

1 **LONG COVID RECOVERY AND EXERCISE ADHERENCE: 32-MONTH STUDY**

2

3 Ana Rolo-Duarte^{1,2*}, Daniela Prada¹, Ana S. M. Carvalho³, Ana Borges¹, Paulo J. G.

4 Bettencourt^{2,4}

5

6 Ana Maria Pissarra Coelho Rolo-Duarte, MD^{1,2*}

7 Daniela Karina Ruiz Prada, MD¹

8 Ana Sofia Marques Carvalho, MSc³

9 Ana Luísa Andrade Borges, MD¹

10 Paulo Jorge Gonçalves de Bettencourt, PhD^{2,4}

11

12 ***Corresponding author.** Ana Rolo-Duarte. Hospital Beatriz Ângelo.

13 Av. Carlos Teixeira 3, 2674-514 Loures, Portugal. Phone 00351916765515.

14 **Fax: +351219847209** anaroloduarte@gmail.com

15

16 **Affiliations:**

17 ¹Department of Physical Medicine and Rehabilitation, Hospital Beatriz Ângelo – ULS

18 Loures/Odivelas, Portugal

19 ²Faculty of Medicine, Universidade Católica Portuguesa, Lisboa, Portugal

20 ³Católica Research Centre for Psychological, Family and Social Wellbeing (CRC-W),

21 Universidade Católica Portuguesa, Lisboa, Portugal.

22 ⁴Center for Interdisciplinary Research in Health, Universidade Católica Portuguesa, Lisboa,

23 Portugal

24

25 **Author Disclosures**

26 **Competing Interests:** The authors declare no competing interests.

27

28 **Funding:** PJGB was supported by internal funding from the Faculty of Medicine,
29 Universidade Católica Portuguesa, and external funding from Fundação para a Ciência e a
30 Tecnologia (FCT), under the grants UIDP/04279/2020, UIDB/04279/2020, and
31 EXPL/SAU-INF/0742/2021.

32

33 **Financial Benefits:** The authors declare no financial interests or personal gains related to
34 this study.

35

36 **Previous Presentation:** This research has not been presented in any form, including
37 abstracts, posters, or conferences.

38

39

40

41

42

43

44

45

46

47 **ABSTRACT**

48 **Objective**

49 To evaluate symptom progression in COVID-19 survivors, adherence to prescribed exercise
50 therapy, and its association with pre-infection physical activity at 21 days (T0), 6 months
51 (T1), and 32 months (T2) post-discharge.

52 **Design**

53 Retrospective longitudinal study in a hospital-based rehabilitation unit in Portugal. The
54 cohort included 276 patients (mean age 56.6 ± 13.5 years) with confirmed SARS-CoV-2
55 infection.

56 **Results**

57 Adherence was higher among patients reporting prior physical activity (48.8%; $p = .003$).
58 Symptom prevalence declined over time: dyspnea (T0 = 22.4%, T2 = 7.3%), fatigue (T0 =
59 32.4%, T2 = 14.5%), and pain (T0 = 17.6%, T2 = 4.8%). Asymptomatic cases increased from
60 27.4% (T0) to 54.5% (T2). Early adherence, particularly by day 15, was associated with
61 continued participation at day 21, and adherence at day 21 correlated with reduced dyspnea
62 at follow-up ($p = .02$). Importantly, patients who remained symptomatic at day 21 took
63 significantly longer to recover ($t = -6.386$; $p < .001$), indicating this time point as a prognostic
64 marker of delayed resolution of exercise-modifiable symptoms.

65 **Conclusion**

66 Early initiation of individualized, structured exercise proved safe, adaptable, and associated
67 with reduced symptom burden, especially dyspnea. Persistence of symptoms at day 21
68 highlights the prognostic value of early follow-up and underscores the decisive role of timely
69 rehabilitation engagement. Structured home-based and tele-rehabilitation programs

70 supported adherence and accessibility, reinforcing exercise as a cornerstone of long COVID
71 management and potentially applicable to other post-respiratory rehabilitation contexts.

72

73 **Keywords:** Long COVID; Rehabilitation; Patient Compliance; Exercise Therapy

74

75

76 INTRODUCTION

77

78 COVID-19 is a multisystemic disease with heterogeneous clinical presentations.
79 While many individuals experience mild and self-limiting illness, the pandemic caused an
80 estimated 15.9 million deaths globally in 2020–2021.[1] Although the World Health
81 Organization (WHO) declared its end in May 2023, the long-term health consequences of
82 SARS-CoV-2 infection remain a major concern.[2]

83 Long COVID, defined by the WHO as the persistence or emergence of symptoms
84 three months after infection, lasting at least two months without alternative explanation,
85 affects up to 50% of hospitalized patients [3] and as many as 70% of those with severe
86 disease.[4] Fatigue, dyspnea, and cognitive impairment are among the most frequent
87 sequelae, contributing to functional limitations, reduced quality of life, and delayed return to
88 work.[5]

89 Multiple mechanisms have been implicated in its pathophysiology, including organ
90 damage, chronic inflammation, endothelial dysfunction, microthrombosis, and
91 autoimmunity.[6-9] Musculoskeletal impairment and critical illness myopathy, already well

92 recognized before the pandemic,[10] are now acknowledged as contributors to long COVID,
93 aggravating weakness and exercise intolerance.[8-10]

94 Physical inactivity is associated with worse COVID-19 outcomes, whereas higher
95 cardiorespiratory fitness appears protective.[11] Individualized, low- to moderate-intensity
96 exercise has been recommended to support recovery and improve function,[12] and phase-
97 adapted rehabilitation strategies have been proposed.[13] However, uncertainties remain
98 regarding the optimal exercise modality, intensity, and particularly the timing of
99 intervention.[14]]

