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Effectiveness of an online multimodal rehabilitation program in long COVID patients: a randomized clinical trial

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Abstract

Background Digital interventions are expected to facilitate the treatment of patients suffering from Long COVID. This trial assesses the effectiveness of a multimodal rehabilitation program —comprising both online and synchronous components— in managing the characteristic symptoms of Long COVID and, consequently, in improving quality of life. It also aims to identify which changes in measured variables from baseline (T0) to post-intervention (T1) predict an improvement in quality of life.

Methods A blind randomized controlled trial was conducted with two parallel groups: (1) the control group, which received usual treatment from the primary care physician and (2) the intervention group, which received usual treatment in addition to an online multimodal rehabilitation program. The data were collected at two time points: prior to the start of the intervention and three months after it. The main outcome variable was quality of life, encompassing both mental health and physical health-related quality of life. Sociodemographic and clinical variables were collected as secondary variables.

Results A total of 134 participants (age 48.97 ± 7.64 ; 84.33% female) were included and randomized into the control group (67 participants) and the intervention group (67 participants). Comparative analyses conducted before and after the intervention showed a significant improvement in the mental health-related quality of life of the participants who received the intervention, with a mean increase of 1.98 points ($p < 0.05$). Linear regression analyses revealed that both received the intervention ($b = 3.193$; $p < 0.05$) and an increased self-efficacy ($b = 0.298$; $p < 0.05$) were predictors of greater improvement in mental health-related quality of life.

Keywords Long COVID, Effectiveness, Telerehabilitation, Multimodal, Quality of life, Self-efficacy

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Text box 1. Contributions to the literature

- Approaches for treating Long COVID syndrome are still limited due to the lack of knowledge about this new disease. This research sheds light on this topic.
 - Digital interventions are expected to support face-to-face and group treatment for Long COVID patients. This study tests the effectiveness of an online rehabilitation program.
 - Telerehabilitation may be a useful tool when addressing mental health-related quality of life in patients suffering from Long COVID.
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Background

One of the uncertainties that remains a concern in the aftermath of the COVID-19 pandemic is the prognosis of post-COVID or Long COVID syndrome, along with its clinical reality, treatment needs, and the necessary health services and resources [1]. In October 2021, the WHO defined this pathology as symptoms of a probable or confirmed SARS-CoV-2 infection that persist or develop three months after the initial infection, and that cannot be explained by an alternative diagnosis [2].

It is estimated that at least 65 million people are battling this debilitating illness, in which over 200 different symptoms have been documented. These symptoms predominantly manifest as cardiorespiratory, musculoskeletal, neurocognitive, and gastrointestinal symptoms, and they affect their ability of infected individuals to perform activities of daily living (ADLs) for months or even years after infection [3–5]. Indeed, it has been identified as a potentially disabling condition—at least in the short term—that seriously affects quality of life. Quality of life can be defined as the state of personal well-being derived from satisfaction with areas of significance to the individual [6–8]. Evidence regarding the long-term impact of Long COVID on the lives of affected patients is still limited, as is the evidence regarding the efficacy of randomized trials on interventions and treatments that improve the health and quality of life of these patients [9–11].

Rehabilitation represents a key resource for the improvement and recovery of the impaired functionality of patients with Long COVID, when possible [12]. However, the complexity of the symptoms, as well as the absence of effective treatment approaches, adversely affect the provision of services and, of course, the experiences of the patients themselves [13].

Despite the limited options available due to the lack of knowledge about this disease, some clinical management guidelines have been proposed, emphasizing the importance of a personalized and holistic perspective based on the control of symptoms and complications [14]. This is due to the fact that recovery from this disease is not linear and occurs in a heterogeneous manner, with each individual experiencing the evolution, needs, and expectations of recovery differently [15, 16]. Long

COVID has also been recognized as a multisystemic condition that requires comprehensive continuous rehabilitation provided by a multidisciplinary team. This should include the participation of family physicians, physiotherapists, speech therapists, psychologists, nutritionists, occupational therapists, and social workers, among others. These professionals could provide guidelines for the management and self-control of some symptoms such as arthralgia, fatigue, dyspnea, cognitive impairment, sleep problems, depression, and anxiety [12, 17, 18].

