (2.28 to 5.06)	<0.001
45 to 59	1.91 (1.72 to 2.12)	<0.001	4.36 (3.48 to 5.46)	<0.001	7.62 (5.22 to 11.10)	<0.001
≥60	2.32 (2.08 to 2.57)	<0.001	5.68 (4.51 to 7.15)	<0.001	12.03 (8.20 to 17.66)	<0.001
Marital status						
Single	1.0		1.0		1.0	
Married	1.09 (0.96 to 1.07)	0.521	1.20 (1.07 to 1.33)	0.001	1.21 (1.03 to 1.42)	0.017

Separated/ Divorced	1.00 (0.91 to 1.10)	0.961	1.24 (1.06 to 1.45)	0.006	0.93 (0.72 to 1.21)	0.620
Widower	0.96 (0.87 to 1.06)	0.475	1.18 (1.01 to 1.38)	0.032	0.99 (0.77 to 1.26)	0.962
Skin colour						
White/yellow	1.0		1.0		1.0	
Black/brown/ Indigenous	1.10 (1.02 to 1.18)	0.006	1.04 (0.93-1.16)	0.474	0.89 (0.75 to 1.05)	0.175
Socioeconomic block ‡						
Education						
High education or above	1.0		1.0		1.0	
High school	1.00 (0.87 to 1.14)	0.976	0.89 (0.71 to 1.12)	0.357	0.73 (0.50 to 1.05)	0.091
Middle school	0.98 (0.84 to 1.13)	0.754	0.81 (0.63 to 1.06)	0.135	0.80 (0.53 to 1.20)	0.289
Elementary school or less	1.12 (0.98 to 1.29)	0.106	1.01 (0.80 to 1.28)	0.877	1.08 (0.75 to 1.55)	0.667
Economic classification						
A – B	1.0		1.0		1.0	
C	1.04 (0.96 to 1.13)	0.361	1.01 (0.87 to 1.17)	0.881	1.05 (0.83 to 1.33)	0.656
D – E	1.06 (0.97 to 1.16)	0.207	1.15 (0.98 to 1.36)	0.075	1.15 (0.89 to 1.49)	0.254
Occupation						
Formal job	1.0		1.0		1.0	
Informal job	0.95 (0.87 to 1.03)	0.223	0.97 (0.83 to 1.13)	0.728	0.98 (0.76 to 1.28)	0.929
Retired	0.95 (0.86 to 1.06)	0.363	1.11 (0.92 to 1.32)	0.258	1.39 (1.02 to 1.88)	0.033
Student/ housewife	0.96 (0.87 to 1.05)	0.331	0.97 (0.83 to 1.14)	0.767	1.05 (0.81 to 1.36)	0.671
Unemployed	1.09 (0.99 to 1.20)	0,081	0.99 (0.81 to 1.20)	0.949	1.13 (0.83 to 1.54)	0.404
Health block §						
Private health insurance						
No	1.0		1.0		1.0	
Yes	0.99 (0.91 to 1.07)	0.913	1.03 (0.90 to 1.18)	0.593	1.04 (0.84 to 1.28)	0.771
Health status						
Very good	1.0		1.0		1.0	
Good	1.43 (1.24 to 1.64)	<0.001	1.63 (1.23 to 2.15)	<0.001	1.81 (1.09 to 2.99)	0.020
Fair	1.94 (1.69 to 2.23)	<0.001	2.84 (2.15 to 3.76)	<0.001	4.21 (2.56 to 6.93)	<0.001
Bad	2.01 (1.80 to 2.41)	<0.001	3.53 (2.64 to 4.71)	<0.001	6.25 (3.74 to 10.47)	<0.001
Very bad	1.91 (1.60 to 2.27)	<0.001	3.70 (2.73 to 5.00)	<0.001	7.89 (4.71 to 13.23)	<0.001
Health reference						
No	1.0		1.0		1.0	
Yes	1.12 (1.06 to 1.19)	<0.001	1.33 (1.19 to 1.47)	<0.001	1.40 (1.20 to 1.63)	<0.001
Physician visit						
No	1.0		1.0		1.0	
Yes	1.13 (1.05 to 1.22)	<0.001	1.22 (1.07 to 1.40)	0.002	1.33 (1.09 to 1.64)	0.005
Hospitalization						
No	1.0		1.0		1.0	
Yes	1.18 (1.09 to 1.27)	<0.001	1.36 (1.20 to 1.54)	<0.001	1.43 (1.17 to 1.74)	<0.001
Dengue						

No	1.0		1.0		1.0	
Yes	1.07 (0.99 to 1.16)	0.079	1.23 (1.08 to 1.41)	0.001	1.36 (1.13 to 1.64)	0.001
Malaria						
No	1.0		1.0		1.0	
Yes	0.98 (0.82 to 1.01)	0.109	0.96 (0.81 to 1.13)	0.653	0.99 (0.78 to 1.26)	0.947
Type of service						
Primary	1.0		1.0		1.0	
Secondary	1.02 (0.95 to 1.09)	0.518	1.07 (0.95 to 1.22)	0.265	1.15 (0.95 to 1.40)	0.129
Tertiary	0.95 (0.89 to 1.00)	0.086	1.01 (0.92 to 1.12)	0.780	1.05 (0.90 to 1.25)	0.489
Outros	0.92 (0.82 to 1.03)	0.180	0.97 (0.80 to 1.17)	0.723	1.13 (0.85 to 1.51)	0.374

Significant variables kept in each block of analysis:
Any chronic disease: †sex, age, marital status and race; ǂsex, age, marital status, education, income, occupation; §sex, age, marital status, income, occupation, private health insurance, health status, health reference, medical consultation in last 12 months, hospital admission in last 12 months, dengue, malaria and type of health service that usually comes
≥2 morbidities: †sex, age, marital status and race; ǂsex, age, marital status, education, income, occupation; §sex, age, marital status, income, occupation, private health insurance, health status, health reference, medical consultation in last 12 months, hospital admission in last 12 months, dengue, malaria and type of health service that usually comes
≥3 morbidities: †sex, age, marital status and race; ǂsex, age, marital status, education, income, occupation; §sex, age, marital status, income, occupation, private health insurance, health status, health reference, medical consultation in last 12 months, hospital admission in last 12 months, dengue, malaria and type of health service that usually comes

dengue in the last year, poor health status, reference health service use, physician visits and hospitalization presented associations with multimorbidity. Chronic spinal problems were the most commonly reported diseases. Diabetes was the most common disease in women aged 18-34 years with multimorbidity ≥2, and hypercholesterolemia was the corresponding disease in men aged 35-59 years.

The main limitation of this research is the way in which the outcome was measured, the participants' self-report, and consequently, our data were error-prone and influenced by memory bias. This bias is more common in elderly individuals of lower socioeconomic and educational levels, who are susceptible to underreporting.[7 27] Survival bias also influenced the results, since patients who died prematurely from those causes, were hospitalized or had more serious diseases were not available in the household to participate in the survey. In addition, we did not investigate disease severity. Previous studies recommend inquiring about the degree of disease intensity, the diseases' interference with routine activities and disabilities,[5 28] which were not measured in this study.

This is the first local study to estimate the prevalence of multimorbidity in adults in the state of Amazonas. We used a list of 12 diseases and cut-off point of two or more and three or more multimorbidity, in accordance with previous studies.[3 5]

Table 4. Factor score of each chronic disease in women and men, Manaus metropolitan region, Brazil, 2015

Morbidities	Women (N=2,113)	Men (N=1,888)	
	Factor 1	Factor 1	Factor 2
Hypercholesterolemia	0.70		0.62
Hypertension	0.64		0.78
Heart disease	0.72	0.40	0.47
Diabetes	0.63		0.85
Chronic kidney disease	0.46	0.73	
Stroke	0.66	0.61	
Arthritis	0.65	0.40	0.35
Chronic spinal problem	0.46	0.44	
Depressive disorder	0.49	0.58	
Asthma or asthmatic bronchitis	0.44	0.48	
Lung diseases†	0.53	0.76	
Cancer	0.52	-	
Proportion of variance (%)	81.0	62.0	56.0
Kaiser-Meyer-Olkin	0.82	0.78	

Note: Kept factors were those with scores ≥ 0.30 after oblique rotation; cancer showed negative values in men and was excluded
† pulmonary emphysema, bronchitis, chronic obstructive lung disease

We obtained a 76% response rate, which may constitute a source of selection bias. Efforts were employed to improve representativeness by using predefined sex and age quotas and interviewing one individual per family, according to official estimates.[29]

A systematic review that summarized 39 observational studies conducted between 1993 and 2013 identified a range of five to 335 diseases for the study of multimorbidity.[3] As expected, the lower the number of diseases included in the research, the lower the prevalence observed.[30] Regardless of the number of chronic conditions reported and how they were defined, multimorbidity estimates are influenced by self-report. Although widely applied,[3 5 28] self-reports are more likely to suffer classification bias or have no validated instrument for confirmation.

We identified the most vulnerable multimorbidity groups were women and the elderly. A National Health Survey conducted in Brazil reported that women are most affected in all socioeconomic groups, especially the elderly.[31]

Back pain was the most frequent disease, reported by one-third of the sample. In our study, this morbidity was assessed using different terms, which may have increased the sensitivity of the assessment. An even higher proportion (49.4%) of vertebral spine/back issues was observed in a representative cross-sectional survey of Brazilian adults.[31] In other contexts, similar prevalence values were estimated.[32]

Two findings of our research are rarely described in previous studies: the higher frequency of multimorbidity in younger adults and the lack of association with economic status. One-half of adults aged 25-34 years and almost two-thirds of interviewees aged 35-44 years reported any chronic condition, and almost one-third had multimorbidity. It is important to emphasize that half of the Manaus metropolitan region is concentrated in this age range (25-44 years old). A systematic review of 24 cross-sectional studies on multimorbidity found income as a conflicting factor across studies, associated either with richer or poorer individuals, while lower educational attainment was associated with a 64% higher chance of multimorbidity.[33] A Mendelian analysis of 543 733 individuals from high-income countries has found that 3.6 more years of education reduces the risk of coronary heart disease by one-third.[34]

In lower-income countries, such as Brazil, which also faces economic austerity policies, rising unemployment and unstable social and health policies, [35] it is possible to predict a reduction in access to health services, with a consequent increase in morbidity. This effect was observed in other austerity scenarios, in which this type of policy reduced jobs, education and use of health services, resulting in an increase of chronic diseases.[36 37]

A single multimorbidity pattern was identified in women, which included cardiometabolic, skeletal, respiratory, psychosomatic, and cancer diseases. Since only one pattern was identified out of all reported diseases, it is possible that the risk factors are similar and are triggering a sequence of diseases, or one disease may be leading to another. In men, factor 1 included musculoskeletal, respiratory and psychosomatic diseases, and factor 2 included cardiometabolic diseases. Elderly men were assumed to be in factor 1, since they had worse outcomes. Factor 2 included younger men with diseases developed from risk factors such as sedentary lifestyle and obesity.

Our results showed similarities to a cross-sectional study conducted in 2012 in the southern region of Brazil with 2927 subjects, in which 29.1% of the interviewees had more

than two chronic diseases and 14% had three or more.[38] The 2013 National Health Survey also confirmed these findings: 22% reported two or more chronic diseases, and 10% were affected by more than three.[14] The highest prevalence was observed in the south (26-29%) and southeast (23-25%), which are more economically developed and have greater access to health services.[15] Similarly, any chronic disease occurred in 45% of Brazilians, with a lower prevalence in the north region.[39]

Greater or lesser use of health services influences the multimorbidity self-report.[40 41] A systematic review including 27 cross-sectional population-based studies conducted between 1992 and 2013 in Brazil estimated lower prevalence of medical consultation in the north region and greater in the south region.[15]

In contexts of higher economic development, a lower prevalence of multimorbidity was found. A survey conducted in 2012 in Italy, with 3 759 836 adults, detected that 15% of individuals presented two or more chronic diseases.[10] In Ireland, a representative sample of the population (11.3% of subjects ≥50 years) presented multiple diseases.[12] Furthermore, an electronic medical data analysis, conducted in 2007 with 1 751 841 users of the Scottish Health Service, found that 23% had multimorbidity.[9] In a comparable economic context to Brazil's, a population-based Indian study conducted in 2007 with 10 973 interviewees identified smaller proportions (28% had any chronic disease and approximately 9% had multimorbidity).[42]

Diabetes was a common chronic condition coexisting with two or more morbidities in young women, while heart diseases were the most common in those aged 35-59 years. In men, arthritis and hypercholesterolemia were more frequent. In a study conducted in Portugal, diabetes, osteoarthritis and lipid disorders were more common in women with more than two morbidities, while hypertension, osteoarthritis and obesity were more common in men.[43]

The presence of dengue was higher in individuals with multimorbidity, possibly due to the lower immunologic response observed in chronic diseases such as diabetes, rheumatoid arthritis, and asthma. [44 45] A systematic review including 16 cohort and case-control studies conducted between 2007 and 2013 showed that chronic diseases were risk factors for severe forms of dengue.[46] In another meta-analysis of 10 studies conducted between 2006 and 2014,[47] diabetes was significantly associated with haemorrhagic dengue:

regardless of demographic and socioeconomic characteristics, the association was 5% higher compared to individuals who did not have diabetes.

CONCLUSION

Multimorbidity was common in residents of the metropolitan region of Manaus and was associated with female sex, elderly people and poorer health perception. Prevention and control strategies should prioritize these groups. Future analyses may investigate the relationship between multimorbidity and physical and psychic disorders, as well as the impact on the use and costs of health services in the region.

Contributors MTS, TFG, and MEAA designed the study. MEAA, MTS and BNP performed the statistical analyses. MEAA, MTS, TFG, BNP and MGP interpreted the results and drafted the manuscript. All authors made critical revisions and provided intellectual content to the manuscript, approved the final version and agree to be accountable for all aspects of this work.

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Competing interest None declared

Patient consent Obtained

Ethics approval The research project was approved by the Research Ethics Committee of the Federal University of Amazonas. All the individuals who agreed to participate signed a free and informed consent form.

