Brazil and associated determinants: a cross-sectional study

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To cite: Araujo MEA, Silva MT, Galvao TF, et al. Prevalence and patterns of multimorbidity in Amazon Region of Brazil and associated determinants: a cross-sectional study. BMJ Open 2018;8:e023398. doi:10.1136/ bmjopen-2018-023398

Prepublication history and additional material for this paper are available online. To view, please visit the journal (http:// dx.doi.org/10.1136/bmjopen-2018-023398).

Received 4 April 2018
Revised 21 August 2018
Accepted 26 September 2018
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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 4001 adults aged $\geq 18$ years. Primary outcome measures Multimorbidity, measured by the occurrence of $\geq 2$ and $\geq 3$ 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 $57.2 \%$ ( $95 \% \mathrm{Cl} 56.6 \%$ to $59.7 \%$ ) of the interviewees, and the mean morbidity was 1.2 (1.1-1.2); $29.0 \%$ ( $95 \% \mathrm{Cl} 27.6 \%$ to $30.5 \%$ ) reported $\geq 2$ morbidities and $15.2 \%$ ( $95 \%$ CI $14.1 \%$ to $16.4 \%$ ) reported $\geq 3$ chronic conditions. Back pain was reported by one-third of the interviewees. Multimorbidity was highest in women, $\mathrm{PR}=1.66$ ( $95 \% \mathrm{Cl}$ 1.50 to 1.83 ); the elderly, $\mathrm{PR}=5.68$ ( $95 \% \mathrm{Cl} 4.51$ to 7.15 ) and individuals with worse health perception, $\mathrm{PR}=3.70$ ( $95 \% \mathrm{Cl} 2.73$ to 5.00 ). Associated factors also included undergoing medical consultations, hospitalisation 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.


## BACKGROUND

Multimorbidity is the occurrence of different chronic clinical conditions in an individual, without a single condition being considered

## 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 popu-lation-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 knowledge about the epidemiological factors associated with multimorbidity.
- The method used to measure outcomes, self-report, is subject to errors and influenced by memory bias.
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 socioeconomic 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, hospitalisation, 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 $>60 \%$ 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 categorised as $\geq 2$ or $\geq 3$ 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 4000 adults aged $\geq 18$ years 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 (18-24; 25-34; $35-44 ; 45-59$ and $\geq 60$ 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); hospitalisation 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, 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 (suy command).

Descriptive statistics were initially obtained through prevalence calculation. The respective CIs and P values of difference were calculated by Pearson's $\mathrm{X}^{2}$ 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 $95 \%$ 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, hospitalisation, 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 $\leq 0.05$. 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, that is, 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 $\geq 0.70$, and the Bartlett sphericity test, which was considered adequate if its p value was $\leq 0.05 .{ }^{30}{ }^{33}$ 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 $\geq 0.30^{30}$ (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 predefined 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 4001 adults and had a response rate of $76 \%$. Women constituted over half of the sample. About one-half of the interviewees were aged between 25 and 44 years, 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 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 $\pm$ SD of $1.2 \pm 1.5$ chronic disease per person. This average increased with age $(0.5 \pm 0.8$ in the group aged $18-24$ years and $2.5 \pm 1.9$ in those 60 aged years or above).

## Prevalence of multimorbidity

The prevalence of $\geq 2$ chronic conditions was $29 \%$ ( $95 \%$ CI $27.6 \%$ to $30.5 \%$ ), and that of $\geq 3$ 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 hospitalised 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 35-59 years reported $\geq 2$ morbidities (table 2). Back pain was the most frequently reported health problem in both women and men, followed by hypertension. Women $\geq 60$ years with two or more morbidities reported more hypertension ( $92.0 \%$ ) than men did in the same age group ( $79.5 \%$ ).