100 This study evaluated symptom progression and adherence to prescribed exercise
101 therapy in COVID-19 survivors over 32 months. Special attention was given to the
102 prognostic significance of day 21 post-discharge, to determine whether early rehabilitation
103 engagement influences recovery trajectories and long-term outcomes

104

105

106

METHODS

107

Study Design and Ethical Approval

109 During the COVID-19 pandemic, to better characterize the clinical course and ensure
110 continuity of Physical Medicine and Rehabilitation (PM&R) care initiated during
111 hospitalization at Hospital Beatriz Ângelo (HBA), Portugal, patients were systematically
112 evaluated in the hospital's outpatient PM&R clinic following discharge. Informed consent
113 was obtained by phone and documented in the medical records, approved by the Ethics
114 Committee. The study was approved by the research department and the Ethics Committee

115 of HBA, with Ethics Approval Reference 3734/2021_MJHMAB/FB and
116 4692/2025_MJH/CL for study n.º576_LH n.º329. The data were collected between 1 May
117 2020 and 31 July 2025. Data were accessed for research purposes on the 31 July 2025. Only
118 the medical authors who were responsible for monitoring the patients had access to the
119 participants' identities.

120

121 *Participants*

122 Adult patients with clinically and laboratory-confirmed SARS-CoV-2 infection,
123 diagnosed by reverse transcription polymerase chain reaction (RT-PCR), were included.

124 Patients were considered eligible after achieving clinical stability in the general
125 COVID-19 ward. In-hospital exercise therapy was initiated in those meeting predefined
126 clinical safety criteria, including comprehensive assessment of respiratory, cardiovascular,
127 and neurological systems, as well as hematologic and laboratory parameters [15,16] (see S1
128 Appendix).

129 The final sample included 276 hospitalized patients, aged 20 to 86 years (mean = 56.6
130 \pm 13.5), of whom 194 (71.1%) were male. Among them, 163 patients (59.7%) required
131 admission to the intensive care unit (ICU), mainly due to hypoxemic respiratory failure.
132 Invasive mechanical ventilation (IMV) was necessary in 79 patients (29.2%), and prone
133 positioning was frequently employed. Prior physical activity was reported by 97 patients
134 (35.1%) and was defined as meeting the World Health Organization's recommended levels:
135 150–300 minutes of moderate-intensity or 75–150 minutes of vigorous-intensity aerobic
136 activity per week.[17]

137 The most common comorbidities were hypertension (58.3%), obesity (57.4%),
138 dyslipidemia (41.1%), and diabetes mellitus (32.4%). Other relevant conditions included
139 psychiatric disorders (10.2%), malignancy (7.0%), chronic pulmonary disease (6.6%), and
140 asthma (6.1%). Notably, 45.5% of patients had no comorbidities.

141

142 *In-Hospital Rehabilitation Program*

143 During isolation, the PM&R department developed an exercise plan to continue
144 rehabilitation started during hospitalization. After clinical stabilization (typically by day 2–
145 3), the team provided education and individualized instruction.

146 Patients received a printed guide with 10 standardized exercises (breathing, limb and
147 trunk strength, and balance), illustrated with photos, plus a resistance band (TheraBand®).
148 Intensity was progressively adapted (3–20 repetitions), with adjustments based on tolerance
149 under physiotherapist supervision. Oxygen saturation and heart rate were monitored with a
150 pulse oximeter, and symptoms were assessed using the Modified Borg Scale (mBorg).
151 Exercise was discontinued if saturation dropped >4% from baseline, fell below 90%, or if
152 fatigue, dyspnea, or pain exceeded 3 on the mBorg. Progression, including increased
153 repetitions, was implemented under physiotherapist supervision.

154

155 *Post-Discharge Home-Based Program*

156 Upon discharge, all instructional materials and equipment except for the pulse
157 oximeter were provided to patients to continue the home-based program. Exercise
158 compliance was monitored through structured follow-up, including three telephone contacts
159 by the clinical team, forming part of a tele-rehabilitation strategy to support adherence and

160 address any emerging complications related to the prescribed exercise plan. The first call
161 occurred between the 5th and 10th day after discharge, the second on the 15th day (both by
162 physiotherapists), and the third on the 21st day, conducted by a physician. Patients were also
163 encouraged to begin walking after the isolation period, with appropriate safety precautions
164 (Figure 1).

165 Due to fluctuations in healthcare response capacity during the pandemic, only 231 of
166 the 276 patients (83.7%) received at least one follow-up call. Due to the absence of adherence
167 data, the remaining 45 patients (16.3%) could not be included in analyses examining exercise
168 compliance or symptom progression related to follow-up timing. Of those contacted, 93
169 (33.7%) received the first call, 63 (22.8%) received the second, and 227 (82.2%) were
170 reached on the 21st day post-discharge.

171

172 *Outpatient Follow-Up and Clinical Monitoring*

173 Compliance with the prescribed exercise program was assessed, and symptoms were
174 recorded during the day-21 teleconsultation. If symptoms or disability persisted, a face-to-
175 face PM&R consultation was scheduled between the second and fourth months, post-
176 discharge, depending on appointment availability.

177 Pain was defined as new-onset or worsening of prior symptoms. When appropriate, a
178 6-minute walk test (6MWT) was performed during in-person visits to assess oxygen
179 desaturation, heart rate, and functional capacity. Referrals to other specialties and
180 neuropsychology were made when needed.[18] Follow-up diagnostics were limited due to
181 infection risk and logistical constraints.

182

183 *Rehabilitation Prescription and Long-Term Monitoring*

184 During in-person PM&R consultations, patients received a comprehensive clinical
185 assessment and a tailored rehabilitation prescription (RP), which included physiotherapy and
186 occupational therapy, primarily delivered at the hospital. Follow-up appointments were
187 scheduled every 2 to 3 months. Monitoring continued until rehabilitation-responsive
188 symptoms (e.g., fatigue, dyspnea, pain, myalgias, peripheral sequelae, muscle weakness,
189 imbalance, reduced effort tolerance) had resolved, or until the study database closed at 32
190 months.

