

Review

Not peer-reviewed version

Tailored Physical Activity Interventions for Long COVID: Current Approaches and Benefits- a Narrative Review

Guhua Jia and [Chun-Hsien Su](#)*

Posted Date: 4 July 2024

doi: 10.20944/preprints202407.0438.v1

Keywords: exercise therapy; physical endurance; post-acute sequelae of sars-cov-2; quality of life; rehabilitation; symptom management



Preprints.org is a free multidiscipline platform providing preprint service that is dedicated to making early versions of research outputs permanently available and citable. Preprints posted at Preprints.org appear in Web of Science, Crossref, Google Scholar, Scilit, Europe PMC.

Copyright: This is an open access article distributed under the Creative Commons Attribution License which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Review

Tailored Physical Activity Interventions for Long COVID: Current Approaches and Benefits—A Narrative Review

Guhua Jia ¹ and Chun-Hsien Su ^{2,3,*}

¹ Sports Teaching Department, Shanghai University of Medicine & Health Sciences, Shanghai 201318, China

² Department of Exercise and Health Promotion, Chinese Culture University, Taipei City 111369, Taiwan

³ College of Kinesiology and Health, Chinese Culture University, Taipei City 111369, Taiwan

* Correspondence: chsu@ulive.pccu.edu.tw; Tel.: +886-975159678

Abstract: This narrative review examines the crucial role of physical activity in managing long COVID, characterized by persistent symptoms such as fatigue, breathlessness, and cognitive impairments following SARS-CoV-2 infection. The methodology involved a comprehensive literature search across PubMed, EBSCO (EDS), and Google Scholar, selecting peer-reviewed articles from December 2019 focusing on long-term COVID physical activity interventions. The review highlights that tailored exercise programs, adjusted to individual health status and abilities, significantly alleviate symptoms and enhance psychological well-being. Key findings emphasize the importance of personalized exercise prescriptions due to the variability in patient responses and the need for a multidisciplinary approach in developing and monitoring interventions. Despite promising outcomes, the review identifies research gaps, including the need for long-term studies, randomized controlled trials, and deeper mechanistic insights. It suggests that standardized reporting, templates like CERT, and integrating digital health tools are essential for optimizing interventions. Overall, the review advocates including personalized physical activity programs in standard care for long COVID to improve patient outcomes and quality of life.

Keywords: exercise therapy; physical endurance; post-acute sequelae of sars-cov-2; quality of life; rehabilitation; symptom management

1. Introduction

1.1. Background

Long COVID, or Post-Acute Sequelae of SARS-CoV-2 infection (PASC), is a multifaceted condition with a substantial global impact, characterized by persistent symptoms such as fatigue, breathlessness, and "brain fog" following the resolution of the acute phase of COVID-19, affecting a significant global population [1,2]. This syndrome leads to notable declines in physical and mental well-being, challenging individuals' daily functioning and quality of life. The variability in symptoms necessitates personalized and multidisciplinary care approaches due to the impacts on physical function, mental health, and economic productivity [3–5]. The current understanding of the long-term pathophysiology of COVID-19 is limited, indicating a need for effective treatments and rehabilitation strategies. Research has highlighted physical activity as a critical area with potential benefits [6,7]. Physical activity, encompassing a range of exercises from aerobic and resistance training to flexibility and balance exercises, has improved cardiovascular health, muscle strength, mental health, and overall quality of life. Tailoring these interventions to individual needs, considering the heterogeneity of long COVID symptoms, is essential for maximizing their efficacy [8,9].

Emerging evidence suggests that structured physical activity can mitigate some chronic symptoms of long COVID. For instance, regular aerobic exercise has been shown to reduce fatigue and improve cardiovascular endurance, while resistance training can enhance muscle strength and

physical function [10,11]. Moreover, incorporating elements of flexibility and balance training can aid in reducing the risk of falls and improving overall mobility, which is particularly beneficial for those experiencing dizziness or muscle weakness [12]. Implementing physical activity interventions for long COVID patients poses several clinical challenges despite the potential benefits. These include determining the appropriate intensity and duration of exercise, managing symptom fluctuations, and addressing the psychological barriers to physical activity, such as fear of symptom exacerbation and lack of motivation [13,14]. Multidisciplinary approaches involving physiotherapists, occupational therapists, psychologists, and other healthcare professionals are crucial for developing and implementing effective rehabilitation programs [15]. The economic implications of long COVID are also significant, as prolonged illness can lead to reduced work capacity and increased healthcare costs. Effective rehabilitation strategies, including tailored physical activity interventions, can alleviate these economic burdens by enhancing patients' functional abilities and facilitating their return to work [16–19].

Addressing COVID-19 impacts through tailored physical activity interventions is crucial for improving affected individuals' health and quality of life amid the pandemic. This narrative review explores current approaches and clinical challenges in managing long COVID through tailored physical activity interventions to provide insights into effective rehabilitation strategies for this complex condition. It emphasizes the importance of individualized care and the integration of multidisciplinary support to address the diverse needs of long COVID patients.

1.2. Purpose and Scope

This narrative review aims to explore the role of physical activity in managing long-term COVID-19 symptoms and improving patient outcomes. Long COVID, characterized by persistent symptoms such as fatigue, breathlessness, and brain fog, poses significant challenges to healthcare providers and patients, impacting physical, mental, and social well-being. This review examines various exercise intensities, frequencies, and types through observational studies, clinical trials, systematic reviews, and qualitative research to assess their effectiveness in alleviating symptoms and enhancing well-being. Key aspects include the optimal duration and intensity of exercises, the benefits of different exercise forms, and the importance of personalized exercise programs tailored to individual needs. Additionally, it addresses the safety and tolerability of physical activities, emphasizing the need for tailored exercise prescriptions to minimize risks and maximize recovery benefits.

