# Multimorbidity and associated factors in adult users of Primary Health Care in northern Rio Grande do Sul, Brazil 

Multimorbidade e fatores associados em adultos usuários da Atenção Primária à Saúde no norte do Rio Grande do Sul<br>Multimorbidad y factores asociados en adultos en usuarios de Atención Primaria de Salud en el norte de Rio Grande do Sul<br><br>${ }^{1}$ Universidade Federal da Fronteira Sul - Passo Fundo (RS), Brazil.


#### Abstract

Introduction: Lifestyle changes have led to an increased exposure to risk factors for chronic diseases, making the coexistence of such conditions more frequent, even at younger ages. This complex and challenging health condition is characterized by the simultaneous presence of multiple diseases. Objective: To analyze the prevalence and factors associated with multimorbidity in users of Primary Health Care (PHC) in Passo Fundo, northern Rio Grande do Sul, Brazil. Methods: A cross-sectional study was conducted. Data were collected by applying questionnaires to adults assisted by the urban network of PHC from May to August 2019. The prevalence of the outcome was estimated, with a $95 \%$ confidence interval ( $95 \% \mathrm{Cl}$ ), as well as crude and adjusted Prevalence Ratios (PR) to identify associated factors. Results: The prevalence of multimorbidity in the sample of 958 participants was $31 \%(95 \% \mathrm{Cl} 28-34)$, and its associated factors were age between 50 and 59 years ( $\mathrm{PR}=5.47 ; 95 \% \mathrm{Cl} 3.54-8.45$ ), negative self-perception of health ( $\mathrm{PR}=1.61 ; 95 \% \mathrm{Cl}$ 1.29-2.01), overweight ( $\mathrm{PR}=3.14$; $95 \% \mathrm{Cl} 2.21-4.44$ ), and polypharmacy ( $\mathrm{PR}=1.55$; $95 \% \mathrm{Cl} 1.33-$ 1.81). Conclusion: Multimorbidity is prevalent in the population assisted by PHC, suggesting that healthcare teams should seek strategies for investigating this condition and associated factors.


Keywords: Primary health care; Comorbidity; Multimorbidity.

[^0]
#### Abstract

Resumo

Introdução: As mudanças no estilo de vida levam ao aumento da exposição a fatores de risco a doenças crônicas e, diante disso, torna-se mais frequente a simultaneidade de tais doenças, em idades cada vez mais precoces, o que caracteriza uma condição complexa e desafiadora na área da saúde. Objetivo: Analisar a prevalência e os fatores associados à multimorbidade em usuários da Atenção Primária à Saúde (APS) de Passo Fundo, norte do Rio Grande do Sul, Brasil. Métodos: Realizou-se um estudo transversal, cujos dados foram coletados por meio da aplicação de questionários a adultos atendidos na rede urbana da APS de maio a agosto de 2019. Calculou-se a prevalência do desfecho, com intervalo de confiança de 95\% (IC95\%) e as razões de prevalência (RP) brutas e ajustadas, visando identificar os fatores associados. Resultados: A prevalência de multimorbidade na amostra de 958 participantes foi de 31\% (IC95\% 28-34) e seus fatores associados foram idade de 50-59 anos ( $R P=5,47$; IC95\% 3,54-8,45), autopercepção negativa de saúde ( $R P=1,61$; IC95\% 1,29-2,01), excesso de peso ( $R P=3,14 ; I C 95 \% 2,21-4,44$ ) e polifarmácia ( $R P=1,55$; IC95\% 1,33-1,81). Conclusão: A multimorbidade é prevalente na população atendida na APS, e sugere-se que as equipes de saúde busquem estratégias de investigação dessa condição e dos fatores que possam estar associados.


Palavras-chave: Atenção Primária à Saúde; Comorbidade; Multimorbidade.

