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Association of Sleep Duration and Use of Sleeping Medication with Multimorbidity in Adults: Results from the PAMPA (Brazil) Cohort Study

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Abstract

Objective To analyze the association of sleep duration and use of sleeping medication with multimorbidity.

Materials and Methods We conducted a cross-sectional study using data from the Prospective Study about Mental and Physical Health (PAMPA) cohort. Multimorbidity was defined as the presence of two or more conditions from a list of twelve health problems. Descriptive analyses were performed considering proportion and its 95% confidence interval (95%CI). We performed logistic regression (to obtain odds ratios, ORs) to estimate the associations, including models adjusted for confounding factors.

Results In total, 2,936 participants were included, 79,1% of them women, 54.2% aged between 18 and 39 years, and 88.9% with white skin color. Compared with regular sleep (seven to eight hours a day), five hours or less of sleep increased the odds of multimorbidity by 145% (95%CI: 1.90–3.14), and 9 hours or more of sleep increased the odds by 49% (95%CI: 1.14–1.95) for the crude model; the results remained significant even in the adjusted models.

Discussion Consumption of sleeping medication was associated with multimorbidity. Short and prolonged sleep duration increased the odds of multimorbidity, regardless of the sociodemographic and behavior characteristics. The regular use of sleeping medication was also associated with multimorbidity. The results of the present study are important but require caution due to reverse causality, and longitudinal studies are needed to confirm the findings.

Keywords
- diseases
- multimorbidity
- sleep
- sleep deprivation

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Introduction

Multimorbidity has been defined as the presence of two or more health issues;[1] however, there is no clear consensus regarding its concept and evaluation methods. A review[2] on the prevalence of multimorbidity that included 68 articles found high heterogeneity, especially in the number of diseases investigated, which ranged from 4 to 40 among the studies. Moreover, a recent review[3] found a variety of measures of multimorbidity, including two main groups, one consisting of a simple count of diseases from a list and another with a weighting for the chronic conditions included. With the high heterogeneity, it becomes challenging to standardize a way of measuring multimorbidity. The prevalence of multimorbidity may vary from 29.7% in low- and middle-income countries to 37.9% in high-income countries.[2] Other variations can be observed according to the number of diseases evaluated, measurement methods (subjective or objective), and cutoff point.[2] In Brazil, $\sim$ 25% of the population is diagnosed with multimorbidity,[4,5] with a higher prevalence in older adults and women.[4–6] Recent evidence[7] suggests an increase in multimorbidity prevalence in Brazilian adults, from 18.7% in 2013 to 22.3% in 2019. Data from high-income countries also showed that multimorbidity has increased in the last few years.[8,9] Low quality of life,[10] mental health problems,[10] and early death[11] may be listed as consequences of multimorbidity. Moreover, the coronavirus disease 2019 (COVID-19) pandemic impacted the routine of health systems, reducing access to healthcare among people with chronic diseases.[12]

Population aging may explain in part the occurrence of multimorbidity;[9] however, several other factors might be related to new cases,[9] such as the quality and duration of sleep. People who sleep around seven to eight hours regularly are more likely to live one to three years more without chronic diseases when compared with those who sleep less than seven or more than nine hours a day.[13]

Longitudinal studies[14] have evidenced that short sleep duration increases the risk of chronic conditions, such as stroke and cancer. Moreover, data from 27 cohort samples,[15] including more than 1.3 million participants, evidenced that short sleep duration increased the risk of all-cause mortality by 12%, whereas long sleep duration increased it by 30%. A recent meta-analysis[16] showed that people who sleep less than seven hours a day had an increased risk of all-cause mortality. Furthermore, in comparison to adequate sleep duration ($\sim$seven hours a day), an increase or decrease in an hour of sleep increases the risk of cardiovascular disease.[16]

A study[17] with data from Brazilian Basic Health Care Units patients associated sleep disorders with chronic diseases such as osteoporosis, arthritis/osteoarthritis, low back pain, depression, and obesity. Another study[18] evidenced the association of short sleep duration with comorbidities and unhappiness. Given the growing evidence linking short and prolonged sleep duration to disease accumulation, carrying out a study with a representative sample of a Brazilian state maybe be helpful to provide evidence to health professionals and managers regarding case management, health promotion, and prevention of chronic diseases. In addition, the COVID-19 pandemic might have changed the time and quality of sleep,[19,20] which can impact the future prevalence of chronic diseases. Thus, we aimed to analyze the association of sleep duration and use of sleeping medication with multimorbidity.