2. Relevant Collection of Research for Review

A comprehensive literature search was carried out across several electronic databases, namely PubMed, EBSCO (EDS), and Google Scholar, to gather a broad spectrum of research on the intersection of physical activity and long COVID. The search strategy employed a combination of keywords such as "long COVID," "Post-Acute Sequelae of SARS-CoV-2 infection (PASC)," alongside terms linked to "physical activity," "exercise," "rehabilitation," and specific modalities like "aerobic" and "strength training," using Boolean operators for precision. This search spanned publications from the onset of the COVID-19 pandemic in December 2019 to the latest available research, ensuring the inclusion of up-to-date findings. Selection criteria were strictly adhered to, encompassing peer-reviewed English language articles that delved into physical activity interventions for long COVID sufferers. These included a range of study designs, from observational studies and clinical trials to qualitative research. Exclusions were made for content not directly related to long COVID, such as editorials, commentaries, and studies focusing solely on the acute phase of COVID-19 without considering the implications for long-term recovery, ensuring a focused and relevant collection of research for review. The study selection process was meticulously conducted in phases, starting with an initial screening where titles and abstracts were evaluated for relevance to the review's goals, promptly excluding those not aligning with the set inclusion criteria. This was followed by a thorough full-text review of the potentially relevant studies to assess their conformity to the predefined selection criteria closely. Finally, those studies that fulfilled all inclusion requirements and

successfully passed the full-text assessment were chosen for inclusion in the review, ensuring a focused and pertinent compilation of research for analysis.

The review analyzed studies with diverse designs, including observational studies, clinical trials, systematic reviews, and qualitative research. Participant demographics varied widely, encompassing different ages, genders, and stages of long COVID, thus providing a broad perspective on the condition. Study characteristics included a range of physical activity interventions, from low-intensity exercises such as walking and gentle stretching to vigorous activities like aerobic exercise and strength training. Outcome measures were equally diverse, covering symptom improvement, quality of life, physical function, and psychological well-being, allowing for a multifaceted understanding of physical activity's impact on long COVID. These varied study characteristics comprehensively overview how physical activity interventions affect individuals with long COVID.

3. Effects of Physical Activity on Long COVID Symptoms

Findings consistently demonstrated positive effects of physical activity on long COVID symptoms. Participants highlighted the importance of outdoor spaces for physical activity and the impact of changes in daily routines and COVID-19 restrictions on their ability to be active. Many mentioned risks or threats to participation, such as fear of contracting COVID-19. Physical and mental health were also highlighted as essential motivators for physical activity, with many using technology to support their active lifestyle [20].

Moderate long-term exercise training might be an effective strategy to reduce the likelihood of severe presentation of COVID-19. Improved resistance to infection can be seen in two ways: by affecting the immune-regulatory pathway (IL-6/cortisol) [21]. Articles revealed a significant association between sufficient physical activity and reduced COVID-19 hospitalization and mortality. The analysis showed a weighted odds ratio of 0.541 for hospitalization and 0.61 for mortality, indicating a protective effect of physical activity [22].

Early physical rehabilitation interventions applied to COVID-19 patients who were discharged from the hospital improved multiple parameters related to functional capacity, pulmonary function, quality of life, and mental health status [23–25]. Regular moderate-intensity exercise was associated with significant energy and endurance improvements for fatigue, a common and debilitating symptom. The study found that physical activity during the pandemic was associated with a reduced likelihood of long COVID and a shorter duration of symptoms. Those who remained physically active from before to during the pandemic were less likely to report long COVID, fatigue, neurological complications, cough, and loss of sense of smell or taste [26,27].

Physical activity programs could help counteract muscle atrophy and fatigue observed in long COVID patients [28]. Breathlessness also saw improvement through tailored aerobic exercises that enhanced lung capacity and efficiency. A review of articles accessed through electronic databases found that exercise interventions and pulmonary rehabilitation have shown promise in improving functional exercise capacity, dyspnea, and fatigue in people with long COVID [27,29]. Additionally, strength and flexibility exercises contributed to alleviating joint and muscle pain. In contrast, targeted breathing exercises helped manage respiratory symptoms and anxiety, showcasing the multifaceted benefits of exercise on long COVID recovery [13,30,31]. Table 1 in our research concisely summarizes the effects of physical activity on long COVID symptoms.

Table 1. Summary of the effects of physical activity on long COVID symptoms.

Symptom	Type of Exercise	Effect	Reference: Grade ¹
Fatigue	Moderate-intensity exercise	significant improvements in energy and endurance.	
		reduction in fatigue scores, increased exercise capacity, enhanced daily activity levels, improved muscle strength,	[26]: D
		better quality of sleep, decreased perceived exertion, and enhanced mental well-being.	[27]: C [28]: D
Breathlessness	Tailored aerobic exercises	enhanced lung capacity and efficiency. increased forced vital capacity, increased forced expiratory volume,	[27]: C [29]: D

		improved peak expiratory flow rate, reduced breathlessness scores, improved exercise tolerance, and increased maximal voluntary ventilation.	
Joint and Muscle Pain	Strength and flexibility exercises	alleviation of joint and muscle pain. reduced pain scores, increased range of motion, improved muscle strength, enhanced functional mobility, decreased stiffness scores, and increased daily activity levels.	[13]: D [30]: C [31]: A
Respiratory Symptoms	Targeted breathing exercises	management of respiratory symptoms and anxiety. reduced breathlessness scores, improved lung function, decreased respiratory rate, and improved anxiety scores.	[13]: D [30]: C [31]: A
Mental Health	Moderate-intensity exercise, Technology-supported physical activity	improved mental health and motivation. reduced anxiety scores, reduced depression scores, improved mood scores, enhanced self-reported motivation levels, and increased overall well-being scores.	[20]: C
Functional Capacity	Early physical rehabilitation interventions	increased exercise tolerance, enhanced muscle strength, improved balance and stability, increased range of motion, improved functional mobility, and enhanced daily activity levels.	[23]: A [24]: C [25]: A
Pulmonary Function	Early physical rehabilitation interventions	improvement in pulmonary function. increased forced vital capacity, increased forced expiratory volume, improved peak expiratory flow rate, enhanced oxygen saturation levels, and improved maximal voluntary ventilation.	[23]: A [24]: C [25]: A
Quality of Life	Early physical rehabilitation interventions	enhanced quality of life. improved scores on quality of life questionnaires, increased vitality and energy levels, reduced pain scores, and improved performance in activities of daily living (adls).	[23]: A [24]: C [25]: A
Neurological Complications	General physical activity	reduced likelihood of neurological complications. improved cognitive function scores, reduced incidence of neurological symptoms (e.g., headaches, dizziness), improved balance and coordination, and lowered inflammation markers (e.g., c-reactive protein, interleukin-6 levels).	[26]: D [27]: C

