Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Original Research

Physical activity and long COVID: findings from the Prospective Study About Mental and Physical Health in Adults cohort

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ABSTRACT

Objectives: The study investigated the longitudinal association between physical activity and the risk of long COVID in patients who recovered from COVID-19 infection.
Study design: We analyzed longitudinal data of the Prospective Study About Mental and Physical Health cohort, a prospective cohort study with adults living in Southern Brazil.
Methods: Participants responded to an online, self-administered questionnaire in June 2020 (wave 1) and June 2022 (wave 4). Only participants who self-reported a positive test for COVID-19 were included. Physical activity was assessed before (wave 1, retrospectively) and during the pandemic (wave 1). Long COVID was assessed in wave 4 and defined as any post-COVID-19 symptoms that persisted for at least 3 months after infection.
Results: A total of 237 participants (75.1% women; mean age [standard deviation]: 37.1 [12.3]) were included in this study. The prevalence of physical inactivity in baseline was 71.7%, whereas 76.4% were classified with long COVID in wave 4. In the multivariate analysis, physical activity during the pandemic was associated with a reduced likelihood of long COVID (prevalence ratio [PR]: 0.83; 95% confidence interval [CI]: 0.69–0.99) and a reduced duration of long COVID symptoms (odds ratio: 0.44; 95% CI: 0.26–0.75). Participants who remained physically active from before to during the pandemic were less likely to report long COVID (PR: 0.74; 95% CI: 0.58–0.95), fatigue (PR: 0.49; 95% CI: 0.32–0.76), neurological complications (PR: 0.47; 95% CI: 0.27–0.80), cough (PR: 0.40; 95% CI: 0.22–0.71), and loss of sense of smell or taste (PR: 0.43; 95% CI: 0.21–0.87) as symptom-specific long COVID.
Conclusion: Physical activity practice was associated with reduced risk of long COVID in adults.

Introduction

More than 671 million have been diagnosed with COVID-19 since March 2020.[1] However, the World Health Organization has noticed that many survivors may suffer from a long, persistent form of the disease known as long COVID.[2] Long COVID condition refers to patients with probable or confirmed SARS-CoV-2 infection whose symptoms persisted for at least 3 months.[3] Recent estimates suggested a prevalence as high as 75% of long COVID in the general population. The most common symptomology is fatigue, followed by respiratory and neurological complications.[4] Identifying protective mechanisms to reduce the risk of this condition is an

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emerging priority in public health to reduce the projected burden of long COVID.

Physical activity is associated with reduced risk of infection, hospitalization, and mortality related to COVID-19.[5,6] However, the levels of physical activity were drastically disrupted during social distancing restrictions.[7–9] A body of evidence demonstrates the deleterious impact of physical inactivity on cardiovascular, muscular, respiratory, neurological, and immune systems, which are all affected by COVID-19 infection.[10,11] Previous studies have suggested an association between physical inactivity and the risk of long COVID.[12,13] Although these investigations suggested a higher prevalence of long COVID-19 in physically inactive adults, the association between different trajectories of physical activity from before to during the pandemic is scanty. Therefore, this study aimed to investigate the longitudinal association between physical activity and the risk of long COVID.

Methods

Study design

We analyzed data from the Prospective Study About Mental and Physical Health (PAMPA) cohort, a prospective study that evaluates the effects of the COVID-19 pandemic on health parameters in Southern Brazil. The ethics board approved the study from the Physical Education Faculty (Universidade Federal de Pelotas, Brazil; CAAE: 31906920.7.0000.5313). More details about study design and recruitment can be found elsewhere.[14]

Participants recruitment and sample

Adults (aged ≥18 years) living in the Rio Grande do Sul state were recruited by a four-arm approach aiming to reach participants in all state regions. Researchers spread the questionnaire's weblink via (1) messages to their personal and professional contacts over the state, (2) social media campaigns, (3) local media and state agencies, and (4) universities' staff and students.[14] For this study, we used data from wave 1 (assessed in June and July 2020) and wave 4 (assessed in June and July 2022), as we first included questions on persistent symptoms after COVID-19 infection in the latest wave. Wave 1 assessed two periods: before (retrospectively) and during the first months of the pandemic (present). A total of 2239 participants were recruited in wave 1, and 462 participants were followed up in wave 4. Overall, 237 participants reported a positive COVID-19 test and were included in the study (Fig. 1).

