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Multimorbidity in adults from a southern Brazilian city: occurrence and patterns

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Abstract

Objectives   The aim of this study was to evaluate occurrences and patterns of multimorbidity in adults from a southern Brazilian city.

Methods   A population-based cross-sectional study was carried out in 2012 through face-to-face interviews with adults (20 or more years) living in Pelotas, southern Brazil. Multimorbidity was evaluated by a list of 11 morbidities (based on medical diagnosis; Patient Health Questionnaire 9 for depression; and Anatomical Therapeutic Chemical index) and operationalized according to two cutoff points: ≥ 2 and ≥ 3 morbidities. Descriptive analysis and factor analysis (FA) were performed.

Results   The sample was made up of 2927 adults. Multimorbidity reached 29.1 % (95 % CI: 27.1; 31.1) for ≥ 2, and 14.3 % (95 % CI: 12.8; 15.8) for ≥ 3 morbidities and was greater in females, older people, those with less schooling and those from lower economic classes. Four pairs (frequency ≥ 5 %) and four triplets (frequency ≥ 2 %) were observed. Two patterns of morbidities (cardiometabolic and joint problems; and respiratory diseases) explained 93 % of total variance.

Conclusions   Multimorbidity was common in the studied population. The observed patterns may be used to generate and improve Brazilian diseases guidelines.

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Keywords   Comorbidity · Multimorbidity · Chronic diseases · Statistical disease clustering · Elderly · Brazil

Introduction

Multimorbidity, which is the occurrence of different diseases in the same individual (Le Reste et al. 2013), is a public health problem due to its occurrence, consequences and impact on the health system and services (Dias da Costa and Victora 2006).

International studies with an elderly population have identified multimorbidity with a frequencies greater than 60 % (Fortin et al. 2012), but findings with adult population are scarce. Among existing results, a Scottish study found multimorbidity in 11.3 % of individuals between 25 and 44 years old and 30.4 % for those between 45 and

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64 years old (Barnett et al. 2012). Nevertheless, low frequency in adults does not represent a less relevant problem as, in absolute number, this population concentrates most cases of multimorbidity.

In addition to the high prevalence, the consequences of multimorbidity also include greater risk of disabilities, death and decrease in quality of life (Gijsen et al. 2001). These consequences are strongly associated with complications of chronic health problems. Thus, information about concomitant occurrence of diseases can contribute to prevent complications and avoid unnecessary health service use.

Regarding health systems and services, the knowledge and monitoring of multimorbidity is a challenge in managing chronic health conditions (Moraes 2012), mainly in Brazil, where the demographic and epidemiological transitions have been faster than in high-income countries (Schmidt et al. 2011). Nowadays, the majority of clinical guidelines are targeted at specific problems, which increase the risk of iatrogenic events (Guthrie et al. 2012; Moraes 2012; Salisbury 2012).

The scarce information about multimorbidity in Brazil makes the planning of health services and the developing of health professionals' knowledge regarding the adequate management of chronic conditions more difficult. Thus, the aim of the study was to evaluate the occurrences and patterns of multimorbidity in adults from a southern Brazilian city.

Methods

A population-based cross-sectional study was performed. The present paper is part of a survey conducted in 2012 in the urban area of Pelotas (Barros et al. 2008), a city in the state of Rio Grande do Sul, southern Brazil (latitude: $31°46'19''$/longitude: $2°20'19''$). In 2010, Pelotas had 306,193 inhabitants in the urban area (93.3 % of total population) presenting 203,89 inhabitants/km^2. The HDI ranged from 0.558 in 1991 to 0.739 in 2010 (Brazil range from 0.590 in 1990 to 0.726 in 2010).

The sampling procedure was conducted in two stages. The first stage comprised the selection of census sectors from the 2010 census and the second stage the selection of households. From the 495 census sectors from urban areas, 130 were selected. Out of these, 1722 households were located, with respect to the strategy of systematic sampling proportional to the sector size. In each selected household, all individuals aged 10 years or more were invited to participate. The exclusion criteria were the following: patients who were institutionalized and those with severe mental or emotional disabilities which could jeopardize the completion of the survey. This analysis was restricted to adults and the elderly population (individuals aged ≥ 20 years).