¹ Each reference's evidence level is graded as A: systematic reviews and meta-analyses; C: cohort studies, case-control studies, cross-sectional surveys, case studies, and/or observational studies; D: review or evidence insufficient for categories A or C.

4. Variability in Response to Physical Activity Interventions

The review highlighted the variability in response to physical activity interventions, noting that individual outcomes could differ based on several factors, including baseline severity of symptoms, pre-existing conditions, and the specific type and intensity of physical activity undertaken. Physical activity plays a crucial role in preventing and treating COVID-19, promoting the recovery of bodily function, alleviating post-acute COVID-19 syndromes, and improving psychological well-being. It is recommended that appropriate exercise prescriptions for different populations be developed under the guidance of a physician [7].

Some studies reported that patients with more severe long COVID symptoms at baseline experienced more significant improvements with tailored exercise programs. For instance, a study comparing high-intensity interval training (HIIT) and moderate-intensity training (MIT) found that both were effective in improving mental well-being during COVID-19 confinement, with HIIT being more beneficial for reducing depression [32]. Conversely, other studies found that mild to moderate-

intensity exercises were more useful for individuals with less severe symptoms, emphasizing the need for personalized exercise prescriptions.

A systematic review of seven studies revealed that resistance and aerobic exercise programs can improve functional capacity and quality of life in post-COVID-19 patients. These studies demonstrated improvements in muscle strength, functional capacity, fatigue, and quality of life following exercise interventions [33,34]. For a detailed overview of the variability in response to physical activity interventions in long COVID, please refer to Table 2.

Table 2. Variability in response to physical activity interventions in long COVID.

Factor	Details	Reference: Grade ¹
Baseline Severity of Symptoms	Patients with more severe long COVID symptoms at baseline experienced more significant improvements with tailored exercise programs.	[7]: D
Type of Exercise	High-Intensity Interval Training (HIIT) and Moderate-Intensity Training (MIT) improved mental well-being, with HIIT being more beneficial for reducing depression during COVID-19 confinement.	[32]: B
Intensity of Exercise	Mild to moderate-intensity exercises were more beneficial for individuals with less severe symptoms, emphasizing the need for personalized exercise prescriptions.	[7]: D
Exercise Programs	Resistance and aerobic exercise programs improved functional capacity and quality of life in post-COVID-19 patients, demonstrating improvements in muscle strength, functional capacity, fatigue, and quality of life.	[33]: A [34]: A
Personalized Exercise Prescriptions	Personalized exercise prescriptions are essential, developed under the guidance of a physician to cater to different populations and individual needs.	[7]: D
Mental Well-being	Exercise interventions, including HIIT and MIT, improved mental well-being during confinement, demonstrating the psychological benefits of physical activity.	[32]: B
Functional Capacity and Quality of Life	Exercise programs showed significant improvements in muscle strength, functional capacity, fatigue reduction, and overall quality of life in post-COVID-19 patients.	[33]: A [34]: A

¹ Each reference's evidence level is graded as A: systematic reviews and meta-analyses; B: randomized controlled trials (RCTs); D: review or evidence insufficient for categories A or B.

5. Safety and Feasibility of Physical Activity Interventions

Overall, physical activity interventions were safe and feasible for individuals with long COVID, with few adverse events reported. Most studies emphasized the importance of gradually increasing the intensity and duration of exercise to avoid exacerbating symptoms. Physical activity may have a protective effect against fatal outcomes in patients with COVID-19. The protective effect of physical activity on COVID-19 outcomes may be attributed to specific types of exercise, such as resistance and endurance exercises. Further research is needed to understand the biological mechanisms behind these findings [35]. Physical exercise has been shown to modulate interferon responses and innate immune cell activity, which are crucial in the initial defense against viral infections. By enhancing the immune system and improving overall health, physical exercise may serve as a valuable complementary tool in preventing and treating COVID-19. In addition to its immunomodulatory effects, exercise can help control inflammation, oxidative stress, and nitric oxide synthesis, contributing to a comprehensive approach to combating the virus [36]. The review underscored the necessity of closely monitoring individuals during physical activity interventions, particularly those with severe long-term COVID or underlying health conditions, to ensure their safety and optimize the benefits of exercise. A meta-analysis of existing literature was conducted, analyzing various outcome measures related to physical function in COVID-19 patients. The results indicated that physical activity interventions effectively improved the 6-minute Walk Test, 30-second Sit-to-Stand

Test, Timed Up-and-go test, Forced Vital Capacity, and Forced Expiratory Volume in COVID-19 patients. Overall, physical activity was found to play a crucial role in enhancing exercise capacity and pulmonary function in COVID-19 patients, promoting their overall physical health and recovery. COVID-19 patients must undergo an accurate physical assessment before physical activity to ensure their safety and well-being [7,37]. Table 3 highlights the safety and feasibility of physical activity interventions for individuals recovering from long COVID, underscoring the importance of gradual progression and close monitoring to minimize risks and enhance recovery outcomes.

Table 3. Safety and feasibility of physical activity interventions in long COVID.