## Resumen

Introducción: Los cambios en el estilo de vida han llevado a un aumento en la exposición a factores de riesgo para enfermedades crónicas, lo que hace más frecuente la coexistencia de tales condiciones, incluso a edades más tempranas. Esta compleja y desafiante condición de salud se caracteriza por la presencia simultánea de múltiples enfermedades. Objetivo: Analizar la prevalencia y los factores asociados a la multimorbilidad en usuarios de la Atención Primaria a la Salud (APS) de Passo Fundo, norte de Rio Grande do Sul, Brasil. Métodos: Se realizó un estudio transversal, y los datos se recopilaron a través de la aplicación de cuestionarios a adultos atendidos en la red urbana de APS de mayo a agosto de 2019. Se calculó la prevalencia del resultado, con un intervalo de confianza del 95\% (IC95\%), así como las Razones de Prevalencia (RP) crudas y ajustadas para identificar los factores asociados. Resultados: La prevalencia de multimorbilidad en la muestra de 958 participantes fue del $31 \%$ (IC95\% 28-34), y sus factores asociados fueron edad entre 50 y 59 años (RP=5,47; IC95\% 3,54-8,45), percepción negativa de la salud (RP=1,61; IC95\% 1,29-2,01), sobrepeso (RP=3,14; IC95\% 2,21-4,44) y polifarmacia (RP=1,55; IC95\% 1,33-1,81). Conclusión: La multimorbilidad es prevalente en la población atendida en APS, lo que sugiere que los equipos de salud deben buscar estrategias de investigación para esta condición y los factores asociados.
Palabras clave: Atención primaria de salud; Comorbilidad; Multimorbilidad.

## INTRODUCTION

In Brazil, considering demographic and lifestyle changes, including changes in eating habits and exposure to environmental agents, we have been witnessing a process of modification in the situation of population mortality. ${ }^{1-3}$ In recent decades, an epidemiological profile of increased deaths from noncommunicable diseases (NCDs) has prevailed. ${ }^{4}$

This change in the epidemiological profile in which NCDs predominate highlights multimorbidity, a condition defined as the occurrence of two or more diseases in the same individual. ${ }^{5,6}$ In view of its severity, prevalence, manageability, and impact on quality of life, multimorbidity has become an important public health issue. ${ }^{7}$

Thus, understanding multimorbidity at early stages during adulthood is important for many reasons. During this period, usually, individuals deal with often demanding and conflicting social roles when managing professional, personal, and family relationships. ${ }^{8,9}$ The effort to manage these multiple social roles can increase the vulnerability to chronic diseases or can make it more difficult to manage existing chronic conditions. ${ }^{10,11}$

Studies show that the prevalence of multimorbidity in adults ranges from 25 to $30 \%$, 6,12 with a predominance of women, lower level of education, ${ }^{6}$ and obese individuals. ${ }^{13}$

In addition to the high prevalence, the effects of multimorbidity may include an increased risk of death, worsening of quality of life, functional disabilities, and increased use of healthcare services. ${ }^{6}$

Despite the impact and clinical importance of multimorbidity, there is little scientific evidence to assess this problem in the adult population assisted by Primary Health Care (PHC) in Brazil. Thus, the objective of this study is to describe the prevalence and factors associated with multimorbidity in adults assisted by PHC in a medium-sized city in the north of the state of Rio Grande do Sul (RS), Brazil.

## METHODS

This study represents a selection of a broader cross-sectional study, which aimed to describe different characteristics of PHC users and whose data were collected from May to August 2019, in the urban PHC network of Passo Fundo, northern RS.

The sample size was estimated in two ways, considering the confidence level of $95 \%$ and the study power of $80 \%$ for both. The first calculation, to identify a $10 \%$ prevalence of the outcome, assuming a margin of error of five percentage points, resulted in 138 participants. The second, to identify the association between the different outcomes and exposure factors, was carried out based on the unexposed/exposed ratio of 9:1, total prevalence of the outcome of $10 \%$, expected frequency of the outcome in the unexposed group of $9.1 \%$, and a prevalence ratio (PR) of 2. Thus, 1,220 respondents would be required. Adding $15 \%$ for confounding factors to this number, the required sample would be 1,403 participants.

The following eligibility criteria were considered: age $\geq 18$ years, both sexes, residing in the municipality, receiving care in the network during the collection period, and being able to respond to the questionnaire. Thus, the research population consisted of adults and older people, sampled in a non-probabilistic way, with participants selected by convenience, and consecutively among those who sought the services provided at the units in the period stipulated for collection. To this end, sampling was carried out in two stages in the 34 urban PHC units. Initially, to define the quantity per unit, the number of respondents in each location was proportional to the number of procedures performed in each unit in the month prior to the onset of data collection and, subsequently, consecutively, all users who were in the unit to undergo some procedure were included until reaching the $n$ stipulated for each location or until all those present in the last collection shift were invited to participate. The instrument used for data collection was a standardized questionnaire, applied by trained interviewers, who approached the users according to the eligibility criteria. For this study, older people and pregnant women were excluded from the sample.