During the prolonged period of the COVID-19 pandemic, the use of technology in social health care and rehabilitation services increased due to the elevated risk of contagion. Digital health interventions are considered to be as effective as conventional face-to-face interventions. However, they present several advantages such as low cost, wide reach, and adaptability. It is expected that these interventions will also support face-to-face and group treatment for Long COVID patients, especially given that many of these patients express concern about reinfection, which could potentially worsen their health condition. Additionally, their numerous physical and cognitive limitations make it difficult or impossible for them to travel to other locations to receive treatment. The efficacy of telerehabilitation in post-COVID conditions has already been demonstrated, resulting in improvements in various domains such as dyspnea, fatigue, functionality, and physical components of quality of life. However, although technology offers greater accessibility, it also presents some challenges such as possible technical problems or the limited technological literacy of some patients [12, 19–21].

With the emergence of initial cases of Long COVID and the subsequent dissemination of shared experiences via social networks, group support among the affected individuals has been identified as a crucial element in their recovery process [22, 23]. In fact, despite concerns about reinfection, some studies have also demonstrated the effectiveness of group interventions in the management of patients with Long COVID, with positive results related to the participants' well-being [24–26].

The objective of this trial was to investigate Long COVID and to evaluate the efficacy of multidisciplinary social health care teams in its management. The study aimed to analyze the effectiveness of a multimodal rehabilitation program, comprising online and synchronous components, in alleviating the characteristic symptoms of Long COVID and, consequently, in improving quality of life. A secondary purpose was to identify which changes in measured variables from baseline (T0) to post-intervention (T1) predict an improvement in quality of life in individuals with Long COVID.

Methods

Study design

This study employed a Randomized Clinical Trial that included two parallel groups of Long COVID patients: patients from the first group followed their usual treatment as prescribed by their primary care practitioner (control group; treatment as usual, TAU), and patients from the second group followed their TAU and additionally participated in an online multimodal rehabilitation program (intervention group).

This study complies with the guidelines prescribed by the Consolidated Standards of Reporting Trials (CONSORT) checklist [see Additional file 1] and was registered with the ISRCTN Registry (registration no.: ISRCTN15414370). The original study protocol has been recently published [27] and specifies multiple methodological issues.

Patient recruitment

A purposive sampling method was used to invite individuals to participate in this research. Potential participants were those who had been diagnosed with Long COVID syndrome and who were members of Spanish Long-COVID collectives and associations.

The research team informed the presidents of Long-COVID Spanish associations about the project and its objective through an invitation letter, with all the necessary information for members to participate. Those who expressed interest were requested to contact the project researchers through the contact details provided in said letter. An evaluating researcher then contacted them and determined whether they met the study's inclusion criteria.

The study population consisted of individuals aged 18 to 80, with persistent COVID symptoms for at least three months since the acute infection for which alternative diagnosis could not be provided, and who were part of Spanish Long-COVID associations. The exclusion criteria were: having a serious uncontrolled medical condition that could interfere with adherence to the rehabilitation program; undergoing structured rehabilitation or psychotherapeutic treatment provided by health professionals; participating in another clinical trial within the previous six months; being pregnant or lactating; having considerable risk of suicide; or having any medical, psychological or social issues that could seriously affect the patient's participation in the study.

Recruitment was carried out consecutively until the estimated sample size was reached. The recruitment period spanned a two-months interval, from November 2022 to January 2023. A total of 134 patients from different Spanish Long-COVID associations were recruited.

Sample size

In accordance with the results obtained in the existing literature [28], a sample size of 53 subjects per group (106 subjects in total) was required to detect a mean difference of 20 points on the physical scale of the 36-Item Short Form Health Survey Questionnaire (SF-36), with a standard deviation (SD) between the groups of 36.16, an alpha value of 0.05 and a power of 80%. To account for potential losses, the minimum sample size was increased by 10%, resulting in a total of 116 subjects. Considering a mental health scale, in order to detect a mean difference of 20 points, with an SD of 29.99 between the groups, an alpha value of 0.05 and a power of 80%, it was necessary to recruit 35 subjects per group (70 subjects in total). This sample size was increased by 10% to counter possible losses, resulting in 77 subjects. Accordingly, the minimum sample size required for the study was determined to be 58 subjects per group (116 subjects in total). The sample size was calculated using Fistera's Guide for Determination of Sample Size [29] and the formula was specified in the protocol of this study [27].

Given the high volume of participants who showed interest in participating in the study, the final sample size included a total of 134 participants, 18 more than the required sample size.