Aspect	Details	Reference: Grade ¹
Safety and Feasibility	Physical activity interventions were found to be safe and feasible for individuals with long COVID, with few adverse events reported.	[35]: A
Gradual Progression	It is important to gradually increase the intensity and duration of exercise to avoid exacerbating symptoms.	[35]: A
Protective Effects	Physical activity may protect against fatal outcomes in patients with COVID-19, attributed to specific types of exercise such as resistance and endurance.	[35]: A
Immunomodulatory Effects	Physical exercise modulates interferon responses and innate immune cell activity, enhancing initial defense against viral infections.	[36]: D
Control of Inflammation	Exercise helps control inflammation, oxidative stress, and nitric oxide synthesis, contributing to a comprehensive approach to combating the virus.	[36]: D
Close Monitoring	There is a need to closely monitor individuals during physical activity interventions, particularly those with severe long-term COVID or underlying health conditions.	[7]: D [37]: A
Improvement in Physical Function	Physical activity interventions improved the 6-minute Walk Test, 30-second Sit-to-Stand Test, Timed Up-and-go test, Forced Vital Capacity, and Forced Expiratory Volume.	[7]: D [37]: A
Enhancement of Exercise Capacity	Physical activity enhances exercise capacity and pulmonary function in COVID-19 patients, promoting overall physical health and recovery.	[7]: D [37]: A
Pre-activity Physical Assessment	COVID-19 patients must undergo an accurate physical assessment before physical activity to ensure safety and well-being.	[7]: D [37]: A

¹ Each reference's evidence level is graded as A: systematic reviews and meta-analyses; D: review or evidence insufficient for categories A.

6. Discussion

The review provides a comprehensive synthesis of evidence indicating that physical activity can significantly manage long COVID symptoms. Tailored exercise programs have demonstrated substantial improvements in patients with severe long COVID symptoms at baseline, emphasizing the importance of personalized exercise prescriptions [13]. Mild to moderate-intensity exercises, on the other hand, have shown more significant benefits for individuals with less severe symptoms [26]. These findings highlight the necessity of individualized exercise regimens in rehabilitating long COVID patients, enabling targeted interventions that address specific needs, thereby enhancing functional capacity and quality of life [38]. Personalized exercise prescriptions consider factors such as obesity and vaccination status, which influence the response to rehabilitation [39]. The evidence underscores that personalized approaches are crucial for optimizing rehabilitation benefits. Case studies, such as those by Torres et al., illustrate significant improvements in lung function, cardiorespiratory fitness, endurance capacity, and muscle strength following exercise interventions using FITT-VP principles and the Consensus on Exercise Reporting Template (CERT) [40]. Similarly, Binetti et al. reported enhanced 6-minute walk test results and reduced fatigue levels in long COVID patients participating in supervised exercise programs, with biomarkers like creatinine potentially

predicting rehabilitation response [26]. Rehabilitation interventions have also improved lung function, exercise capacity, dyspnea severity, quality of life, and mental health outcomes [41]. The synthesis of these findings underscores the critical role of individualized exercise prescriptions in the rehabilitation process for long-term COVID-19. These interventions, tailored to each patient's unique needs, significantly enhance health outcomes and emphasize healthcare professionals' need to integrate diverse physical rehabilitation strategies. Using standardized reporting templates, such as CERT, facilitates the optimization of rehabilitation practices by ensuring detailed documentation and enabling the identification of predictors for rehabilitation response. Despite the promising results, limitations exist, including variability in study quality, small sample sizes, and a lack of long-term follow-up data, which may affect the generalizability and durability of the findings.

Physical activity benefits individuals with long COVID through several potential mechanisms. Regular exercise can mitigate the pandemic's impact at both personal and societal levels [24]. Long COVID patients often exhibit reduced aerobic capacity, cardiocirculatory limitations, dysfunctional breathing patterns, and impaired oxygen utilization during exercise [13]. Physical activity addresses these issues by improving the quality of life through molecular mechanisms, such as stimulating the inflammatory response and enhancing immune system function [13,41]. Exercise-induced increases in blood flow and lymphatic circulation facilitate the removal of inflammatory mediators and promote tissue repair and recovery. Moreover, physical activity may enhance vaccine-induced antibody responses, as suggested by previous research [9,11]. By modulating interferon responses and innate immune cell activity, exercise improves the body's initial defense against viral infections and controls inflammation, oxidative stress, and nitric oxide synthesis [36]. The engagement of the parasympathetic nervous system during physical activity could also explain the reductions in stress-related symptoms and improvements in autonomic regulation observed in long COVID patients [13,41].

Incorporating physical activity as a critical component of therapeutic management for long-term COVID-19 is essential. Tailored exercise programs should be recommended based on symptom severity, baseline physical condition, and personal preferences, as patient engagement and adherence are crucial for the success of the program [42–44]. A multidisciplinary approach involving physiotherapists, exercise physiologists, and mental health professionals is vital for comprehensively addressing the complex needs of long-term COVID patients [24,40,45,46]. Despite the lack of standardization in reporting exercise interventions, templates like CERT and FITT-VP exercise prescription principles show promise in developing best practice guidelines [13,47,48]. Rehabilitation interventions such as endurance, flexibility, strength training, pulmonary rehabilitation, task-specific exercises, psychological rehabilitation, and pain management can significantly improve functional capacity and quality of life in long COVID patients [26,49–51]. Cardiopulmonary exercise testing (CPET) and pulmonary rehabilitation are particularly effective in managing dyspnea and muscle fatigue [41,52].

Despite promising evidence, several research gaps remain. More significant, well-designed, randomized controlled trials are needed to establish causal relationships between specific types and intensities of physical activity and improvements in long COVID symptoms. Longitudinal studies are essential to understand the long-term effects of exercise interventions and identify potential delayed adverse outcomes, such as overuse injuries or exacerbation of pre-existing conditions. Further research should explore the underlying mechanisms of physical activity benefits to develop targeted interventions and provide insights into optimizing rehabilitation strategies. This review has limitations, including potential biases in study selection and reliance on published literature, which may influence the findings. The heterogeneity of the studies in design, population, and interventions complicates the direct comparison of results. Additionally, the rapidly evolving nature of long COVID research necessitates ongoing updates to the evidence base, as newer studies may provide further insights and refine current knowledge.