191

192 *Study Variables*

193 Variables included demographic data (age, sex), ICU admission, IMV, discharge
194 date, prior physical activity, comorbidities, follow-up contact dates, exercise adherence, and
195 symptom evolution (see S2 Appendix).

196

197 *Data Analysis*

198 Statistical analysis was performed using **IBM** Statistical Package for the Social
199 Sciences (SPSS), version 28 (IBM Corp., Armonk, NY, USA). Descriptive and frequency
200 analyses were conducted for demographic and clinical variables. Frequency analyses, chi-
201 square tests of independence, and independent-sample t-tests were used to assess associations
202 between the study variables. Patients who did not receive any follow-up calls (n = 45;16.3%)
203 were excluded from analyses involving exercise adherence and its association with outcomes,
204 due to lack of relevant data. However, they were retained in overall descriptive statistics

205 where applicable. No data imputation was performed. Full details of the statistical procedures
206 are provided in S3 Appendix.

207 RESULTS

208

209 *Exercise adherence*

210 Most patients adhered consistently to the prescribed exercise program throughout
211 follow-up (Figure 2). A significant association was found between adherence at day 15 and
212 adherence at day 21 post-discharge (Table 1; $\chi^2 = 4.712$; $p = .03$), with 83.6% of individuals
213 who exercised on day 15 also adhering on day 21 (Table 1).

214

215 Table 1. Association between early exercise adherence and day 21 adherence in covid-19
216 survivors

Adherence to exercise				21st day after discharge		χ^2
				No	Yes	
5-10th day after discharge	No	1 (33.3%)	2 (66.7%)	1.552 ($p=.21$)		
	Yes	9 (10.3%)	78 (89.7%)			
15th day after discharge	No	1(100.0%)*	0 (0.0%)*	4.712 ($p=.03$)		
	Yes	10(16.4%)*	51 (83.6%)*			

217 * $p < .05$

218

219

220

221 *Symptom Burden and Adherence*

222 Intervention strategies aimed at enhancing patients' understanding of the importance
223 of exercise for physical rehabilitation promoted sustained adherence, even 21 days post-
224 discharge. Additionally, analysis of long COVID symptoms revealed that the majority
225 (83.2%) of patients who performed the exercises on day 21 did not experience dyspnea post-
226 discharge ($\chi^2(1) = 5.289, p = .02$) (Table 2). The average follow-up time in the PM&R
227 consultation was 6.1 months (M = 6.1; SD = 6.2).

228

229 Table 2. Day 21 Exercise and Post-COVID Symptom Burden

Symptoms	Adherence to exercise		χ^2
	No	Yes	
Pain	No	32 (18.5%)	0.193 ($p=.66$)
	Yes	141 (81.5%)	
Fatigue	No	8 (21.6%)	0.915 ($p=.34$)
	Yes	132 (82.5%)	
Dyspnea	No	12 (23.5%)	5.289 ($p=.02$)
	Yes	39 (76.5%)	
Neurologic sequelae	No	31 (16.8%)*	0.231 ($p=.63$)
	Yes	154 (83.2%)*	
Myalgias	No	9 (36.0%)*	0.509 ($p=.48$)
	Yes	16 (64.0%)*	

Decline in muscular strength	No	35 (18.7%)	152 (81.3%)	0.121 ($p=.73$)
	Yes	5 (21.7%)	18 (78.3%)	
Imbalance	No	37 (18.5%)	163 (81.5%)	0.817 ($p=.37$)
	Yes	3 (30.0%)	7 (70.0%)	
Decreased effort tolerance	No	40 (19.5%)	165 (80.5%)	1.205 ($p=.27$)
	Yes	0 (0.0%)	5 (100.0%)	
Paresthesias	No	39 (19.0%)	166 (81.0%)	0.003 ($p=.96$)
	Yes	1 (20.0%)	4 (80.0%)	

230 * $p<.05$

231 *Effect of Prior Physical Activity on Adherence*

232 Patients were asked about their exercise habits prior to COVID-19 infection. A
 233 significant association was observed between previous habits and adherence on day 21 ($\chi^2(1)$
 234 = 8.991, $p = .003$), Nearly half of adherent patients (48.8%) reported meeting WHO physical
 235 activity guidelines prior to COVID-19 infection. (Table 3).

236

237 Table 3. Pre-Infection Physical Activity and Day-21 Exercise Adherence

Adherence to exercise		Previous exercise habits		χ^2
		No	Yes	
5-10th day after discharge	No	1 (33.3%)	2 (66.7%)	0.346 ($p=.56$)
	Yes	41 (50.6%)	40 (49.4%)	
15th day after discharge	No	1 (100.0%)	0 (0.0%)	

	Yes	27 (49.1%)	28 (50.9%)	1.018 ($p=.31$)
21st day after discharge	No	29 (78.4%)*	8 (21.6%)*	
	Yes	82 (51.2%)*	78 (48.8%)*	8.991
				($p=.003$)

238 * $p<.01$ *Long-Term Symptom Evolution*

239 Most patients were aged 55–64 years (34.4%, 50.0%, and 28.0% at T0, T1, and T2,
 240 respectively). Males predominated at T0 (65.6%) and T2 (72.0%), while females were more
 241 frequent at T1 (58.3%). Symptoms were assessed at follow-up consultations every 2–3
 242 months, with data compared at T0 (21 days), T1 (6 months), and T2 (32 months) post-
 243 discharge. Figure 3 shows symptom evolution across these time points.