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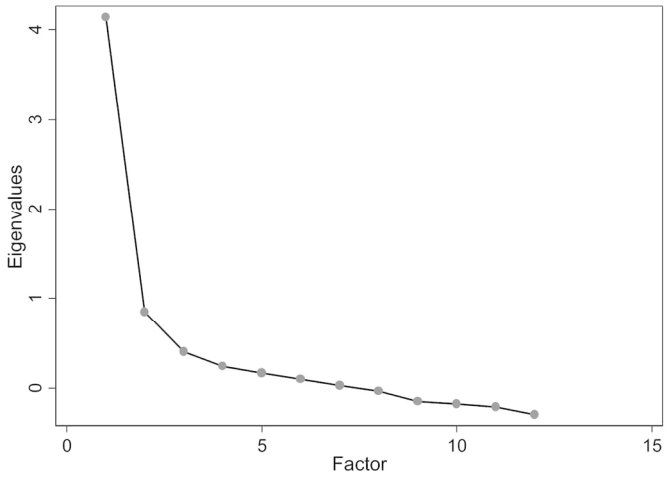

Figure 1 - Scree plot for women

Note: One factor was identified according to the inflection point in the curve (eigenvalue >1)

599x776mm (72 x 72 DPI)

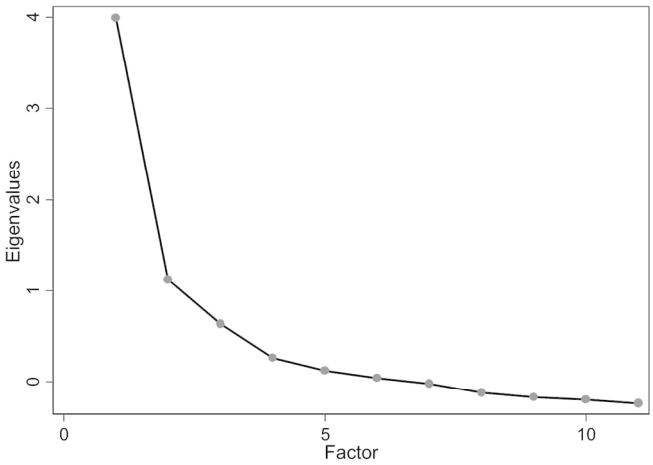

Figure 2 - Scree plot for men

Note: Two factors were identified according to the inflection point in the curve (eigenvalue >1)

599x776mm (72 x 72 DPI)

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1,2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any pre-specified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	3,4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—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 *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	4
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—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	4
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	4
Bias	9	Describe any efforts to address potential sources of bias	4
Study size	10	Explain how the study size was arrived at	-
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5
		(*b*) Describe any methods used to examine subgroups and interactions	-
		(*c*) Explain how missing data were addressed	-
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	4

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*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	6
		(b) Give reasons for non-participation at each stage	-
		(c) Consider use of a flow diagram	na
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6
		(b) Indicate number of participants with missing data for each variable of interest	-
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	-
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	-
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	-
		Cross-sectional study—Report numbers of outcome events or summary measures	6
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	7,8,9
		(*b*) Report category boundaries when continuous variables were categorized	6
		(*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	10 and 12
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	12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13,14
Generalisability	21	Discuss the generalisability (external validity) of the study results	14,15
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	16

*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.

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Prevalence and patterns of multimorbidity in Amazon Region of Brazil and associated determinants: a cross-sectional study

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Prevalence and patterns of multimorbidity in Amazon Region of Brazil and associated determinants: a cross-sectional study

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Word count: 2999

ABSTRACT

Objectives: To estimate the prevalence of multimorbidity and to identify factors associated with it in the adult population from the metropolitan region of Manaus.

Design: Cross-sectional population-based study.

Setting: Interviews conducted between May and August of 2015 in eight cities that compose the metropolitan region of Manaus, Amazonas, Brazil.

Participants: 4000 adults aged ≥18 years

Primary outcome measures: Multimorbidity, measured by the occurrence of ≥2 and ≥3 chronic diseases, was the primary outcome. The associated factors were investigated by calculating the prevalence ratio (PR) obtained by Poisson regression, with robust adjustment of the variance in a hierarchical model. A factor analysis was conducted to investigate multimorbidity clusters.

Results: Half of the interviewees were women. The presence of a chronic disease was reported by 57.2% (95% CI 56.6% to 59.7%) of the interviewees, and the mean morbidity was 1.2 (1.1-1.2); 29.0% (95% CI 27.6% to 30.5%) reported ≥2 morbidities, and 15.2% (95% CI 14.1% to 16.4%) reported ≥3 chronic conditions. Back pain was reported by one-third of the interviewees. Multimorbidity was higher in women PR = 1.66 (95% CI 1.50 to 1.83), the elderly, PR = 5.68 (95% CI 4.51 to 7.15) and individuals with worse health perception, PR = 3.70 (95% CI 2.73-5.00). Associated factors also included undergoing medical consultations, hospitalization in the last year, suffering from dengue in the last year and using a reference health service. Factor analysis revealed a pattern of multimorbidity in women. The factor loading the most strength of association in women was heart disease. In men, an association was identified in two groups and lung disease was disease with higher factorial loading.

Conclusion: Multimorbidity was frequent in the metropolitan region of Manaus. It occurred more in women, in the elderly and in those with worse health perception.

Keywords: Prevalence, Multimorbidity, Cross-Sectional Studies, Population Surveys, Brazil.

Strengths and limitations of this study:

This is the first study on the prevalence of multimorbidity in adults from the metropolitan region of Manaus, Amazonas, Brazil, using data from a population-based survey.

We used probabilistic complex sampling in three stages: census track, household and individual to include 4001 adults living in one of the eight cities of the metropolitan region.

This research increases the knowledge about the epidemiologic factors associated with multimorbidity.

The measurement method of the outcome, self-report, is subject to errors and influenced by memory bias.

BACKGROUND

Multimorbidity is the occurrence of different chronic clinical conditions in an individual, without a single condition being considered the main cause.[1 2] It is operationally defined as the occurrence of two or more chronic diseases.[3-5] In recent decades, population ageing, lifestyle changes, improved socio-economic conditions, and increased diagnostic ability of health services have contributed to a significant rise in the population that survives serious diseases, causing an accumulation of health problems in specific population groups. This situation has contributed to the increased prevalence of multimorbidity.[6-8]

The multimorbidity frequency varies according to the evaluated diseases, the age of the population, the individual's socioeconomic and demographic level, and the individual's health condition. The rising prevalence of multimorbidity has resulted in higher costs to health services.[9-12] The costs associated with multimorbidity can reach 75% of total health expenditures, which includes physician consultation, hospitalization, odontological care, medication and rehabilitation.[13]

In Brazil, the 2013 National Health Survey (*Pesquisa Nacional de Saúde*), including 64 308 individuals over 18 years old, and the most extensive evidence on population multimorbidity, has identified that the prevalence of multimorbidity was 26% to 29% in the southern region and 14% to 19% in the northern region.[14]. Studies in specific populations conducted on the south and southeast regions identified higher multimorbidity prevalence in women and elderly.[15 16] The differences found suggest heterogeneity in socioeconomic development.[17] However, there is a lack of studies on the north region to identify more susceptible groups and expand our knowledge about multimorbidity at the local level.

The present research estimated the prevalence of and identified the factors associated with multimorbidity in the adult population of the metropolitan region of Manaus, the most populated region and largest economic cluster in northern Brazil.

METHODS

Study design

This is a cross-sectional population-based study in the metropolitan region of Manaus, composed by the capital of Amazonas, Manaus, and seven surrounding cities.

Multimorbidity was considered a primary outcome, which was categorized as ≥2 or ≥3 chronic diseases. The present analysis is part of a larger study, which aimed to study the use of health services and inputs in the region from May to August 2015.[18]

Participants and study size

We calculated the sample size as 4000 adults ≥18 years old to be interviewed, who were selected by probabilistic complex sampling—by cluster and stratified by sex and age—in three stages (census track, household and individual).[18] We assume an estimated 50% prevalence of use of health services, considering a CI of 95%, accuracy of 2% and a design effect value of 1.5.[19] We added 10% to compensate for possible losses and refusals.

Variables and data collection

The primary outcome was self-reported multimorbidity, defined as two or more affirmative answers to any of the following questions: "Have any doctors ever diagnosed you with [...]?" [1] hypertension, [2] diabetes, [3] high cholesterol, [4] heart disease (heart attack, angina, heart failure or other), [5] stroke, [6] asthma or asthmatic bronchitis, [7] arthritis or rheumatism, [8] depression, [9] pulmonary disease (pulmonary emphysema, chronic bronchitis or chronic obstructive pulmonary disease), [10] cancer, or [11] chronic kidney disease, and [12] “Do you have any chronic spinal problems, such as chronic back or neck pain, low back pain, sciatic pain, vertebral or disc problems?” These questions were previously used in the National Health Survey.[20]

The independent variables were sex; age (18 to 24; 25 to 34; 35 to 44; 45 to 59 and ≥60 years);[21] marital status; self-reported skin colour; education; social class;[22] occupation; private health insurance (yes, no); self-perception of health status; place of attendance (capital, countryside); using a reference health service, that is, use of the same healthcare professional for attendance (yes, no); physician visit in the last 12 months (yes, no); hospitalization in the last year (yes, no); malaria in the last 12 months (yes, no); dengue in the last 12 months (yes, no); and types of services one usually seeks when in need of medical care (primary, secondary, or tertiary).

Interviewers with experience in conducting home interviews collected the data on a mobile electronic device (Samsung® Galaxy Tab3 SM-T110). Interview records were transmitted over the Internet and stored using Survey To Go software (Dooblo Ltd., Israel).

Statistical analyses

Statistical analyses were carried out in Stata v. 14.2. In all calculations, the complex sampling design was weighted by incorporating sample weights (*svy* command).

Descriptive statistics were initially obtained through prevalence calculation. The respective confidence intervals and P values of difference were calculated by Pearson's chi-square between sociodemographic characteristics and multimorbidity. The prevalence of the most common diseases stratified by sex, age group and multimorbidity was also calculated. At this stage, morbidities with a prevalence of <5% were excluded.

Bivariate analyses were performed between all independent and dependent variables to calculate prevalence ratios (PRs) and 95% confidence intervals (CIs). To identify the factors associated with multimorbidity, PRs were adjusted using Poisson regression with robust variance adjustment.[23-25]

A hierarchical model consisting of three blocks was constructed of the most distal to the most proximal determinants of multimorbidity: (1) demographic variables (sex, age, race, marital status); (2) socioeconomic variables (economic, education classification, occupation); and (3) health variables (private health insurance, health status, demand for the same health service, physician visit, hospitalization, dengue, malaria and type of service usually used). The variables from the first block were kept for the next stage if they presented a p-value ≤0.05. Multicollinearity among the independent variables was discarded by assessing the variance inflation factors.[26]

To analyse whether the diseases grouped in patterns, an exploratory factor analysis was conducted, stratified by sex.[27 28] This technique allowed us to identify the tendency of coexisting diseases and to select a set of variables with potentially common causal factors, such as interaction between diseases and/or their treatments and/or common risk factors, which were interpreted as multimorbidity patterns. The tetrachoric correlation coefficient was used in the analysis because it is better than Pearson's correlation coefficient for dichotomous outcomes.[29] The suitability of the sampling was evaluated by the Kaiser-Meyer-Olkin test (KMO), which was considered adequate if the index was ≥0.70, and the Bartlett sphericity test, which was considered adequate if its p-value was ≤0.05.[27 30] To establish the number of factors to be maintained, Cattell's graphic (Cattell's scree plot) was used, which represents the eigenvalues of the correlation matrix in descending order. The factor number extracted corresponds to the eigenvalue that produces the inflection point in

the curve (eigenvalue> 1) and explains the minimum variance (>10% for each component). Variables were defined as being associated with a factor if they presented loads ≥0.30 [27] (the closer to 1, the greater the association). Oblique rotation (promax) was performed to allow for better interpretation of the factor analysis.[27]

Patient and public involvement

Patients and public were not involved in the design of the research question nor were they involved in developing plans for design or implementation of the study. The study had no patient advisers. Outcomes were self-reported by patients based on pre-defined questions. Due to the cross-sectional nature of the study, a feedback of the results was not planned to those involved.

RESULTS

Participant characteristics

Table 1 shows the characteristics of the participants and the prevalence of multimorbidity. The sample was composed of 4001 adults and had a response rate of 76%. Women constituted over half of the sample. About one-half of the interviewees were between 25 and 44 years old, and 81% were black, brown or indigenous. The predominant social stratum was the lower middle class (57%), and about one-third of the participants were students or housewives. More than half reported good health (54%), and the majority had had a physician visit in the last year (76%). In the last 12 months, 7% reported dengue and 6% reported malaria. One-half of respondents reported seeking a tertiary health service when they needed care (47%).

Prevalence of multimorbidity

The prevalence of at least one chronic disease was 57.2% (95% CI 56.6 to 58.7%), with a mean of 1.2 ± 1.5 diseases. The prevalence of ≥2 chronic conditions was 29% (95% CI 27.6 to 30.5%) and ≥3 chronic diseases was 15.2% (95% CI 14.1 to 16.4%). Higher prevalence was observed in women, in widowers, in individuals with lower education, in retired individuals, in individuals who had the worst perceptions of health and in those who visited a doctor and were hospitalized in the last year (Table 1). The mean of any chronic disease and the multimorbidity increased with age (0.5 ± 0.8 in the 18 to 24 year-old group

and 2.5 ± 1.9 in those 60 years or above). In the previous year, dengue was reported by 44% of those who had two or more chronic conditions.

About half of women aged 35 to 59 years reported ≥2 morbidities (Table 2). Back pain was the most reported health problem in both women and men.