Material and Methods

We conducted a cross-sectional study using data from wave 3 of the Prospective Study about Mental and Physical Health (PAMPA) cohort, a longitudinal study, with adults aged 18 or older, performed in the state of Rio Grande do Sul, Brazil. The data 3 was collected between June and September 2021. The Research Ethics Board of the School of Physical Education of Universidade Federal de Pelotas, Brazil, approved the study (under protocol number 4.093.170)

Recruitment Phase

We contacted the participants through university professors, social media, local media, and personal contacts from all macro-regions in the state of Rio Grande do Sul during the recruitment phase.

Sample Size

The sample size was calculated based on the three primary outcomes of the cohort: low back pain, depressive and anxiety symptoms, and access to the healthcare system.[21] According to the last Brazilian Census (2010), the total population of the state of Rio Grande do Sul was of 10,693,929 inhabitants in 2010. A required sample of 1,767 participants was defined considering a 95% confidence level, a margin of error of 1.8, and a possible loss-to-follow-up rate of 30%. The state was divided into seven macro-regions (with the names in Portuguese): Serra, Norte, Nordeste, Centro-Oeste, Vales, Metropolitana, and Sul. The required sample size was divided proportionally to the number of people living in each region.

Outcomes

The primary outcome was multimorbidity, defined as the presence of two or more and three or more health issues. We assessed multimorbidity using the same question previously used by the Brazilian Telephone-based Surveillance System for Noncommunicable Diseases:[22] "Has any doctor ever told you that you have the following health issues?". Multimorbidity was defined based on the following diseases: hypertension or high blood pressure, diabetes, high levels of cholesterol, cancer, arthritis/arthrosis/fibromyalgia, asthma/bronchitis, back problems, heart disease, depression, memory problems, HIV/AIDS, and other chronic diseases.

Exposures

The primary exposure was the duration of sleep, assessed through the following question: "Thinking about the last two weeks, how many hours per night did you sleep on average?". Based on this question, sleep duration was categorized as follows: 1) five hours or less; 2) six hours; 3) seven to eight hours (adequate sleep); and 4) nine hours or more.

Sleeping medication was used as additional exposure, categorized through the following yes-no question: "In the last two weeks, did you use any medication to sleep?".

The following sociodemographic variables were considered as potential confounders: sex (male or female); age in years (18–39, 40–59, and $\geq$ 60 years); skin color (white or non-white); level of schooling (secondary or lower, higher education, and specialized, masters, or Ph.D.). The behavioral variables included: practice of physical activity in the previous week, categorized as "No" or "Yes," as well as smoking, which was classified as "smoker," "former smoker," or "never smoked."

Data Analysis

Descriptive data were reported as proportions with a 95% confidence interval (95%CI). Data were presented for the total sample and stratified according to multimorbidity occurrence (two or more diseases and three or more diseases). For the association analysis, seven to eight hours of sleep per night was considered the reference, whereas the other categories were used as exposure. As for sleeping medications, their use was considered exposure, whereas non-use was considered the reference. Crude and multivariable analyses were performed using the logistic regression model and reported as odds ratio (ORs) with 95%CIs. Regarding the multivariable analysis, two models were built: 1) adjusting sleeping duration to sociodemographic variables (age, sex, skin color, and level of schooling), and; 2) adjusting sleeping duration to model 1, behavioral variables (physical activity and smoking), in addition to sleep duration and sleeping medication. The analyses were performed using the Stata (StataCorp, College Station, TX, US) software, version 15.1.

Results

►**Table 1** shows the sociodemographic and behavioral characteristics of the general sample and according to the

Table 1 Sociodemographic and behavioral characteristics of the study participants ($N = 2{,}936$).