244 At T0, the most common symptoms were fatigue (32.4%), dyspnea (22.4%), and pain
 245 (17.6%); at T1, pain (37.5%), fatigue (34.4%), and dyspnea (28.1%); and at T2, fatigue
 246 (14.5%), dyspnea (7.3%), and reduced strength (5.5%). The proportion of asymptomatic
 247 patients increased from 27.4% at T0 to 54.5% at T2.

248 A significant association was found between symptoms reported on the day-21 phone call
 249 and delayed resolution of exercise-modifiable symptoms, with symptomatic patients taking
 250 longer to become asymptomatic ($t = -6.386$; $p < .001$) (Table 4).

251

252

253 Table 4. Impact of Day-21 Symptom Status on Time to Resolution of Exercise-Modifiable
254 Symptoms

Time to resolution of exercise-modifiable symptoms			
Symptomatic patients	n	<i>M (SD)</i>	<i>t</i>
No	73	4.32 (3.80)	
Yes	95	9.48 (6.06)	-6.386 (<i>p</i> <.001)

255

256

257

DISCUSSION

258

259 This retrospective longitudinal study highlighted the potential benefits of early,
260 structured exercise therapy in post-COVID rehabilitation and provided novel data on
261 symptom evolution up to 32 months after hospital discharge.

262 The cohort was predominantly male and middle-aged, with a high prevalence of
263 comorbidities - particularly hypertension, followed by obesity and dyslipidemia. Most
264 participants were aged between 55 and 64 years. In this study, the majority of patients with
265 long COVID were male at T0 and T2, and female at T1. Previous studies identified a higher
266 risk of developing long COVID in association with several factors, including female sex,
267 middle age, obesity, infection severity, hospital admission (particularly requiring oxygen
268 therapy), symptom burden (such as dyspnea and chest pain), and pre-existing comorbidities
269 such as asthma.[19-22] While the age distribution in this cohort aligns with prior studies,[22]
270 the predominance of male patients contrasts with most reports.[20] This discrepancy may

271 reflect the higher proportion of male hospitalizations during the study period. These
272 comorbidities are well-established risk factors for severe COVID-19 and have been linked to
273 delayed recovery and greater symptom burden in post-acute and long COVID populations.
274 In this cohort, early adherence to the exercise regimen, particularly by day 15, was strongly
275 associated with continued participation through day 21, underscoring the value of early
276 rehabilitation engagement. Moreover, patients with a history of physical activity prior to
277 infection demonstrated better adherence post-discharge, reinforcing the influence of lifestyle
278 factors on recovery. Notably, adherence at day 21 was associated with reduced dyspnea at
279 final consultation.

280 An important finding of this study is the identification of day 21 as a critical
281 prognostic time point. Patients who still reported symptoms and did not adhere to the exercise
282 program at this stage took significantly longer to become asymptomatic. This emphasizes
283 that, while the benefits of exercise in long COVID are recognized, the timing of initiation is
284 decisive: patients who fail to engage in exercise early—within the first three weeks after
285 discharge—are at substantially higher risk of prolonged recovery. Clinically, this suggests
286 that day-21 follow-up is valuable not only for monitoring adherence but also for identifying
287 high-risk patients who may require intensified rehabilitation strategies and closer
288 supervision.

289 Long-term symptom monitoring revealed a progressive decline in key symptoms
290 (fatigue, dyspnea, and pain) and an increase in asymptomatic individuals over time.
291 However, patients who remained symptomatic at day 21 experienced significantly slower
292 recovery, suggesting early symptom persistence as a potential prognostic marker of
293 prolonged rehabilitation.

294 The pathophysiological mechanisms underlying long COVID remain incompletely
295 understood. Prolonged systemic inflammatory responses have been proposed as a potential
296 mechanism for long COVID, particularly in patients with mild acute infection who develop
297 persistent symptoms despite no detectable organ damage.[19,23] Several mechanisms have
298 been implicated in the pathogenesis of long COVID, including alterations in the angiotensin-
299 converting enzyme 2 (ACE2) pathway and dysregulation of the renin–angiotensin–
300 aldosterone system (RAAS)[24], endothelial dysfunction [25], neuromuscular
301 impairment²⁶, and autonomic dysregulation.[27] Given these complex mechanisms,
302 interventions that target systemic inflammation and functional impairment—such as
303 exercise—are increasingly supported by evidence. Exercise plays a key role in post-COVID
304 rehabilitation, not only by enhancing functional capacity but also through its anti-
305 inflammatory effects. Regular moderate-intensity exercise reduces systemic inflammatory
306 mediators (CRP, IL-6, TNF- α) through improved immune regulation, increased anti-
307 inflammatory cytokines, and enhanced vagal tone. Given the contribution of chronic low-
308 grade inflammation to long COVID, exercise may directly modulate its pathophysiology and
309 support recovery. [28,29]

310 This study underscores the importance of individualized rehabilitation strategies and
311 multidisciplinary care in long COVID.³⁰ Exercise interventions were adapted to patient
312 tolerance and adjusted progressively based on symptom response, accommodating the
313 heterogeneity of clinical presentations. Supervision by physiotherapists and physicians,
314 including structured telephone follow-up, enabled safe and remote engagement, particularly
315 during isolation periods. These findings highlight the utility of tele-rehabilitation in

316 supporting adherence and extending access to care, reinforcing its role within comprehensive
317 post-COVID rehabilitation protocols.

318

319 Limitations

320 This study has several limitations. First, pre-existing symptomatology data were
321 unavailable, potentially confounding persistent symptom interpretation. Second, symptom
322 severity assessment was limited by data granularity constraints. Third, excluding patients
323 without follow-up calls may have introduced selection bias. Additionally, this single-center
324 study lacked a control group of patients discharged after non-COVID illnesses. Since
325 prolonged symptoms may occur after community-acquired pneumonia, findings may have
326 broader relevance beyond COVID-19

327

328

329 CONCLUSION

330

331 This study evaluated post-discharge symptoms in COVID-19 survivors and their
332 adherence to a rehabilitation program for long COVID. The findings reinforce the importance
333 of early and individualized rehabilitation, particularly through structured therapeutic
334 exercise. Interventions were safe, adaptable, and associated with reduced symptom burden—
335 most notably dyspnea.