Data were collected between February and June 2012. The structured electronic questionnaires containing precoded questions were administered using netbooks. Interviews which were not performed after three attempts on different days and times, with one of these attempts being made by a study supervisor, were considered losses or refusals. Quality control was ensured using different data collection strategies, e.g., checking for database inconsistencies. After the interviews, a new visit was randomly made to 10.0 % of the study sample. Quality control was ensured by using a short questionnaire containing 14 questions.

The outcome multimorbidity was operationalized by a list of 11 morbidities based on three measurement forms. Six diseases were based on self-report of a physician diagnosis [high blood pressure—HBP, diabetes, heart problem, asthma/wheezy bronchitis (Oliveira et al. 2013), bronchitis (Oliveira et al. 2013) and emphysema (Oliveira et al. 2013)]. Depression was measured by Patient Health Questionnaire-9 (PHQ-9) which was validated in the population of the present analysis (Santos et al. 2013). The other four diseases were based on use of medicines classified by Anatomical Therapeutic Chemical—ATC (joint disorders—rheumatism, arthritis and arthrosis, osteoporosis, hypothyroidism and hypercholesterolemia) (WHO Collaborating Centre for Drug Statistics Methodology 2013). Multimorbidity was evaluated in two ways according to the literature (Fortin et al. 2012; Harrison et al. 2014): (a) two or more morbidities; and (b) three or more morbidities.

Exposure variables included sex (male; female), age in years (20–29; 30–39; 40–49; 50–59; 60 or more), self-reported skin color (white; black; brown, yellow and indigenous), marital status (with partner; without partner), economic status measured by *Associação Brasileira de Empresas de Pesquisas—ABEP*—which is a measure of the purchasing power based on the ownership of assets (A and B—richer; C; D and E) (Associação Brasileira de Empresas de Pesquisa 2010) and education in years (4 or less; 5–8; 9 or more).

Descriptive analysis involved the calculation of prevalence and its respective confidence intervals and p values for difference (Pearson Chi square). The pairs (frequency 5 % or more) and triplets (frequency 2 % or more) of morbidities were calculated to evaluate the major combinations between diseases. The relation between the observed (O) and expected (E) frequencies was calculated to measure morbidities occurrence beyond expected by chance. By multiplying individual prevalence of the diseases, we calculated the expected frequencies of diseases.

Statistical analyses were performed using Stata 12.1 software and the *syv* command was used to consider the sampling process of the study. Exploratory factor analysis

(FA), through principal factor method, was performed to identify the patterns of morbidities (Schäfer et al. 2010). Analysis was based on tetrachoric correlation as used variables were dichotomous. This analysis is more appropriate than Pearson correlation to these variables (Kubinger 2003). Before FA analysis, Kaiser–Meyer–Olkin (KMO) and Bartlett sphericity tests were used to evaluate the applicability of this approach. Oblique (oblimin or promax) rotation was performed. To establish the number of components to be retained, we used Cattel graphics, Kaiser criteria (eigenvalue >1), minimum explained variance (>10 % by each component), accumulated variance by retained components (>70 %) and, at least, two variables in the final solution. Variables with loadings $|\geq 0.3|$ were kept (Norman and Streiner 2008).

The project was submitted and approved by the Ethics Committee of the Medical School of the Federal University of Pelotas, registered by protocol number 77/11. The interviewers were performed after acceptance of the participant by signing the Instrument of Consent.

Results

The sample was made up of 2.927 adults with 20 or more years. The participation rate was 86.6 %. Males refused more than females ($p < 0.001$). There was no difference on age mean of participants [45.7 (SD = 16.6)] compared to losses and refusals [45.8 (SD = 17.4); $p = 0.095$].

Of the total, 58.9 % were female. White skin color was the most common (80.1 %) followed by black (12.1 %). Individuals with partner represented 59.4 %. Half of the sample (54.1 %) studied for 9 years or more and 18.0 % studied up to 4 years. The predominant economic class was A/B—the richest one (46.4 %) followed by C (43.4 %) and D/E (10.2 %). The most frequent morbidities were HBP (32.7 %) and depression (20.4 %). The least frequent ones were joint disorders (3.4 %) and emphysema (1.6 %) (Table 1).

The individuals who presented zero, one, two and three morbidities represented 41.9, 29.0, 14.8 and 8.4 %, respectively. Less than 1 % presented six or more morbidities. Two or more morbidities increased with age, whereas the frequency of one disease was similar among the age groups (Fig. 1).