Table 3 shows the results obtained for factors associated with multimorbidity. After adjustment, multimorbidity ( $\geq 2$ diseases) was associated with female sex ( $\mathrm{PR}=1.66,95 \% \mathrm{CI} 1.50$ to 1.83 ), age between 45 and 59 years ( $\mathrm{PR}=4.36,95 \% \mathrm{CI} 3.48$ to 5.46 ) and age $\geq 60$ years ( $\mathrm{PR}=5.68,95 \% \mathrm{CI} 4.51$ to 7.15 ). The presence of $\geq 3$ diseases was associated with female sex ( $\mathrm{PR}=2.19,95 \% \mathrm{CI}$ 1.88 to 2.56 ), age $45-59$ years ( $\mathrm{PR}=7.62,95 \% \mathrm{CI} 5.22$ to 11.10 ), age $\geq 60$ years ( $\mathrm{PR}=12.03,95 \%$ CI 8.20 to 17.66 ), dengue in the last 12 months ( $\mathrm{PR}=1.36,95 \% \mathrm{CI} 1.13$ to 1.64) and very poor health status ( $\mathrm{PR}=7.89,95 \%$ CI 4.71 to 13.23). Having $\geq 3$ chronic conditions increased the demand for physician visits, hospitalisation 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 0.82 for women and 0.78 for men, and the Bartlett sphericity test presented a p value $\leq 0.001$ for both, suggesting an adequate factor analysis. In women, one multimorbidity pattern (see online supplemental figure 1) explained $81 \%$ of the total variance, including the 12 chronic diseases analysed. In men, two factors were identified (see online 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.

## 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 25 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 hospitalisation presented associations with multimorbidity. Chronic spinal problems were the most commonly reported diseases.

We used a list of 12 self-reported chronic conditionssome of which were very broad-to assess the primary outcome of this study. A systematic review summarised 39 observational studies from 1993 to 2013 and identified a range of 5-335 diseases for the study of multimorbidity. ${ }^{3}$ In previous studies, the fewer diseases included in the research was, the lower the prevalence observed became. ${ }^{534}$ Regardless of the number of chronic conditions reported
Table 1 Characteristics of participants and prevalence of multimorbidity (\%), Manaus metropolitan region, Brazil, 2015 ( $n=4001$ ) * Multimorbidity \% (95\% CI)

| $\geq 3$ | P values |
| :--- | :--- |
| $15.2(14.1$ to 16.4$)$ |  |
|  | $<0.001$ |
| $9.3(8.1$ to 10.7$)$ |  |
| $20.5(18.8$ to 22.3$)$ |  |
|  | $<0.001$ |
| $3.5(2.5$ to 5.0$)$ |  |
| $6.9(5.6$ to 8.5$)$ |  |
| $12.7(10.6$ to 15.1$)$ |  |
| $28.1(25.1$ to 31.4$)$ |  |
| $44.4(39.6$ to 49.3$)$ |  |

 10.3 (8.8 to 11.3)
19.6 (17.6 to 21.8) 19.9 (15.5 to 25.2)

39.9 (32.5 to 47.7 ) 0.0016 |  |
| :--- |
|  |
| 0 |
| 0 |
| 0 | to 28.9) $<0.001$

<0.001

| Table 1 Continued |  |  |  |  |
| :--- | :---: | :--- | :--- | :--- | :--- | :--- | :--- |
|  |  |  |  |  |

Table 1 Continued


Physician visit, hospitalisation, dengue and malaria in last 12 months.
*Descriptive statistics using simple frequency and Pearson's $\chi^{2}$ test. †Tertiary education or higher.
$\ddagger$ 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.
and how they were defined, multimorbidity estimates are influenced by self-report. Although widely applied, ${ }^{3} 535$ such assessments are more likely to suffer classification bias or have no validated instrument for confirmation. In the present research, over-reporting or under-reporting 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. ${ }^{737}$ 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. ${ }^{535}$ 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 hospitalised 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 $\geq 2$ and $\geq 3$ chronic diseases, as performed in previous studies. ${ }^{35}$ 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. ${ }^{59}{ }^{23}$ 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 $(26 \%-29 \%),{ }^{14}$ which is more economically developed and has greater access to health services than the north does. ${ }^{1741}$ 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 3759 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 $\geq 50$ years) presented multiple diseases. ${ }^{12}$ Furthermore, an electronic medical data analysis conducted in 2007 with 1751841 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 10973 interviewees identified