The evidence underscores the critical role of personalized exercise interventions in managing long COVID symptoms. Tailoring exercise programs to individual needs and integrating multidisciplinary support can significantly enhance patient outcomes and improve functional

capacity and quality of life. Continued research and refinement of personalized rehabilitation approaches and standardized reporting practices are essential to optimize long COVID management and support the recovery of affected individuals.

7. Conclusions

This review emphasizes the pivotal role of physical activity in managing long COVID, a condition marked by persistent symptoms such as fatigue, breathlessness, and muscle pain following an initial SARS-CoV-2 infection. Tailored exercise programs, customized to each individual's health status and abilities, have shown significant potential in alleviating these symptoms and enhancing psychological well-being. The variability in patient responses to physical activity highlights the need for personalized exercise prescriptions considering symptom severity, pre-existing health conditions, and prior physical activity levels. The findings underscore the importance of a flexible, patient-centered approach, supported by a multidisciplinary team of healthcare professionals, to develop and monitor effective and safe exercise interventions.

Future research should prioritize long-term studies, well-designed randomized controlled trials, and mechanistic investigations to deepen the understanding of how physical activity benefits long COVID patients. Additionally, standardized reporting using templates like CERT, identifying predictors of rehabilitation response, and integrating digital health tools are crucial for refining these interventions. Overall, this review advocates integrating personalized physical activity programs into the standard care for long COVID. It emphasizes their potential to significantly improve patient outcomes and quality of life while calling for continued research to address existing gaps and optimize rehabilitation strategies.

Author Contributions: G.J. and C.-H.S. contributed to this review of experts. All authors have read and agreed to the published version of the manuscript.

Funding: This work was supported by the Beijing Jingti da Culture Development Co., Ltd. (Grant No. HXXM-18-10-006)

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Conflicts of Interest: The authors declare no conflicts of interest.

References

1. Lambert, N.; Survivor Corps; El-Azab, S. A.; Ramrakhiani, N. S.; Barisano, A.; Yu, L.; Taylor, K.; Esperança, Á.; Mendiola, C.; Downs, C. A.; Abraham, H. L.; Hughes, T.; Rahmani, A. M.; Borelli, J. L.; Chakraborty, R.; Pinto, M. D. The Other COVID-19 Survivors: Timing, Duration, and Health Impact of Post-Acute Sequelae of SARS-CoV-2 Infection. *J. Clin. Nurs.* 2024, 33 (1), 76–88. <https://doi.org/10.1111/jocn.16541>
2. Naeije, R.; Caravita, S. Phenotyping Long COVID. *Eur. Respir. J.* 2021, 58, <https://doi.org/10.1183/13993003.01763-2021>
3. O'Connor, R. C.; Wetherall, K.; Cleare, S.; McClelland, H.; Melson, A. J.; Niedzwiedz, C. L.; O'Carroll, R. E.; O'Connor, D. B.; Platt, S.; Scowcroft, E.; Watson, B.; Zortea, T.; Ferguson, E.; Robb, K. A. Mental Health and Well-Being During the COVID-19 Pandemic: Longitudinal Analyses of Adults in the UK COVID-19 Mental Health & Wellbeing Study. *Br. J. Psychiatry* 2021, 218 (6), 326–333. <https://doi.org/10.1192/bjp.2020.212>
4. Melo-Oliveira, M. E.; Sá-Caputo, D.; Bachur, J. A.; Paineiras-Domingos, L. L.; Sonza, A.; Lacerda, A. C.; Mendonça, V.; Seixas, A.; Taiar, R.; Bernardo-Filho, M. Reported Quality of Life in Countries with Cases of COVID-19: A Systematic Review. *Expert Rev. Respir. Med.* 2021, 15 (2), 213–220. <https://doi.org/10.1080/17476348.2021.1826315>
5. Bong, C. L.; Brasher, C.; Chikumba, E.; McDougall, R.; Mellin-Olsen, J.; Enright, A. The COVID-19 Pandemic: Effects on Low- and Middle-Income Countries. *Anesth. Analg.* 2020, 131 (1), 86–92. <https://doi.org/10.1213/ANE.0000000000004846>
6. Rooney, S.; Webster, A.; Paul, L. Systematic Review of Changes and Recovery in Physical Function and Fitness After Severe Acute Respiratory Syndrome-Related Coronavirus Infection: Implications for COVID-19 Rehabilitation. *Phys. Ther.* 2020, 100 (10), 1717–1729. <https://doi.org/10.1093/ptj/pzaa129>