Multimorbidity reached 29.1 % (95 % CI: 27.1; 31.1) for two or more, and 14.3 % (95 % CI: 12.8; 15.8) for three or more morbidities. For both cutoff points, individuals who were females, older, with fewer years of schooling and from lower economic classes presented more multimorbidity. The frequency of multimorbidity was similar for skin color and marital status categories (Table 1).

The observed pairs of morbidities with frequency of 5 % or higher were the following: HBP/heart problem; HBP/

depression; HBP/diabetes; and HBP/hypercholesterolemia. With the exception of HBP/depression pair, the other pairs presented occurrences two times greater than expected by chance which is similar to triplets of diseases (Table 2).

In the FA analysis, the KMO coefficient was 0.61, with $p \leq 0.001$ in Bartlett test, suggesting an FA adequacy. Two patterns of morbidities explained 93 % of the total variance. The following components were identified: (1) cardiometabolic problems (HBP, heart disease, hypercholesterolemia and diabetes) + joint problems + osteoporosis; (2) respiratory (asthma/wheezy bronchitis, bronchitis and emphysema) (Table 3). The score and loading plots are available in Online Resource 1.

Discussion

The occurrence of two or more and three or more morbidities achieved almost 1/3 and 1/5 of the individuals, respectively. The frequency of multimorbidity was greater in the lower purchasing power group. The HBP was present in all evaluated pairs and triplets. The factor analysis showed an occurrence of the patterns of morbidities. To our knowledge, this is the first evidence about frequency and pattern of multimorbidity in Brazilian adults, which may contribute to plan actions related to the management of multiple health chronic conditions.

The occurrence of a morbidity was similar among the different age groups despite the expected increase of morbidity numbers with the increase in age. Approximately, 30 % of the individuals at 20 years or more have a chronic disease. Regarding two, three and four morbidities, the gap between extreme groups (60 or more and 20–29) was, at least, higher than nine percentage points. The greater percentage of morbidities in the elderly population promotes relevant implications to the health system, but, in absolute numbers, there are more adults with multiple health problems. For instance, when extrapolating the data to the whole population of Pelotas, approximately 21,000 adults (20–59 years) and 11,000 of the elderly (60 or more) presented two chronic conditions. Thus, for policy makers, the planning of actions to address complications of concomitant occurrence of multiple diseases should include the elderly (high prevalence) and the adults (high number of absolute cases).

The frequency of two or more morbidities was higher than the ones found in Spain (Garin et al. 2014) (individuals with 18 or more years = 20.0 %; 95 % CI: 18.8–21.2) and similar to the ones found in Scotland (Barnett et al. 2012) (25 or more years = 31.1 %) and Canada (Agborsangaya et al. 2013) (18 or more years = 30.9 %; 95 % CI 29.5–32.4). Methodologically, these are the most comparable studies in relation to the present work. The

Table 1 Demographic, socioeconomic and morbidity characteristics and multimorbidity frequency in the adult population. Pelotas, Rio Grande do Sul state, Brazil, 2012

