ORIGINAL ARTICLE

Correlation between physical activity practice and mortality from COVID-19: an ecological study

Correlação entre prática de atividade física e mortalidade por COVID-19: um estudo ecológico

Correlación entre la práctica de actividad física y la mortalidad por COVID-19: un estudio ecológico

Lucas Paes de Oliveira¹ ORCID 0000-0002-7096-496X Helena Martinez Faria Bastos Régis Hughes¹ ORCID 0000-0001-5718-2173 Raquel Alencastro Veiga Domingues Carneiro¹ ORCID 0000-0002-0770-9771 Cleverton José Teixeira da Silva¹ ORCID 0000-0001-7108-9717 Kamille Feltrin Ronsoni¹ ORCID 0000-0002-6944-5791 Andreia Morales Cascaes¹ ORCID 0000-0001-9412-8299 Danúbia Hillesheim¹ ORCID 0000-0003-0600-4072 Ana Luiza de Lima Curi Hallal¹ ORCID 0000-0003-4761-0001

¹Universidade Federal de Santa Catarina Florianópolis, SC, Brasil

Endereço: Rua Delfino Conti, S/N, Bloco H, Florianópolis, SC, Brasil. E-mail: nubiah12@yahoo.com.br

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ABSTRACT

Background and objective: new population-level studies are needed to better assess the relationship between physical inactivity and mortality from COVID-19. The aim of the study was to evaluate the correlation between population prevalence of physical activity and standardized mortality rates by COVID-19 in Brazilian capital cities and the Federal District. **Methods**: this is an ecological study, whose analysis is secondary. The prevalence of physical inactivity, insufficient physical activity, and physical activity during free time was obtained from the Surveillance of Risk Factors and Protection for Chronic Diseases by Telephone Survey 2019 (VIGITEL), according to minutes spent on leisure, commuting, and household activities. The COVID-19 mortality data was obtained

from the Influenza Epidemiological Surveillance Information System (SIVEP-Gripe), adding the accumulated deaths until December 31, 2020. The resident population was estimated from the Instituto Brasileiro de Geografia e Estatística (IBGE) for the year 2020. Pearson Correlation evaluated the correlation between the prevalence of different physical activity practices and the standardized mortality rate from COVID-19, in total, and according to age groups. **Results:** there was a significant positive correlation (r = 0.420; p = 0.029) between the overall prevalence of insufficient physical activity and the standardized COVID-19 mortality rate. No correlation was observed between the other prevalence of physical activity and the standardized mortality rate from COVID-19. **Conclusion:** there was a correlation between insufficient levels of physical activity and the standardized mortality rate from COVID-19.

Keywords: COVID-19; Mortality; Physical Exercise; Sedentary Behavior; Correlation of Data.

RESUMO

Justificativa e objetivo: novos estudos em nível populacional são necessários para avaliar a relação entre inatividade física e mortalidade por COVID-19. O objetivo deste estudo foi avaliar a correlação entre as prevalências populacionais de prática de atividade física e as taxas padronizadas de mortalidade por COVID-19 nas cidades capitais brasileiras e no Distrito Federal. Métodos: trata-se de um estudo ecológico, cuja análise é secundária. As prevalências de inatividade física, atividade física insuficiente e atividade física no tempo livre foram obtidas do inquérito Vigilância de Fatores de Risco e Proteção para Doenças Crônicas por Inquérito Telefônico 2019 (VIGITEL). Os dados de mortalidade por COVID-19 foram obtidos do Sistema de Informação de Vigilância Epidemiológica da Gripe (SIVEP-Gripe), somando os óbitos acumulados até 31 de dezembro de 2020. A população residente foi estimada a partir do Instituto Brasileiro de Geografia e Estatística (IBGE) para o ano de 2020. A Correlação de Pearson avaliou a correlação entre a prevalência de diferentes práticas de atividade física e a taxa padronizada de mortalidade por COVID-19, no total e segundo faixas etárias. **Resultados:** houve correlação significativa positiva (r = 0,420; p = 0,029) entre a prevalência geral de atividade física insuficiente e a taxa padronizada de mortalidade por COVID-19. Não foi observada correlação entre as demais prevalências de prática de atividade física e taxa padronizada de mortalidade por COVID-19. Conclusão: houve correlação entre os níveis insuficientes de atividade física e a taxa padronizada de mortalidade por COVID-19 em pessoas que vivem nas cidades capitais brasileiras.

Palavras-chave: COVID-19; Mortalidade; Exercício Físico; Comportamento Sedentário; Correlação de Dados.