The outcome - multimorbidity - was operationalized by the simultaneous prevalence of two or more noncommunicable diseases, considering the self-reported medical diagnosis of cancer, diabetes mellitus, dyslipidemia, heart disease, and hypertension. ${ }^{5}$

Sociodemographic variables included sex (men; women), age in full years (18-29; 30-39; 40-49; 50-59), self-reported skin color (white; other); level of education (elementary school, high school, and college education), marital status (with and without a partner), paid work (no; yes), and monthly per capita family income in minimum wages (value of BRL 998 during the data collection period). Furthermore, the following aspects were analyzed: self-perception of health (positive; negative), overweight (evaluated based on self-reported weight and height and classified according to body mass index), ${ }^{14,15}$ polypharmacy (concurrent use of five or more medications), ${ }^{16}$ smoking habit (no; yes), alcohol consumption (no; yes), and physical activity (no; yes).

After double entry and data validation, descriptive statistics were used to characterize the sample and estimate the prevalence of the outcome with a $95 \%$ confidence interval $(95 \% \mathrm{Cl})$. Factors associated with multimorbidity were verified by using Poisson Regression; initially, with bivariate analysis, the crude PR and their $95 \%$ CI were generated. Subsequently, to control for possible confounding factors, multivariate analysis with robust variance for clusters was performed, estimating the adjusted PR and their Cl . In this analysis, of the backward stepwise type, a hierarchical model ${ }^{17}$ previously established and composed of three levels of determination (demographic and socioeconomic variables, health characteristics, and lifestyle habits, respectively) was considered. At each level, the variables were adjusted among themselves and those with $p \leq 0.20$ remained for adjustment with the next level. For polychotomous categorical variables, when there was ordering between the categories, the Wald test for linear trend was performed and, if not, or with a non-significant result, the heterogeneity was tested. In all tests, an $\alpha$ error of $5 \%$ was admitted, with $\mathrm{p}<0.05$ being considered significant for two-tailed tests.

The study protocol was approved by the Human Research Ethics Committee of the proposing institution (Opinion No. 3.219.633), in compliance with Resolution No. 466/2012 of the National Health Council and with the ethical principles contained in the Declaration of Helsinki. All participants were asked to sign an Informed Consent Form.

## RESULTS

The total research sample consisted of 1,443 adults and older people. For this selection, excluding older adults and pregnant women, the sample consisted of 958 participants ( $66.4 \%$ ) and their characterization is presented in Table 1. We verified that $72.8 \%$ were women, $27 \%$ aged between 30 and 39 years old, $63.6 \%$ self-reported to be white, $40.5 \%$ had elementary education, $75.3 \%$ mentioned having a partner (spouse), $55.3 \%$ had a paid job, and $74.5 \%$ reported a monthly per capita family income of up to one minimum wage. In addition, we verified that $58.4 \%$ had a positive self-perception of their health, $68.2 \%$ were overweight, $8.5 \%$ were polymedicated, $20.8 \%$ were smokers, $33.2 \%$ reported alcohol consumption, and $61.4 \%$ did not practice physical activity.

The prevalence of multimorbidity was $31 \%(95 \% \mathrm{Cl} 28-34)$. After the adjusted analysis, as shown in Table 2, there was a trend towards an increase in the probability of the outcome as the age group increased, with PR=5.47 ( $95 \% \mathrm{Cl} 3.54-8.45$ ) among those aged 50 to 59 years. Regarding the second level variables, we found that the prevalence of the outcome was positively influenced by negative self-perception of health ( $\mathrm{PR}=1.61$; 95\%CI 1.29-2.01), overweight ( $\mathrm{PR}=3.14 ; 95 \% \mathrm{Cl} 2.21-4.44$ ), and polypharmacy ( $\mathrm{PR}=1.55$; $95 \% \mathrm{Cl} 1.33-1.81$ ). Finally, among the behavioral variables, we observed a lower probability of the outcome among participants who did not practice physical activity ( $\mathrm{PR}=0.81$; 95\%Cl 0.66-0.98).