Outcome

Participants who reported a positive test for COVID-19 were asked to indicate for how long they had COVID-related symptoms. A list of symptoms was displayed (e.g. fatigue, cough, headache), and for each one, there were the following answering options: (1) did not have, (2) 3 months, (3) 6 months, (4) 12 months, (5) 15 months, and (6) ≥18 months. Based on this information, two outcome variables were built, as follows: (1) presence of general long COVID symptoms (any COVID-related symptoms that lasted at least 3 months) and (2) duration of long COVID symptoms (<6 months, >6 and <12 months, and 12 or more months). We also analyzed the association between physical activity and the presence of each persistent symptom, henceforward referred to as symptom-specific long COVID. Only symptoms with a prevalence ≥20% were analyzed for analysis purposes. Memory and concentration problems, irritability, depression, and anxiety were grouped as neurological complications in these analyses.

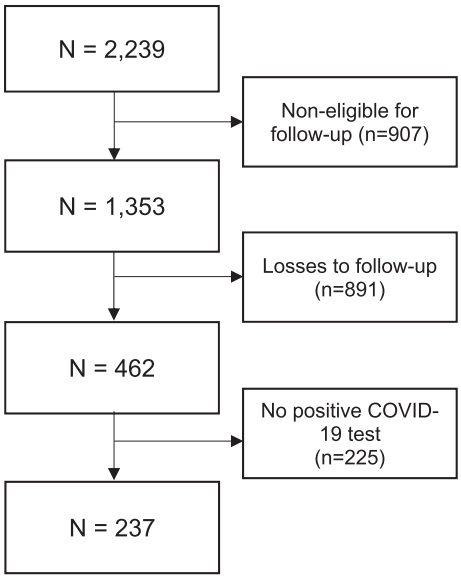

Fig. 1. Study sampling process.

Exposure

Physical activity was assessed on wave 1, with two-time references: before (retrospectively) and during the pandemic (at survey's week). Participants were asked if they engaged in regular physical activities before the pandemic and in the last 7 days. Those who answered yes were asked about the frequency (days per week) and time (minutes per day) the activities lasted.[15] Two main exposure variables were built. Participants were considered inactive if they engaged in <150 min/week and active if they engaged in ≥150 min/week.13 The trajectory of physical activity from before (retrospectively) to during wave 1 (baseline) was examined using a four-category variable that classified participants based on their physical activity status in both periods as follows: remained inactive, became inactive, remained active, or became active.

Potential confounders

Sex, age, educational level, ethnicity, marital status, comorbidities, body mass index (BMI), pandemic routine behavior (stayed at home always, left home to essentials only, left home all days), family income, and vaccination status (unvaccinated, one to four doses) were used as possible confounders. Self-reported weight and height were assessed to calculate BMI, which was categorized as follows: normal (<25 kg/m^2), overweight (≥25 and <30 kg/m^2), and obese (≥30 kg/m^2). Participants reported their daily routine during wave 1 and were categorized as follows: stayed at home always, left home to essentials only, and left home all days. Negative economic impact of COVID-19 was assessed, with participants reporting whether monthly income decreased from before to during the social distancing restrictions (wave 1). Finally, participants were asked about the number of vaccine doses they took until wave 4 (June 2022).

Data analyses

Descriptive data are presented as total and relative frequencies. A Chi-square test was used to check for associations between outcomes and exposures, and when necessary, the Fisher exact test was used. Robust Poisson regression models were used to evaluate

the association between physical activity assessed in wave 1 and the presence of general and specific long COVID symptoms 2 years later in wave 4. Data are presented as prevalence ratio (PR) with their respective 95% confidence interval (95% CI). Ordinal logistic regression models were used for the association between physical activity and duration of general and specific long COVID symptoms, with data presented as odds ratio (OR) with their respective 95% CI. Because of our low follow-up rate (51.3%), we conducted inverse probability weights models for successful follow-up for general and specific long COVID symptom and physical activity variables. This method is used in situations with unequal selection probabilities to avoid censoring or non-response bias.[16] All models were adjusted for age, sex, education, ethnicity, income, presence of comorbidities, and vaccination status. In addition, we used structural equation modeling to examine the possible mediation role of income and education in the association between physical activity and the long COVID.[17]

Results

We included 237 participants with a mean age of 37.1 ± 12.3 years, with most being women, White, and with at least one university degree (Table 1). The prevalence of physical inactivity increased from before (49.8%) to during (71.7%) the pandemic (wave 1). Three in four participants had general long COVID (76.4%; 95% CI: 70.5%, 81.4%). The most common symptomatology was fatigue (53.2%), followed by neurological complications (40.1%), cough (39.7%), headache (35.9%), and loss of sense of smell or taste (27.8%). Symptoms lasted from 3 to 6 months in 38.5% and more than 6 months in 37.5% of the included participants.