RESUMEN

Justificación y objetivo: nuevos estudios a nivel poblacional son necesarios para evaluar la relación entre la inactividad física y la mortalidad por COVID-19. Evaluar la correlación entre la prevalencia poblacional de actividad física y las tasas estandarizadas de mortalidad por COVID-19 en las capitales brasileñas y el Distrito Federal. **Métodos:** se trata de un estudio ecológico, cuyo análisis es secundario. Las prevalencias de sedentarismo, actividad física insuficiente y actividad física en el tiempo libre se obtuvieron de la Encuesta Telefónica de Vigilancia de Factores de Riesgo y Protección de Enfermedades Crónicas 2019 (VIGITEL). Los datos de mortalidad por COVID-19 se obtuvieron del Sistema de Información de Vigilancia Epidemiológica de Influenza (SIVEP-Gripe), sumando las muertes acumuladas hasta el 31 de diciembre de 2020. La población residente se estimó del Instituto Brasileiro de Geografia e Estatística (IBGE) para el año. 2020. Pearson Correlation evaluó la correlación entre la prevalencia de diferentes prácticas de actividad física y la tasa de mortalidad estandarizada por COVID-19, en total y según grupos de edad. **Resultados:** hubo una correlación positiva significativa (r = 0,420; p = 0,029) entre la prevalencia general de actividad física insuficiente y la tasa de mortalidad estandarizada por COVID-19. No se observó correlación entre la otra prevalencia de actividad física y la tasa de mortalidad física y la tasa de mortalidad estandarizada por COVID-19. Conclusión: hubo una correlación entre los niveles insuficientes de actividad física y la tasa de mortalidad estandarizada por COVID-19 en personas que viven en las capitales brasileñas.

Palabras clave: COVID-19; Mortalidad; Ejercicio Físico; Comportamiento Sedentario; Correlación de Datos.

INTRODUCTION

The first alert of a possible Public Health Emergency of International Concern (PHEIC) reporting the emergence of pneumonia of unknown cause in Wuhan, China, was released by the International Health Regulations (IHR, 2005) on December 31, 2019. Soon, researchers from the World Health Organization (WHO) gathered to identify the new infectious agent from the spread of cases to other Asian countries, until the outbreak was finally declared as PHEIC on January 30, 2020.¹

After more than a year of its beginning, the pandemic epicenter moved from the Asian continent to the Americas region, which, in December 2021, had more than 96 million cases of the disease (37.01% of the world total) and 2.3 million deaths (45.06% of the world total). Looking at Latin America, Brazil stands out by ranking third in the global ranking of disease cases, with about 22 million cases, and second in the world ranking of deaths, with approximately 614,000 deaths.² The challenge that COVID-19 poses for the Brazilian territory is accentuated by regional differences, with an uneven distribution of mortality and infections by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) among states.^{3,4} Such regional differences have already been discussed by another study, which found higher mortality from COVID-19 in the northern region of the country, when compared with the same variable in the southeast

region. The authors related this difference in mortality to the greater number of comorbidities present in places with a lower level of socioeconomic development.⁵

Regarding comorbidities considered risk factors for death from COVID-19, until October 2021, the Centers for Disease Control and Prevention (CDC) highlighted arterial hypertension, cardiovascular diseases, diabetes, cancer, chronic kidney disease, chronic lung disease, advanced age, and obesity as aggravating factors and indicators of poor prognosis.⁶ However, the search for new risk factors associated with SARS-CoV-2 infection remains active. The regular practice of physical activity is already being discussed in the medical literature as a protective factor against chronic non-communicable diseases such as breast cancer, colorectal cancer, type II diabetes mellitus, ischemic heart disease, coronary heart disease, and stroke.⁷ Regarding SARS-CoV-2 infection, a US hospital observational study associated constant physical inactivity with severe COVID-19 development. Also, in terms of poor disease evolution, the authors equate physical inactivity with other comorbidities and risk factors identified by the CDC, with the exception of advanced age and previous organ transplantation.⁸

Although this study suggests physical inactivity as a possible risk factor for COVID-19 mortality, further population-level studies are required to better understand this relationship. This is the first study to analyze variables of physical inactivity and insufficient physical activity prevalence correlated with COVID-19 mortality at the population level in capital cities in Brazil. Additionally, age stratification analysis can be an important factor in guiding actions, potentially generating implications for clinical practice.

Thus, considering the scarcity of population-level studies on the topic of physical inactivity as a possible risk factor for death from COVID-19, the unequal distribution of mortality rates in Brazilian territory and the availability of population-level data on these different variables, the present study aimed to evaluate the correlation between population prevalence of physical activity and standardized mortality rates by COVID-19 in Brazilian capital cities and the Federal District.

METHODS

Study design and data source

This is an ecological study, whose units of analysis were the 26 Brazilian capitals and the Federal District (FD). To obtain information about the practice of physical activity, data from the national Surveillance of Risk and Protection Factors for Chronic Diseases Survey by Telephone (VIGITEL) of the year 2019 was used. Managed by the Ministry of Health of Brazil, VIGITEL has collected data since 2006 on noncommunicable chronic diseases and associated factors in the population aged 18 years old and over, with the aim of knowing the health status of these people and guiding programs and actions that reduce the occurrence of chronic diseases.⁹ Detailed information about the VIGITEL sampling and data collection process was previously described.¹⁰ Furthermore, data on mortality from COVID-19 was obtained from the Severe Acute Respiratory Syndrome (SARS) database, made available by the Influenza Epidemiological Surveillance Information System (SIVEP-Gripe).¹¹ Deaths accumulated up to December 31, 2020 and with laboratory confirmation for COVID-19 in the same capital cities evaluated by VIGITEL were included. Data on the resident population of cities was obtained from the Instituto Brasileiro de Geografia e Estatística (IBGE), the Brazilian statistics bureau, in the year 2020.¹²

Death rate from COVID-19

First, the crude mortality rate for COVID-19 was calculated through the ratio of the number of deaths in each capital city divided by the estimated population of the same city, multiplied by 100,000 population. Then, the rates were standardized by age, using the direct method¹³ (10-year age groups), using the estimated age structure of the Brazilian population in 2020 as a standard. It is worth noting that this rate reflects the general population, as no data was found regarding the estimated population for 2020 in each capital city that included the age division " \geq 18 years old" for the standardization calculation.