336 An important finding of this study was the identification of day 21 as a critical
337 prognostic point: patients who remained symptomatic and did not adhere to exercise at this

338 stage took significantly longer to recover. This underscores that early initiation of low- to
339 moderate-intensity exercise under professional supervision is decisive for optimizing
340 recovery, beyond its role as a functional enhancer and immune modulator.

341 Additionally, the successful implementation of tele-rehabilitation highlights its
342 potential to enhance accessibility and support patient management. Collectively, these results
343 suggest that structured and early rehabilitation strategies may be extended to other
344 populations recovering from severe respiratory illnesses.

345

346

347 Acknowledgements

348 The authors would like to acknowledge Gisela Gomes, PT; Patricia Martins, PT;
349 Carla Rodrigues, PT; and Tânia Bastos, PT for performing physiotherapy sessions,
350 conducting follow-up phone calls, and assisting with data collection. The authors also thank
351 Cláudia Abreu, PT for her contribution in designing the patient exercise brochure.
352 Additionally, ARD, DP, and AB acknowledge Ana Filipa Regadas, PT for her support in the
353 organizational aspects of the study.

354

355

REFERENCES

356

357 1. GBD 2021 Demographics Collaborators. Global age-sex-specific mortality, life
358 expectancy, and population estimates in 204 countries and territories and 811 subnational
359 locations, 1950–2021, and the impact of the COVID-19 pandemic: a comprehensive

- 360 demographic analysis for the Global Burden of Disease Study 2021. *Lancet*.
361 2024;403(10440):1989–2056. doi:10.1016/S0140-6736(24)00476-8
- 362 2. World Health Organization. Post COVID-19 condition (Long COVID). Published
363 December 7, 2022. Accessed June 19, 2025. [https://www.who.int/europe/news-room/fact-](https://www.who.int/europe/news-room/fact-sheets/item/post-covid-19-condition)
364 [sheets/item/post-covid-19-condition](https://www.who.int/europe/news-room/fact-sheets/item/post-covid-19-condition)
- 365 3. Shi J, Lu R, Tian Y, Wu F, Geng X, Zhai S, et al. Prevalence of and factors associated
366 with long COVID among US adults: a nationwide survey. *BMC Public Health*. 2025;
367 25:1758. doi:10.1186/s12889-025-22987-8
- 368 4. Davis HE, McCorkell L, Moore Vogel J, Topol EJ. Long COVID: major findings,
369 mechanisms and recommendations. *Nat Rev Microbiol*. 2023;21(3):133–146.
370 doi:10.1038/s41579-022-00846-2
- 371 5. Halpin SJ, McIvor C, Whyatt G, Adams A, Harvey O, McLean L, et al. Postdischarge
372 symptoms and rehabilitation needs in survivors of COVID-19 infection: a cross-sectional
373 evaluation. *J Med Virol*. 2021;93(2):1013-1022. doi:10.1002/jmv.26368;93(2):1013–1022.
374 doi:10.1002/jmv.26368
- 375 6. Xie Y, Bowe B, Al-Aly Z. Long-term cardiovascular outcomes of COVID-19. *Nat Med*.
376 2022;28(3):583–590. doi:10.1038/s41591-022-01689-3
- 377 7. Carvalho-Schneider C, Laurent E, Lemaigen A, Beaufils E, Bourbao-Tournois C, Laribi
378 S, et al. Follow-up of adults with noncritical COVID-19 two months after symptom onset.
379 *Clin Microbiol Infect*. 2021;27(2):258–263. doi:10.1016/j.cmi.2020.09.052
- 380 8. Agergaard J, Khan BYA, Engell-Sørensen T, Schiøttz-Christensen B, Østergaard L,
381 Hejbøl EK, et al. Myopathy as a cause of Long COVID fatigue: Evidence from quantitative

- 382 and single fiber EMG and muscle histopathology. *Clin Neurophysiol.* 2023;148:65–75.
383 doi:10.1016/j.clinph.2023.01.010
- 384 9. Ramírez-Vélez R, Legarra-Gorgoñon G, Oscoz-Ochandorena S, García-Alonso Y, García-
385 Alonso N, Oteiza J, et al. Reduced muscle strength in patients with long-COVID-19
386 syndrome is mediated by limb muscle mass. *J Appl Physiol.* 2023;134(1):50–58.
387 doi:10.1152/jappphysiol.00599.202
- 388 10. Schefold JC, Wollersheim T, Grunow JJ, Luedi MM, Z'Graggen WJ, Weber-Carstens S.
389 Muscular weakness and muscle wasting in the critically ill. *J Cachexia Sarcopenia Muscle.*
390 2020;11(6):1399–1412. doi:10.1002/jcsm.12620
- 391 11. Rahmati M, Shamsi MM, Khoramipour K, Malakoutinia F, Woo W, Park S, et al.
392 Baseline physical activity is associated with reduced mortality and disease outcomes in
393 COVID-19: A systematic review and meta-analysis. *Rev Med Virol.* 2022;32(5):e2349.
394 doi:10.1002/rmv.2349
- 395 12. Zheng C, Chen XK, Sit CH-P, Liang X, Li MH, Ma ACH-H, et al. Effect of physical
396 exercise-based rehabilitation on long COVID: a systematic review and meta-analysis. *Med*
397 *Sci Sports Exerc.* 2024;56(1):143-154. doi:10.1249/MSS.0000000000003280
- 398 13. Gutenbrunner C, Nugraha B, Martin LT. Phase-adapted rehabilitation for acute
399 coronavirus disease-19 patients and patients with long-term sequelae of coronavirus disease-
400 19. *Am J Phys Med Rehabil.* 2021;100(6):533–538. doi:10.1097/PHM.0000000000001762
- 401 14. Besnier F, Malo J, Mohammadi H, Clavet S, Klai C, Martin N, et al. Effects of
402 cardiopulmonary rehabilitation on cardiorespiratory fitness and clinical symptom burden in
403 Long COVID: results from the COVID-Rehab randomized controlled trial. *Am J Phys Med*
404 *Rehabil.* 2025;104(2):163-171. doi:10.1097/PHM.0000000000002559