Participants who reported being physically active during the pandemic showed a lower likelihood of general long COVID as well as fatigue, neurological complications, and cough as symptom-specific long COVID (Table 2). Participants who were active before the pandemic showed a lower likelihood of fatigue, neurological complications, and headache as symptom-specific long COVID. Structural equation modeling indicated that income ($P = 0.834$ for indirect effect) and education ($P = 0.849$ for indirect effect) do not mediate the association between physical activity and the likelihood of long COVID.

We also investigated the association between changes in physical activity status and long COVID, as described in Table 3. Participants who were physically active before and during the pandemic showed a lower probability of long COVID than those who remained physically inactive. This protective association was also observed for persistent fatigue, neurological complications, cough, loss of sense of smell or taste, and headache. In addition, those who became active showed a lower likelihood of neurological

Table 1
Characteristics of the included participants (N = 237).

Variables	Overall, *n* (%)	Long COVID, *n* (%)		*P*-value
		No (*n* = 56)	Yes (*n* = 181)	
Sex				0.074[a]
Male	59 (24.9)	19 (33.9)	40 (22.1)	
Female	178 (75.1)	37 (66.1)	141 (77.9)	
Age in years				0.937[b]
18–30	92 (38.8)	23 (41.1)	69 (38.1)	
31–59	131 (55.3)	30 (53.6)	101 (55.8)	
≥60	14 (5.9)	3 (5.4)	11 (6.1)	
Skin color				0.086[b]
White	213 (89.9)	46 (82.1)	167 (92.3)	
Mixed	14 (5.9)	6 (10.7)	8 (4.4)	
Black	10 (4.2)	4 (7.1)	6 (3.3)	
Highest education achievement				0.632[a]
High school or less	66 (27.8)	17 (30.4)	49 (27.1)	
University degree or higher	171 (72.2)	39 (69.6)	132 (72.9)	
Conjugal situation				0.387[a]
Living with partner	158 (66.7)	40 (71.4)	118 (65.2)	
Living alone	79 (33.3)	16 (28.6)	63 (34.8)	
Daily routine during pandemic				0.161[b]
Stayed at home always	11 (4.6)	3 (5.4)	8 (4.4)	
Left home to essentials only	160 (67.5)	43 (76.8)	117 (64.6)	
Left home all days	66 (27.8)	10 (17.9)	56 (30.9)	
Chronic conditions, yes (%)	141 (59.5)	29 (51.8)	112 (61.9)	0.179[a]
Reduced income during pandemic, yes (%)	100 (42.2)	20 (35.7)	80 (44.2)	0.261[a]
COVID-19 vaccine				0.866[b]
Two doses	19 (8.0)	4 (7.1)	15 (8.3)	
Three doses	131 (55.3)	33 (58.9)	98 (54.1)	
Four doses	87 (36.7)	19 (33.9)	68 (37.6)	
Physical activity before pandemic				0.035[a]
No	118 (49.8)	21 (37.5)	97 (53.6)	
Yes	119 (50.2)	35 (62.5)	84 (46.4)	
Physical activity during pandemic				0.015[a]
No	170 (71.7)	33 (58.9)	137 (75.7)	
Yes	67 (28.3)	23 (41.1)	44 (24.3)	
Change in physical activity status				0.017[b]
Sustained inactive	95 (41.5)	17 (31.5)	78 (44.6)	
Become inactive	67 (29.3)	14 (25.9)	53 (30.3)	
Become active	15 (6.6)	2 (3.7)	13 (7.4)	
Sustained active	52 (22.7)	21 (38.9)	31 (17.7)	

Physical activity before the pandemic was assessed retrospectively during wave 1 (June 2020).
Physical activity during the pandemic was assessed during wave 1 (June 2020).
[a] Pearson's Chi-squared.
[b] Fisher exact.

Table 2
Association of physical activity before and during the pandemic with the presence of general and symptoms specific long COVID in adults (N = 237).