Practice of physical activity

The practice of physical activity was assessed through three variables related to the prevalence of physical inactivity, insufficient physical activity, and physical activity during free time, as defined in VIGITEL, according to minutes spent on leisure, commuting, and household activities. Individuals who did not practice any physical activity in their free time in the last three months and who did not perform intense physical efforts at work, did not go to work or course/school by walking or cycling, for a minimum of 20 minutes in a one-way journey and, moreover, did not participate in the heavy cleaning of their homes were considered physically inactive. Individuals whose sum of minutes spent on physical activities in their free time, commuting to work/school and occupational activity did not reach the equivalent of at least 150 minutes per week of moderate intensity activities (or at least 75 minutes per week of vigorous-intensity activity) were classified as having insufficient physical activity. Finally, individuals with free time physical activity were those who practiced at least 150 minutes a week of moderate-intensity physical activity or commuting to school/work, or at least 75 minutes a week of vigorous-intensity physical activity. All variables were stratified according to age categories (18 to 24; 25 to 39; 40 to 59; 60 to 79; 80 years or older).¹⁰

Data analysis

Data was stored in *Microsoft Excel spreadsheets* and later exported and analyzed using software Stata , version 14.0 (StataCorp LP, College Station, United States). For the description of continuous variables, data was expressed as means, with their respective minimum and maximum values and 95% confidence intervals (95% CI). Shapiro-Wilk test was used to test the normality of the data for COVID-19 standardized mortality rate variable, in which the null hypothesis is that the population has a normal distribution. The prevalence of variables related to the practice of physical activity were weighted to adjust the sociodemographic distribution of the VIGITEL sample to the distribution of the city's adult population projected for the year 2019.

To assess the degree of correlation between the standardized mortality rate from COVID-19 and the variables related to the prevalence of physical inactivity, insufficient physical activity and physical activity during free time, Pearson's Correlation analysis was used to obtain the Coefficient Correlation (r), total and stratified for each age group (18 to 24; 25 to 39; 40 to 59; 60 to 79; 80 years or older). The statistical significance value adopted in this study was p < 0.05.

Ethical aspects

VIGITEL was approved by the Brazilian National Research Ethics Commission (CAAE: 65610017.1.0000.0008). The data used in this research is in the public domain and was analyzed in aggregate, without identifying the participants, without the need for approval of the Research Ethics Committee (CEP), according to resolution No. 510, of April 7, 2016, of the Brazilian National Council of Health (CNS).

RESULTS

The average standardized mortality rate from COVID-19 in Brazilian capitals and the FD was 125.1 deaths per 100,000 population. The lowest rate (51.6/100,000 population) was found in Florianópolis (SC) and the highest (246.6/100,000 population) was found in Porto Velho (RO) (Table 1).

Capital cities	Population	Deaths*	Crude mortality	Standardized
			rate ⁺	mortality rate ^{+,++}
Aracaju	664,908	898	135.1	147.3
Belém	1,499,641	2268	151.2	163.1
Belo Horizonte	2,521,564	2082	82.6	65.3
Boa vista	419,652	334	79.6	151.7
Campo Grande	906,092	1045	115.3	116.8
Cuiabá	617,848	646	104.6	122.1
Curitiba	1,948,626	2384	122.3	109.3
Florianópolis	508,826	310	60.9	51.6
Fortaleza	2,686,612	4267	158.8	174.3
Goiânia	1,536,097	1952	127.1	136.1
João Pessoa	817,511	1106	135.3	143.0
Macapá	512,902	284	55.4	101.0
Maceió	1,025,360	1192	116.3	136.5
Manaus	2,219,580	2962	133.4	221.1
Natal	890,480	1070	120.2	119.7
Palmas	306,296	199	65.0	126.0
Porto Alegre	1,488,252	1898	127.5	89.9
Porto Velho	539,354	763	141.5	246.6
Recife	1,653,461	3410	206.2	186.9
Rio Branco	413,418	491	118.8	188.1
Rio de Janeiro	6,747,815	10752	159.3	123.2
Salvador	2,886,698	2952	102.3	107.5
São Luís	1,108,975	1009	91.0	113.2
São Paulo	12,325,232	15553	126.2	112.1
Teresina	868,075	1168	134.6	168.6
Vitória	365,855	613	167.6	139.9
Distrito Federal	3,055,149	3930	128.6	160.9
Total capital cities	50,534,279	65,538	129.7	125.1

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Table 1. Estimated resident population in 2020, accumulated deaths, crude, and age-standardized COVID-19 mortality rates in the 26 capital cities and the Federal District. Brazil, 2020.