## DISCUSSION

An analysis conducted by the National Health Interview Survey (NHIS) in 2012 showed that approximately $25 \%$ of US adults aged 18 and over have more than two chronic illnesses. ${ }^{11,18}$ A similar result was observed in a study conducted in Pelotas (RS), Brazil, which showed a general prevalence of multimorbidity of $29.1 \%$ in the adult population. ${ }^{6}$ In the present study, we verified a prevalence of $31 \%$, a value similar to the aforementioned.

| Variables | n | \% |
| :---: | :---: | :---: |
| Sex |  |  |
| Men | 261 | 27.2 |
| Women | 697 | 72.8 |
| Age (full years) |  |  |
| 18-29 | 241 | 25.2 |
| 30-39 | 259 | 27.0 |
| 40-49 | 212 | 22.1 |
| 50-59 | 246 | 25.7 |
| Self-reported skin color ( $\mathrm{n}=957$ ) |  |  |
| White | 609 | 63.6 |
| Other | 348 | 36.4 |
| Level of education ( $\mathrm{n}=914$ ) |  |  |
| Elementary school | 370 | 40.5 |
| High school | 341 | 37.3 |
| College education | 203 | 22.2 |
| Marital status |  |  |
| Without a partner | 236 | 24.7 |
| With a partner | 718 | 75.3 |
| Paid work |  |  |
| No | 428 | 44.7 |
| Yes | 530 | 55.3 |
| Monthly per capita family income* ( $n=901$ ) |  |  |
| >1 minimum wage | 230 | 25.5 |
| $\leq 1$ minimum wage | 671 | 74.5 |
| Self-perception of health |  |  |
| Positive | 554 | 58.4 |
| Negative | 395 | 41.6 |
| Overweight ( $\mathrm{n}=850$ ) |  |  |
| No | 270 | 31.8 |
| Yes | 580 | 68.2 |
| Polypharmacy |  |  |
| No | 877 | 91.5 |
| Yes | 81 | 8.5 |
| Smoking habit ( $\mathrm{n}=957$ ) |  |  |
| No | 758 | 79.2 |
| Yes | 199 | 20.8 |
| Consumption of alcoholic beverages |  |  |
| No | 640 | 66.8 |
| Yes | 318 | 33.2 |
| Practice of physical activity ( $\mathrm{n}=957$ ) |  |  |
| Yes | 369 | 38.6 |
| No | 588 | 61.4 |

*BRL 998.00

Table 2. Crude and adjusted analysis of factors associated with multimorbidity among adult users of Primary Health Care. Passo Fundo (RS), 2019 ( $n=958$ ).