Characteristics	Total sample (N)	Total sample (%): mean (range)	Proportion of participants with MM2: mean (range)	Proportion of participants with MM3: mean (range)
Sex				
Male	678	20.9 (19.6–22.4)	38.0 (34.3–42.0)	20.0 (17.0–23.7)
Female	2,560	79.1 (77.6–80.4)	50.7 (48.6–52.7)	30.6 (28.8–32.5)
Age (years)				
18–39	1,746	54.2 (52.5–55.9)	33.7 (31.5–36.1)	17.1 (15.4–19.1)
40–59	1,137	35.3 (33.7–37.0)	64.3 (61.3–67.2)	41.3 (38.3–44.3)
$\geq$ 60	338	10.5 (9.5–11.6)	72.2 (66.7–77.1)	46.5 (40.7–52.3)
Skin color				
White	2,866	88.9 (87.8–90.0)	48.0 (46.1–50.0)	28.1 (26.5–30.0)
Non-white	357	11.1 (10.0–12.2)	48.4 (42.9–54.0)	30.6 (25.8–36.0)
Level of Schooling				
Secondary or lower	1,163	35.9 34.2–37.6	48.2 45.1–51.3	30.6 (27.8–33.5)
Higher education	780	24.1 22.6–25.6	47.9 44.3–51.6	27.4 (24.3–30.9)
Specialized, masters, PhD	1,298	40.0 (38.4–41.7)	48.0 (45.2–50.8)	27.2 (24.7–29.7)
Sleep duration (hours)				
$<$ 5	1,650	11.3 (10.1–12.5)	65.1 (59.8–70.1)	47.8 (42.4–53.3)
6	324	22.9 (21.4–24.5)	49.9 (46.1–53.7)	28.8 (25.5–32.4)
7–8	659	57.3 (55.5–59.1)	43.3 (40.9–45.7)	23.7 (21.7–25.8)
$\geq$ 9	246	8.5 (7.6–9.6)	53.3 (47.0–59.4)	34.1 (28.5–40.3)
Sleeping medication				
No	2,454	84.6 (83.3–85.9)	43.2 (41.2–45.1)	23.5 (21.9–25.2)
Yes	445	15.4 (14.1–16.7)	75.1 (70.8–78.9)	55.5 (50.8–60.1)
Physical activity (previous week)				
No	1,455	49.6 (47.8–51.4)	55.1 (52.5–57.6)	33.3 (30.9–35.7)
Yes	1,479	50.4 (48.6–52.2)	41.1 (38.6–43.6)	23.4 (21.3–25.6)

Abbreviations: MM2, multimorbidity: two or more diseases; MM3, multimorbidity: three or more diseases.

Table 2 Association of sleep duration and sleeping medication use with multimorbidity ($N = 2{,}869$).

	Crude OR (95%CI)	Model 1 OR (95%CI)	Model 2 OR (95%CI)
Two or more diseases			
Daily sleep duration (hours)			
7–8	Ref.	Ref.	Ref.
< 5	2.45 (1.90–3.14)	2.41 (1.88–3.10)	1.80 (1.36–2.38)
6	1.31 (1.09–1.57)	1.30 (1.08–1.56)	1.26 (1.03–1.54)
≥ 9	1.49 (1.14–1.95)	1.60 (1.20–2.13)	1.44 (1.07–1.94)
Sleeping medication			
No	Ref	Ref	Ref
Yes	3.96 (3.15–4.98)	3.85 (3.06–4.85)	3.41 (2.67–4.36)
Three or more diseases			
Daily sleep duration (hours)			
7–8	Ref.	Ref.	Ref.
< 5	2.95 (2.31–3.78)	2.81 (2.19–3.60)	2.12 (1.61–2.79)
6	1.30 (1.06–1.60)	1.29 (1.05–1.58)	1.24 (0.99–1.55)
≥ 9	1.67 (1.25–2.22)	1.72 (1.27–2.33)	1.57 (1.14–2.15)
Sleeping medication			
No	Ref.	Ref.	Ref.
Yes	4.06 (3.29–5.00)	3.93 (2.19–4.86)	3.46 (2.77–4.32)

Abbreviations: 95%CI, 95% confidence interval; N, number; OR, odds ratio.
Notes: Model 1: adjusted for age, sex, skin color, and level of schooling. Model 2: adjusted for model 1 plus physical activity, smoking. When the sleep duration was exposure, the model was adjusted for sleeping medication and vice versa.

occurrence of multimorbidity. A total of 2,936 subjects were included (79.1% of them women). Most of the participants were aged between 18 and 39 years (54.2%; 95%CI: 52.5–55.9%) and were white (88.9%; 95%CI: 87.8–90.0%).