*Deaths registered until 12/31/20 with laboratory confirmation for the disease.

+ Rates calculated per 100,000 population.

+ Rate standardized by the direct method and by age, by the estimated population of Brazil in 2020.

Deaths from COVID-19 occurred predominantly in the age group 60 to 79 years old (48.4%), followed by the age groups ≥ 80 (28.7%) and 40 to 59 years old (18.8%). Among individuals aged less than or equal to 39 years old, 4.1% of the deaths occurred.

Regarding the total prevalence of physical activity (physical inactivity, insufficient physical activity, and physical activity in their free time), it was observed that, among adults, 41.1% practiced physical activities during their free time and 44.4% had insufficient practice. Individuals aged 60-79 and 80 years old or older had the highest prevalence of physical inactivity and insufficient physical activity, while the groups 18-24 and 25-39 years old had the highest prevalence of free-time physical activity (Table 2).

Variable*	Average Prevalence	95% CI	Minimum	Maximum
Physical inactivity				
18 to 24	12.8	11.3 - 14.4	6.6	24.5
25 to 39	11.3	10.0 - 12.5	7.3	21
40 to 59	10.9	10.1 - 11.7	7.4	14.8
60 to 79	24.1	22.5 - 25.8	15.8	31
80 or older	51.1	47.8 - 54.4	36.3	69.8
Total	14.0	13.2 - 14.8	10.2	17.4
Insufficient physical activity				
18 to 24	36.3	34.6 - 38.1	29.6	44.3
25 to 39	38.9	36.9 - 40.8	32	51.9
40 to 59	44.6	43.2 - 45.9	37.3	53.7
60 to 79	60.2	58.5 - 61.8	53	70
80 or older	80.5	78.4 - 82.6	67.8	90.3
Total	44.4	43.2 - 45.6	39	49.8
Physical activity during free time				
18 to 24	51.6	49.8 - 53.4	44.1	60.6
25 to 39	46.4	44.6 - 48.2	36.8	53.4
40 to 59	36.8	35.3 - 38.3	30.7	44.9
60 to 79	30.5	28.7 - 32.3	22.4	41.4
80 or older	16.7	14.5 – 18.9	6.4	30.6
Total	41.1	39.6 - 42.5	34.6	49.9

 Table 2. Average, minimum, and maximum prevalence of physical inactivity, insufficient physical activity, and free time in the 26 capital cities and the Federal District according to age groups. Brazil, 2019.

* Weighted prevalence to adjust the sociodemographic distribution of the Vigitel sample to the distribution of the adult population from each city projected for the year 2019.

A significant positive correlation (r = 0.420; p = 0.029) was found between the prevalence of insufficient physical activity and the standardized mortality rate from

COVID-19, in total. There was no significant correlation between the prevalence of physical inactivity and the standardized COVID-19 mortality rate (r = 0.293; p = 0.138) and between the prevalence of free-time physical activity and the standardized COVID-19 mortality rate (r = -0.153; p = 0.445), in total (Figure 1).

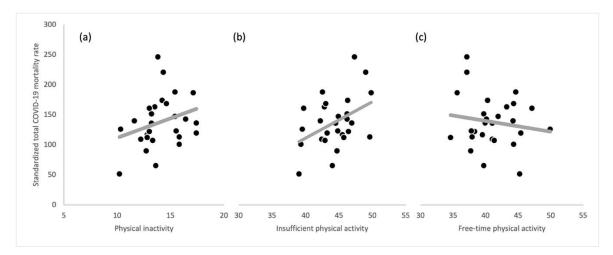


Figure 1. Correlation analysis between: (a) prevalence of total physical inactivity and standardized total COVID-19 mortality rate (r = 0.293; p = 0.138); (b) prevalence of total insufficient physical activity and standardized total COVID-19 mortality rate (r = 0.420; p = 0.029); (c) total free-time physical activity prevalence and total standardized COVID-19 mortality rate (r = -0.153; 0.445). Capital cities and the Federal District. Brazil. 2019-2020. $r = Pearson \ correlation \ coefficient$.

In the analysis stratified by age groups, a significant positive correlation was found between the prevalence of physical inactivity and the standardized rate of mortality from COVID-19 for groups aged 18 to 24 (r = 0.460; p = 0.015), 60 to 79 (r = 0.545; p = 0.003), and 80 years old or older (r = 0.648; p < 0.001). At the same time, a significant positive correlation was found between the prevalence of insufficient physical activity and the standardized COVID-19 mortality rate for groups aged 18 to 24 (r = 0.426; p = 0.026), 25 to 39 (r = 0.428; p = 0.025) and 40 to 59 years old (r = 0.404; p = 0.036). No significant result was found for the correlation between physical activity in free time and standardized mortality rate by COVID-19 in all age groups analyzed (Table 3).

 Table 3. Correlation analysis between the prevalence of different levels of physical activity and standardized COVID-19 mortality rates in capital cities and the Federal District. Brazil. 2019-2020.