| Variables | Crude PR (95\%CI) | p | Adjusted PR (95\%CI) | p |
| :---: | :---: | :---: | :---: | :---: |
| $1^{\text {st }}$ level: demographic and socioeconomic variables ( $\mathrm{n}=857$ ) |  |  |  |  |
| Sex |  |  |  |  |
| Men | 1.00 | $0.875^{\dagger}$ | 1.00 | $0.321^{\dagger}$ |
| Women | 1.01 (0.87-1.18) |  | 1.09 (0.92-1.29) |  |
| Age in full years |  |  |  |  |
| 18-29 | 1.00 |  | 1.00 |  |
| 30-39 | 2.29 (1.48-3.55) | <0.001 ${ }^{\ddagger}$ | 2.29 (1.49-3.53) | $<0.001^{\ddagger}$ |
| 40-49 | 3.74 (2.53-5.54) |  | 3.82 (2.58-5.66) |  |
| 50-59 | 5.63 (3.65-8.67) |  | 5.47 (3.54-8.45) |  |
| Self-reported skin color |  |  |  |  |
| White | 1.00 | $0.824^{\dagger}$ | 1.00 | $0.519^{\dagger}$ |
| Other | 0.98 (0.78-1.22) |  | 1.08 (0.86-1.64) |  |
| Level of education |  |  |  |  |
| Elementary school | 1.00 |  | 1.00 |  |
| High school | 0.76 (0.64-0.91) | $0.008^{\S}$ | 0.96 (0.81-1.14) | $0.511^{\S}$ |
| College education | 0.88 (0.68-1.13) |  | 1.14 (0.88-1.48) |  |
| Marital status |  |  |  |  |
| Without spouse | 1.00 | $0.346^{\dagger}$ | 1.00 | $0.179^{\dagger}$ |
| With a spouse | 1.10 (0.91-1.32) |  | 1.13 (0.95-1.35) |  |
| Paid work |  |  |  |  |
| No | 1.00 | $0.008^{\dagger}$ | 1.00 | $0.055^{\dagger}$ |
| Yes | 0.80 (0.67-0.94) |  | 0.83 (0.69-1.00) |  |
| Monthly per capita family income* |  |  |  |  |
| >1 minimum wage | 1.00 | $0.587^{\dagger}$ | 1.00 | $0.745^{\dagger}$ |
| $\leq 1$ minimum wage | 0.95 (0.78-1.15) |  | 1.03 (0.86-1.24) |  |
| $2{ }^{\text {nd }}$ level: health characteristics ( $\mathrm{n}=840$ ) |  |  |  |  |
| Self-perception of health |  |  |  |  |
| Positive | 1.00 | <0.001 ${ }^{\text {+ }}$ | 1.00 | <0.001 ${ }^{\dagger}$ |
| Negative | 2.29 (1.84-2.85) |  | 1.61 (1.29-2.01) |  |
| Overweight |  |  |  |  |
| No | 1.00 | <0.001 ${ }^{\dagger}$ | 1.00 | <0.001 ${ }^{\dagger}$ |
| Yes | 4.07 (2.89-5.72) |  | 3.14 (2.21-4.44) |  |
| Polypharmacy |  |  |  |  |
| No | 1.00 | <0.001 ${ }^{\dagger}$ | 1.00 | <0.001 ${ }^{\dagger}$ |
| Yes | 3.11 (2.69-3.60) |  | 1.55 (1.33-1.81) |  |
| $3{ }^{\text {rd }}$ level: lifestyle habits ( $\mathrm{n}=838$ ) |  |  |  |  |
| Smoking habit |  |  |  |  |
| No | 1.00 | $0.447^{\dagger}$ | 1.00 | $0.221^{\dagger}$ |
| Yes | 0.92 (0.73-1.15) |  | 0.88 (0.71-1.08) |  |
| Consumption of alcoholic beverages |  |  |  |  |
| No | 1.00 | $0.006{ }^{\dagger}$ | 1.00 | $0.758^{\dagger}$ |
| Yes | 0.74 (0.60-0.92) |  | 0.97 (080-1.18) |  |
| Practice of physical activity |  |  |  |  |
| Yes | 1.00 | $0.276{ }^{\dagger}$ | 1.00 | $0.033^{\dagger}$ |
| No | 0.89 (0.72-1.10) |  | 0.81 (0.66-0.98) |  |

[^1]According to the literature, the condition is related to increasing age, ${ }^{6}$ which was also verified in this study, with a linearly higher prevalence as years of life increases. This can be explained by the fact that with aging, the body's natural process, the human body modifies its homeostasis, decreasing its effectiveness against endogenous and exogenous agents and thus increasing the risk for the onset of diseases. ${ }^{19}$

In addition, inadequate lifestyle habits, such as smoking and excessive alcohol consumption, are recognized risk factors for the increased frequency of NCDs. ${ }^{20,21}$ However, in this study, we observed no association between multimorbidity and smoking and alcohol consumption, which can be explained by the possibility of reverse causality, as avoiding smoking and alcohol is part of the non-drug therapy of many NCDs. It is, therefore, a basic and fundamental recommendation, especially among adults assisted by PHC.

Regarding self-perception of health, authors of a study carried out on older people in northern Rio Grande Sul showed that multimorbidity is associated with a negative self-perception of health. ${ }^{22}$ We verified the same association in this study, although with a sample of adults. The relation between the factors can be explained by the fact that individuals with multimorbidity have a deficit in self-care concerning their health, worse quality of life, and a greater degree of dependence for activities of daily living, with negative repercussions on their functional capacity. ${ }^{23}$

Moreover, the association between polypharmacy and multimorbidity in the older adult population is known, ${ }^{22}$ which was also verified in this study. Simultaneous use of several medications and reports of poor or terrible health seem to be a consequence of the accumulation of chronic diseases, and not the opposite. Polypharmacy can be justified by the frequent need of older adults to take medication for the treatment of chronic diseases, while self-perception regarding their health tends to be negative due to the greater number of hospitalizations of these older adults due to multimorbidity. ${ }^{24}$

With regard to the association between overweight and multimorbidity, the results indicate that it is positive, which corroborates previous findings from a study also carried out on adults. ${ }^{25}$ This reiterates the fact that obesity is an underlying risk factor for a number of chronic diseases and, consequently, for multimorbidity.