Regarding sleep duration, 57.3% (95%CI: 55.5–59.1%) of the participants slept 7 to 8 hours. A linear positive association between multimorbidity and age was observed, with older individuals having a higher prevalence of multimorbidity than younger subjects, both for two or more and three or more diseases. Comparing the practice of physical activity in the previous week, the prevalence of multimorbidity was lower among those who reported practicing physical activity at both cutoff points for multimorbidity.

►**Fig. 1** shows that the prevalence of multimorbidity was higher among those with short sleep duration compared with the total sample, as well as for those with long sleep duration. Regarding patients with adequate sleep time (seven to eight hours a day), the proportion of multimorbidity was lower. The prevalence of multimorbidity was higher among participants who reported the use of sleeping medication.

►**Table 2** shows the association of sleep duration and sleeping medication use with multimorbidity, considering multimorbidity as ≥ 3 diseases, ≤ 5 hours of sleep a day increased the odds by 195% (OR: 2.95; 95%CI: 2.31–3.78). Nine or more hours also increased the multimorbidity odds compared with the reference group (OR: 1.67; 95%CI: 1.25–2.22). The use of sleeping medication increased the odds of multimorbidity by 306% (OR: 4.06; 95%CI: 3.29–5.00). Prolonged sleep duration (nine hours or more per day) was associated with multimorbidity, increasing its odds by 83% (OR: 1.49; 95%CI: 1.14–1.95). Compared with non-users of sleeping medication, the users had a high probability of having multimorbidity (OR: 3.96; 95%CI: 3.15–4.98).

Discussion

The present cross-sectional study evaluated the association between sleep duration and sleeping medication with multimorbidity during the COVID-19 pandemic. Our results showed that the prevalence of multimorbidity was lower among individuals with regular sleep (seven to eight hours a day) compared with the total sample. Otherwise, the prevalence was higher among those sleeping less than five hours a day and nine hours or more. Short and prolonged sleep duration were associated with multimorbidity (for two or more or there or more diseases), even after the adjustment for sociodemographic and behavioral characteristics. The use of sleeping medication increased the probability of having multimorbidity in the crude and adjusted analyses. This association may occur due to drug interaction; therefore, more studies evaluating this association are required. Despite this, a study[23] presented null results for chronic diseases (OR: 1.89; 95%CI: 0.56–6.35).

Cross-sectional analyses from the Canadian Longitudinal Study on Aging (CLSA) evidenced a high probability of

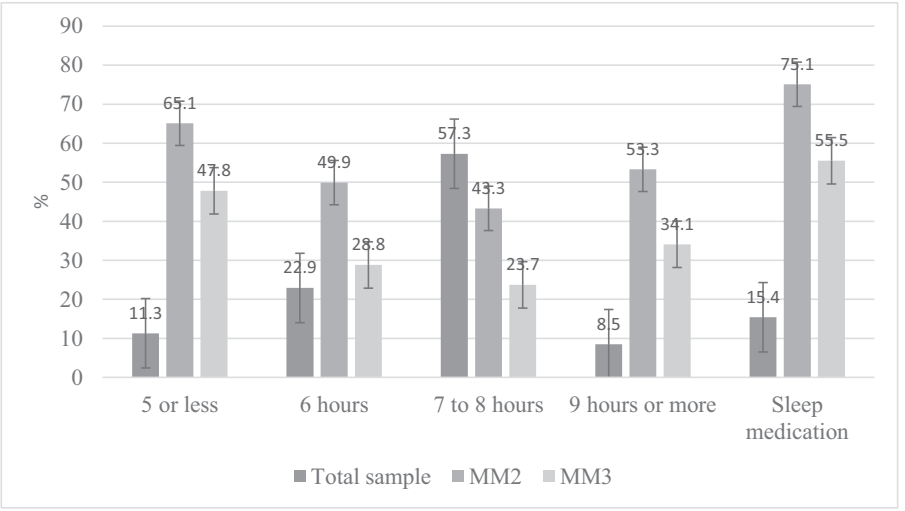

Fig. 1 Frequency of sleep duration and use of sleeping medication for the total sample and among multimorbidity participants.