Outcome	Before pandemic		During pandemic	
	PR (95% CI)	*P*-value	PR (95% CI)	*P*-value
Long COVID	0.88 (0.76, 1.02)	0.090	0.83 (0.69, 0.99)	0.041
Symptom-specific long COVID				
Fatigue	0.67 (0.52, 0.86)	0.002	0.66 (0.48, 0.92)	0.015
Neurological complications	0.71 (0.51, 0.97)	0.032	0.48 (0.30, 0.77)	0.002
Cough	0.73 (0.53, 1.01)	0.056	0.58 (0.38, 0.89)	0.013
Loss of sense of smell or taste	0.72 (0.47, 1.10)	0.131	0.63 (0.37, 1.09)	0.097
Headache	0.57 (0.40, 0.82)	0.003	0.75 (0.49, 1.16)	0.197

CI, confidence intervals; PR, prevalence ratio.
General long COVID was defined as any post-COVID-19 symptoms that persisted for at least 3 months.
Symptom-specific long COVID were based on individual symptoms.
Physical activity before the pandemic was assessed retrospectively during wave 1 (June 2020).
Physical activity during the pandemic was assessed during wave 1 (June 2020).
PR was estimated using robust Poisson regression models adjusted for age, sex, education, skin color, income, presence of comorbidities, and vaccination status.

complications after COVID-19 infection. Physical activity before the pandemic was associated with a lower probability of fatigue as symptom-specific long COVID, even in participants who became inactive during the pandemic.

Finally, physical activity was associated with a shorter duration of symptoms (Table 4). Physical activity before the pandemic was associated with briefer fatigue, neurological complications, and headache as symptom-specific long COVID. Participants who became physically inactive from before to during the pandemic were less likely to report persistent fatigue and headache, whereas neurological complications were less likely in those who became active in the same period (Table 5). Persistent fatigue, neurological complications, and cough after COVID-19 infection were briefer in participants who were physically active during the pandemic than in inactive participants in the same period (Table 4). General and symptom-specific long COVID was less likely in participants who remained physically active during the pandemic (Table 5).

The association between physical activity and long COVID remained significant after inverse probability weighting for successful follow-up (Supplementary Table 1). In this sensitivity analysis, cough and headache were associated with physical activity before the pandemic. In contrast, loss of sense of smell or taste was associated with physical activity during the pandemic. Remaining physically active from before to during the pandemic was consistently associated with long COVID, although becoming physically inactive was no longer related to long COVID (Supplementary Table 2).

Discussion

Our findings demonstrate the protective association between physical activity and long COVID. Adults who persisted physically active during the COVID-19 pandemic showed a lower likelihood of long COVID, including long-lasting fatigue, neurological complications, cough, loss of sense of smell or taste, and headache. Up to 80% of COVID-19 survivors live with persistent symptoms after SARS-CoV-2 infection.[4,10,18] Considering the 640 million cases of COVID-19 since the pandemic's beginning, physical activity has been shown as a potential non-pharmacological strategy to reduce the forecasted burden of long COVID-19 worldwide. Consequently, public policies focused on reducing the risk of long COVID, especially in those at higher risk, are urgently needed.

We demonstrated that people who survived COVID-19 and were physically active before and during the pandemic showed a lower likelihood of respiratory sequelae after SARS-CoV-2 infection.

Table 3
Association between change in physical activity status and the presence of general and symptoms specific long COVID in adults (N = 237).

Outcome	Persisted inactive	Became inactive	Became active	Persisted active
		PR (95% CI)	PR (95% CI)	PR (95% CI)
Long COVID	Ref	0.98 (0.83, 1.15)	1.06 (0.85, 1.33)	0.74 (0.58, 0.95)
P-value		*0.811*	*0.581*	*0.016*
Symptom-specific long COVID				
Fatigue	Ref	0.74 (0.56, 0.99)	0.87 (0.56, 1.33)	0.49 (0.32, 0.76)
P-value		*0.035*	*0.519*	*0.001*
Neurological complications	Ref	0.75 (0.53, 1.07)	0.34 (0.13, 0.88)	0.47 (0.27, 0.80)
P-value		*0.112*	*0.025*	*0.006*
Cough	Ref	0.99 (0.69, 1.41)	1.17 (0.69, 1.97)	0.40 (0.22, 0.71)
P-value		*0.956*	*0.566*	*0.002*
Loss of sense of smell or taste	Ref	0.85 (0.53, 1.36)	1.00 (0.47, 2.11)	0.43 (0.21, 0.87)
P-value		*0.452*	*0.988*	*0.018*
Headache	Ref	0.65 (0.43, 0.99)	1.14 (0.68, 1.92)	0.48 (0.27, 0.86)
P-value		*0.049*	*0.579*	*0.015*