- 405 15. Zhao HM, Xie YX, Wang C. Recommendations for respiratory rehabilitation in adults
406 with coronavirus disease 2019. *Chin Med J (Engl)*. 2020;133(13):1595-1602.
407 doi:10.1097/CM9.0000000000000848
- 408 16. Conceição T, Gonzales AI, Figueiredo F, Vieira DSR, Bundchen DC. Safety criteria to
409 start early mobilization in intensive care units: systematic review. *Rev Bras Ter Intensiva*.
410 2017;29(4):509–519. doi:10.5935/0103-507X.20170076
- 411 17. Bull FC, Al-Ansari SS, Biddle S, Borodulin K, Buman MP, Cardon G, et al. World Health
412 Organization 2020 guidelines on physical activity and sedentary behaviour. *Br J Sports Med*.
413 2020;54(24):1451–1462. doi:10.1136/bjsports-2020-102955
- 414 18. Ceravolo MG, Anwar F, Andrenelli E, Udensi C, Qureshi J, Sivan M, et al. Evidence-
415 based position paper on physical and rehabilitation medicine professional practice for
416 persons with COVID-19, including post COVID-19 condition: the European PRM position
417 (UEMS PRM Section). *Eur J Phys Rehabil Med*. 2023;59(6):789-799. doi:10.23736/S1973-
418 9087.23.08315-6
- 419 19. Sudre CH, Murray B, Varsavsky T, Graham MS, Penfold RS, Bowyer RC, et al.
420 Attributes and predictors of long COVID. *Nat Med*. 2021;27(4):626-631.
421 doi:10.1038/s41591-021-01292-y
- 422 20. Moritani I, Yamanaka K, Nakamura T, Tanaka J, Kainuma K, Okamoto M, et al.
423 Prevalence of and risk factors for long COVID following infection with the COVID-19
424 omicron variant. *Med Int (Lond)*. 2025;5(2):17. doi:10.3892/mi.2025.216
- 425 21. Castanares-Zapatero D, Chalon P, Kohn L, Dauvrin M, Detollenaere J, Maertens de
426 Noordhout C, et al. Pathophysiology and mechanism of long COVID: a comprehensive
427 review. *Ann Med*. 2022;54(1):1473-1487. doi:10.1080/07853890.2022.2076901

- 428 22. Guan WJ, Liang WH, Zhao Y, Liang HR, Chen ZS, Li YM, et al. Comorbidity and its
429 impact on 1590 patients with COVID-19 in China: a nationwide analysis. *Eur Respir J*.
430 2020;55(5):2000547. doi:10.1183/13993003.00547-2020
- 431 23. Wirth KJ, Scheibenbogen C. Dyspnea in post-COVID syndrome following mild acute
432 COVID-19 infections: potential causes and consequences for a therapeutic approach.
433 *Medicina (Kaunas)*. 2022;58(3):419. doi:10.3390/medicina58030419
- 434 24. Astin R, Banerjee A, Baker MR, Dani M, Ford E, Hull JH, et al. Long COVID:
435 mechanisms, risk factors and recovery. *Exp Physiol*. 2023;108(1):12-27.
436 doi:10.1113/EP090802
- 437 25. Gleeson M, Bishop NC, Stensel DJ, Lindley MR, Mastana SS, Nimmo MA. The anti-
438 inflammatory effects of exercise: mechanisms and implications for the prevention and
439 treatment of disease. *Nat Rev Immunol*. 2011;11(9):607–615. doi:10.1038/nri3041
- 440 26. Swarnakar R, Yadav SL. Rehabilitation in long COVID-19: A mini-review. *World J*
441 *Methodol*. 2022;12(4):235–245. doi:10.5662/wjm.v12.i4.235
- 442 27. Vassiliou AG, Vrettou CS, Keskinidou C, Dimopoulou I, Kotanidou A, Orfanos SE.
443 Endotheliopathy in acute COVID-19 and long COVID. *Int J Mol Sci*. 2023;24(9):8237.
444 doi:10.3390/ijms24098237
- 445 28. Jimeno-Almazán A, Pallarés JG, Buendía-Romero Á, Martínez-Cava A, Franco-López
446 F, Sánchez-Alcaraz Martínez BJ, et al. Post-COVID-19 syndrome and the potential benefits
447 of exercise. *Int J Environ Res Public Health*. 2021;18(10):5329. doi:10.3390/ijerph18105329
- 448 29. Gleeson M, Bishop NC, Stensel DJ, Lindley MR, Mastana SS, Nimmo MA. The anti-
449 inflammatory effects of exercise. *Nat Rev Immunol*. 2011;11(9):607–615.
450 doi:10.1038/nri3041

451 30. Swarnakar R, Yadav SL. Rehabilitation in long COVID-19: A mini-review. World J
452 Methodol. 2022;12(4):235–245. doi:10.5662/wjm.v12.i4.235