As for the practice of physical activity, authors of a survey carried out on adults in the state of Santa Catarina, Brazil, observed that it is a protective factor against multimorbidity. ${ }^{26}$ However, in our study, we verified that the probability of the outcome is lower among those who do not practice physical activity, a finding that possibly derived from the reverse causality between the variables.

Regarding level of education, researchers of a study carried out in the United States of America found that, among adults aged 30-64 years, lower levels of education were associated with greater chances of multimorbidity. ${ }^{10}$ In Brazil, authors of a research conducted in Pelotas (RS) also verified such association. ${ }^{6}$ However, in the present study, multimorbidity is not associated with low levels of education.

Likewise, in the present investigation, the participants' skin color was not associated with the outcome, which is not in line with the literature; ${ }^{6}$ in addition, we identified no association between per capita income, paid work, sex, ${ }^{6,12}$ alcohol consumption, and smoking habit. ${ }^{20}$

One of the possibilities for such divergences is that the aforementioned studies were not conducted exclusively with PHC users. Differences may arise from regional differences in population profiles, originating from the historical context of settlement and population constitution, as well as from differences in economic and social development and access to healthcare services.

It is noteworthy that this is one of the few studies to analyze multimorbidity in adults. Furthermore, it is worth emphasizing that over $70 \%$ of Brazilians use public healthcare services and, among them, approximately $48 \%$ have Health Centers (Unidades Básicas de Saúde - UBS) as the main gateway to the system. ${ }^{18}$ Thus, research like ours, which aim to investigate PHC users, become fundamental, especially regarding conditions that can bring harmful consequences to health, as is the case of multimorbidity.

As a limitation of the study, it should be noted that the presented results may be under- or overestimated due to the possibility of information bias, as the NCDs computed in the definition of the outcome were evaluated by medical diagnosis self-reported by the interviewees, and not independently by a specialist or verified in medical records. Although respondents can be aware of their condition, this cannot be taken with the certainty that would be attributed if the illnesses were objectively measured.

In addition, as this is a sample of PHC users composed of those who sought care at healthcare services during the data collection period, we must consider the possibility of selection bias by favoring the inclusion of those with compromised health. This could generate overestimated results in terms of estimated prevalence, as well as leading to a lack of association with some of the independent variables potentially related to the outcome. Furthermore, it is worth stressing the possibility of reverse causality between some independent variables and the outcome, as this is a cross-sectional study. And, finally, considering that this is a selection of a broader research, with a small sample size, there may not have been enough statistical power in some comparisons.

## CONCLUSION

We identified the prevalence of multimorbidity in the sample and described the PHC user population in Passo Fundo (RS).

By observing the demographic variables, we confirmed that multimorbidity is more frequent in overweight people, individuals using polypharmacy, and with a negative perception of health; however, there was no association with women and level of education.

Thus, we expect that this scenario related to multimorbidity in Passo Fundo will alert healthcare professionals about the prevalence and the sociodemographic and health profile that these patients present, aiming at establishing early diagnoses as well as the treatment and proper follow-up of diseases, especially in PHC. Moreover, we suggest that research be carried out in other places, with adult samples composed exclusively of PHC users and the general population, aiming to better elucidate the prevalence of multimorbidity and associated factors in this population. Consequently, the results can serve as a basis for the definition of public health and education policies and intervention strategies aimed both at raising awareness and specific care and at an increasingly early prevention of NCDs in the different age groups of the population, in such a way to positively impact morbidity and mortality indicators.

## CONFLICT OF INTERESTS

Nothing to declare.

## AUTHORS' CONTRIBUTIONS

VES: Project administration, Conceptualization, Writing - original draft, Writing - review \& editing, Investigation, Methodology, Software. MB: Formal analysis, Writing - review \& editing, Investigation, Supervision. GOA: Formal analysis, Writing - review \& editing. ILL: Project administration, Formal analysis, Data curation, Writing - review \& editing, Software, Supervision, Validation.

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[^0]:    How to cite: Albergaria VE, Biffi M, Acrani GO, Lindemann IL. Multimorbidity and associated factors in adult users of Primary Health Care in northern Rio Grande do Sul, Brazil. Rev Bras Med Fam Comunidade. 2023;18(45):3504. https://doi.org/10.5712/rbmfc18(45)3504

[^1]:    *BRL 998,00; ${ }^{\text {tchi-square test; }}$ flinear trend test; sheterogeneity test.