Variables	COVID-19 mortality rates		
	\mathbf{r}^*	P value	
Physical inactivity			
18 to 24	0.460	0.015	
25 to 39	0.061	0.760	

40 to 59	0.162	0.418
60 to 79	0.545	0.003
80 or older	0.648	<0.001
Total	0.293	0.138
Insufficient physical activity		
18 to 24	0.426	0.026
25 to 39	0.428	0.025
40 to 59	0.404	0.036
60 to 79	0.369	0.057
80 or older	0.224	0.260
Total	0.420	0,029
Physical activity during free time		
18 to 24	-0.179	0.371
25 to 39	-0.230	0.247
40 to 59	-0.184	0.357
60 to 79	-0.281	0.155
80 or older	-0.262	0.186
Total	-0.153	0.445

* Pearson correlation.

DISCUSSION

In the present study, all correlation coefficients were positive and significant in the physical inactivity category, with the exception of people aged 25 to 59 years old. In the case of the insufficient physical activity category, all the correlation coefficients obtained were positive, and only for people over 60 years old the value was not statistically significant. Still, analyzing the category of physical activity in free time, all correlation coefficients showed a negative correlation without statistical significance for all age groups. Finally, when the age groups were analyzed together, a significant result was noticed only for the prevalence of insufficient physical activity.

Since the declaration of PHEIC by the WHO,¹ lockdown and social distancing policies have been adopted by different authorities around the world. Such policies immediately resulted in necessary changes in habits and greater confinement of the population in their homes, which may have directly or indirectly limited the practice of physical activity in a diffuse way in these locations.¹⁴ A survey review analyzed data from about 2 million participants in 168 countries, demonstrating that the prevalence of physical activity was low even before the pandemic, estimating approximately 1.4 billion people around the world at risk of exacerbation of diseases related to physical inactivity.¹⁵ In Brazil, the effects of policies adopted to contain the pandemic, such as social distancing and quarantine, were also related to increased risk behaviors.¹⁶

Public policies to contain the pandemic in Brazil faced numerous challenges given the spread of fake news, misinformation, devaluation of vaccines, and promotion of disbelief in non-pharmacological actions as effective protective measures.¹⁷⁻¹⁹ Still, there was no effective investigation through mass testing as in other countries because it was restricted only to individuals with severe symptoms, which may culminate in the difficulty of tracking viral spread.²⁰ Finally, there was little federal intervention in funding means to support the recovery of those infected,¹⁹ when only about 23% of the Brazilian population has benefits through private health insurance plans.²¹ The set of all these factors may be associated with a worse result of the country in facing the pandemic, reaching a greater number of cases and deaths.

The importance of physical activity in protecting against infections and systemic inflammation can be explained by several physiological processes. Among these effects, the following stand out: reduction in the amounts of molecules characteristic of the acute inflammatory phase, such as C-Reactive Protein (CRP) and interleukin-6 (IL-6); the maintenance and increase of muscle mass; ²² balance between the levels of antiinflammatory (IL-4 and IL-1ra) and pro-inflammatory (IL-8, IL-1 and IL-1 β) cytokines;²³ and increased recirculation of immune cells and greater efficacy of cytotoxic cells.²⁴ The regular practice of moderate physical activity is also associated with a lower number of infections of the upper respiratory tract ^{25,26} and a better response of the body to the application of vaccines, for example, against the Influenza virus.²⁷ Finally, there is evidence of a relationship between physical activity and changes in volume and muscle concentrations of the angiotensin-converting enzyme II (ACE II), ²⁸ the main human binding receptor for the Spike antigen of the SARS-CoV-2 virus.²⁹ Thus, the documented role of physical activity in better immune functioning and in the maintenance of human physiology could help in the study at the population level.

The total analysis, without stratification by age groups, found a statistically significant result only for the prevalence of insufficient physical activity. This corroborates the results of national and hospital observational studies carried out in other countries, which associated the practice of physical inactivity with the development of severity by COVID-19 and reached the conclusion that there may be an increase in severity and mortality from COVID-19 according to previous levels of physical inactivity.³⁰⁻³² The results of these studies could encourage further investigation, as they present physical inactivity as a possible new risk factor for COVID-19.

When evaluating age stratification, not all correlations were statistically significant. However, the correlation patterns obtained in the analysis without age stratification were maintained: Negative correlation for physical activity during free time and positive correlation for insufficient physical activity and physical inactivity. Among the results highlights, there was a significance between the standardized mortality rate and the prevalence of physical inactivity for people aged over 60 years old. This is worth noting, as advanced age is one of the main independent factors associated with mortality from COVID-19, since about 81% of deaths from the disease occurred in people over 65 years of age,^{7,33} which determined the need for standardization to reduce this effect on correlation for this study. In addition, the age group between 18 and 24 years deserves mention for presenting significant results to positive correlations for the prevalence of physical inactivity and insufficient physical activity with the standardized mortality rate. A possible explanation for this finding is the fact that this population may have comorbidities. A person's risk of severe illness from COVID-19, and even death, increases as the number of underlying medical conditions they have increases, even in the young adult population.⁶ In Brazil, Law N°. 14,124, of March 10, 2021, pointed out that young people with comorbidity enter a priority group for vaccination against COVID-19.