Table 1. Characteristics of participants and prevalence of multimorbidity (%), Manaus metropolitan region, Brazil, 2015 (n= 4001)*

Variable	% (n)	Any chronic disease % (95% CI)	P value	Mean number of chronic health problems (95% CI)	Multimorbidity % (95% CI)			
					≥2	P value	≥3	P value
Overall		57.2 (55.6 to 58.7)		1.17 (1.1 to 1.2)	29.0 (27.6 to 30.5)		15.2 (14.1 to 16.4)	
Sex			<0.001			<0.001		<0.001
Male	47.2 (1888)	52.1 (49.8 to 54.0)		0.9 (0.8 to 0.9)	21.5 (19.7 to 23.4)		9.3 (8.1 to 10.7)	
Female	52.7 (2113)	61.8 (59.7 to 63.8)		1.39 (1.3 to 1.4)	35.8 (33.8 to 37.8)		20.5 (18.8 to 22.3)	
Age (years)			<0.001			<0.001		<0.001
18 to 24	20.8 (838)	37.0 (33.8 to 40.3)		0.5 (0.4 to 0.5)	9.8 (7.9 to 12.0)		3.5 (2.5 to 5.0)	
25 to 34	28.7 (1152)	49.6 (46.7 to 52.5)		0.8 (0.7 to 0.8)	18.6 (16.4 to 20.9)		6.9 (5.6 to 8.5)	
35 to 44	21.1 (843)	61.0 (57.6 to 64.2)		1.1 (1.0 to 1.2)	30.0 (27.0 to 33.2)		12.7 (10.6 to 15.1)	
45 to 59	19.3 (772)	71.4 (68.0 to 74.4)		1.7 (1.6 to 1.8)	46.6 (13.1 to 50.2)		28.1 (25.1 to 31.4)	
≥60	9.9 (396)	86.1 (82.3 to 89.2)		2.5 (2.3 to 2.7)	63.5 (58.6 to 68.1)		44.4 (39.6 to 49.3)	
Marital status			<0.001			<0.001		<0.001
Single	54.2 (2173)	51.5 (49.3 to 53.5)		0.9 (0.8 to 0.9)	20.8 (19.1 to 22.6)		10.3 (8.8 to 11.3)	
Married	35.2 (1409)	62.0 (59.4 to 64.5)		1.3 (1.2 to 1.4)	35.3 (32.9 to 37.9)		19.6 (17.6 to 21.8)	
Separated/Divorced	6.5 (260)	65.6 (59.6 to 71.2)		1.5 (1.3 to 1.7)	42.6 (36.8 to 48.7)		19.9 (15.5 to 25.2)	
Widower	4.0 (159)	79.3 (72.3 to 84.9)		2.2 (1.9 to 92.5	63.1 (55.3 to 70.2)		39.9 (32.5 to 47.7)	
Skin colour			<0.001			0.0021		0.0016
White/yellow	19.3 (774)	51.7 (48.2 to 55.2)		1.1 (1.0 to 1.2)	27.1 (24.1 to 30.4)		15.7 (13.3 to 18.5)	
Black/brown/ indigenous	80.5 (3227)	58.5 (56.8 to 60.2)		1.2 (1.1 to 1.2)	29.5 (27.9 to 31.1)		15.1 (13.9 to 16.4)	
Schooling level			<0.001			<0.001		<0.001
High education or above§	3.9 (158)	57.1 (49.3 to 64.6)		1.2 (1.0 to 1.5)	32.6 (25.7 to 40.4)		16.1 (11.7 to 23.7)	
High school	47.5 (1903)	51.0 (48.8 to 53.3)		0.9 (0.8 to 1.0)	22.5 (20.7 to 24.5)		9.0 (7.8 to 10.4)	
Middle school	16.2 (649)	50.0 (46.2 to 53.8)		0.9 (0.8 to 1.0)	21.1 (18.2 to 24.4)		10.7 (0.8 to 13.3)	
Elementary school or less	32.2 (1291)	69.9 (67.4 to 72.4)	<0.001	1.7 (1.6 to 1.8)	42.1 (39.5 to 44.8)		26.5 (24.1 to 28.9)	
Economic classification†						<0.001		<0.001
A - B	15.7 (629)	51.2 (47.2 to 55.1)		0.9 (0.8 to 1.1)	24.6 (21.4 to 28.2)		11.1 (8.8 to 13-8)	
C	57.1 (2285)	55.5 (53.4 to 57.5)		1.0 (1.0 to 1.1)	26.1 (24.3 to 27.9)		13.2 (11.9 to 14.7)	
D - E	27.2 (1087)	64.3 (61.4 to 67.2)		1.5 (1.4 to 1.6)	37.7 (34.9 to 40.7)		21.8 (19.4 to 24.3)	
Occupation			<0.001			<0.001		<0.001

Variable	% (n)	Any chronic disease % (95% CI)	P value	Mean number of chronic health problems (95% CI)	Multimorbidity % (95% CI)			
					≥2	P value	≥3	P value
Formal job	19.0 (761)	52.7 (49.1 to 56.2)		0.9 (0.8 to 1.0)	22.7 (19.8 to 25.8)		9.2 (7.3 to 11.5)	
Informal job	28.7 (1149)	55.9 (53.0 to 58.7)		1.0 (1.0 to 1.1)	27.6 (25.1 to 30.3)		12.9 (11.1 to 15.0)	
Retired	7.9 (315)	79.2 (74.3 to 83.3)		2.4 (2.2 to 2.6)	60.5 (55.4 to 65.8)		43.4 (38.0 to 49.0)	
Student/ housewife	29.8 (1199)	55.0 (52.2 to 57.8)		1.1 (1.1 to 1.2)	29.0 (25.5 to 31.6)		15.8 (13.8 to 18.0)	
Unemployed	14.4 (577)	58.3 (54.2 to 62.3)		1.0 (0.9 to 1.1)	23.1 (19.8 to 26.7)		11.2 (8.9 to 14.1)	
Private health insurance			0.348			0.697		0.616
Yes	13.0 (523)	55.3 (51.0 to 59.5)		1.0 (0.9 to 1.29	28.0 (24.6 to 32.3)		14.5 (11.7 to 17.8)	
No‡	87.0 (3478)	57.5 (55.8 to 59.1)		1.2 (1.1 to 1.2)	29.0 (27.6 to 30.7)		15.3 (14.2 to 16.6)	
Health status			<0.001			<0.001		<0.001
Very good	11.9 (471)	30.8 (26.8 to 35.2)		0.4 (0.47 to 0.5)	9.7 (7.3 to 12.7)		3.1 (1.9 to 5.1)	
Good	54.3 (2175)	50.4 (48.3 to 52.5)		0.8 (0.8 to 0.9)	20.3 (18.7 to 22.0)		7.9 (6.8 to 9.1)	
Fair	27.7 (1108)	75.1 (72.5 to 77.5)		1.7 (1.6 to 1.8)	45.2 (42.3 to 48.1)		26.0 (23.5 to 28.6)	
Bad	4.8 (193)	88.6 (83.2 to 93.3)		2.6 (2.4 to 2.9)	68.4 (61.6 to 74.6)		50.3 (43.3 to 57.3)	
Very bad	1.3 (54)	81.5 (68.9 to 89.7)		3.6 (3.0 to 4.3)	77.7 (64.8 to 86.9)		70.3 (57.0 to 81.0)	
City			<0.001			<0.001		<0.001
Capital	86.8 (3479)	58.4 (56.8 to 60.0)		1.2 (1.1 to 1.2)	30.2 (28.7 to 31.7)		15.8 (14.6 to 17.1)	
Countryside	13.1 (522)	49.2 (44.9 to 53.5)		0.9 (0.8 to 1.0)	21.5 (18.2 to 25.3)		11.3 (0.8 to 14.3)	
Health reference			<0.001			<0.001		<0.001
Yes	60.7 (2434)	62.3 (60.3 to 64.2)		1.3 (1.2 to 1.4)	34.4 (31.5 to 36.3)		18.7 (17.1 to 20.3)	
No	39.2 (1567)	49.4 (46.9 to 51.9)		0.9 (0.8 to 0.9)	20.8 (18.9 to 22.9)		9.8 (17.2 to 20.3)	
Physician visit			<0.001			<0.001		<0.001
Yes	76.5 (3066)	60.8 (59.0 to 62.5)		1.2 (1.2 to 1.3)	32,1 (30.5 to 33.8)		17.4 (16.1 to 18.8)	
No	23.4 (935)	45.5 (42.3 to 48.7)		0.8 (0.7 to 0.9)	18,9 (16.5 to 21.5)		8.2 (6.6 to 10.2)	
Hospitalization			<0.001			<0.001		<0.001
Yes	7.0 (273)	72.9 (67.3 to 77.8)		1.2 (1.2 to 1.3)	47,2 (41.4 to 53.2)		28.1 (23.1 to 33.8)	
No	93.0 (3728)	56.1 (67.3 to 77.8)		0.8 (0.7 to 0.9)	27,7 (26.3 to 29.2)		14.3 (13.2 to 15.4)	
Dengue			0.002			<0.001		<0.001
Yes	7.0 (281)	65.9 (60.1 to 71.2)		1.6 (1.4 to 1.8)	44.2 (38.5 to 50.1)		27.6 (22.7 to 33.1)	
No	93.0 (3720)	56.5 (54.9 to 58.1)		1.1 (1.0 to 1.1)	27.9 (26.5 to 29.3)		14.3 (13.2 to 15.5)	
Malaria			0.420			0.122		0.014
Yes	5.9 (234)	54.6 (48.2 to 60.9)		1.3 (1.1 to 1.5)	33.5 (27.7 to 39.8)		20.8 (16.1 to 26.5)	
No	94.0 (3767)	57.3 (0.55 to 0.58)		1.1 (1.1 to 1.2)	28.8 (27.3 to 30.2)		14.9 (13.8 to 16.0)	
Medical attention			<0.001			0.048		0.531

Variable	% (n)	Any chronic disease % (95% CI)	P value	Mean number of chronic health problems (95% CI)	Multimorbidity % (95% CI)			
					≥2	P value	≥3	P value
Primary	30.2 (1208)	60.8 (58.0 to 63.5)		1.2 (1.1 to 1.3)	29.9 (27.3 to 32.5)		15.2 (13.3 to 17.3)	
Secondary	14.9 (598)	62.3 (58.3 to 66.1)		1.3 (1.2 to 1.5)	33.0 (29.4 to 36.9)		18.9 (15.9 to 22.2)	
Tertiary	47.2 (1886)	54.0 (51.8 to 56.3)		1.1 (1.0 to 1.2)	27.7 (25.7 to 29.8)		14.3 (12.8 to 15.9)	
Others	7.7 (309)	52.7 (47.2 to 58.3)		1.0 (0.9 to 1.2)	26.2 (21.6 to 31.4)		14.2 (10.7 to 18.5)	

* Descriptive statistics using simple frequency and Pearson $\chi 2$ test

CI: confidence interval; physician visit, hospitalization, dengue and malaria in last 12 months; § tertiary education or higher; † Average household income in 2015: A-B, US$6500-US$1419; C, US$463-US$772; D-E, US$205; ‡ People who use the public health service.

Table 2. Prevalence (%) of most common diseases stratified by sex, age and multimorbidity group, Manaus metropolitan region, Brazil, 2015*

Morbidities	%(n)	Multimorbidity ≥2			Multimorbidity ≥3		
		18 to 34 % (n)	35 to 59 % (n)	≥60 % (n)	18 to 34 % (n)	35 to 59 % (n)	≥60 % (n)
Women (2113)		18.4 (195)	47.0 (394)	76.9 (168)	7.0 (78)	28.1 (236)	55.0 (120)
Chronic spinal problem †	35.3 (747)	42.6 (135)	75.6 (248)	96.1 (99)	20.1 (64)	53.6 (176)	75.7 (78)
Hypertension	24.4 (516)	62.3 (78)	83.0 (211)	92.0 (126)	32.7 (94)	58.7 (149)	71.6 (98)
Arthritis or rheumatism	19.5 (414)	79.5 (66)	91.6 (197)	94.8 (110)	39.7 (33)	67.7 (146)	79.3 (92)
Hypercholesterolemia	20.1 (425)	79.5 (66)	90.8 (217)	97.0 (100)	55.4 (46)	62.4 (149)	82.5 (85)
Diabetes	7.4 (157)	93.7 (15)	90.2 (82)	96.0 (48)	87.4 (14)	76.6 (70)	84.5 (42)
Asthma or asthmatic bronchitis	7.3 (155)	68.5 (50)	85.6 (54)	100.0 (19)	38.3 (28)	73.0 (46)	100.0(19)
Depressive disorder	7.4 (158)	71.0 (44)	91.9 (69)	100.0 (21)	30.6 (19)	73.2 (55)	95.2 (20)
Heart disease ǂ	5.6 (119)	71.8 (23)	98.1 (52)	100.0 (34)	53.0 (17)	86.7 (46)	94.0 (32)
Men (1888)		10.9 (102)	28.2 (220)	47.1 (84)	3.4 (32)	11.4 (89)	31.4 (56)
Chronic spinal problem†	35.0 (662)	27.5 (77)	49.7 (149)	65.8 (54)	7.1 (20)	21.0 (63)	51.4 (42)
Hypertension	14.4 (271)	77.1 (37)	76.7 (112)	79.5 (61)	35.3 (17)	41.1 (60)	58.6 (45)
Arthritis or rheumatism	9.5 (179)	89.3 (25)	86.8 (80)	84.9 (50)	46.1 (13)	48.9 (45)	64.5 (38)
Hypercholesterolemia	9.0 (171)	57.1 (24)	87.6 (85)	87.6 (28)	33.3 (14)	49.4 (48)	78.2 (25)

P values of all variables were ≤0.002
* multimorbidity with prevalence ≥5%.
† chronic back pain or neck, low back pain, sciatica, vertebral or disc pain
ǂ heart disease, or heart attack, angina, cardiac insufficiency

Table 3 shows the investigation for factors associated with multimorbidity. After adjustment, multimorbidity (≥2 diseases) was associated with female sex (PR = 1.66, 95% CI 1.50 to 1.83), age between 45 and 59 years (PR = 4.36, 95% CI 3.48 to 5.46) and age ≥60 years (PR = 5.68, 95% CI 4.51 to 7.15). The presence of ≥3 diseases was associated with female sex (PR = 2.19, 95% CI 1.88 to 2.56), age 45 to 59 years (PR = 7.62, 95% CI 5.22 to 11.10), age ≥60 years (PR = 12.03, 95% CI 8.20 to 17.66), dengue in the last 12 months (PR = 1.36, 95% CI 1.13 to 1.64), and very poor health status (PR = 7.89, 95% CI 4.71 to 13.23). Having ≥3 chronic conditions increased the demand for physician visits, hospitalization in the last year, and demand for the same health service. Education, income, occupation, and malaria in the last 12 months did not show associations with multimorbidity.