Randomization, allocation and masking of the study groups

Once the initial data were collected, all participants were randomized in a blinded sequence. Individual randomization was performed by an independent statistician, who arranged the list of participants in alphabetical order. Due to the nature of the interventions, it was not feasible to blind the participants to their allocation. A research assistant (RA) informed the participants about their assigned group, and the intervention group was informed about the nature of the intervention, as well as the location and time frame for its implementation. In addition, the RA requested that participants refrain from disclosing their group assignment to other research.

Data collection and monitoring

A RA collected the data, and another one entered and encoded the identification data. All RAs who handled the data were blinded to patient assignment, as was the RA who performed outcome assessment and data analysis. All the information collected was treated in accordance with the provisions of the current legislation on the protection of personal data.

Control group

Patients assigned to the control group followed the usual treatment provided by their general practitioner (GP), and/or other specialist professionals. This included

standard medical care typically prescribed for their condition. Usual treatment varied based on individual patient's needs and could encompass regular consultations, prescription medications and any other routine healthcare intervention recommended by their healthcare providers. The control group did not receive the specific multimodal intervention provided to the intervention group.

Intervention group

Patients assigned to the intervention group, besides following the usual treatment provided by their GPs, participated in a multidisciplinary online rehabilitation program. The program aimed to address the symptoms of individuals with Long COVID and to improve their quality of life. To meet this objective, patients were offered exercises and therapeutic recommendations regarding physical activity, respiratory rehabilitation, cognitive rehabilitation, diet, sleep hygiene, the use of community resources and emotional management.

Intervention tools

The program was carried out using two techniques that are particularly suited to the field of telerehabilitation. On the one hand, a weekly group videoconference was held, during which all patients were monitored, and the contents of the intervention were personalized. On the other hand, a Modular Object-Oriented Dynamic Learning Environment (Moodle) platform was used as a support mechanism, containing all the materials provided to the participants during the videoconferences.

In total, eight videoconference sessions (one per week), each approximately 1.5 hours in duration, were held through the Google Meet application. Three different meetings were scheduled for each telerehabilitation session, with the aim of allowing participants to choose their preferred group based on their personal availability. This approach ensured that the maximum possible assistance was achieved. Dividing all patients into three smaller intervention groups (approximately 23 participants per group) significantly enhanced the individualization of the intervention. Smaller groups facilitated more interactive sessions, allowing for a great focus on each individual's specific needs. This also enabled more personalized guidance and support, ensuring that the therapeutic recommendations were tailored to the unique challenges of each group. Moreover, participants were able to engage more actively, discuss their experiences, and receive feedback that was suited to their individual preferences.

Each session focused on the management of each type of symptomatology (physical, cognitive, respiratory, etc.), and their impact on the quality of life (work, social and emotional impact). Therapeutic recommendations were provided with the aim of improving the health of the

population in question. The same content was provided in all three meeting groups.

Regarding the Moodle Platform, the provided material was divided into eight sections, each bearing the same name and content as the corresponding videoconference session.

Specifically, the Moodle platform allowed patients to:

- Access the link to each video conference (carried out through Google Meet).
- Review PowerPoint presentations shown during videoconferences.
- Download exercises and therapeutic recommendations (cognitive stimulation notebooks, videos with respiratory physiotherapy exercises, list of dietary recommendations, etc.).
- Participate and debate in forums about the topics addressed during the videoconference.
- Access to other resources of interest (web pages or social networks, current news, glossary of terms, etc.).

Before the beginning of the intervention, to each patient was furnished with instructions regarding the access to the online platform and the weekly videoconferences, through both verbal (by phone) and in written (by email) formats. During the program, patients could use any of their personal digital devices (mobile phones, computers, tablets, etc.), although the professionals of the team recommended the use of a computer to avoid visual fatigue.

Content of the online multimodal rehabilitation program

The design of the content of each program session was based on scientific evidence on how to address the symptoms of Long COVID with the goal of improving the quality of life of the population suffering from it [30–34]. All the contents of the Multimodal Rehabilitation Program are fully detailed in both the protocol article [27] and supplementary material, which includes some examples of specific exercises [see Additional file 2].

Due to the heterogeneity of this disease, patients had to adapt each intervention to their health status, choosing those recommendations and exercises that could help in the recovery of their own symptoms. Any recommendations or exercises that caused any harm or discomfort to patients had to be suspended immediately.

The rehabilitation sessions consisted of the following content:

1. Approach to neurological and neurocognitive symptoms: Recommendations about which cognitive exercises to practice, when and how to do them; Implementation of these recommendations and exercises.