Variables	N	%	Multimorbidity	
			≥2 % (95 % CI)	≥3 % (95 % CI)
Gender (n = 2,927)			p < 0.001	p < 0.001
Male	1203	41.1	20.4 (17.7; 23.0)	8.6 (6.9; 10.2)
Female	1724	58.9	35.2 (32.6; 37.7)	18.4 (16.3; 20.5)
Age (in years) (n = 2,927)			p < 0.001	p < 0.001
20–29	612	20.9	8.0 (5.8; 10.2)	3.1 (1.8; 4.5)
30–39	540	18.4	14.4 (11.4; 17.5)	4.3 (2.7; 5.9)
40– 49	595	20.3	22.2 (18.4; 26.1)	8.2 (5.8; 10.7)
50–59	514	17.6	40.3 (35.9; 44.7)	19.5 (16.1; 22.8)
60 or more	666	22.8	57.9 (54.1; 61.7)	34.4 (30.4; 38.4)
Skin color (n = 2,926)			p = 0.457	p = 0.162
White	2345	80.1	29.6 (27.4; 31.8)	14.9 (13.2; 16.6)
Black	354	12.1	28.0 (23.4; 32.5)	12.4 (9.0; 15.8)
Brown/yellow/indigenous	227	7.8	26.0 (20.0; 32.0)	11.5 (7.7; 15.2)
Marital status (n = 2,923)			p = 0.554	p = 0.197
With partner	1736	59.4	28.6 (26.0; 31.3)	13.5 (11.7; 15.3)
Without partner	1187	40.6	29.8 (26.9; 31.34)	15.5 (12.9; 18.1)
Schooling (in years) (n = 2,924)			p < 0.001	p < 0.001
≤4	526	18.0	49.1 (44.1; 54.3)	30.4 (26.0; 34.9)
5–8	817	27.9	28.5 (25.2; 31.8)	13.5 (11.1; 15.9)
≥9	1581	54.1	22.7 (20.4; 24.9)	9.4 (7.8; 10.9)
Economic class—ABEP (n = 2,905)			p = 0.010	p = 0.001
A/B (the richest)	1349	46.4	27.5 (25.0; 30.1)	12.5 (10.6; 14.5)
C	1261	43.4	28.9 (25.9; 31.9)	14.4 (12.1; 16.6)
D/E	295	10.2	36.7 (31.2; 42.2)	22.1 (17.0; 27.3)
Morbidities				
High blood pressure (n = 2,926)	958	32.7	65.3 (62.0; 68.7)	35.5 (32.2; 38.9)
Depression (n = 2,925)	596	20.4	59.5 (55.5; 63.5)	34.0 (29.9; 38.0)
Heart disease (n = 2,927)	336	11.5	89.6 (86.1; 92.9)	65.1 (60.3; 69.9)
Hypercholesterolemia (n = 2,925)	230	7.9	93.0 (89.8; 96.3)	69.1 (63.1; 75.2)
Diabetes (n = 2,927)	230	7.9	87.4 (83.0; 91.8)	66.1 (59.8; 72.3)
Bronchitis (n = 2,927)	179	6.1	80.0 (73.9; 85.4)	53.1 (45.1; 61.1)
Asthma/wheezy bronchitis (n = 2,927)	175	6.0	78.3 (71.6; 85.0)	52.0 (44.6; 59.4)
Hypothyroidism (n = 2,925)	144	4.9	70.8 (62.9; 78.8)	44.4 (36.8; 52.1)
Osteoporosis (n = 2,925)	100	3.4	82.0 (74.0; 90.0)	48.0 (38.6; 57.4)
Joint problems (n = 2,925)	99	3.4	83.8 (76.0; 91.6)	59.6 (49.3; 69.9)
Emphysema (n = 2,927)	48	1.6	93.5 (86.3; 100.0)	71.7 (59.1; 84.3)
Total	2927	100.0	29.1 (27.1; 31.1)	14.3 (12.8; 15.8)

differences among these studies can be attributed mainly to the different number of diseases included to define multimorbidity. To do so, 11, 40 and 14 diseases were used in Spain, Scotland and Canada, respectively. Taking into account the number of morbidities, the frequency found in these studies seems higher than international standards. Meanwhile, the comparability of multimorbidity frequency is hampered due to methodological differences among