7. Yang, J.; Li, X.; He, T.; Ju, F.; Qiu, Y.; Tian, Z. Impact of Physical Activity on COVID-19. *Int. J. Environ. Res. Public Health* 2022, 19 (21), 14108. <https://doi.org/10.3390/ijerph192114108>
8. Colas, C.; Le Berre, Y.; Fanget, M.; Savall, A.; Killian, M.; Goujon, I.; Labeix, P.; Bayle, M.; Féasson, L.; Roche, F.; Hupin, D. Physical Activity in Long COVID: A Comparative Study of Exercise Rehabilitation Benefits in Patients with Long COVID, Coronary Artery Disease and Fibromyalgia. *Int. J. Environ. Res. Public Health* 2023, 20 (15), 6513. <https://doi.org/10.3390/ijerph20156513>
9. Thirupathi, A.; Yong, W.; Oflaz, O.; Agascioglu, E.; Gu, Y. Exercise and COVID-19: Exercise Intensity Reassures Immunological Benefits of Post-COVID-19 Condition. *Front. Physiol.* 2023, 14, 1036925. <https://doi.org/10.3389/fphys.2023.1036925>
10. Yang, G.; Li, Z.; Li, Z.; Huang, L.; Liang, P.; Liu, L.; Li, D. Meta-Analysis of the Impact of Physical Activity on the Recovery of Physical Function in COVID-19 Patients. *Heliyon* 2023, 9 (9), e19339. <https://doi.org/10.1016/j.heliyon.2023.e19339>
11. Kurowski, M.; Seys, S.; Bonini, M.; Del Giacco, S.; Delgado, L.; Diamant, Z.; Kowalski, M. L.; Moreira, A.; Rukhadze, M.; Couto, M. Physical Exercise, Immune Response, and Susceptibility to Infections—Current Knowledge and Growing Research Areas. *Allergy* 2022, 77 (9), 2653–2664. <https://doi.org/10.1111/all.15328>
12. da Silveira, M. P.; da Silva Fagundes, K. K.; Bizuti, M. R.; Starck, É.; Rossi, R. C.; de Resende E Silva, D. T. Physical Exercise as a Tool to Help the Immune System Against COVID-19: An Integrative Review of the Current Literature. *Clin. Exp. Med.* 2021, 21 (1), 15–28. <https://doi.org/10.1007/s10238-020-00650-3>
13. Rathore, F. A.; Khalil, M. T.; Khan, O. J. Rehabilitation Perspectives in Long COVID-19. *J. Pak. Med. Assoc.* 2023, 73 (7), 1553–1555. <https://doi.org/10.47391/JPMA.23-54>
14. Frändin, K.; Grönstedt, H.; Helbostad, J. L.; Bergland, A.; Andresen, M.; Puggaard, L.; Harms-Ringdahl, K.; Granbo, R.; Hellström, K. Long-Term Effects of Individually Tailored Physical Training and Activity on Physical Function, Well-Being and Cognition in Scandinavian Nursing Home Residents: A Randomized Controlled Trial. *Gerontology* 2016, 62 (6), 571–580. <https://doi.org/10.1159/000443611>
15. Draud, S.; Prado, J.; Hass, T.; Ramirez, J. Long COVID: The Silent Pandemic. *Norton Healthc. Med. J.* 2023, 1 (1). <https://doi.org/10.59541/001c.81031>
16. Zakia, H.; Pradana, K.; Iskandar, S. Risk Factors for Psychiatric Symptoms in Patients with Long COVID: A Systematic Review. *PLoS One* 2023, 18 (4), e0284075. <https://doi.org/10.1371/journal.pone.0284075>
17. Baig AM, Rizvi S, Pardhan S, et al. Long-COVID and Its Physical and Neurological Symptoms in Adults: A Systematic Review. *Pak J Med Health Sci.* 2023;17(04). doi:10.53350/pjmhs20231742.
18. Hossain, M. M.; Das, J.; Rahman, F.; Nesa, F.; Hossain, P.; Islam, A. M. K.; Tasnim, S.; Faizah, F.; Mazumder, H.; Purohit, N.; Ramirez, G. Living with "Long COVID": A Systematic Review and Meta-Synthesis of Qualitative Evidence. *PLoS One* 2023, 18 (2), e0281884. <https://doi.org/10.1371/journal.pone.0281884>
19. Davis, H. E.; McCorkell, L.; Vogel, J. M.; Topol, E. J. Long COVID: Major Findings, Mechanisms and Recommendations. *Nat. Rev. Microbiol.* 2023, 21, 133–146. <https://doi.org/10.1038/s41579-022-00846-2>
20. Hailey, V.; Burton, A.; Hamer, M.; Fancourt, D.; Fisher, A. Physical Activity during the COVID-19 Pandemic in the UK: A Qualitative Analysis of Free-Text Survey Data. *Int. J. Environ. Res. Public Health* 2022, 19 (22), 14784. <https://doi.org/10.3390/ijerph192214784>
21. Seman, S.; Dražilov, S. S.; Ilić, V.; Tešić, M.; Stojiljković, S.; Arena, R.; Popović, D. Physical Activity and Exercise as an Essential Medical Strategy for the COVID-19 Pandemic and Beyond. *Exp. Biol. Med.* 2021, 246 (21), 2324–2331. <https://doi.org/10.1177/15353702211028543>
22. Halabchi, F., Mahdavian, B., Tazesh, B., Shab-Bidar, S., & Selk-Ghaffari, M. (2023). Association between physical activity and risk of COVID-19 infection or clinical outcomes of the patients with COVID-19: A systematic review and meta-analysis. *Journal of preventive medicine and hygiene*, 64(2), E123–E136. <https://doi.org/10.15167/2421-4248/jpmh2023.64.2.2625>
23. Rahmati, M.; Molanouri Shamsi, M.; Woo, W.; Koyanagi, A.; Won Lee, S.; Keon Yon, D.; Shin, J. I.; Smith, L. Effects of Physical Rehabilitation Interventions in COVID-19 Patients Following Discharge from Hospital: A Systematic Review. *J. Integr. Med.* 2023, 21 (2), 149–158. <https://doi.org/10.1016/j.joim.2023.01.003>
24. Ambrosio, L.; Morris, J.; Lambrick, D.; Faulkner, J.; Compton, E.; Portillo, M. C. Physical Activity and Mental Health Experiences of People Living with Long Term Conditions during COVID-19 Pandemic: A Qualitative Study. *PLoS One* 2023, 18 (7), e0285785. <https://doi.org/10.1371/journal.pone.0285785>
25. Rejeki, P. S.; Witarto, B. S.; Witarto, A. P.; Rifdah, S. N.; Wafa, I. A.; Utami, D. M.; Izzatunnisa, N.; Kencono Wungu, C. D.; Khaerunnisa, S.; Sakina; Fazleen Mohd Fathil, N. E. Importance of Moderate-to-Vigorous Physical Activity during the COVID-19 Pandemic: A Systematic Review and Meta-Analysis. *J. Basic Clin. Physiol. Pharmacol.* 2023, 34 (3), 311–320. <https://doi.org/10.1515/jbcpp-2023-0040>
26. Binetti, J.; Real, M.; Renzulli, M.; Bertran, L.; Riesco, D.; Perpiñan, C.; Mohedano, A.; Segundo, R. S.; Ortiz, M.; Porrás, J. A.; Pineda, D. R.; Auguet, T. Clinical and Biomarker Profile Responses to Rehabilitation Treatment in Patients with Long COVID Characterized by Chronic Fatigue. *Viruses* 2023, 15 (7), 1452. <https://doi.org/10.3390/v15071452>