2. Approach to respiratory symptoms: Recommendations about breathing exercises, when and how to practice them; Implementation of these exercises.
3. Approach to physical symptoms: Recommendations about physical activities and exercises, when and how to do them; Implementation of these exercises.
4. Recommendations for a healthy diet: Healthy eating recommendations mainly based on following the classic Mediterranean diet.
5. Approach to sleep and rest disorders: Sleep hygiene program; Recommendations for a good rest.
6. Managing emotional impact: Recommendations about emotional management; Explanation about first steps in meditation; Implementation of two meditation dynamics.
7. Behavioral activation and promotion of participation in the community: Brief description and examples of community health assets; Benefits of using resources offered by the community itself in health recovery; Recommendations about which community resources to use, when and how to use them.
8. Compilation of important aspects, resolution of doubts, and farewell: The last session, which took place in the last week of the program, aimed to compile and summarize the key therapeutic recommendations as well as to address the doubts and questions that had arisen throughout the sessions.

It is noteworthy that, although each session was mainly designed to address a specific type of symptomatology, the exercises explained in the previous sessions continued to be performed and any questions arising were resolved.

Outcomes and measures

Two individualized measurements were carried out three months apart. The baseline assessment was conducted between December 2022 and January 2023, and the three-months follow-up assessment was performed between April and May 2023. Both evaluations were conducted over a period of three consecutive weeks. In general, the measurements were completed online, by videoconference via Google Meet, except in some cases where in-person assessment at a Primary Health Care (PHC) Center in Zaragoza (Spain) was deemed more appropriate.

Two independent researchers with experience in similar projects performed these evaluations. Both were instructed to do so in a manner that would avoid biases in the process.

Primary outcome

The main variable of this study was quality of life, evaluated through the 36-Item Short Form Health Survey (SF-36) [35]. This survey measures eight different dimensions: physical functioning, physical role, pain, general health, vitality, social functioning, emotional role and mental health; in addition to including an item regarding the participant's declared health evolution. Its eight dimensions define two main components of health: the physical and the mental. In this survey, a score higher or lower than 50 indicates a health-related quality of life better or worse than the average of the reference population, respectively. Items are rated on a Likert-type scale from 1 to 3.5 or 6, depending on the type of item. The total score of the eight scales ranges from 0 to 100, with higher scores indicating better health-related quality of life. The validated Spanish version of the questionnaire was used [36]. The Cronbach's alpha obtained in this study was 0.80.

Secondary outcomes

Regarding the secondary variables of the study, an ad hoc questionnaire was designed to collect some sociodemographic and clinical variables from the participants. In addition, eleven validated scales were used with the aim of further exploring the profile of each Long COVID patient. In all cases, the validated Spanish version of the original scale was used.

- The following sociodemographic variables were collected: current age, self-perceived age (how individuals perceive their own age compared to their actual chronological age), gender (man, woman, other), marital status (single, separated, divorced, or widowed/married or in a relationship), education level (no studies or primary studies/secondary or university studies), living area (rural or urban) and occupational status (employed, unemployed, temporary work disability, permanent work disability, retired, or others).
- The analyzed clinical variables related to Long COVID syndrome were the date of contracting COVID-19 and the number and severity of self-reported persistent symptoms at the time of each assessment, as measured by the 1–10 Visual Analog Scale [37]. To record these symptoms, a list of 30 typical persistent symptoms of patients with Long COVID was used according to previous literature [38–40].
- The official Spanish version of the Montreal Cognitive Assessment (MoCA) [41–43] was used to assess the presence of cognitive impairment in the participants of this study. This test evaluates six cognitive domains: memory, attention, language, executive function, visuospatial ability, and

orientation. The cutoff point of this scale for the detection of mild cognitive impairment is twenty-six points. The Cronbach's alpha obtained in this study was 0.59.