CI, confidence interval; PR, prevalence ratio.
General long COVID was defined as any post-COVID-19 symptoms that persisted for at least 3 months.
Symptom-specific long COVID were based on individual symptoms.
Physical activity before the pandemic was assessed retrospectively during wave 1 (June 2020).
Physical activity during the pandemic was assessed during wave 1 (June 2020).
PR was estimated using robust Poisson regression models adjusted for age, sex, education, skin color, income, presence of comorbidities, and vaccination status.

Table 4
Association of physical activity before and during the pandemic and duration of general and symptoms specific long COVID in adults (N = 237).

Outcome	Before pandemic		During pandemic	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Long COVID	0.62 (0.38, 1.00)	0.051	0.44 (0.26, 0.75)	0.003
Symptom-specific long COVID				
Fatigue	0.35 (0.21, 0.59)	<0.001	0.41 (0.23, 0.74)	0.003
Neurological complications	0.53 (0.31, 0.90)	0.018	0.30 (0.15, 0.59)	0.001
Cough	0.60 (0.35, 1.03)	0.064	0.39 (0.21, 0.74)	0.004
Loss of sense of smell or taste	0.60 (0.33, 1.08)	0.087	0.54 (0.27, 1.08)	0.081
Headache	0.39 (0.22, 0.68)	0.001	0.61 (0.32, 1.15)	0.124

CI: confidence interval; OR: odds ratio.
OR >1 indicates higher odds for persistent symptoms lasting longer.
General long COVID was defined as any post-COVID-19 symptoms that persisted for at least 3 months.
Symptom-specific long COVID were based on individual symptoms.
Physical activity before the pandemic was assessed retrospectively during wave 1 (June 2020).
Physical activity during the pandemic was assessed during wave 1 (June 2020).
OR were estimated using proportional ordinal logistical regression models adjusted for age, sex, education, skin color, income, presence of comorbidities, and vaccination status.

Fatigue was the most common long COVID symptomatology, with previous corroborating studies on COVID-19, SARS-CoV-1, and MERS-COV.[4,18–20] Most patients with decreased respiratory function after SARS-CoV-1 infection also presented muscle wasting and fatigue.[27] In addition, Ahmed et al.[19] estimated a reduction of 461 m in a six-minute walking test, an indicator of exercise capacity, in patients who survived SARS-CoV-1 and MERS-COV. Decreased exercise tolerance may also be associated with modifications in peripheric oxygen uptake. After COVID-19 infection, patients showed preserved oxygen availability with reduced peripheral oxygen extraction rate and increased venous saturation, which may explain the lower cardiorespiratory fitness in these patients compared with healthy controls.[21] On the other hand, physical activity can improve mitochondrial activity and oxygen uptake, preserving energy production during cellular respiration.[22,23] For example, a previous study revealed that eight weeks of endurance and resistance training was safe and more effective than self-care recommendations and inspiratory muscle training alone to regain cardiovascular and muscular fitness and improve symptom severity and health status in adults with long COVID.[24] Thus, physical activity maintenance before and during the COVID-19 pandemic may have promoted cellular and systemic protective mechanisms, preserving pulmonary function in COVID-19 survivors.

Our findings suggest that physical activity was associated with a lower likelihood of neurological complications after COVID-19. Neurological complications were among the most common symptomatology of long COVID, known as brain 'fog'.[4,18] Different mechanisms have been suggested for the beneficial effects of physical activity on brain function. For example, regular physical activity seems to preserve brain health through the upregulation of neurotrophic factors and anti-inflammatory cytokines,[25,26] resulting in the generation of new astrocytes and promotion of neurogenesis and synaptic plasticity. These physical activity–induced modifications can improve cognitive function and reduce the risk of neurological complications and degenerative processes. Also, previous evidence suggests the critical role of astrocytes in this complication.[27–29] Astrocytes are the most abundant cells in the central nervous system and perform various functions, such as regulating the concentration of neurotransmitters and other substances with the potential to interfere with neuronal functioning, the integrity of the blood–brain barrier, and helping to maintain cerebral homeostasis.