27. Feter, N.; Caputo, E. L.; Delpino, F. M.; Leite, J. S.; da Silva, L. S.; de Almeida Paz, I.; Santos Rocha, J. Q.; Vieira, Y. P.; Schröder, N.; da Silva, C. N.; Baptista Gonçalves, J. C.; da Costa Pereira, H.; Barbosa, T. A.; Cassuriaga, J.; da Silva, M. C.; Reichert, F. F.; Rombaldi, A. J. Physical Activity and Long COVID: Findings from the Prospective Study About Mental and Physical Health in Adults Cohort. *Public Health* 2023, 220, 148–154. <https://doi.org/10.1016/j.puhe.2023.05.011>
28. Coscia, F.; Di Filippo, E. S.; Gigliotti, P. V.; Fano Illic, G. Effect of Physical Activity on Long COVID Fatigue: An Unsolved Enigma. *Eur. J. Transl. Myol.* 2023, 33 (3), 11639. <https://doi.org/10.4081/ejtm.2023.11639>
29. Burnett, D. M.; Skinner, C. E. Year in Review: Long COVID and Pulmonary Rehabilitation. *Respir. Care* 2023, 68 (6), 846–851. <https://doi.org/10.4187/respcare.10928>
30. Smith, J. L.; Deighton, K.; Innes, A. Q.; Holl, M.; Mould, L.; Liao, Z.; Doherty, P.; Whyte, G.; King, J. A.; Deniszczyc, D.; Kelly, B. M. Improved Clinical Outcomes in Response to a 12-Week Blended Digital and Community-Based Long-COVID-19 Rehabilitation Programme. *Front. Med.* 2023, 10, 1149922. <https://doi.org/10.3389/fmed.2023.1149922>
31. Ahmed, I.; Mustafaoglu, R.; Yeldan, I.; Yasaci, Z.; Erhan, B. Effect of Pulmonary Rehabilitation Approaches on Dyspnea, Exercise Capacity, Fatigue, Lung Functions, and Quality of Life in Patients With COVID-19: A Systematic Review and Meta-Analysis. *Arch. Phys. Med. Rehabil.* 2022, 103 (10), 2051–2062. <https://doi.org/10.1016/j.apmr.2022.06.007>
32. Borrega-Mouquinho, Y.; Sánchez-Gómez, J.; Fuentes-García, J. P.; Collado-Mateo, D.; Villafaina, S. Effects of High-Intensity Interval Training and Moderate-Intensity Training on Stress, Depression, Anxiety, and Resilience in Healthy Adults During Coronavirus Disease 2019 Confinement: A Randomized Controlled Trial. *Front. Psychol.* 2021, 12, 643069. <https://doi.org/10.3389/fpsyg.2021.643069>
33. Ahmadi Hekmatikar, A. H.; Ferreira Júnior, J. B.; Shahrbani, S.; Suzuki, K. Functional and Psychological Changes after Exercise Training in Post-COVID-19 Patients Discharged from the Hospital: A PRISMA-Compliant Systematic Review. *Int. J. Environ. Res. Public Health* 2022, 19 (4), 2290. <https://doi.org/10.3390/ijerph19042290>
34. Chtourou, H.; Trabelsi, K.; H'mida, C.; Boukhris, O.; Glenn, J. M.; Brach, M.; Bentlage, E.; Bott, N.; Shephard, R. J.; Ammar, A.; Bragazzi, N. L. Staying Physically Active During the Quarantine and Self-Isolation Period for Controlling and Mitigating the COVID-19 Pandemic: A Systematic Overview of the Literature. *Front. Psychol.* 2020, 11, 1708. <https://doi.org/10.3389/fpsyg.2020.01708>
35. Rahmati, M.; Shamsi, M. M.; Khoramipour, K.; Malakoutinia, F.; Woo, W.; Park, S.; Yon, D. K.; Lee, S. W.; Shin, J. I.; Smith, L. Baseline Physical Activity Is Associated with Reduced Mortality and Disease Outcomes in COVID-19: A Systematic Review and Meta-Analysis. *Rev. Med. Virol.* 2022, 32 (5), e2349. <https://doi.org/10.1002/rmv.2349>
36. Fernández-Lázaro, D.; González-Bernal, J. J.; Sánchez-Serrano, N.; Navascués, L. J.; Ascaso-Del-Río, A.; Mielgo-Ayuso, J. Physical Exercise as a Multimodal Tool for COVID-19: Could It Be Used as a Preventive Strategy? *Int. J. Environ. Res. Public Health* 2020, 17 (22), 8496. <https://doi.org/10.3390/ijerph17228496>
37. Yang, G.; Li, Z.; Li, Z.; Huang, L.; Liang, P.; Liu, L.; Li, D. Meta-Analysis of the Impact of Physical Activity on the Recovery of Physical Function in COVID-19 Patients. *Heliyon* 2023, 9 (9), e19339. <https://doi.org/10.1016/j.heliyon.2023.e19339>
38. Dumitrescu, A.; Doros, G.; Lazureanu, V. E.; Septimiu-Radu, S.; Bratosin, F.; Rosca, O.; Patel, H.; Porosnicu, T. M.; Vitcu, G. M.; Mirea, A.; Oancea, C.; Mihaicuta, S.; Stoicescu, E. R.; Barata, P. I. Post-Severe-COVID-19 Cardiopulmonary Rehabilitation: A Comprehensive Study on Patient Features and Recovery Dynamics in Correlation with Workout Intensity. *J. Clin. Med.* 2023, 12 (13), 4390. <https://doi.org/10.3390/jcm12134390>
39. Frisk, B.; Jürgensen, M.; Espehaug, B.; Njøten, K. L.; Sjøteland, E.; Aarli, B. B.; Kvale, G. A Safe and Effective Micro-Choice Based Rehabilitation for Patients with Long COVID: Results from a Quasi-Experimental Study. *Sci. Rep.* 2023, 13 (1), 9423. <https://doi.org/10.1038/s41598-023-35991-y>
40. Torres, G.; Rains, N.; Gradidge, P. J.; Constantinou, D. Exercise Intervention for Post-Acute COVID-19 Syndrome - Do FITT-VP Principles Apply? A Case Study. *S. Afr. J. Sports Med.* 2023, 35 (1), v35i1a15284. <https://doi.org/10.17159/2078-516X/2023/v35i1a15284>
41. Chen, H.; Shi, H.; Liu, X.; Sun, T.; Wu, J.; Liu, Z. Effect of Pulmonary Rehabilitation for Patients With Post-COVID-19: A Systematic Review and Meta-Analysis. *Front. Med.* 2022, 9, 837420. <https://doi.org/10.3389/fmed.2022.837420>
42. Chen, Y.; Klein, S. L.; Garibaldi, B. T.; Li, H.; Wu, C.; Osevala, N. M.; Li, T.; Margolick, J. B.; Pawelec, G.; Leng, S. X. Aging in COVID-19: Vulnerability, Immunity and Intervention. *Ageing Res. Rev.* 2021, 65, 101205. <https://doi.org/10.1016/j.arr.2020.101205>
43. Tang, T.; Bidon, M.; Jaimes, J. A.; Whittaker, G. R.; Daniel, S. Coronavirus Membrane Fusion Mechanism Offers a Potential Target for Antiviral Development. *Antiviral Res.* 2020, 178, 104792. <https://doi.org/10.1016/j.antiviral.2020.104792>
44. Zhang, X.; Tan, Y.; Ling, Y.; Lu, G.; Liu, F.; Yi, Z.; Jia, X.; Wu, M.; Shi, B.; Xu, S.; Chen, J.; Wang, W.; Chen, B.; Jiang, L.; Yu, S.; Lu, J.; Wang, J.; Xu, M.; Yuan, Z.; Zhang, Q.; Zhang, X.; Zhao, G.; Wang, S.; Chen, S.; Lu,