Table 3. Adjusted prevalence ratio (PRs) and 95% CIs for any chronic disease and multimorbidity ≥2 and ≥3, according to sociodemographic and health variables based on hierarchical Poisson regression. Manaus metropolitan region, Brazil, 2015 (n=4001)

Variable	Any chronic disease PR (95% CI)	P value	Multimorbidity PR (95% CI)			
			≥2	P value	≥3	P value
Demographic block†						
Sex						
Male	1.00		1.00		1.00	
Female	1.19 (1.12 to 1.25)	<0.001	1.66 (1.50 to 1.83)	<0.001	2.19 (1.88 to 2.56)	<0.001
Age group						
18 to 24	1.00				1.00	
25 to 34	1.33 (1.19 to 1.48)	<0.001	1.81 (1.42 to 2.30)	<0.001	1.88 (1.24 to 2.84)	0.003
35 to 44	1.63 (1.47 to 1.81)	<0.001	2.85 (2.26 to 3.60)	<0.001	3.40 (2.28 to 5.06)	<0.001
45 to 59	1.91 (1.72 to 2.12)	<0.001	4.36 (3.48 to 5.46)	<0.001	7.62 (5.22 to 11.10)	<0.001
≥60	2.32 (2.08 to 2.57)	<0.001	5.68 (4.51 to 7.15)	<0.001	12.03 (8.20 to 17.66)	<0.001
Marital status						
Single	1.00		1.00		1.00	
Married	1.09 (0.96 to 1.07)	0.521	1.20 (1.07 to 1.33)	0.001	1.21 (1.03 to 1.42)	0.017
Separated/ Divorced	1.00 (0.91 to 1.10)	0.961	1.24 (1.06 to 1.45)	0.006	0.93 (0.72 to 1.21)	0.620
Widower	0.96 (0.87 to 1.06)	0.475	1.18 (1.01 to 1.38)	0.032	0.99 (0.77 to 1.26)	0.962
Skin colour						
White/yellow	1.00		1.00		1.00	
Black/brown/ Indigenous	1.10 (1.02 to 1.18)	0.006	1.04 (0.93 to 1.16)	0.474	0.89 (0.75 to 1.05)	0.175
Socioeconomic block ǂ						
Education						
High education or above	1.00		1.00		1.00	
High school	1.00 (0.87 to 1.14)	0.976	0.89 (0.71 to 1.12)	0.357	0.73 (0.50 to 1.05)	0.091
Middle school	0.98 (0.84 to 1.13)	0.754	0.81 (0.63 to 1.06)	0.135	0.80 (0.53 to 1.20)	0.289
Elementary school or less	1.12 (0.98 to 1.29)	0.106	1.01 (0.80 to 1.28)	0.877	1.08 (0.75 to 1.55)	0.667
Economic classification						
A – B	1.00		1.00		1.00	
C	1.04 (0.96 to 1.13)	0.361	1.01 (0.87 to 1.17)	0.881	1.05 (0.83 to 1.33)	0.656
D – E	1.06 (0.97 to 1.16)	0.207	1.15 (0.98 to 1.36)	0.075	1.15 (0.89 to 1.49)	0.254
Occupation						
Formal job	1.00		1.00		1.00	
Informal job	0.95 (0.87 to 1.03)	0.223	0.97 (0.83 to 1.13)	0.728	0.98 (0.76 to 1.28)	0.929
Retired	0.95 (0.86 to 1.06)	0.363	1.11 (0.92 to 1.32)	0.258	1.39 (1.02 to 1.88)	0.033
Student/ housewife	0.96 (0.87 to 1.05)	0.331	0.97 (0.83 to 1.14)	0.767	1.05 (0.81 to 1.36)	0.671
Unemployed	1.09 (0.99 to 1.20)	0.081	0.99 (0.81 to 1.20)	0.949	1.13 (0.83 to 1.54)	0.404
Health block §						

Private health insurance						
No	1.00		1.00		1.00	
Yes	0.99 (0.91 to 1.07)	0.913	1.03 (0.90 to 1.18)	0.593	1.04 (0.84 to 1.28)	0.771
Health status						
Very good	1.00		1.00		1.00	
Good	1.43 (1.24 to 1.64)	<0.001	1.63 (1.23 to 2.15)	<0.001	1.81 (1.09 to 2.99)	0.020
Fair	1.94 (1.69 to 2.23)	<0.001	2.84 (2.15 to 3.76)	<0.001	4.21 (2.56 to 6.93)	<0.001
Bad	2.01 (1.80 to 2.41)	<0.001	3.53 (2.64 to 4.71)	<0.001	6.25 (3.74 to 10.47)	<0.001
Very bad	1.91 (1.60 to 2.27)	<0.001	3.70 (2.73 to 5.00)	<0.001	7.89 (4.71 to 13.23)	<0.001
Health reference						
No	1.00		1.00		1.00	
Yes	1.12 (1.06 to 1.19)	<0.001	1.33 (1.19 to 1.47)	<0.001	1.40 (1.20 to 1.63)	<0.001
Physician visit						
No	1.00		1.00		1.00	
Yes	1.13 (1.05 to 1.22)	<0.001	1.22 (1.07 to 1.40)	0.002	1.33 (1.09 to 1.64)	0.005
Hospitalization						
No	1.00		1.00		1.00	
Yes	1.18 (1.09 to 1.27)	<0.001	1.36 (1.20 to 1.54)	<0.001	1.43 (1.17 to 1.74)	<0.001
Dengue						
No	1.00		1.00		1.00	
Yes	1.07 (0.99 to 1.16)	0.079	1.23 (1.08 to 1.41)	0.001	1.36 (1.13 to 1.64)	0.001
Malaria						
No	1.00		1.00		1.00	
Yes	0.98 (0.82 to 1.01)	0.109	0.96 (0.81 to 1.13)	0.653	0.99 (0.78 to 1.26)	0.947
Type of service						
Primary	1.00		1.00		1.00	
Secondary	1.02 (0.95 to 1.09)	0.518	1.07 (0.95 to 1.22)	0.265	1.15 (0.95 to 1.40)	0.129
Tertiary	0.95 (0.89 to 1.00)	0.086	1.01 (0.92 to 1.12)	0.780	1.05 (0.90 to 1.25)	0.489
Outros	0.92 (0.82 to 1.03)	0.180	0.97 (0.80 to 1.17)	0.723	1.13 (0.85 to 1.51)	0.374

Significant variables kept in each block of analysis:
Any chronic disease: †sex, age, marital status and race; ǂsex, age, marital status, education, income, occupation; §sex, age, marital status, income, occupation, private health insurance, health status, health reference, medical consultation in last 12 months, hospital admission in last 12 months, dengue, malaria and type of health service that usually comes
≥2 morbidities: †sex, age, marital status and race; ǂsex, age, marital status, education, income, occupation; §sex, age, marital status, income, occupation, private health insurance, health status, health reference, medical consultation in last 12 months, hospital admission in last 12 months, dengue, malaria and type of health service that usually comes
≥3 morbidities: †sex, age, marital status and race; ǂsex, age, marital status, education, income, occupation; §sex, age, marital status, income, occupation, private health insurance, health status, health reference, medical consultation in last 12 months, hospital admission in last 12 months, dengue, malaria and type of health service that usually comes

The factor analysis is presented in Table 4. The KMO coefficient was 0.82 for women and 0.78 for men, and the Bartlett sphericity test presented a p-value ≤0.001 for both, suggesting an adequate factor analysis. In women, one multimorbidity pattern (supplemental figure 1) explained 81% of the total variance, including the 12 chronic

diseases analysed. In men, two factors were identified (supplemental figure 2). In the first factor, heart diseases, chronic kidney disease, stroke, arthritis or rheumatism, chronic spinal problems, depressive disorders, asthma or bronchitis and lung diseases were the associated chronic diseases, which explained a total of 62% of the variance. In the second, the associated chronic diseases were hypercholesterolemia, hypertension, heart disease, diabetes and arthritis, which explained 56% of the variance.

Table 4. Factor score of each chronic disease in women and men, Manaus metropolitan region, Brazil, 2015

Morbidities	**Women (n=2113)**	**Men (n=1888)**	
	Factor 1	**Factor 1**	**Factor 2**
Hypercholesterolemia	0.70		0.62
Hypertension	0.64		0.78
Heart disease	0.72	0.40	0.47
Diabetes	0.63		0.85
Chronic kidney disease	0.46	0.73	
Stroke	0.66	0.61	
Arthritis	0.65	0.40	0.35
Chronic spinal problem	0.46	0.44	
Depressive disorder	0.49	0.58	
Asthma or asthmatic bronchitis	0.44	0.48	
Lung diseases†	0.53	0.76	
Cancer‡	0.52		
Proportion of variance (%)	81.0	62.0	56.0
Kaiser-Meyer-Olkin	0.82	0.78	

Note: Kept factors were those with scores ≥ 0.30 after oblique rotation;
† pulmonary emphysema, bronchitis, chronic obstructive lung disease
‡cancer showed negative values in men and was excluded

DISCUSSION

More than half of the adults had some chronic disease. The occurrence of two or more morbidities was reported by more than a quarter of the adults. Four out of twenty-five individuals reported a multimorbidity of three or more. Female sex, elderly age, dengue in the last year, poor health status, usage of a reference health, physician visits and hospitalization presented associations with multimorbidity. Chronic spinal problems were the most commonly reported diseases.

We used a list of 12 self-reported chronic conditions – of which some were very broad – to assess the primary outcome of this study. A systematic review summarized 39

observational studies from 1993 to 2013 identified a range of five to 335 diseases for the study of multimorbidity.[3] In previous studies, the lower the number of diseases included in the research, the lower the prevalence observed.[5 31] Regardless of the number of chronic conditions reported and how they were defined, multimorbidity estimates are influenced by self-report. Although widely applied,[3 5 32] such assessments are more likely to suffer classification bias or have no validated instrument for confirmation. In present research over-reporting or underreporting may have occurred,[33] as well as recall bias, which is more common in elderly individuals of lower socioeconomic and educational levels.[7 34] In addition, we did not investigate disease severity. Previous studies recommend inquiring about the degree of disease intensity, the diseases' interference with routine activities and disabilities.[5 32] More reliable estimates of multimorbidity, using medical records, for example, are not available in the region.

The response rate was 76%, which may constitute a source of selection bias. Efforts were employed to improve representativeness by using predefined sex and age quotas and interviewing one individual per family, according to official estimates.[35] Survival bias may also influenced the results, since patients who died prematurely from those causes, were hospitalized or had more serious diseases were not available in the household to participate in the survey. The cross-sectional nature of the study does not allow temporal associations investigation.

This is the first local study to estimate the prevalence of multimorbidity in adults in the state of Amazonas. We used a cut-off point of ≥2 and ≥3 chronic diseases, as previous studies did.[3 5] We identified the most vulnerable multimorbidity groups were women and the elderly. The multimorbidity was higher in older people and it increases with age, this outcome was observed in previous studies.[5 9 20] The National Health Survey conducted in Brazil in 2013 reported that women are most affected in all socioeconomic groups, especially the elderly.[36]

Our results showed similarities to a cross-sectional study conducted in 2012 in Pelotas city in the southern region of Brazil with 2927 subjects, in which 29.1% of the interviewees had more than two chronic diseases and 14% had three or more.[37] The 2013 National Health Survey also confirmed these findings: 22% of Brazilians reported two or more chronic diseases, and 10% were affected by more than three.[14] The highest prevalence

was observed in the south (26 to 29%),[14] which is more economically developed and have greater access to health services.[17 38] Any chronic disease occurred in 45% of Brazilians, with a lower prevalence in the north region.[39]

In other contexts, lower prevalence of multimorbidity was found. A survey conducted in 2012 in Italy, with 3 759 836 adults, detected that 15% of individuals presented two or more chronic diseases.[10] In Ireland, a representative sample of the population (11.3% of subjects ≥50 years) presented multiple diseases.[12] Furthermore, an electronic medical data analysis, conducted in 2007 with 1 751 841 users of the Scottish Health Service, found that 23% had multimorbidity.[9] In a comparable economic context to Brazil's, a population-based Indian study conducted in 2007 with 10 973 interviewees identified smaller proportions (28% had any chronic disease and approximately 9% had multimorbidity).[40]

Two findings of our research are rarely described in previous studies: the higher frequency of multimorbidity in younger ages and the lack of association with economic status. One-half of adults aged 25 to 34 years and almost two-thirds of interviewees aged 35 to 44 years reported any chronic condition, and almost one-third had multimorbidity. The development of multimorbidity in young adults is agreement with previous data from Brazil.[20 36 37] It is important to emphasize that half of the Manaus metropolitan region is concentrated in this age range (49% aged 25 to 44 years). A systematic review of 24 cross-sectional studies on multimorbidity found income as a conflicting factor across studies, associated either with richer or poorer individuals, while lower educational attainment was associated with a 64% higher chance of multimorbidity.[41] We identified lack of association after adjusting for socioeconomic block.