- The physical functioning variable was determined using the 30-second version of the Sit to Stand Test which measures the strength and endurance of the lower limbs [44–46].
- The affective state was evaluated applying the Hospital Anxiety and Depression Scale (HADS) questionnaire [47]. This self-report-based scale consists of 14 items that assess symptoms of anxiety and depression (the HADS-A and HADS-D, respectively). The score ranges from 0 to 21 for anxiety symptoms and depression symptoms. Higher scores indicate more severe symptoms [48]. The Cronbach's alpha obtained in this study was 0.91.
- The Insomnia Severity Index (ISI) was used to measure the participants' sleep quality [49]. This is a self-report scale that measures the patient's perception of nocturnal and daytime symptoms of insomnia. The total score ranges from 0 to 28, with a higher score indicating more severe insomnia. The Cronbach's alpha obtained in this study was 0.86.
- The following personal factors related to behavior were evaluated in this study:
 - a) Self-efficacy was measured through the Self-Efficacy Scale-12 [50]. The total score ranges between 12 and 60, with higher scores indicating greater self-efficacy. The scale obtained a Cronbach's alpha of 0.87 in this study.
 - b) The Health Literacy Europe Questionnaire (HLS-EUQ16) was used to measure the health literacy of the participants [51]. The final score can be converted into a dichotomous answer: very difficult and difficult = 0; easy and very easy = 1. Higher scores indicate poorer health literacy [52]. The Cronbach's alpha obtained in this study was 0.82.
 - c) Patient's activation on his own health was measured by using the Patient Activation Measure (PAM) [53]. The resulting score ranges from 13 to 52, with higher scores indicating higher levels of activation. The Cronbach's alpha obtained in this study was 0.85.

Statistical analysis

A normality analysis was conducted using the Kolmogorov-Smirnov test, revealing that most variables followed a normal distribution. Subsequently, a descriptive and exploratory analysis of the variables was performed to rule out the presence of outliers. To facilitate data

interpretation and considering that, in large samples, statistical tests tend to approximate normality, even in the absence of a normal data distribution [54], parametric statistics were employed in the statistical analyses. Additionally, for variables that did not follow a normal distribution, non-parametric tests were conducted to confirm the robustness of our findings, which indicated that the significance levels did not change.

After randomization, a between-groups comparison was performed (chi-square test for qualitative variables and Student's t test for continuous variables) to examine the data and to test whether there were baseline differences between the groups. To analyze the effectiveness of the online program, a per-protocol analysis was performed, which compared baseline, three months, and the three-month-baseline differences between the two groups using Student's t test.

To address the secondary objective, a linear regression was conducted with mental health-related quality of life as the dependent variable, which was found to be significant in the mean comparison analysis. The independent variables of sex, current age, occupational status, intervention, and improvements in secondary clinical variables were entered into the model.

Data collection and statistical analysis were performed via Excel software and SPSS software (version 25.0) [55].

Results

Initially, 163 patients from different communities in Spain were interested in participating in the study, 29 of whom (17.79%) did not participate once eligibility was evaluated. As shown in Fig. 1, 25 participants did not meet the inclusion criteria and 4 did not participate due to loss of interest after receiving the pertinent information. Ultimately, 134 participants were included and randomized, 67 in the control group and 67 in the intervention group. The evaluation at three months from baseline was completed by 124 participants, 62 of whom belonged to the intervention group, and 62 to the control group. A total of 10 participants did not complete this analysis, 3 for preferring to participate in other studies, 1 for personal and work-related reasons, 1 due to a serious state of health incompatible with the continuity of the study and 5 for not attending the evaluation session.

Firstly, a descriptive analysis was carried out, and the results are shown in Table 1. Of the 134 participants, 113 were women and 21 were men, and the mean age was 48.97 (SD 7.64) years old. The sample profile was female, married or in a relationship, with secondary or university education and living in an urban area. The mean number of persistent symptoms was 17.07 (SD 6.28). The mean scores in the assessments of physical and cognitive functioning indicated impairment. The mental health and the quality of life of the participants were also affected.