studies. The variation of diseases included in multimorbidity is broad. Some studies included acute diseases in the definition, i.e., flu and pneumonia. Despite the important burden of morbidity and mortality attributed to these problems, mainly in the elderly population and low-income countries, these diseases hampered the comparability among studies due to greater influence from geographical and seasonal characteristics. So, it is suggested to use
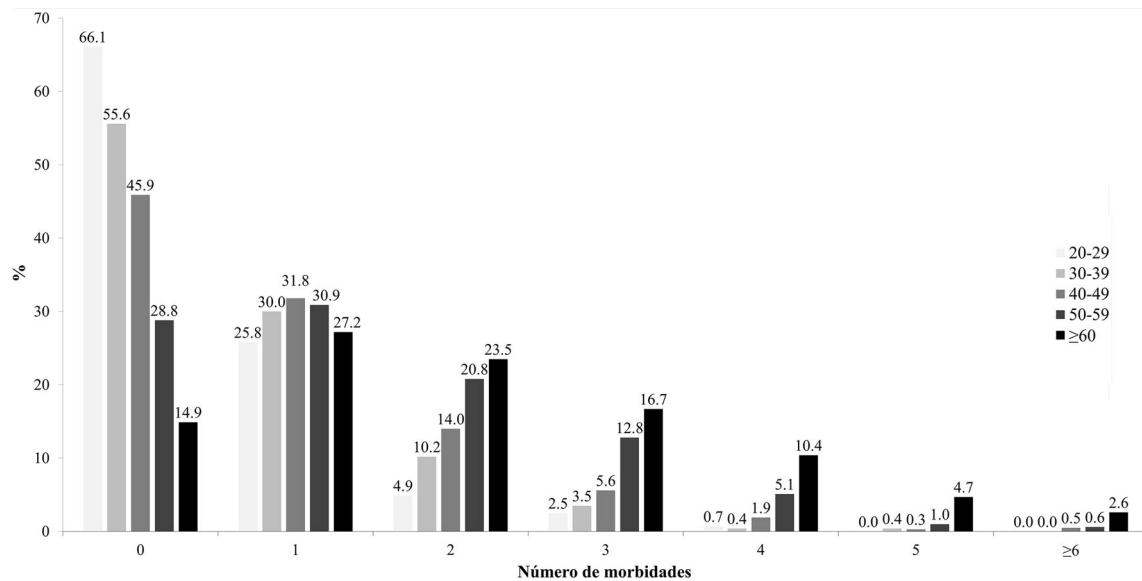
Fig. 1 Frequency of morbidity numbers in the adult population according to age groups ($n = 2,923$). Pelotas, Rio Grande do Sul State, Brazil, 2012

Table 2 Pairs (frequency 5 % or higher) and triplets (frequency 2 % or higher) of morbidities in the adult population. Pelotas, Rio Grande do Sul state, Brazil, 2012 ($n = 2,923$)

Pairs and triplets	Observed—O (%)	Expected—E (%)	O/E	95 % CI
Pairs				
High blood pressure/heart disease	8.3	3.8	2.21	1.97–2.48
High blood pressure/depression	8.3	6.7	1.24	1.13–1.37
High blood pressure/diabetes	5.8	2.6	2.26	1.97–2.60
High blood pressure/hypercholesterolemia	5.4	2.6	2.09	1.82–2.41
Triplets				
High blood pressure/heart disease/depression	3.1	0.8	4.06	3.21–5.14
High blood pressure/heart disease/ hypercholesterolemia	2.5	0.3	8.40	5.87–12.03
High blood pressure/diabetes/heart disease	2.1	0.3	7.13	4.96–10.25
High blood pressure/diabetes/depression	2.0	0.5	3.83	2.88–5.10

chronic conditions for the multimorbidity operationalization (Salive 2013).

Multimorbidity distribution showed a similar pattern according to socio-demographic characteristics. Females presented, at least, 12 percentage points higher of multimorbidity than males. This result is not consistent with the literature (Agborsangaya et al. 2012, 2013; Barnett et al. 2012), but may be explained as follows: as women use health services more often, as a result they receive more diagnosis (Mendoza-Sassi and Béria 2001). Another explanation is the survival bias which may increase multimorbidity in females, since males tend to die earlier and those who live longer are usually healthier compared to males who died. Higher multimorbidity with increasing age may be explained by the fact that the elderly are more exposed to lifetime events

which damage the physiological system and therefore facilitate the onset of chronic diseases, corroborating findings from other studies (Agborsangaya et al. 2012, 2013; Barnett et al. 2012; Fortin et al. 2012).

Individuals with lower schooling and purchasing power presented more multimorbidity as found in the majority of studies which evaluated this relationship (Agborsangaya et al. 2012, 2013; Barnett et al. 2012; Jerliu et al. 2013) and as a result highlighting the social determinant in multimorbidity occurrences (CSDH 2008). Longitudinal studies have also found a greater incidence of multimorbidity among individuals from a lower socioeconomic status (Violan et al. 2014). More longitudinal evaluations may contribute to a better understanding of the multimorbidity social determinants (Vellakkal et al. 2014).