In lower-income countries, such as Brazil, which also faces economic austerity policies, rising unemployment and unstable social and health policies, [42] it is possible to predict a reduction in access to health services, with a consequent increase in morbidity. This effect was observed in other austerity scenarios, in which this type of policy reduced jobs, education and use of health services, resulting in an increase of chronic diseases.[43 44] High-income countries has found that 3,6 more years of education reduces the risk of cardiovascular disease by one third.[45]

Back pain was the most frequent disease, reported by one-third of the sample. In our study this morbidity was assessed using several questions, which may have increased the sensitivity of the assessment. An even higher proportion (49%) of vertebral spine/back issues was observed in a representative cross-sectional survey of Brazilian adults.[36] In other contexts, similar prevalence values were estimated.[46]

The presence of dengue was higher in individuals with multimorbidity, possibly due to the lower immunologic response observed in chronic diseases such as diabetes, rheumatoid arthritis, and asthma. [47 48] A systematic review of 16 cohort and case-control studies from 2007 to 2013 showed chronic diseases as risk factors for severe dengue.[49] In another meta-analysis of 10 studies conducted between 2006 and 2014,[50] diabetes was significantly associated with haemorrhagic dengue: regardless of demographic and socioeconomic characteristics, the association was 5% higher compared to individuals who did not have diabetes.

A single multimorbidity pattern was identified in women, which included the 12 researched diseases. The factor loading the most strength of association in women was heart disease. In previous studies conducted in Brazil with similar questions, up to three multimorbidity pattern have been identified, and hypertension had the most strength of association, but no stratification by sex was done.[20] It is possible that the lowest number of pattern for women in our research may be due to stratification or to the broad categories of diseases. In men, lung disease was disease with higher factorial loading, comparable to a Spanish population-based cross-sectional study.[51] Based on assumptions, elderly men could be clustered in factor 1, since they had worse outcomes. Factor 2 would include younger men with diseases developed from risk factors such as sedentary lifestyle and obesity.

According to the results, it is estimated that over 1 300 000 residents of the metropolitan region of Manaus have a chronic condition, and almost 700 000 have multimorbidity. Early diagnosing and treatment of chronic diseases, centred in primary care services, is a priority to allow sustainability of the health system and a healthier society. [52]

CONCLUSION

Multimorbidity was common in residents of the metropolitan region of Manaus and was associated with female sex, elderly people and poorer health perception. Prevention

and control strategies should prioritize these groups. Future analyses should investigate the relationship between multimorbidity and use and costs of health services in the region.

Contributors MTS, TFG, and MEAA designed the study. MEAA, MTS and BNP performed the statistical analyses. MEAA, MTS, TFG, BNP and MGP interpreted the results and drafted the manuscript. All authors made critical revisions and provided intellectual content to the manuscript, approved the final version and agree to be accountable for all aspects of this work.

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Competing interest None declared

Patient consent Obtained

Ethics approval The research project was approved by the Research Ethics Committee of the Federal University of Amazonas. All the individuals who agreed to participate signed a free and informed consent form.

Data sharing statement: Data are available and can be accessed by contacting MTS.

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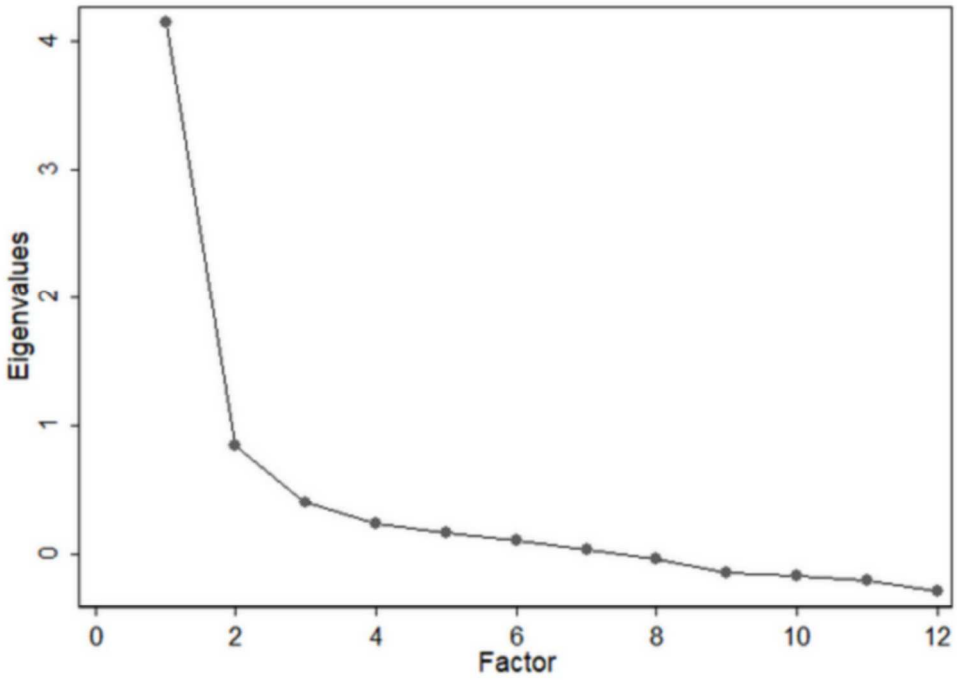

Figure 1 Scree plot for women
Note: The graph shows one factors before the inflection point in the curve (eigenvalue >1)

143x104mm (300 x 300 DPI)

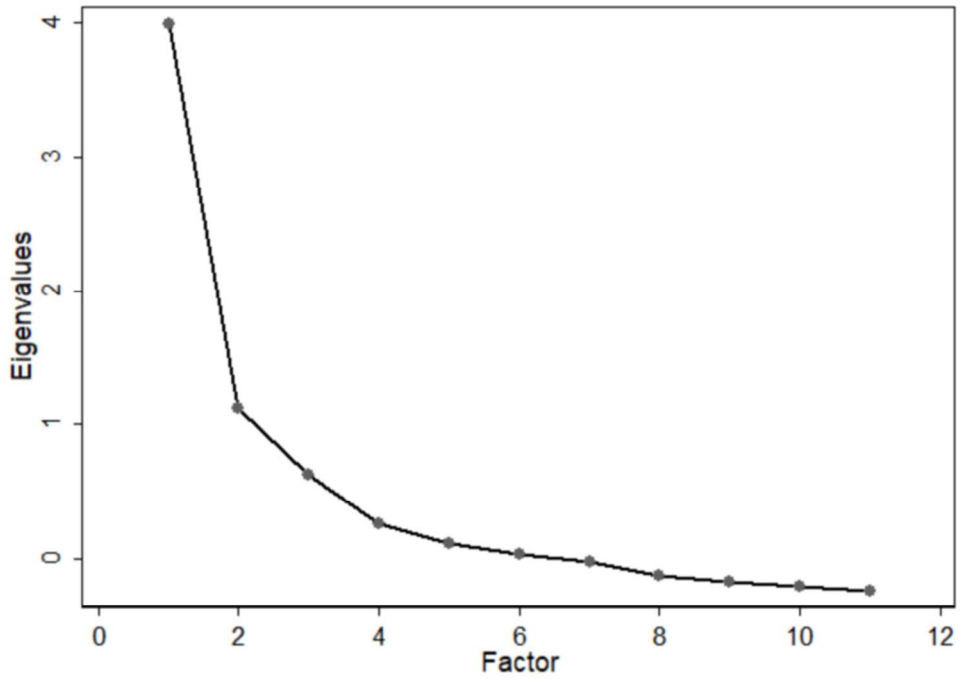

Figure 2 Scree plot for men
Note: The graph shows two factors before the inflection point in the curve (eigenvalue >1)

125x91mm (300 x 300 DPI)

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1,2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any pre-specified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	3,4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—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 *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	4
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—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	4
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	4
Bias	9	Describe any efforts to address potential sources of bias	-
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5
		(*b*) Describe any methods used to examine subgroups and interactions	-
		(*c*) Explain how missing data were addressed	-
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	4

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*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	6
		(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	6
		(b) Indicate number of participants with missing data for each variable of interest	-
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	-
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	-
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	-
		Cross-sectional study—Report numbers of outcome events or summary measures	6
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	7,8,9,10,11
		(*b*) Report category boundaries when continuous variables were categorized	6
		(*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	12,13
Discussion			
Key results	18	Summarise key results with reference to study objectives	13,14
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	14,15,16
Generalisability	21	Discuss the generalisability (external validity) of the study results	16
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	17

*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.

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Prevalence and patterns of multimorbidity in Amazon Region of Brazil and associated determinants: a cross-sectional study

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ABSTRACT

Objectives: To estimate the prevalence of multimorbidity and to identify factors associated with it in the adult population from the metropolitan region of Manaus.

Design: Cross-sectional population-based study.

Setting: Interviews conducted between May and August of 2015 in eight cities that compose the metropolitan region of Manaus, Amazonas, Brazil.

Participants: 4 001 adults aged ≥18 years.

Primary outcome measures: Multimorbidity, measured by the occurrence of ≥2 and ≥3 chronic diseases, was the primary outcome. The associated factors were investigated by calculating the prevalence ratio (PR) obtained by Poisson regression, with robust adjustment of the variance in a hierarchical model. A factor analysis was conducted to investigate multimorbidity clusters.

Results: Half of the interviewees were women. The presence of a chronic disease was reported by 57.2% (95% CI 56.6% to 59.7%) of the interviewees, and the mean morbidity was 1.2 (1.1-1.2); 29.0% (95% CI 27.6% to 30.5%) reported ≥2 morbidities, and 15.2% (95% CI 14.1% to 16.4%) reported ≥3 chronic conditions. Back pain was reported by one-third of the interviewees. Multimorbidity was highest in women, PR = 1.66 (95% CI 1.50 to 1.83); the elderly, PR = 5.68 (95% CI 4.51 to 7.15); and individuals with worse health perception, PR = 3.70 (95% CI 2.73-5.00). Associated factors also included undergoing medical consultations, hospitalization in the last year, suffering from dengue in the last year and seeking the same healthcare service. Factor analysis revealed a pattern of multimorbidity in women. The factor loading the most strength of association in women was heart disease. In men, an association was identified in two groups, and lung disease was the disease with the highest factorial loading.

Conclusion: Multimorbidity was frequent in the metropolitan region of Manaus. It occurred most often in women, in the elderly and in those with worse health perception.

Keywords: Prevalence, Multimorbidity, Cross-Sectional Studies, Population Surveys, Brazil.

Strengths and limitations of this study:

This is the first study on the prevalence of multimorbidity in adults from the metropolitan region of Manaus, Amazonas, Brazil, using data from a population-based survey.

We used probabilistic complex sampling in three stages, census track, household and individual, to include 4 001 adults living in one of the eight cities of the metropolitan region.

This research increases knowledge about the epidemiologic factors associated with multimorbidity.

The method used to measure outcomes, self-report, is subject to errors and influenced by memory bias.

BACKGROUND

Multimorbidity is the occurrence of different chronic clinical conditions in an individual, without a single condition being considered the main cause.[1 2] Multimorbidity is operationally defined as the occurrence of two or more chronic diseases.[3-5] In recent decades, population ageing, lifestyle changes, improved socio-economic conditions, and increased diagnostic ability of health services have contributed to a significant rise in the population that survives serious diseases, causing an accumulation of health problems in specific population groups. This situation has contributed to the increased prevalence of multimorbidity.[6-8]

The frequency of multimorbidity varies according to the evaluated diseases, the age of the population, the individual's socioeconomic and demographic level, and the individual's health condition. The rising prevalence of multimorbidity has resulted in higher costs of health services.[9-12] The costs associated with multimorbidity can reach 75% of total health expenditures, which includes physician consultation, hospitalization, odontological care, medication and rehabilitation.[13]

In Brazil, multimorbidity ranged from 26% to 29% in adults living in the southern—and more developed—region and from 14% to 19% in the northern region.[14] Studies in specific populations conducted in the south and southeast Brazilian regions identified higher prevalence of multimorbidity in women and the elderly than in other groups.[15 16] Differences detected suggest heterogeneity due to socioeconomic development.[17] In northern Brazil, there is a lack of studies identifying more susceptible groups and studies that expand our knowledge about multimorbidity at the local level.

To obtain evidence of the health status and usage of health services, a large survey was performed in 2015 in the Manaus metropolitan region,[18 19] the most populated region and largest economic cluster in northern Brazil. This region comprises more than 60% of the 3.5 million people of Amazonas, which has the largest land area, the lowest population density, and the highest population of indigenous people (4.7%) in Brazil.[20] Health coverage is mainly public (Unified Health System), and this region had the lowest coverage of health insurance in the country in 2013 (13.0%).[21] The present research estimated the

prevalence of and factors associated with multimorbidity in the adult population of the metropolitan region of Manaus.

METHODS

Study design

This is a cross-sectional population-based study on the urban population of the metropolitan region of Manaus, consisting of the capital of Amazonas, Manaus, and seven surrounding cities. Multimorbidity was considered a primary outcome, which was categorized as ≥2 or ≥3 chronic diseases. The present analysis is part of a larger study aimed to examine the use of health services and inputs in the region from May to August 2015. Details of the study design and the representativeness of the sample are available elsewhere.[18]

Participants and study size

We calculated the sample size as 4 000 adults ≥18 years old to be interviewed, who were selected by probabilistic complex sampling—by cluster and stratified by sex and age—in three stages (census track, household and individual).[18] We assume an estimated 50% prevalence of use of health services, considering a CI of 95%, absolute precision of 2% and a design effect of 1.5.[22] We added 10% to compensate for possible losses and refusals.

Variables and data collection

The primary outcome was self-reported multimorbidity, defined as two or more affirmative answers to any of the following questions: "Have any doctors ever diagnosed you with [...]?" [1] hypertension, [2] diabetes, [3] high cholesterol, [4] heart disease (heart attack, angina, heart failure or other), [5] stroke, [6] asthma or asthmatic bronchitis, [7] arthritis or rheumatism, [8] depression, [9] pulmonary disease (pulmonary emphysema, chronic bronchitis or chronic obstructive pulmonary disease), [10] cancer, or [11] chronic kidney disease, and [12] “Do you have any chronic spinal problems, such as chronic back or neck pain, low back pain, sciatic pain, vertebral or disc problems?” These questions were previously used in the National Health Survey.[23]

The independent variables were sex; age (18 to 24; 25 to 34; 35 to 44; 45 to 59 and ≥60 years);[24] marital status; self-reported skin colour; education; social class;[25] occupation; private health insurance (yes, no); self-perception of health status; place of attendance

(capital, countryside); seeking the same healthcare service when in need of attendance (health reference; yes, no); physician visit in the last 12 months (yes, no); hospitalization in the last year (yes, no); malaria in the last 12 months (yes, no); dengue in the last 12 months (yes, no); and types of services one usually seeks when in need of medical care (primary, secondary, or tertiary).