This study has limitations due to the use of secondary data sources, as justified by the absence of correlation analysis in the age group below 18 years old, since VIGITEL restricts its physical activity prevalence sample to the population above or equal to 18 years old residing in Brazilian capitals and the Federal District. In addition, mortality rates from COVID-19 encompass the overall population, that is, it contains the population under 18 years old, however, it only represents 0.2% of the overall population.¹¹ Added to this, the exclusion of residents without landline telephones can cause a selection bias, since a predominance of certain prevalence for these individuals has already been evidenced: lower education levels, socioeconomic status, and access to health systems; and greater brown/black ethnicity, unemployment, and young age.³⁴ However, VIGITEL sought to apply post-stratification weight adjustments to better estimate survey prevalence and reduce the effect of this bias.³⁵ However it is important to note that data collection from self-reports may present underestimated or overestimated differences compared to measurements by movement tests, such as accelerometers and pedometers, and heart rate. ^{36,37} Regarding the questionnaire, VIGITEL does not use the Global Physical Activity Questionnaire (GPAQ) recommended by the WHO,38 but a

reproducible and already validated adaptation.³⁹ Furthermore, there was no agreement between the periods of the 2020 mortality data and the 2019 prevalence of physical activity, with the study being conducted before the highest peak of cases and deaths in Brazil, in the first semester of 2021.⁴⁰ Finally, the intrinsic limitations of an ecological study should be highlighted, such as dependence on the quality of secondary data and the ecological fallacy, since the latter makes it impossible to associate the practice of physical activity with mortality from the disease at an individual level.

In the present study, we observed a positive correlation between the overall prevalence of insufficient physical activity and the standardized mortality rate of COVID-19. Based on this finding, some implications for clinical practice can be cited, such as: recommending and encouraging regular physical activity for patients at increased risk of COVID-19, especially elderly individuals; identifying and addressing the lack of physical activity as a modifiable risk factor for worse outcomes in patients with COVID-19 and other chronic diseases; incorporating the evaluation of physical activity in the risk assessment for COVID-19 and considering physical activity as an integral part of the treatment and prevention plan for the disease; developing adapted and safe exercise programs for COVID-19 patients, including those hospitalized and in rehabilitation, to improve their functional capacity and reduce the risk of complications and mortality.

In addition, this result may encourage further in-depth studies to investigate the relationship between physical activity and COVID-19, including clinical trials to evaluate the effect of physical activity on the prevention and treatment of the disease.

The regular practice of physical activity is essential at any age and has been considered a means of preserving and improving human health and quality of life. By checking the correlation between the prevalence of physical activity practice and the standardized mortality rate from COVID-19 and examining people living in Brazilian capital cities, the total analysis showed a significant correlation when insufficient physical activity was studied. When analyzing the age groups, there was a significant correlation for groups from 18 to 24, 60 to 79, and 80 years old or older, for the prevalence of physical inactivity; and for groups 18 to 24, 25 to 39, and 40 to 59 years old, for the prevalence of insufficient physical activity.

REFERENCES

1. WHO. World Health Organization. 2019-nCoV outbreak is an emergency of international concern; 2020 Jan 31 <u>https://www.euro.who.int/en/health-topics/health-emergencies/international-health-regulations/news/2020/2/2019-ncov-outbreak-is-an-emergency-of-international-concern</u>

2. WHO. World Health Organization. WHO Coronavirus (COVID-19) Dashboard; 2020 Jan 30. <u>https://covid19.who.int</u>

3. Orellana JDY, Cunha GM da, Marrero L, et al. Excess deaths during the COVID-19 pandemic: underreporting and regional inequalities in Brazil. Cad Saude Publica. 2021;37(1):e00259120. <u>https://doi.org/10.1590/0102-311X00259120</u>

4. Demenech LM, Dumith S de C, Vieira MECD, et al. Income inequality and risk of infection and death by COVID-19 in Brazil. Rev Bras Epidemiol. 2020;23:e200095. https://doi.org/10.1590/1980-549720200095

5. Baqui P, Bica I, Marra V, et al. Ethnic and regional variations in hospital mortality from COVID-19 in Brazil: a cross-sectional observational study. Lancet Glob Heal. 2020 Aug 1;8(8):e1018–26. <u>https://doi.org/10.1016/S2214-109X(20)30285-0</u>

6. CDC. Centers for Disease Control and Prevention. People with Certain Medical Conditions. USA; 2021.<u>https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html</u>

7. Kyu HH, Bachman VF, Alexander LT, et al. Physical activity and risk of breast cancer, colon cancer, diabetes, ischemic heart disease, and ischemic stroke events: systematic review and dose-response meta-analysis for the Global Burden of Disease Study 2013. BMJ. 2016 Aug;354:i3857. <u>https://doi.org/10.1136/bmj.i3857</u>