Table 5
Association between change in physical activity status and duration of general and symptoms specific long COVID in adults (N = 237).

Outcome	Persisted inactive	Became inactive	Became active	Persisted active
		OR (95% CI)	OR (95% CI)	OR (95% CI)
Long COVID	Ref	0.76 (0.42, 1.37)	0.58 (0.23, 1.49)	0.33 (0.17,0.64)
P-value		*0.364*	*0.227*	*0.001*
Symptom-specific long COVID				
Fatigue	Ref	0.42 (0.23, 0.78)	0.68 (0.24, 1.88)	0.20 (0.09, 0.41)
P-value		*0.025*	*0.494*	<0.001
Neurological complications	Ref	0.60 (0.32, 1.12)	0.21 (0.05, 0.79)	0.26 (0.12, 0.58)
P-value		*0.110*	*0.016*	*0.002*
Cough	Ref	1.01 (0.53, 1.92)	1.18 (0.41, 3.43)	0.23 (0.10, 0.53)
P-value		*0.953*	*0.799*	*0.001*
Loss of sense of smell or taste	Ref	0.72 (0.36, 1.43)	0.98 (0.31, 3.09)	0.30 (0.13, 0.75)
P-value		*0.313*	*0.882*	*0.009*
Headache	Ref	0.45 (0.23, 0.88)	1.14 (0.39, 3.30)	0.28 (0.12, 0.64)
P-value		*0.022*	*0.836*	*0.003*

CI: confidence interval; OR, odds ratio.
OR >1 indicates higher odds for persistent symptoms lasting longer.
General long COVID was defined as any post-COVID-19 symptoms that persisted for at least 3 months.
Symptom-specific long COVID were based on individual symptoms.
Physical activity before the pandemic was assessed retrospectively during wave 1 (June 2020).
Physical activity during the pandemic was assessed during wave 1 (June 2020).
OR were estimated using proportional ordinal logistical regression models adjusted for age, sex, education, skin color, income, presence of comorbidities, and vaccination status.

Physical activity before and during the pandemic was associated with shorter lengths of long COVID symptoms. A previous cross-sectional, population-based analysis suggested an inverse association between physical activity and the duration of symptoms.[30] However, to our knowledge, this is the first study to assess the longitudinal association of physical activity with the presence and duration of long COVID. Exposure to physical activity across the life course results in long-term benefits in different body systems. For example, physical activity during adolescence showed a lower risk of depression[31] and improved cognitive function[32] in adulthood. However, during the more restricted phases of the COVID-19 pandemic, physical activity practice in sports clubs, gyms, and public spaces were limited to control virus spreading. Alternative methods, such as online platforms, surged as options to preserve physical activity levels. Unfortunately, inequity in opportunities to continue physical activity practice during these stages may lead to an increased burden of long COVID in some population groups. Based on the available scientific literature and our findings, physical activity surges as a potential strategy to reduce the likelihood of long COVID in adult populations.

Despite this being the first study to assess the longitudinal association between physical activity and long COVID in Brazil, an epicenter of the COVID-19 pandemic, our study presents some limitations. First, physical activity, persistent symptoms, and COVID-19 infection were self-reported. However, the local ethics committee did not allow in-person research activities during baseline assessments. Also, we acknowledged the low response rate from baseline to wave 4. Data collection for wave 4 occurred between June and August 2022, simultaneously with political campaigns for the Brazilian Presidential Election. The anti-science movement that arose in Brazil during the pandemic resulted in offenses of some eligible participants against the research.[33] In addition, the results may be biased by the limited number of non-long COVID people, explained as a result of loss of follow-up. However, the results were robust after sensitivity analysis with inverse probability weighting to account for losses to follow-up.

Conclusions

In conclusion, physical activity was associated with a lower likelihood of long COVID in adults. Although experimental studies are needed to confirm our findings, public policies focused on reducing the risk of long COVID, especially in those at higher risk, are urgently needed.

Author statements

Acknowledgments

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Ethical approval

The ethics board approved the study from the Physical Education Faculty (Universidade Federal de Pelotas, Brazil; CAAE: 31906920.7.0000.5313).

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Competing interests

None declared.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.puhe.2023.05.011.

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