Table 3 Factor Analysis with loadings |≥0.3|. Pelotas, Rio Grande do Sul state, Brazil, 2012 (n = 2,923)

Morbidities	Factor 1	Factor 2
High blood pressure	0.66	
Heart disease	0.69	
Hypercholesterolemia	0.74	
Diabetes	0.56	
Osteoporosis	0.47	
Joint problems	0.53	
Hypothyroidism	0.38	
Emphysema	0.31	0.44
Bronchitis		0.84
Asthma/wheezy bronchitis		0.88
Depression		
Eigenvalue	2.8	1.6
Explained variance %[a]	56 (54)	32 (39)

[a] Before oblique rotation (after oblique rotation)

The associations of multimorbidity with socio-demographic variables were not adjusted, as the objective of the manuscript is not to evaluate the possible causal relationships among diseases. Moreover, it is believed that descriptive analysis contributes to identifying priority groups to health actions related to multimorbidity despite possible confusion.

As expected, individuals with specific diseases presented more multimorbidity. However, it is worth mentioning that in relation to some diseases, the occurrence of comorbidities comprises almost all individuals (heart diseases, joint disorders and hypercholesterolemia).

We found four pairs and four triplets of diseases with an observed frequency greater than 5 and 2 %, respectively. The HBP was present in all combinations due to its higher frequency and strong relation with other conditions. The observed combinations were, in some ways, the most common ones including heart problems. Notwithstanding, we highlight the presence of depression in one pair and two triplets of diseases. Despite the influence of single prevalence in diseases combinations (Islam et al. 2014), all pairs and triplets presented here showed the observed frequency greater than expected by chance suggestion of a possible causal relationship between morbidities and/or its risk factors (Schafer et al. 2014).

The explanations for the relationship between depression and diabetes are complex and comprise biological and psychological mechanisms (Fiore et al. 2015). On a biological perspective, both depression and diabetes increase the hypothalamic–pituitary adrenal axis as it was observed, resulting in cortisol increase and an increase in the proinflammatory cytokines production (Talbot and Nouwen 2000). In depression, the increase in cytokine concentration is responsible for the reduction of serotonin levels. In diabetes, these factors operate in metabolic dysregulation (apoptosis of beta cells in the pancreas, reduce insulin secretion, insulin resistance) (Fiore et al. 2015). Regarding psychological causes, evidences suggest a lower odds of diabetes treatment adherence (such as weight loss and weight control, proper use of medication, as well as monitoring blood glucose levels) for depressed individuals (Gonzalez et al. 2008). Psychological stress increase, as result of treatment, for example, is reported as a possible risk factor to develop depressed symptoms. Understanding these causal relationships from other study designs will be important to start actions related to multimorbidity prevention.

The observed pairs and triplets may be incorporated in the guidelines for morbidity treatment. In Brazil, some cardiocirculatory problems are reported in the disease guidelines of other morbidities. Depression is seldom mentioned despite its importance in the treatment of others diseases (DiMatteo et al. 2000). The factor analysis was similar to the results found in a systematic review of literature (Prados-Torres et al. 2014). Fourteen studies were found and all of them presented important methodological differences. Even so, the combination of cardiovascular and musculoskeletal diseases was frequent, as found in the present analysis. Depression was not present in any of two factors. This is possibly explained by the lack of information of other mental health problems.

Some limitations of the study should be addressed. First, the prevalence of multimorbidity may be biased. The losses and refusals are greater in male individuals who presented lower occurrence of multimorbidity. This characteristic can produce some underestimation in frequency of multimorbidity, but with a low magnitude as the participation rate was high. Second, with the exception of depression, other morbidities were evaluated by self-reports which may cause misclassification bias. Nevertheless, besides recognized the limitations (Galenkamp et al. 2014; Kriegsman et al. 2006), self-report diagnosis is considered an adequate and common information used in population-based studies on multimorbidity (Fortin et al. 2012; Huntley et al. 2012; Violan et al. 2013), mainly for common diseases which can lead to serious complications and medicine use. Furthermore, a study of the same database showed socioeconomic equity in health service utilization, minimizing the possibility of greater diagnosis by specific socioeconomic groups. Third, subjectivity may be present in different stages of FA and should be taken into account when interpreting the results. To minimize this limitation, a detailed analysis of each step has been described. The number of morbidities (n = 11) may also be considered a limitation. It is possible that with a greater number of morbidities, other groups would be identified. However,

the principal component analysis explained a good proportion (93 %) of the data variance.

Multimorbidity was common in the adult population from the city of Pelotas, RS. The frequency and the observed inequalities highlight the need of actions to prevent multimorbidity and, mainly, its complications. The observed patterns may be used to generate and improve Brazilian disease guidelines.

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