8. Sallis R, Young DR, Tartof SY, et al. Physical inactivity is associated with a higher risk for severe COVID-19 outcomes: a study in 48 440 adult patients. 2021 Apr. Br J Sports Med. <u>http://dx.doi.org/10.1136/bjsports-2021-104080</u>

9. MS. Ministério da Saúde. Vigitel: o que é, como funciona, quando utilizar e resultados. Brasil. <u>https://antigo.saude.gov.br/saude-de-a-z/vigitel</u>

10. MS. Ministério da Saúde. Secretaria de Vigilância em Saúde. Vigitel Brasil, 2019: Vigilância de Fatores de Risco e Proteção para Doenças Crônicas por Inquérito Telefônico (VIGITEL). Brasil, Brasília: Ministério da Saúde, 2016. <u>https://bvsms.saude.gov.br/bvs/publicacoes/vigitel_brasil_2019_vigilancia_fatores_risc</u> <u>o.pdf</u>

11. MS. Ministério da Saúde, Banco de Dados do Sistema Único de Saúde- open DataSUS, Sistema de Informação de Vigilância Epidemiológica da Gripe (SIVEP-Gripe). SRAG 2020 - Banco de Dados de Síndrome Respiratória Aguda Grave - incluindo dados da COVID-19: Vigilância de Síndrome Respiratória Aguda Grave (SRAG). Brasil; 2020 Jul 22. <u>https://opendatasus.saude.gov.br/dataset/bd-srag-2020</u>

12. IBGE. Instituto Brasileiro de Geografia e Estatística. Brasil. <u>https://www.ibge.gov.br/</u>

13. Naing NN. Easy way to learn standardization: direct and indirect methods. Malays JMedSci.2000Jan;7(1):10–5.PMCID:PMC3406211.https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3406211/

14. Ammar A, Brach M, Trabelsi K, et al. Effects of COVID-19 Home Confinement on Eating Behaviour and Physical Activity: Results of the ECLB-COVID19 International Online Survey. 2020 May 28; Vol. 12, Nutrients. 1583. https://doi.org/10.3390/nu12061583

15. Guthold R, Stevens GA, Riley LM, et al. Worldwide trends in insufficient physical activity from 2001 to 2016: a pooled analysis of 358 population-based surveys with 1,9 million participants. Lancet Glob Heal. 2018 Oct 1;6(10):e1077–86. https://doi.org/10.1016/S2214-109X(18)30357-7

16. Malta D, Szwarcwald C, Barros M, et al. A pandemia da COVID-19 e as mudanças no estilo de vida dos brasileiros adultos: um estudo transversal. 2020. Epidemiol e Serviços Saúde. 2020 Sep 25;29. <u>http://dx.doi.org/10.1590/s1679-49742020000400026</u>

17. Chu DK, Akl EA, Duda S, et al. Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: a systematic review and meta-analysis. Lancet. 2020 Jun 27;395(10242):1973–87. https://doi.org/10.1016/S0140-6736(20)31142-9

18. Nussbaumer-Streit B, Mayr V, Dobrescu AI, et al. Quarantine alone or in combination with other public health measures to control COVID- 19: a rapid review. Cochrane Database Syst Rev. 2020;(4). <u>https://doi.org/10.1002/14651858.CD013574</u>

19. Boschiero MN, Palamim CVC, Ortega MM, et al. One Year of Coronavirus Disease 2019 (COVID-19) in Brazil: A Political and Social Overview. Ann Glob Heal. 2021 May 18;87(1):44. <u>https://doi.org/10.5334/aogh.3182</u>

20. Hallal PC, Hartwig FP, Horta BL, et al. SARS-CoV-2 antibody prevalence in Brazil: results from two successive nationwide serological household surveys. Lancet Glob Heal. 2020 Nov 1;8(11):e1390–8. <u>https://doi.org/10.1016/S2214-109X(20)30387-9</u>

21. ANS. Agência Nacional de Saúde, Sistema de Informações de Beneficiários. Dados Gerais: Beneficiários de planos privados de saúde, por cobertura assistencial. Brasil, 2011. <u>https://www.ans.gov.br/perfil-do-setor/dados-gerais</u>

22. Mikkelsen UR, Couppé C, Karlsen A, et al. Life-long endurance exercise in humans: circulating levels of inflammatory markers and leg muscle size. Mech Ageing Dev. 2013;134(11–12):531–40. <u>https://doi.org/10.1016/j.mad.2013.11.004</u>

23. Minuzzi LG, Chupel MU, Rama L, et al. Lifelong exercise practice and immunosenescence: Master athletes cytokine response to acute exercise. Cytokine. 2019 Mar;115:1–7. <u>https://doi.org/10.1016/j.cyto.2018.12.006</u>

24. Simpson RJ, Kunz H, Agha N, et al. Exercise and the Regulation of Immune Functions. Prog Mol Biol Transl Sci. 2015;135:355–80. https://doi.org/10.1016/bs.pmbts.2015.08.001

25. Nieman DC, Nehlsen-Cannarella SL, Markoff PA, et al. The effects of moderate exercise training on natural killer cells and acute upper respiratory tract infections. Int J Sports Med. 1990 Dec;11(6):467–73. <u>https://doi.org/10.1055/s-2007-1024839</u>