- H. Viral and Host Factors Related to the Clinical Outcome of COVID-19. *Nature* 2020, 583, 437–440. <https://doi.org/10.1038/s41586-020-2355-0>
45. Yong, S. J. Long COVID or Post-COVID-19 Syndrome: Putative Pathophysiology, Risk Factors, and Treatments. *Infect. Dis. (Lond.)* 2021, 53 (10), 737–754. <https://doi.org/10.1080/23744235.2021.1924397>
 46. Raman, B.; Bluemke, D. A.; Lüscher, T. F.; Neubauer, S. Long COVID: Post-Acute Sequelae of COVID-19 with a Cardiovascular Focus. *Eur. Heart J.* 2022, 43 (11), 1157–1172. <https://doi.org/10.1093/eurheartj/ehac031>
 47. Klok, F. A.; Boon, G. J. A. M.; Barco, S.; Endres, M.; Geelhoed, J. J. M.; Knauss, S.; Rezek, S. A.; Spruit, M. A.; Vehreschild, J.; Siegerink, B. The Post-COVID-19 Functional Status Scale: A Tool to Measure Functional Status Over Time After COVID-19. *Eur. Respir. J.* 2020, 56 (1), 2001494. <https://doi.org/10.1183/13993003.01494-2020>
 48. Hughes, D. C.; Orchard, J. W.; Partridge, E. M.; La Gerche, A.; Broderick, C. Return to Exercise Post-COVID-19 Infection: A Pragmatic Approach in Mid-2022. *J. Sci. Med. Sport* 2022, 25 (7), 544–547. <https://doi.org/10.1016/j.jsams.2022.06.001>
 49. Dillen, H.; Bekkering, G.; Gijsbers, S.; Vande Weygaerde, Y.; Van Herck, M.; Haesevoets, S.; Bos, D. A. G.; Li, A.; Janssens, W.; Gosselink, R.; Troosters, T.; Verbakel, J. Y. Clinical Effectiveness of Rehabilitation in Ambulatory Care for Patients with Persisting Symptoms After COVID-19: A Systematic Review. *BMC Infect. Dis.* 2023, 23 (1), 419. <https://doi.org/10.1186/s12879-023-08374-x>
 50. Barbara, C.; Clavario, P.; De Marzo, V.; Lotti, R.; Guglielmi, G.; Porcile, A.; Russo, C.; Griffo, R.; Mäkikallio, T.; Hautala, A. J.; Porto, I. Effects of Exercise Rehabilitation in Patients with Long Coronavirus Disease 2019. *Eur. J. Prev. Cardiol.* 2022, 29 (7), e258–e260. <https://doi.org/10.1093/eurjpc/zwac019>
 51. Liu, K.; Zhang, W.; Yang, Y.; Zhang, J.; Li, Y.; Chen, Y. Respiratory Rehabilitation in Elderly Patients with COVID-19: A Randomized Controlled Study. *Complement. Ther. Clin. Pract.* 2020, 39, 101166. <https://doi.org/10.1016/j.ctcp.2020.101166>
 52. Gao, Y.; Chen, R.; Geng, Q.; Mo, X.; Zhan, C.; Jian, W.; Li, S.; Zheng, J. Cardiopulmonary Exercise Testing Might Be Helpful for Interpretation of Impaired Pulmonary Function in Recovered COVID-19 Patients. *Eur. Respir. J.* 2021, 57 (1), 2004265. <https://doi.org/10.1183/13993003.04265-2020>

Disclaimer/Publisher’s Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.