Interviewers with experience in conducting home interviews collected the data on a mobile electronic device (Samsung® Galaxy Tab3 SM-T110). Interview records were transmitted over the Internet and stored using Survey To Go software (Dooblo Ltd., Israel).

Statistical analyses

Statistical analyses were carried out in Stata v. 14.2. In all calculations, the complex sampling design was weighted by incorporating sample weights (*svy* command).

Descriptive statistics were initially obtained through prevalence calculation. The respective confidence intervals and P values of difference were calculated by Pearson's chi-square between sociodemographic characteristics and multimorbidity. The prevalence of the most common diseases stratified by sex, age group and multimorbidity was also calculated. At this stage, morbidities with a prevalence of <5% were excluded.

Bivariate analyses were performed between all independent and dependent variables to calculate prevalence ratios (PRs) and 95% confidence intervals (CIs). To identify the factors associated with multimorbidity, PRs were adjusted using Poisson regression with robust variance adjustment.[26-28]

A hierarchical model consisting of three blocks was constructed of the most distal to the most proximal determinants of multimorbidity: (1) demographic variables (sex, age, race, marital status); (2) socioeconomic variables (economic, education classification, occupation); and (3) health variables (private health insurance, health status, demand for the same health service, physician visit, hospitalization, dengue, malaria and type of service usually used). The variables from the first block were retained for the next stage if they presented a p-value ≤0.05. Multicollinearity among the independent variables was discarded by assessing the variance inflation factors.[29]

Exploratory factor analysis stratified by sex was performed to identify multimorbidity patterns, i.e., to identify associations, selecting variables with potentially common causal factors, such as interaction between diseases and/or common risk factors.[30]

[31] The tetrachoric correlation coefficient was used in the analysis because it is better than Pearson's correlation coefficient for dichotomous outcomes.[32] The suitability of the sampling was evaluated by the Kaiser-Meyer-Olkin test (KMO), which was considered adequate if the index was ≥0.70, and the Bartlett sphericity test, which was considered adequate if its p-value was ≤0.05.[30 33] To establish the number of factors to be maintained, Cattell's scree plot was used, which represents the eigenvalues of the correlation matrix in descending order. The factor number extracted corresponds to the eigenvalue that produces the inflection point in the curve (eigenvalue> 1) and explains the minimum variance (>10% for each component). Variables were defined as associated with a factor if they presented loads ≥0.30 [30] (the closer to 1, the greater the association). Oblique rotation (promax) was performed to allow for better interpretation of the factor analysis.[30]

Patient and public involvement

Patients and public were involved in neither the design of the research question nor in developing plans for the design or implementation of the study. The study had no patient advisers. Outcomes were self-reported by patients based on pre-defined questions. Due to the cross-sectional nature of the study, feedback regarding the results was not planned for those involved.

RESULTS

Participant characteristics

Table 1 shows the characteristics of the participants, prevalence of any chronic disease, and multimorbidity. The sample was composed of 4 001 adults and had a response rate of 76%. Women constituted over half of the sample. About one-half of the interviewees were between 25 and 44 years old, and 81% were black, brown or indigenous. The predominant social stratum was the lower middle class (57%), and approximately one-third of the participants were students or housewives. More than half reported good health status (54%), and the majority had had a physician visit in the last year (76%). In the last 12 months, 7% reported dengue and 6% reported malaria. One-half of respondents reported seeking a tertiary health service when they needed care (47%). The prevalence of any chronic disease was 57.2% (95% CI 56.6 to 58.7%), with a mean ± standard deviation of 1.2 ± 1.5 chronic disease per person. This average increased with age (0.5 ± 0.8 in the 18 to 24-year-old group and 2.5 ± 1.9 in those 60 years or above).

Prevalence of multimorbidity

The prevalence of ≥2 chronic conditions was 29% (95% CI 27.6 to 30.5%), and that of ≥3 chronic diseases was 15.2% (95% CI 14.1 to 16.4%). Higher prevalence was observed in women, in widowers, in individuals with lower education, in retired individuals, in individuals who had the worst perceptions of health and in those who visited a doctor and were hospitalized in the last year than in others (Table 1). In the previous year, dengue was reported by 44% of those who had two or more chronic conditions.

Approximately half of women aged 35 to 59 years reported ≥2 morbidities (Table 2). Back pain was the most frequently reported health problem in both women and men, followed by hypertension. Women ≥60 years with two or more morbidities reported more hypertension (92.0%) than men did in the same age group (79.5%).

Table 1. Characteristics of participants and prevalence of multimorbidity (%), Manaus metropolitan region, Brazil, 2015 (n = 4 001)*

Variable	n (%)	Any chronic disease % (95% CI)	p-value	Mean number of chronic health problems (95% CI)	Multimorbidity % (95% CI)			
					≥2	p-value	≥3	p-value
Overall		57.2 (55.6 to 58.7)		1.17 (1.1 to 1.2)	29.0 (27.6 to 30.5)		15.2 (14.1 to 16.4)	
Sex			<0.001			<0.001		<0.001
Male	1888 (47.2)	52.1 (49.8 to 54.0)		0.9 (0.8 to 0.9)	21.5 (19.7 to 23.4)		9.3 (8.1 to 10.7)	
Female	2113 (52.7)	61.8 (59.7 to 63.8)		1.39 (1.3 to 1.4)	35.8 (33.8 to 37.8)		20.5 (18.8 to 22.3)	
Age (years)			<0.001			<0.001		<0.001
18 to 24	838 (20.8)	37.0 (33.8 to 40.3)		0.5 (0.4 to 0.5)	9.8 (7.9 to 12.0)		3.5 (2.5 to 5.0)	
25 to 34	1152 (28.7)	49.6 (46.7 to 52.5)		0.8 (0.7 to 0.8)	18.6 (16.4 to 20.9)		6.9 (5.6 to 8.5)	
35 to 44	843 (21.1)	61.0 (57.6 to 64.2)		1.1 (1.0 to 1.2)	30.0 (27.0 to 33.2)		12.7 (10.6 to 15.1)	
45 to 59	772 (19.3)	71.4 (68.0 to 74.4)		1.7 (1.6 to 1.8)	46.6 (13.1 to 50.2)		28.1 (25.1 to 31.4)	
≥60	396 (9.9)	86.1 (82.3 to 89.2)		2.5 (2.3 to 2.7)	63.5 (58.6 to 68.1)		44.4 (39.6 to 49.3)	
Marital status			<0.001			<0.001		<0.001
Single	2173 (54.2)	51.5 (49.3 to 53.5)		0.9 (0.8 to 0.9)	20.8 (19.1 to 22.6)		10.3 (8.8 to 11.3)	
Married	1409 (35.2)	62.0 (59.4 to 64.5)		1.3 (1.2 to 1.4)	35.3 (32.9 to 37.9)		19.6 (17.6 to 21.8)	
Separated/divorced	260 (6.5)	65.6 (59.6 to 71.2)		1.5 (1.3 to 1.7)	42.6 (36.8 to 48.7)		19.9 (15.5 to 25.2)	
Widower	159 (4.0)	79.3 (72.3 to 84.9)		2.2 (1.9 to 92.5	63.1 (55.3 to 70.2)		39.9 (32.5 to 47.7)	
Skin colour			<0.001			0.0021		0.0016
White/yellow	774 (19.3)	51.7 (48.2 to 55.2)		1.1 (1.0 to 1.2)	27.1 (24.1 to 30.4)		15.7 (13.3 to 18.5)	
Black/brown/ indigenous	3227 (80.5)	58.5 (56.8 to 60.2)		1.2 (1.1 to 1.2)	29.5 (27.9 to 31.1)		15.1 (13.9 to 16.4)	
Schooling level			<0.001			<0.001		<0.001
High education or above§	158 (3.9)	57.1 (49.3 to 64.6)		.2 (1.0 to 1.5)	32.6 (25.7 to 40.4)		16.1 (11.7 to 23.7)	
High school	1903 (47.5)	51.0 (48.8 to 53.3)		0.9 (0.8 to 1.0)	22.5 (20.7 to 24.5)		9.0 (7.8 to 10.4)	
Middle school	649 (16.2)	50.0 (46.2 to 53.8)		0.9 (0.8 to 1.0)	21.1 (18.2 to 24.4)		10.7 (0.8 to 13.3)	
Elementary school or less	1291 (32.2)	69.9 (67.4 to 72.4)	<0.001	1.7 (1.6 to 1.8)	42.1 (39.5 to 44.8)		26.5 (24.1 to 28.9)	
Economic classification†						<0.001		<0.001
A - B	629 (15.7)	51.2 (47.2 to 55.1)		0.9 (0.8 to 1.1)	24.6 (21.4 to 28.2)		11.1 (8.8 to 13-8)	
C	2285 (57.1)	55.5 (53.4 to 57.5)		1.0 (1.0 to 1.1)	26.1 (24.3 to 27.9)		13.2 (11.9 to 14.7)	
D - E	1087 (27.2)	64.3 (61.4 to 67.2)		1.5 (1.4 to 1.6)	37.7 (34.9 to 40.7)		21.8 (19.4 to 24.3)	
Occupation			<0.001			<0.001		<0.001

Variable	n (%)	Any chronic disease % (95% CI)	p-value	Mean number of chronic health problems (95% CI)	Multimorbidity % (95% CI)			
					≥2	p-value	≥3	p-value
Formal job	761 (19.0)	52.7 (49.1 to 56.2)		0.9 (0.8 to 1.0)	22.7 (19.8 to 25.8)		9.2 (7.3 to 11.5)	
Informal job	1149 (28.7)	55.9 (53.0 to 58.7)		1.0 (1.0 to 1.1)	27.6 (25.1 to 30.3)		12.9 (11.1 to 15.0)	
Retired	315 (7.9)	79.2 (74.3 to 83.3)		2.4 (2.2 to 2.6)	60.5 (55.4 to 65.8)		43.4 (38.0 to 49.0)	
Student/housewife	1199 (29.8)	55.0 (52.2 to 57.8)		1.1 (1.1 to 1.2)	29.0 (25.5 to 31.6)		15.8 (13.8 to 18.0)	
Unemployed	577 (14.4)	58.3 (54.2 to 62.3)		1.0 (0.9 to 1.1)	23.1 (19.8 to 26.7)		11.2 (8.9 to 14.1)	
Private health insurance			0.348			0.697		0.616
Yes	523 (13.0)	55.3 (51.0 to 59.5)		1.0 (0.9 to 1.29	28.0 (24.6 to 32.3)		14.5 (11.7 to 17.8)	
No‡	3478 (87.0)	57.5 (55.8 to 59.1)		1.2 (1.1 to 1.2)	29.0 (27.6 to 30.7)		15.3 (14.2 to 16.6)	
Health status			<0.001			<0.001		<0.001
Very good	471 (11.9)	30.8 (26.8 to 35.2)		0.4 (0.47 to 0.5)	9.7 (7.3 to 12.7)		3.1 (1.9 to 5.1)	
Good	2175 (54.3)	50.4 (48.3 to 52.5)		0.8 (0.8 to 0.9)	20.3 (18.7 to 22.0)		7.9 (6.8 to 9.1)	
Fair	1108 (27.7)	75.1 (72.5 to 77.5)		1.7 (1.6 to 1.8)	45.2 (42.3 to 48.1)		26.0 (23.5 to 28.6)	
Bad	193 (4.8)	88.6 (83.2 to 93.3)		2.6 (2.4 to 2.9)	68.4 (61.6 to 74.6)		50.3 (43.3 to 57.3)	
Very bad	54 (1.3)	81.5 (68.9 to 89.7)		3.6 (3.0 to 4.3)	77.7 (64.8 to 86.9)		70.3 (57.0 to 81.0)	
City			<0.001			<0.001		<0.001
Capital	3479 (86.8)	58.4 (56.8 to 60.0)		1.2 (1.1 to 1.2)	30.2 (28.7 to 31.7)		15.8 (14.6 to 17.1)	
Countryside	522 (13.1)	49.2 (44.9 to 53.5)		0.9 (0.8 to 1.0)	21.5 (18.2 to 25.3)		11.3 (0.8 to 14.3)	
Health reference §			<0.001			<0.001		<0.001
Yes	2434 (60.7)	62.3 (60.3 to 64.2)		1.3 (1.2 to 1.4)	34.4 (31.5 to 36.3)		18.7 (17.1 to 20.3)	
No	1567 (39.2)	49.4 (46.9 to 51.9)		0.9 (0.8 to 0.9)	20.8 (18.9 to 22.9)		9.8 (17.2 to 20.3)	
Physician visit			<0.001			<0.001		<0.001
Yes	3066 (76.5)	60.8 (59.0 to 62.5)		1.2 (1.2 to 1.3)	32,1 (30.5 to 33.8)		17.4 (16.1 to 18.8)	
No	935 (23.4)	45.5 (42.3 to 48.7)		0.8 (0.7 to 0.9)	18,9 (16.5 to 21.5)		8.2 (6.6 to 10.2)	
Hospitalization			<0.001			<0.001		<0.001
Yes	273 (7.0)	72.9 (67.3 to 77.8)		1.2 (1.2 to 1.3)	47,2 (41.4 to 53.2)		28.1 (23.1 to 33.8)	
No	3728 (93.0)	56.1 (67.3 to 77.8)		0.8 (0.7 to 0.9)	27,7 (26.3 to 29.2)		14.3 (13.2 to 15.4)	
Dengue			0.002			<0.001		<0.001
Yes	281 (7.0)	65.9 (60.1 to 71.2)		1.6 (1.4 to 1.8)	44.2 (38.5 to 50.1)		27.6 (22.7 to 33.1)	
No	3720 (93.0)	56.5 (54.9 to 58.1)		1.1 (1.0 to 1.1)	27.9 (26.5 to 29.3)		14.3 (13.2 to 15.5)	
Malaria			0.420			0.122		0.014
Yes	234 (5.9)	54.6 (48.2 to 60.9)		1.3 (1.1 to 1.5)	33.5 (27.7 to 39.8)		20.8 (16.1 to 26.5)	
No	3767 (94.0)	57.3 (0.55 to 0.58)		1.1 (1.1 to 1.2)	28.8 (27.3 to 30.2)		14.9 (13.8 to 16.0)	
Medical attention			<0.001			0.048		0.531