multimorbidity among participants with short or long sleep duration.[24] A longitudinal study[25] using data from the Swedish National Study of Aging and Care in Kungsholmen, showed that moderate and severe sleep disturbances were associated with the accumulation of chronic diseases, in addition to neuropsychiatric and musculoskeletal conditions. However, for cardiovascular diseases, the results were not significant.[25] In older adults from the Cooperative Health Research in Augsburg (KORA), Germany, neither short nor long daily sleep duration was associated with multimorbidity among men. In contrast, among women, both short ($\leq$ 5 hours a day) and prolonged ($\geq$ 10 hours a day) sleep duration were significantly associated with multimorbidity.[26] In Luxembourg, between 2013 and 2015, Ruiz-Castell et al.[23] presented an association between short sleep duration and the number of chronic conditions, regardless of socioeconomic and behavioral characteristics. Short sleep duration may be a risk factor for several chronic conditions, including cardiovascular and metabolic diseases,[27] which represents the current findings of the present study. So far, the results for some diseases, such as cardiovascular diseases, are inconclusive for men, and more studies are needed. However, for the accumulation of conditions (multimorbidity), the association is more solid.

Regarding the quality of sleep, data from the China Health and Retirement Longitudinal Study[28] showed that participants with poor-quality sleep had a higher probability of having multimorbidity compared with those with good-quality sleep. However, this parameter was not evaluated in the present study, making the comparison with other studies unfeasible.

Several mechanisms may explain the association between short sleep duration and health issues. Among the consequences of sleep disturbances, changes in circadian rhythms stand out.[29] An unregulated circadian rhythm can exert deleterious effects on the human body.[30] The molecular circadian clock has functions in several cells in the human body and exerts temporal control over the physiological activity of different tissues and organs.[31] Results from the Whitehall II Study[32] showed that short sleep duration was associated with lower scores on most cognitive function tests. Sleep deprivation was also associated with reduced attention and working memory, in addition to long-term memory reduction and decision-making.[33] Moreover, sleep deprivation may result in a complex set of changes in brain activity and connectivity.[34]

Short sleep duration may result in several consequences for health, such as stress responsivity, somatic issues, reduced quality of life, emotional distress, in addition to mental and memory problems.[29] On the other hand, prolonged sleep duration (here categorized as nine or more hours a day) may lead to chronic diseases, including hypertension, dyslipidemia, cardiovascular diseases, obesity, metabolic syndrome, and diabetes.[29,35,36] Such implications may explain the results of the present study, since multimorbidity comprises most of these health issues.

As observed in our results, in addition to the impact of sleep disorders on several functions of the human body, these changes can cause the accumulation of different chronic diseases, worsening quality of life. Strategies such as exercises, meditation, and healthy eating can improve sleep quality.[37–39] In a meta-analysis with 18 trials and more than 1600 participants, Rusch et al.[38] found evidence that mindfulness meditation may enhance sleep quality. Another meta-analysis,[39] including 557 participants, showed that exercise improved sleep quality without notable adverse effects.

Our data were collected during the COVID-19 pandemic, and they may provide important information on both the burden of multimorbidity and sleep patterns that may have been altered throughout the pandemic. Recently, evaluating data from waves 1 and 2 of the PAMPA study, we found a 27.1% incidence of multimorbidity, with higher rates among women and the elderly.[40] A cross-sectional study[41] conducted in Brazil during the pandemic pointed out that sleep

quality significantly worsened during social distancing. Furthermore, in an online survey[42] of just over 45 thousand respondents from Brazil, 43.5% of the sample reported sleep issues during the pandemic.

To the best of our knowledge, the present is the first study with a Brazilian population investigating the associations of sleep duration and medication use with multimorbidity during the COVID-19 pandemic. The present study includes a high number of participants from one of the largest states in the Brazil. However, the study also has some limitations. First, the fact that the multimorbidity was self-reported may have caused us to include fewer patients with it than there are in reality, as some participants may not know they have a specific chronic condition. The second limitation refers to the fact that our study did not include questions about sleep quality. Finally, the cross-sectional design may imply reverse causality in our association of interest (multimorbidity and sleep duration). Despite this, longitudinal studies with other populations[25,28] have reported results similar to ours, demonstrating that inadequate sleep duration and sleep disturbances are associated with multimorbidity. With the present findings, we recommend that longitudinal studies and clinical trials be performed to confirm the association found in our analyses.

As a conclusion, short (five hours or less) and prolonged (nine hours or more) sleep duration increased the odds of multimorbidity, regardless of sociodemographic and behavioral characteristics. The use of sleeping medication was also associated with multimorbidity. The results of the present study are important but require caution due to reverse causality, and longitudinal studies are needed to confirm the findings.

Conflict of Interests

The authors have no conflict of interests to declare.

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