453 **Figure Legends**

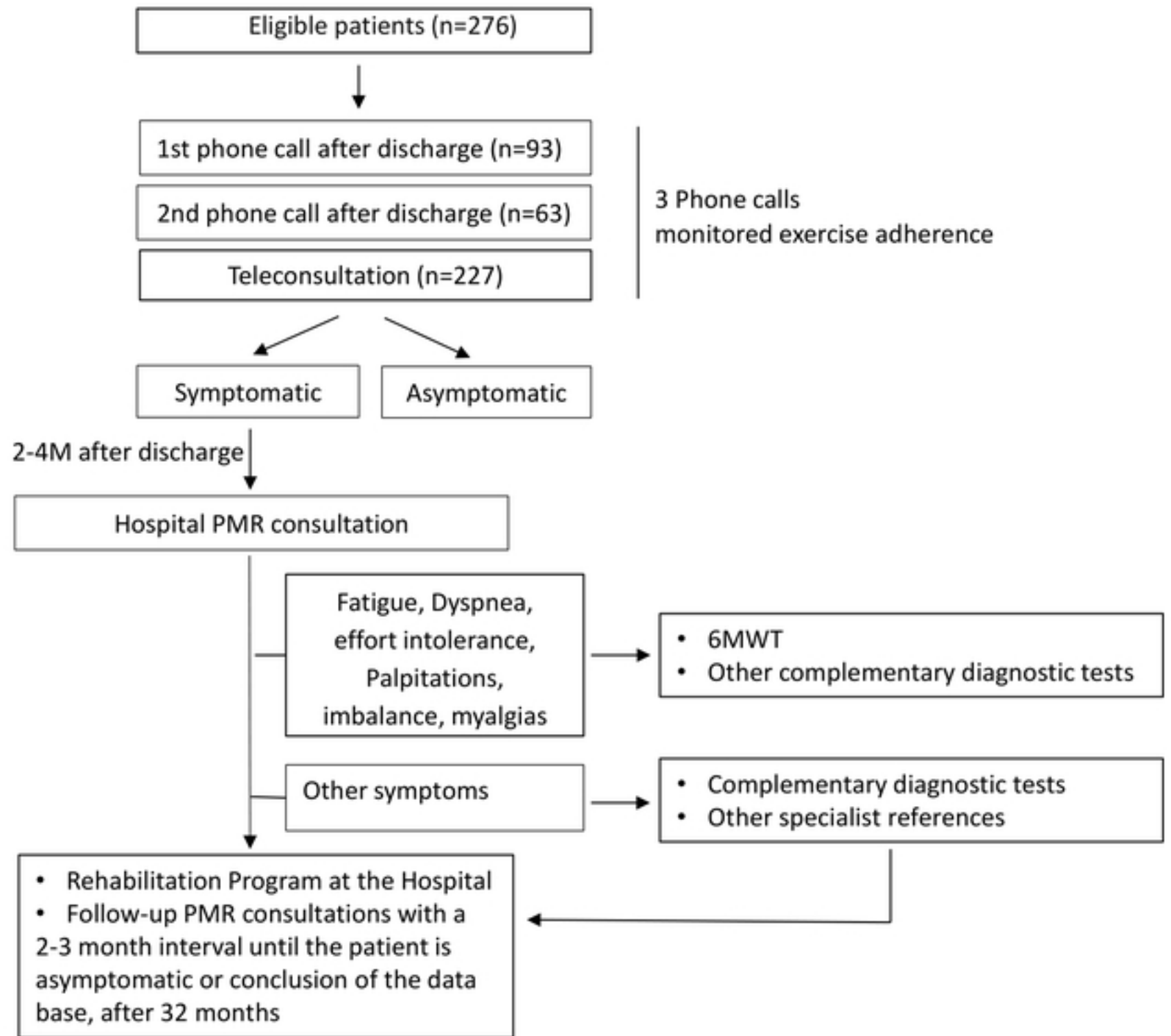
454 Figure 1. *Flow chart of the study*

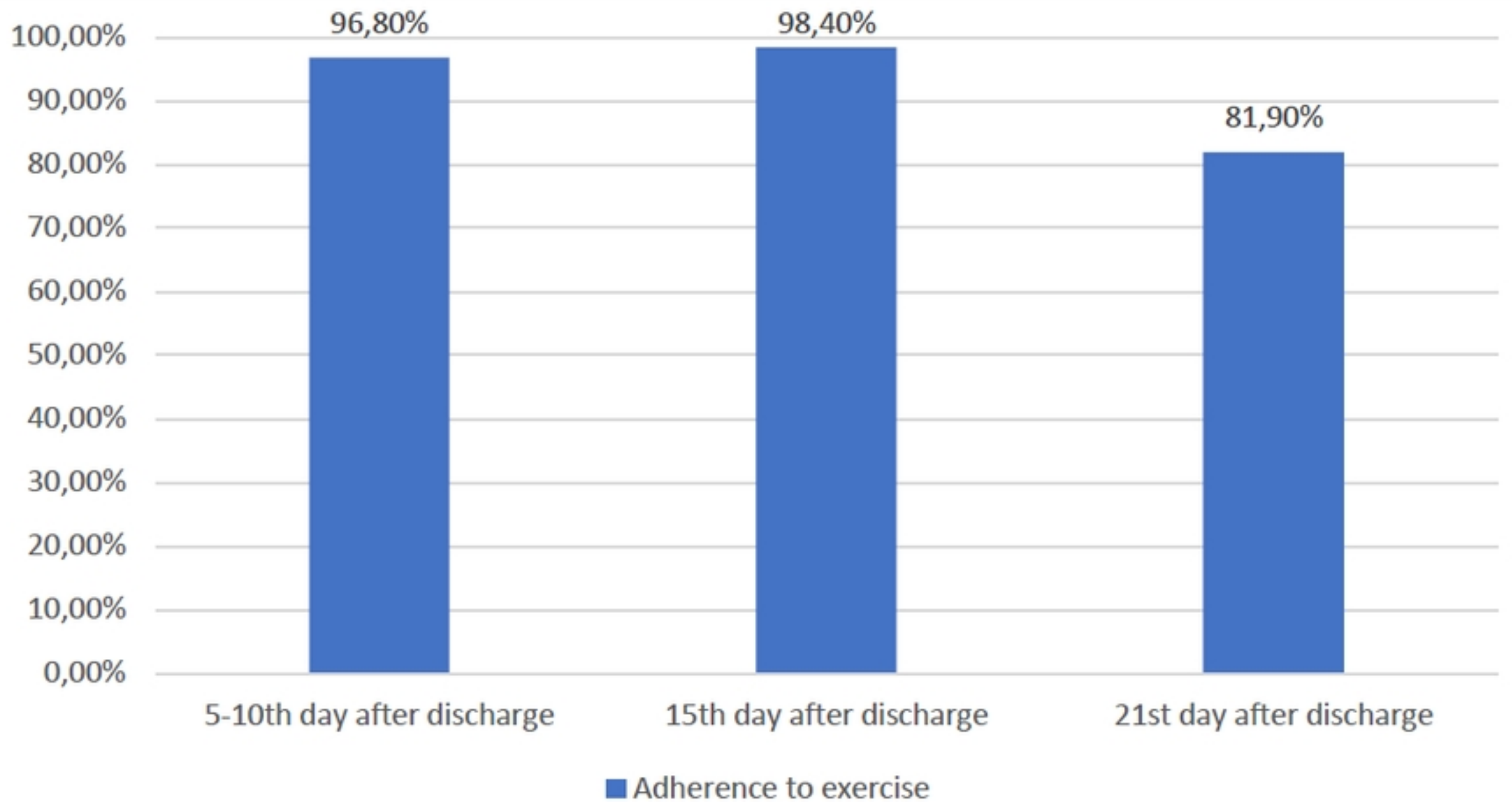
455 Figure 2. *Adherence to exercise at three follow-up points*