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

| Morbidities | n (\%) | Multimorbidity $\geq 2$ |  |  | Multimorbidity $\geq 3$ |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $\begin{aligned} & \text { 18-34 } \\ & \text { n (\%) } \end{aligned}$ | $\begin{aligned} & \text { 35-59 } \\ & \mathrm{n}(\%) \end{aligned}$ | $\begin{aligned} & \geq 60 \\ & \mathrm{n} \text { (\%) } \end{aligned}$ | $\begin{aligned} & \hline \text { 18-34 } \\ & \mathrm{n}(\%) \end{aligned}$ | $\begin{aligned} & \text { 35-59 } \\ & \mathrm{n}(\%) \end{aligned}$ | $\begin{aligned} & \geq 60 \\ & \mathrm{n} \text { (\%) } \end{aligned}$ |
| Women (2113) |  | 195 (18.4) | 394 (47.0) | 168 (76.9) | 78 (7.0) | 236 (28.1) | 120 (55.0) |
| Chronic spinal problem $\dagger$ | 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) |
| Hypercholesterolaemia | 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 $\ddagger$ | 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 $\dagger$ | 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) |
| Hypercholesterolaemia | 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 $\leq 0.002$.
*Multimorbidity with prevalence $\geq 5 \%$. $\dagger$ Chronic back pain or neck, low back pain, sciatica, vertebral or disc pain. $\ddagger$ Heart disease, or heart attack, angina, cardiac insufficiency.
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 25-34 years and nearly two-thirds of interviewees aged 35-44 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. ${ }^{239}{ }^{39}$ It is important to emphasise that half of the population of the Manaus metropolitan region is concentrated in this age range ( $49 \%$ aged $25-44$ 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 low-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. ${ }^{4647}$ 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 immunological 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

Table 3 Adjusted prevalence ratio (PR) and $95 \% \mathrm{Cl}$ for any chronic disease and multimorbidity $\geq 2$ and $\geq 3$, according to sociodemographic and health variables based on hierarchical Poisson regression; Manaus metropolitan region, Brazil, 2015 ( $\mathrm{n}=4001$ )

| Variable | Any chronic disease PR (95\% CI) | $P$ values | Multimorbidity PR (95\% CI) |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  | $\geq 2$ | P values | $\geq 3$ | P values |
| 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 (years) |  |  |  |  |  |  |
| 18-24 | 1.00 |  |  |  | 1.00 |  |
| 25-34 | 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 |
| 35-44 | 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 |
| 45-59 | 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 |
| $\geq 60$ | 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 $\dagger$

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 $\ddagger$ |  |  |  |  |  |  |

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 |  |  | 1.00 |  | 1.00 |  |
| Very good | 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$)$ | $<0.001$ |

Table 3 Continued

| Variable | Any chronic diseasePR (95\% CI) | P values | Multimorbidity PR (95\% CI) |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  | $\geq 2$ | P values | $\geq 3$ | P values |
| 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 |
| Hospitalisation |  |  |  |  |  |  |
| 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; $\ddagger$ 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.
$\geq 2$ morbidities: *sex, age, marital status and race; †sex, age, marital status, education, income, occupation; $\ddagger$ 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.
$\geq 3$ morbidities: *sex, age, marital status and race; tsex, age, marital status, education, income, occupation; $\ddagger$ 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.
conditions investigated. In previous studies conducted in Brazil involving similar questions, up to three multimorbidity patterns have been identified: cardiometabolic, musculoskeletal-mental and respiratory. ${ }^{14} 2340$ Such studies did not stratify by sex when investigating the multimorbidity pattern. An Australian cohort with 13715 women born between 1946 and 1951 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 vs 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 2008 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 1300 000 residents of the metropolitan region of Manaus have a chronic condition, and nearly 700000 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 prioritise these groups. Future analyses should investigate the relationship

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

|  | Women <br> $(\mathbf{n}=2113)$ | Men (n=1888) |  |
| :--- | :---: | :--- | :---: |
| Morbidities | Factor 1 | Factor 1 | Factor 2 |
| Hypercholesterolaemia | 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 | 0.44 | 0.48 |  |
| bronchitis |  |  |  |
| Lung diseases* | 0.53 | 0.76 |  |
| Cancer $\dagger$ | 0.52 |  |  |
| Proportion of variance (\%) | 81.0 | 62.0 | 56.0 |
| Kaiser-Meyer-Olkin | 0.82 | 0.78 |  |

Kept factors were those with scores $\geq 0.30$ after oblique rotation.
*Pulmonary emphysema, bronchitis, chronic obstructive lung disease.
$\dagger$ Cancer showed negative values in men and was excluded.
between multimorbidity and the use and costs of health services in the region.

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Funding This work was funded by the National Council for Scientific and Technological Development (Conselho Nacional para o Desenvolvimento Cientifico e Tecnologico (CNPq) (404990/2013-4 and 448093/2014-6 to MTS) and the Foundation for Research Support of the State of Amazonas (Fundaçao de Amparo à Pesquisa do Estado do Amazonas (FAPEAM) to MEdAA).
Competing interests None declared.
Patient consent Not required.
Ethics approval The research project was approved by the Research Ethics Committee of the Federal University of Amazonas.
Provenance and peer review Not commissioned; externally peer reviewed.
Data sharing statement Data are available and can be accessed by contacting MTS.

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