Variable	n (%)	Any chronic disease % (95% CI)	p-value	Mean number of chronic health problems (95% CI)	Multimorbidity % (95% CI)			
					≥2	p-value	≥3	p-value
Primary	1208 (30.2)	60.8 (58.0 to 63.5)		1.2 (1.1 to 1.3)	29.9 (27.3 to 32.5)		15.2 (13.3 to 17.3)	
Secondary	598 (14.9)	62.3 (58.3 to 66.1)		1.3 (1.2 to 1.5)	33.0 (29.4 to 36.9)		18.9 (15.9 to 22.2)	
Tertiary	1886 (47.2)	54.0 (51.8 to 56.3)		1.1 (1.0 to 1.2)	27.7 (25.7 to 29.8)		14.3 (12.8 to 15.9)	
Others	309 (7.7)	52.7 (47.2 to 58.3)		1.0 (0.9 to 1.2)	26.2 (21.6 to 31.4)		14.2 (10.7 to 18.5)	

* Descriptive statistics using simple frequency and Pearson $\chi 2$ test

CI: confidence interval; physician visit, hospitalization, dengue and malaria in last 12 months; § tertiary education or higher; † Average household income in 2015: A-B, US$6500-US$1419; C, US$463-US$772; D-E, US$205; ‡ People who use the public health service. § Seeking the same healthcare service when in need of attendance.

Table 2. Prevalence (%) of most common diseases stratified by sex, age and multimorbidity group, Manaus metropolitan region, Brazil, 2015*

Morbidities	n (%)	Multimorbidity ≥2			Multimorbidity ≥3		
		18 to 34 n (%)	35 to 59 n (%)	≥60 n (%)	18 to 34 n (%)	35 to 59 n (%)	≥60 n (%)
Women (2113)		195 (18.4)	394 (47.0)	168 (76.9)	78 (7.0)	236 (28.1)	120 (55.0)
Chronic spinal problem †	747 (35.3)	135 (42.6)	248 (75.6)	99 (96.1)	64 (20.1)	176 (53.6)	78 (75.7)
Hypertension	516 (24.4)	78 (62.3)	211 (83.0)	126 (92.0)	94 (32.7)	149 (58.7)	98 (71.6)
Arthritis or rheumatism	414 (19.5)	66 (79.5)	197 (91.6)	110 (94.8)	33 (39.7)	146 (67.7)	92 (79.3)
Hypercholesterolemia	425 (20.1)	66 (79.5)	217(90.8)	100 (97.0)	46 (55.4)	149 (62.4)	85 (82.5)
Diabetes	157 (7.4)	15 (93.7)	82 (90.2)	48 (96.0)	14 (87.4)	70 (76.6)	42 (84.5)
Asthma or asthmatic bronchitis	155 (7.3)	50 (68.5)	54 (85.6)	19 (100.0)	28 (38.3)	46 (73.0)	19(100.0)
Depressive disorder	158 (7.4)	44 (71.0)	69 (91.9)	21 (100.0)	19 (30.6)	55 (73.2)	20 (95.2)
Heart disease ‡	119 (5.6)	23 (71.8)	52 (98.1)	34 (100.0)	17 (53.0)	46 (86.7)	32 (94.0)
Men (1888)		102 (10.9)	220 (28.2)	84 (47.1)	32 (3.4)	89 (11.4)	56 (31.4)
Chronic spinal problem†	662 (35.0)	77 (27.5)	149 (49.7)	54 (65.8)	20 (7.1)	63 (21.0)	42 (51.4)
Hypertension	271 (14.4)	37 (77.1)	112 (76.7)	61 (79.5)	17 (35.3)	60 (41.1)	45 (58.6)
Arthritis or rheumatism	179 (9.5)	25 (89.3)	80 (86.8)	50 (84.9)	13 (46.1)	45 (48.9)	38 (64.5)
Hypercholesterolemia	171 (9.0)	24 (57.1)	85 (87.6)	28 (87.6)	14 (33.3)	48 (49.4)	25 (78.2)

p-values of all variables were ≤0.002
* multimorbidity with prevalence ≥5%.
† chronic back pain or neck, low back pain, sciatica, vertebral or disc pain
‡ heart disease, or heart attack, angina, cardiac insufficiency

Table 3 shows the results obtained for factors associated with multimorbidity. After adjustment, multimorbidity (≥2 diseases) was associated with female sex (PR = 1.66, 95% CI 1.50 to 1.83), age between 45 and 59 years (PR = 4.36, 95% CI 3.48 to 5.46) and age ≥60 years (PR = 5.68, 95% CI 4.51 to 7.15). The presence of ≥3 diseases was associated with female sex (PR = 2.19, 95% CI 1.88 to 2.56), age 45 to 59 years (PR = 7.62, 95% CI 5.22 to 11.10), age ≥60 years (PR = 12.03, 95% CI 8.20 to 17.66), dengue in the last 12 months (PR = 1.36, 95% CI 1.13 to 1.64), and very poor health status (PR = 7.89, 95% CI 4.71 to 13.23). Having ≥3 chronic conditions increased the demand for physician visits, hospitalization in the last year, and demand for the same health service. Education, income, occupation, and malaria in the last 12 months did not show associations with multimorbidity.

Table 3. Adjusted prevalence ratio (PR) and 95% confidence interval (CI) for any chronic disease and multimorbidity ≥2 and ≥3, according to sociodemographic and health variables based on hierarchical Poisson regression. Manaus metropolitan region, Brazil, 2015 (n = 4 001)

Variable	Any chronic disease PR (95% CI)	P value	Multimorbidity PR (95% CI)			
			≥2	P value	≥3	P value
Demographic block†						
Sex						
Male	1.00		1.00		1.00	
Female	1.19 (1.12 to 1.25)	<0.001	1.66 (1.50 to 1.83)	<0.001	2.19 (1.88 to 2.56)	<0.001
Age group						
18 to 24	1.00				1.00	
25 to 34	1.33 (1.19 to 1.48)	<0.001	1.81 (1.42 to 2.30)	<0.001	1.88 (1.24 to 2.84)	0.003
35 to 44	1.63 (1.47 to 1.81)	<0.001	2.85 (2.26 to 3.60)	<0.001	3.40 (2.28 to 5.06)	<0.001
45 to 59	1.91 (1.72 to 2.12)	<0.001	4.36 (3.48 to 5.46)	<0.001	7.62 (5.22 to 11.10)	<0.001
≥60	2.32 (2.08 to 2.57)	<0.001	5.68 (4.51 to 7.15)	<0.001	12.03 (8.20 to 17.66)	<0.001
Marital status						
Single	1.00		1.00		1.00	
Married	1.09 (0.96 to 1.07)	0.521	1.20 (1.07 to 1.33)	0.001	1.21 (1.03 to 1.42)	0.017
Separated/ divorced	1.00 (0.91 to 1.10)	0.961	1.24 (1.06 to 1.45)	0.006	0.93 (0.72 to 1.21)	0.620
Widower	0.96 (0.87 to 1.06)	0.475	1.18 (1.01 to 1.38)	0.032	0.99 (0.77 to 1.26)	0.962
Skin colour						
White/yellow	1.00		1.00		1.00	
Black/brown/ Indigenous	1.10 (1.02 to 1.18)	0.006	1.04 (0.93 to 1.16)	0.474	0.89 (0.75 to 1.05)	0.175
Socioeconomic block ‡						
Education						
High education or above	1.00		1.00		1.00	
High school	1.00 (0.87 to 1.14)	0.976	0.89 (0.71 to 1.12)	0.357	0.73 (0.50 to 1.05)	0.091
Middle school	0.98 (0.84 to 1.13)	0.754	0.81 (0.63 to 1.06)	0.135	0.80 (0.53 to 1.20)	0.289
Elementary school or less	1.12 (0.98 to 1.29)	0.106	1.01 (0.80 to 1.28)	0.877	1.08 (0.75 to 1.55)	0.667
Economic classification						
A – B	1.00		1.00		1.00	
C	1.04 (0.96 to 1.13)	0.361	1.01 (0.87 to 1.17)	0.881	1.05 (0.83 to 1.33)	0.656
D – E	1.06 (0.97 to 1.16)	0.207	1.15 (0.98 to 1.36)	0.075	1.15 (0.89 to 1.49)	0.254
Occupation						
Formal job	1.00		1.00		1.00	
Informal job	0.95 (0.87 to 1.03)	0.223	0.97 (0.83 to 1.13)	0.728	0.98 (0.76 to 1.28)	0.929
Retired	0.95 (0.86 to 1.06)	0.363	1.11 (0.92 to 1.32)	0.258	1.39 (1.02 to 1.88)	0.033
Student/ housewife	0.96 (0.87 to 1.05)	0.331	0.97 (0.83 to 1.14)	0.767	1.05 (0.81 to 1.36)	0.671
Unemployed	1.09 (0.99 to 1.20)	0.081	0.99 (0.81 to 1.20)	0.949	1.13 (0.83 to 1.54)	0.404
Health block §						

Private health insurance						
No	1.00		1.00		1.00	
Yes	0.99 (0.91 to 1.07)	0.913	1.03 (0.90 to 1.18)	0.593	1.04 (0.84 to 1.28)	0.771
Health status						
Very good	1.00		1.00		1.00	
Good	1.43 (1.24 to 1.64)	<0.001	1.63 (1.23 to 2.15)	<0.001	1.81 (1.09 to 2.99)	0.020
Fair	1.94 (1.69 to 2.23)	<0.001	2.84 (2.15 to 3.76)	<0.001	4.21 (2.56 to 6.93)	<0.001
Bad	2.01 (1.80 to 2.41)	<0.001	3.53 (2.64 to 4.71)	<0.001	6.25 (3.74 to 10.47)	<0.001
Very bad	1.91 (1.60 to 2.27)	<0.001	3.70 (2.73 to 5.00)	<0.001	7.89 (4.71 to 13.23)	<0.001
Health reference**						
No	1.00		1.00		1.00	
Yes	1.12 (1.06 to 1.19)	<0.001	1.33 (1.19 to 1.47)	<0.001	1.40 (1.20 to 1.63)	<0.001
Physician visit						
No	1.00		1.00		1.00	
Yes	1.13 (1.05 to 1.22)	<0.001	1.22 (1.07 to 1.40)	0.002	1.33 (1.09 to 1.64)	0.005
Hospitalization						
No	1.00		1.00		1.00	
Yes	1.18 (1.09 to 1.27)	<0.001	1.36 (1.20 to 1.54)	<0.001	1.43 (1.17 to 1.74)	<0.001
Dengue						
No	1.00		1.00		1.00	
Yes	1.07 (0.99 to 1.16)	0.079	1.23 (1.08 to 1.41)	0.001	1.36 (1.13 to 1.64)	0.001
Malaria						
No	1.00		1.00		1.00	
Yes	0.98 (0.82 to 1.01)	0.109	0.96 (0.81 to 1.13)	0.653	0.99 (0.78 to 1.26)	0.947
Type of service						
Primary	1.00		1.00		1.00	
Secondary	1.02 (0.95 to 1.09)	0.518	1.07 (0.95 to 1.22)	0.265	1.15 (0.95 to 1.40)	0.129
Tertiary	0.95 (0.89 to 1.00)	0.086	1.01 (0.92 to 1.12)	0.780	1.05 (0.90 to 1.25)	0.489
Outros	0.92 (0.82 to 1.03)	0.180	0.97 (0.80 to 1.17)	0.723	1.13 (0.85 to 1.51)	0.374

Significant variables kept in each block of analysis:
Any chronic disease: †sex, age, marital status and race; ‡sex, age, marital status, education, income, occupation; §sex, age, marital status, income, occupation, private health insurance, health status, health reference, medical consultation in last 12 months, hospital admission in last 12 months, dengue, malaria and type of health service that usually comes
≥2 morbidities: †sex, age, marital status and race; ‡sex, age, marital status, education, income, occupation; §sex, age, marital status, income, occupation, private health insurance, health status, health reference, medical consultation in last 12 months, hospital admission in last 12 months, dengue, malaria and type of health service that usually comes
≥3 morbidities: †sex, age, marital status and race; ‡sex, age, marital status, education, income, occupation; §sex, age, marital status, income, occupation, private health insurance, health status, health reference, medical consultation in last 12 months, hospital admission in last 12 months, dengue, malaria and type of health service that usually comes
** Seeking the same healthcare service when in need of attendance.

The factor analysis is presented in Table 4. The KMO coefficient was 0.82 for women and 0.78 for men, and the Bartlett sphericity test presented a p-value ≤0.001 for both, suggesting an adequate factor analysis. In women, one multimorbidity pattern

(supplemental figure 1) explained 81% of the total variance, including the 12 chronic diseases analysed. In men, two factors were identified (supplemental figure 2). In the first factor, heart diseases, chronic kidney disease, stroke, arthritis or rheumatism, chronic spinal problems, depressive disorders, asthma or bronchitis, and lung diseases were the associated chronic diseases, which explained a total of 62% of the variance. The second factor was essentially cardiometabolic, which explained 56% of the variance.