456 Figure 3. *Evolution of the most frequent post-COVID symptoms at 21 days (T0), 6 months
457 (T1), and 32 months (T2) after discharge*

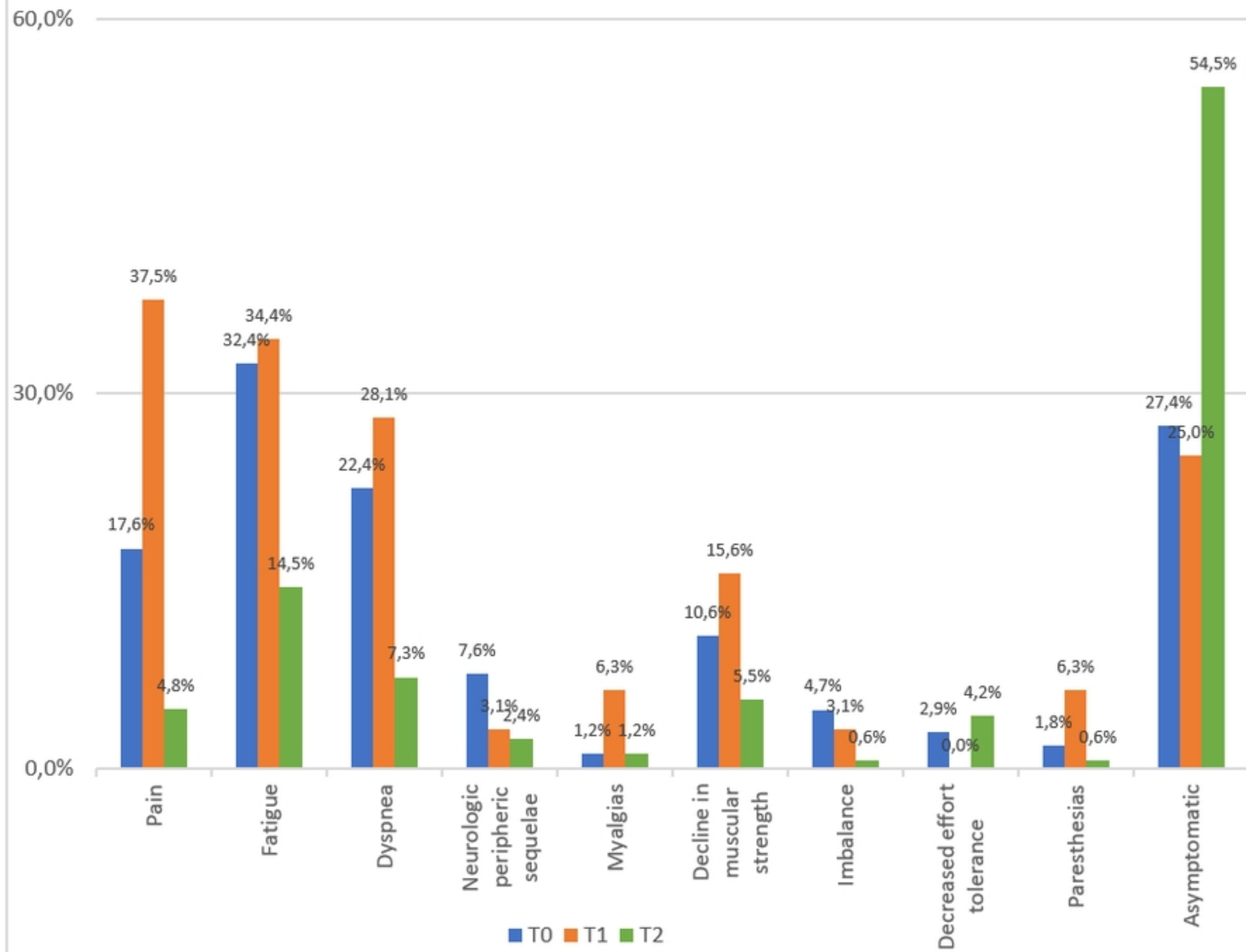
458

Figure 1. Flow chart of the study





Figure



Figure