26. Nieman DC, Henson DA, Austin MD, et al. Upper respiratory tract infection is reduced in physically fit and active adults. Br J Sports Med. 2011 Sep;45(12):987–92. http://dx.doi.org/10.1136/bjsm.2010.077875

27. Woods JA, Keylock KT, Lowder T, et al. Cardiovascular exercise training extends influenza vaccine seroprotection in sedentary older adults: the immune function intervention trial. J Am Geriatr Soc. 2009 Dec;57(12):2183–91. https://doi.org/10.1111/j.1532-5415.2009.02563.x

28. Klöting N, Ristow M, Blüher M. Effects of Exercise on ACE2. Vol. 28, Obesity (Silver Spring, Md.). United States; 2020. p. 2266–7. <u>https://doi.org/10.1002/oby.23041</u>

29. Wan Y, Shang J, Graham R, et al. Receptor Recognition by the Novel Coronavirus from Wuhan: an Analysis Based on Decade-Long Structural Studies of SARS Coronavirus. J Virol. 2020 Mar;94(7). <u>https://doi.org/10.1128/JVI.00127-20</u>

30. Lee SW, Lee J, Moon SY, et al. Physical activity and the risk of SARS-CoV-2 infection, severe COVID-19 illness and COVID-19 related mortality in South Korea: a nationwide cohort study. Br J Sports Med. 2021 Jul. <u>http://dx.doi.org/10.1136/bjsports-2021-104203</u>

31. Yuan Q, Huang H, Chen X, et al. Does pre-existent physical inactivity have a role in the severity of COVID-19? Ther Adv Respir Dis. 2021 Jan 1;15:17534666211025220. https://doi.org/10.1177/17534666211025221

32. Salgado-Aranda R, Pérez-Castellano N, Núñez-Gil I, et al. Influence of Baseline Physical Activity as a Modifying Factor on COVID-19 Mortality: A Single-Center, Retrospective Study. Infect Dis Ther. 2021 Mar;1–14. <u>https://doi.org/10.1007/s40121-021-00418-6</u>

33. Wolff D, Nee S, Hickey NS, et al. Risk factors for Covid-19 severity and fatality: a structured literature review. Infection. 2020/08/28. 2021 Feb;49(1):15–28. https://doi.org/10.1007/s15010-020-01509-1

34. Segri NJ, Galvão CLC, Berti MAB, et al. Inquérito de saúde: comparação dos entrevistados segundo posse de linha telefônica residencial. Rev Saude Publica. 2010 Nov 27;44(3). <u>https://doi.org/10.1590/S0034-89102010005000012</u>

35. Bernal RTI, Iser BPM, Malta DC, et al. Surveillance System for Risk and Protective Factors for Chronic Diseases by Telephone Survey (Vigitel): changes in weighting

methodology. Epidemiol e Serv saude. Rev do Sist Unico Saude do Bras. 2017;26(4):701–12. https://doi.org/10.5123/S1679-49742017000400003

36. Ferrari P, Friedenreich C, Matthews CE. The Role of Measurement Error in Estimating Levels of Physical Activity. Am J Epidemiol. 2007 Oct 1;166(7):832–40. https://doi.org/10.1093/aje/kwm148

37. Skender S, Ose J, Chang-Claude J, et al. Accelerometry and physical activity questionnaires - a systematic review. BMC Public Health. 2016;16(1):515: <u>https://doi.org/10.1186/s12889-016-3172-0</u>

38. WHO. World Health Organization. Global Physical Activity Questionnaire (GPAQ). Switzerland, Geneva. 2021. <u>https://www.who.int/publications/m/item/global-physical-activity-questionnaire</u>

39. Moreira AD, Claro RM, Felisbino-Mendes MS, et al. Validity and reliability of a telephone survey of physical activity in Brazil. Rev Bras Epidemiol. 2017;20(1):136–46. https://doi.org/10.1590/1980-5497201700010012

40. Silva SJR, Pena L. Collapse of the public health system and the emergence of new variants during the second wave of the COVID-19 pandemic in Brazil. One Heal. 2021;13:100287. <u>https://doi.org/10.1016/j.onehlt.2021.100287</u>

Author Contributions

Lucas Paes de Oliveira: conceptualization, data curation; investigation; methodology; project administration; drafting, reviewing, and editing of the manuscript. Helena Martinez Faria Bastos Régis Hughe, Raquel Alencastro Veiga Domingues Carneiro, Cleverton José Teixeira da Silva e Kamille Feltrin Ronsoni: data curation; review and editing of the manuscript. Danúbia Hillesheim: formal analysis; methodology; review and editing of the manuscript. Andreia Morales Cascaes e Ana Luiza de Lima Curi Hallal: conceptualization; methodology; project administration; drafting, reviewing, and editing of the manuscript. All of the authors gave final approval of the version to be published and agreed to be accountable for all aspects of the study, ensuring that questions related to the accuracy or integrity of any of its parts have been appropriately investigated and resolved.