Table 4. Factor score of each chronic disease in women and men, Manaus metropolitan region, Brazil, 2015

Morbidities	**Women (n=2113)**	**Men (n=1888)**	
	Factor 1	**Factor 1**	**Factor 2**
Hypercholesterolemia	0.70		0.62
Hypertension	0.64		0.78
Heart disease	0.72	0.40	0.47
Diabetes	0.63		0.85
Chronic kidney disease	0.46	0.73	
Stroke	0.66	0.61	
Arthritis	0.65	0.40	0.35
Chronic spinal problem	0.46	0.44	
Depressive disorder	0.49	0.58	
Asthma or asthmatic bronchitis	0.44	0.48	
Lung diseases†	0.53	0.76	
Cancer‡	0.52		
Proportion of variance (%)	81.0	62.0	56.0
Kaiser-Meyer-Olkin	0.82	0.78	

Note: Kept factors were those with scores ≥ 0.30 after oblique rotation
† pulmonary emphysema, bronchitis, chronic obstructive lung disease
‡cancer showed negative values in men and was excluded

DISCUSSION

More than half of the adults had some chronic disease. The occurrence of two or more morbidities was reported by more than a quarter of the adults. Four out of twenty-five individuals reported a multimorbidity of three or greater. Female sex, elderly age, dengue in the last year, poor health status, seeking the same healthcare service when in need of attendance, physician visits and hospitalization presented associations with multimorbidity. Chronic spinal problems were the most commonly reported diseases.

We used a list of 12 self-reported chronic conditions—some of which were very broad—to assess the primary outcome of this study. A systematic review summarized 39

observational studies from 1993 to 2013 and identified a range of five to 335 diseases for the study of multimorbidity.[3] In previous studies, the fewer diseases included in the research was, the lower the prevalence observed became.[5 34] Regardless of the number of chronic conditions reported and how they were defined, multimorbidity estimates are influenced by self-report. Although widely applied,[3 5 35] such assessments are more likely to suffer classification bias or have no validated instrument for confirmation. In the present research, over-reporting or underreporting may have occurred,[36] as well as recall bias, which is more common in elderly individuals of lower socioeconomic and educational levels than among other individuals.[7 37] In addition, we did not investigate disease severity. Previous studies recommend inquiring about the degree of disease intensity and diseases' interference with routine activities and disabilities.[5 35] More reliable estimates of multimorbidity, using medical records, for example, are not available in the region.

The response rate was 76%, which may constitute a source of selection bias. Efforts were made to improve representativeness by using predefined sex and age quotas and interviewing one individual per family, according to official estimates.[38] Survival bias may have also influenced the results, as patients who died prematurely from those causes, who were hospitalized or who had more serious diseases were not available in the household to participate in the survey. The cross-sectional nature of the study does not allow for investigation of temporal associations.

This is the first local study to estimate the prevalence of multimorbidity in adults in the state of Amazonas. We used a cut-off point of ≥2 and ≥3 chronic diseases, as performed in previous studies.[3 5] We identified the most vulnerable multimorbidity groups to be women and the elderly. Multimorbidity was higher in older people and increased with age; this finding has been observed in previous studies.[5 9 23] The National Health Survey conducted in Brazil in 2013 reported that women are most affected among all socioeconomic groups, especially the elderly.[39]

Our results showed similarities to a cross-sectional study conducted in 2012 in Pelotas city in the southern region of Brazil with 2927 subjects, in which 29.1% of the interviewees had more than two chronic diseases and 14% had three or more.[40] The 2013 National Health Survey also confirmed these findings: 22% of Brazilians reported two or more chronic diseases, and 10% were affected by more than three.[14] The highest prevalence

was observed in the south (26 to 29%),[14] which is more economically developed and has greater access to health services than the north does.[17 41] Any chronic disease occurred in 45% of Brazilians, with a lower prevalence in the north region.[42]

In other contexts, lower prevalence of multimorbidity was found. A survey conducted in 2012 in Italy, with 3 759 836 adults, detected that 15% of individuals presented two or more chronic diseases.[10] In Ireland, a representative sample of the population (11.3% of subjects ≥50 years) presented multiple diseases.[12] Furthermore, an electronic medical data analysis conducted in 2007 with 1 751 841 users of the Scottish Health Service found that 23% had multimorbidity.[9] In an economic context comparable to Brazil's, a population-based Indian study conducted in 2007 with 10 973 interviewees identified smaller proportions (28% had any chronic disease and approximately 9% had multimorbidity).[43]

Two findings of our research are rarely described in previous studies: the higher frequency of multimorbidity at younger ages and the lack of association with economic status. One-half of adults aged 25 to 34 years and nearly two-thirds of interviewees aged 35 to 44 years reported any chronic condition, and nearly one-third had multimorbidity. The development of multimorbidity in young adults is in agreement with previous data from Brazil.[23 39 40] It is important to emphasize that half of the population of the Manaus metropolitan region is concentrated in this age range (49% aged 25 to 44 years). A systematic review of 24 cross-sectional studies on multimorbidity found income as a conflicting factor across studies, associated either with richer or poorer individuals, while lower educational attainment was associated with a 64% higher chance of multimorbidity.[44] No association was found between income and multimorbidity after adjusting for socioeconomic variables.

In lower-income countries such as Brazil, which also faces economic austerity policies, rising unemployment and unstable social and health policies,[45] it is possible to predict a reduction in access to health services, with a consequent increase in morbidity. This effect has been observed in other austerity scenarios, in which this type of policy reduced jobs, education and use of health services, resulting in an increase of chronic diseases.[46 47] An analysis of high-income countries found that 3.6 more years of education reduces the risk of cardiovascular disease by one-third.[48]

Back pain was the most frequent disease, reported by one-third of the sample. In our study, this morbidity was assessed using several questions, which may have increased the sensitivity of the assessment. An even higher proportion (49%) of vertebral spine/back issues was observed in a representative cross-sectional survey of Brazilian adults.[39] In other contexts, similar prevalence values were estimated.[49]

The presence of dengue was higher in individuals with multimorbidity, possibly due to the lower immunologic response observed in chronic diseases such as diabetes, rheumatoid arthritis, and asthma.[50 51] A systematic review of 16 cohort and case-control studies from 2007 to 2013 showed chronic diseases as risk factors for severe dengue.[52] In another meta-analysis of 10 studies conducted between 2006 and 2014,[53] diabetes was significantly associated with haemorrhagic dengue: regardless of demographic and socioeconomic characteristics, the association was 5% higher than that for individuals who did not have diabetes.

A single multimorbidity pattern with all investigated diseases was identified in women. Heart disease presented the highest factor loading, but disease patterns are poorly explained due to the wide range of diseases included in one factor. This finding may be due to our measurement and analytical approach, including sex stratification, broad categories of diseases, and the number of chronic conditions investigated. In previous studies conducted in Brazil involving similar questions, up to three multimorbidity patterns have been identified: cardiometabolic, musculoskeletal-mental and respiratory.[14 23 40] Such studies did not stratify by sex when investigating the multimorbidity pattern. An Australian cohort with 13 715 women born between 1946-51 identified five multimorbidity patterns (psychosomatic, musculoskeletal, cardiometabolic, cancer and respiratory) after investigating 18 chronic diseases and 13 symptoms.[54] The greater number of diseases and symptoms may explain the number of clustering factors in women relative to our analysis (31 *versus* 12).

In men, lung disease was the disease with the highest factorial loading on factor 1, but no clear pattern of diseases was found in the clustering of this factor. Factor 2 included cardiometabolic diseases, which could be explained by similar risk factors such as sedentary lifestyle and obesity. An analysis of 2 008 electronic medical records from the

Spanish National Health System identified cardiometabolic patterns in both men and women in different age ranges.[55]

According to the results, it is estimated that over 1 300 000 residents of the metropolitan region of Manaus have a chronic condition, and nearly 700 000 have multimorbidity. Early diagnosis and treatment of chronic diseases, centred on primary care services, is a priority for enabling sustainability of the health system and a healthier society.[56]

CONCLUSION

Multimorbidity was common in residents of the metropolitan region of Manaus and was associated with female sex, elderly people and poorer health perception. Prevention and control strategies should prioritize these groups. Future analyses should investigate the relationship between multimorbidity and the use and costs of health services in the region.

Contributors MTS, TFG, and MEAA designed the study. MEAA, MTS and BNP performed the statistical analyses. MEAA, MTS, TFG, BNP and MGP interpreted the results and drafted the manuscript. All authors made critical revisions and provided intellectual content to the manuscript, approved the final version and agreed to be accountable for all aspects of this work.

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Competing interest None declared

Patient consent Obtained

Ethics approval The research project was approved by the Research Ethics Committee of the Federal University of Amazonas. All the individuals who agreed to participate signed a free and informed consent form.

Data sharing statement: Data are available and can be accessed by contacting MTS.

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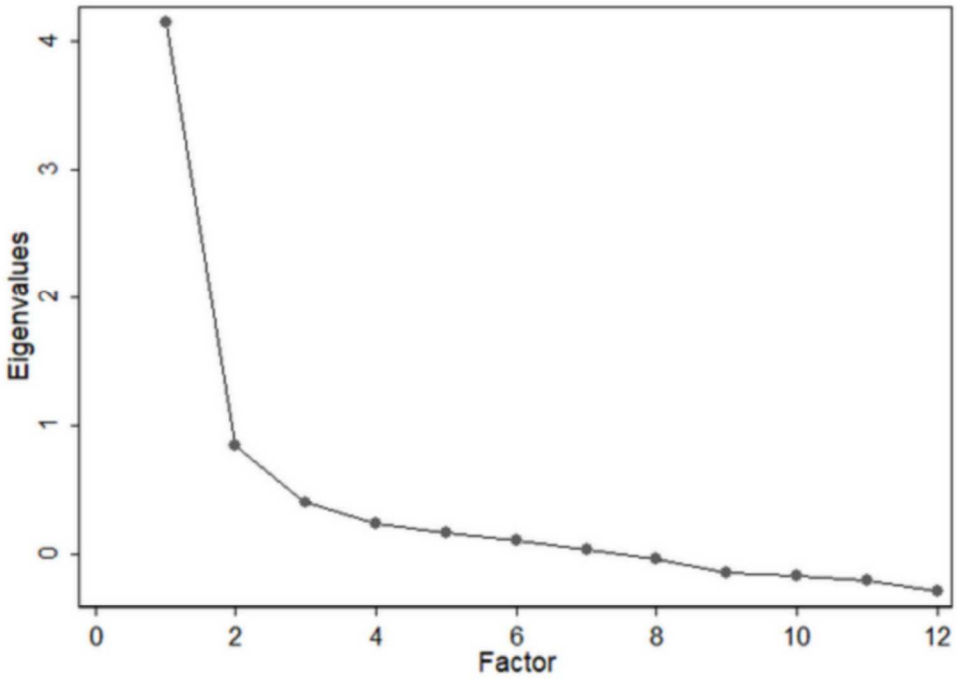

Figure 1 Scree plot for women
Note: The graph shows one factors before the inflection point in the curve (eigenvalue >1)

143x104mm (300 x 300 DPI)

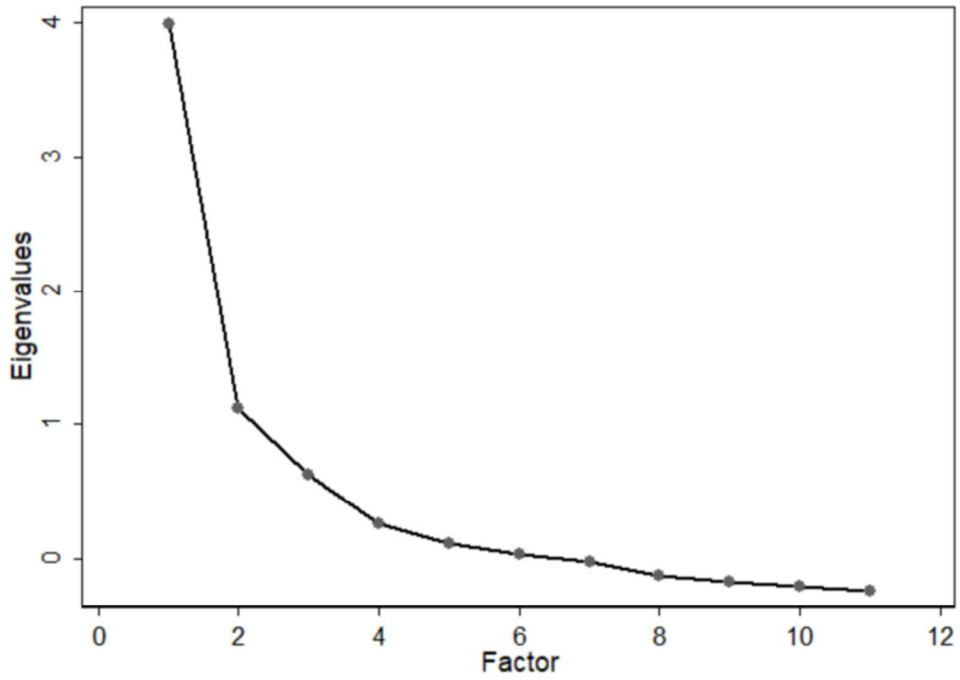

Figure 2 Scree plot for men
Note: The graph shows two factors before the inflection point in the curve (eigenvalue >1)

125x91mm (300 x 300 DPI)

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1,2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any pre-specified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	3,4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—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 *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	4
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—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	4
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	4
Bias	9	Describe any efforts to address potential sources of bias	-
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5
		(*b*) Describe any methods used to examine subgroups and interactions	-
		(*c*) Explain how missing data were addressed	-
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	4

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*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	6
		(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	6
		(b) Indicate number of participants with missing data for each variable of interest	-
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	-
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	-
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	-
		Cross-sectional study—Report numbers of outcome events or summary measures	6
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	7,8,9,10,11
		(*b*) Report category boundaries when continuous variables were categorized	6
		(*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	12,13
Discussion			
Key results	18	Summarise key results with reference to study objectives	13,14
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	14,15,16
Generalisability	21	Discuss the generalisability (external validity) of the study results	16
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	17

*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.