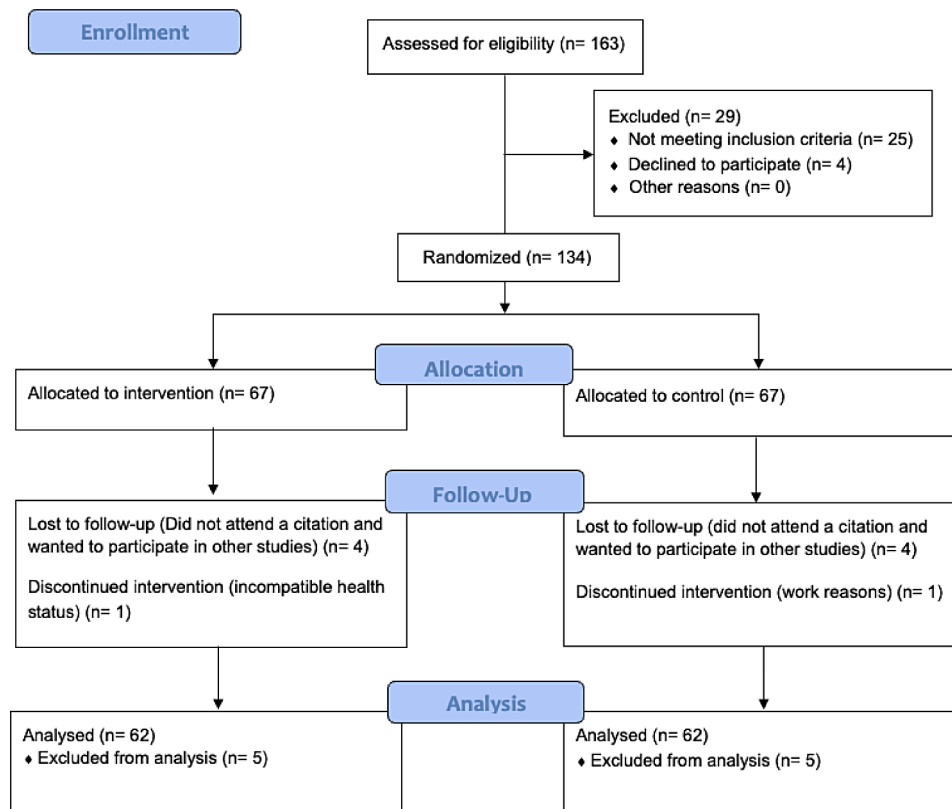


Fig. 1 CONSORT flowchart

Table 1 also presents a comparison of the variables collected between the intervention and control groups. This analysis did not reveal significant differences in the study variables, except for the number of persistent symptoms and the Sit-to-Stand Test score.

Table 2 shows the analysis that compares the data before the intervention and 3 months after it. Considering the raw scores of both groups, a significant improvement was found in the mental health-related quality of life of the participants in the group that received the intervention. However, no significant differences were found in any of the secondary variables of the study. Both groups improved in most of the variables, although the improvements were greater in the group that received the intervention in terms of the number and severity of symptoms, affective state, cognitive state, lower limb functionality, sleep disorders, self-efficacy, and patient activation.

To respond to the secondary study objective, a multivariate analysis was performed, in which the improvement in the mental health-related quality of life was included as a dependent variable, the only variable that showed a significant improvement after intervention. Sociodemographic variables (gender, age, and occupational status), whether or not the participants received the intervention, and the improvements (T1-T0) in the

secondary clinical variables measured through validated questionnaires were introduced as independent variables. The multivariate analysis results are shown in Table 3. Having participated in the study within the group that received the intervention ($b=3.193$; $p<0.05$) and the improvement in perceived self-efficacy ($b=0.298$; $p<0.05$) were predictors of greater improvement in mental health-related quality of life. This model explained 12% of the overall variance [R^2 adjusted=0.126, $F(10,113)=2.767$, $p=0.004$].

Discussion

To the best of our knowledge, this is the first study examining the effectiveness of a multimodal rehabilitation program, comprising online and synchronous components, aimed at improving the symptoms and quality of life of Long COVID patients. The results of this study show significant enhancements in mental health-related quality of life, suggesting a tangible advancement in our understanding of effective interventions that foster psychological well-being among the studied population. The existing scientific evidence has confirmed that the quality of life of these patients is seriously impaired by their disabling symptoms [56–58], which is why studies such as the present one are needed, addressing new approaches and treatment tools whose objective is the recovery, to

Table 1 Description of sociodemographic and clinical variables and comparison of intervention-control groups

| Variables | Total sample (N=134) | Intervention group (N=67) | Control group (N=67) | p-value |
|---|----------------------|---------------------------|----------------------|--------------|
| Current age | 48.97 (7.64) | 48.27 (7.97) | 49.67 (7.29) | 0.290 |
| Self-perceived age | 65.40 (12.91) | 65.34 (13.06) | 65.45 (12.85) | 0.963 |
| *Gender (%) | | | | |
| Men | 21 (15.67%) | 11 (16.41%) | 10 (14.92%) | 0.812 |
| Women | 113 (84.33%) | 56 (83.59%) | 57 (85.08%) | |
| Other | 0 (0%) | 0 (0%) | 0 (0%) | |
| *Marital status (%) | | | | |
| Single, separated, divorced, widowed | 47 (35.07%) | 21 (31.34%) | 26 (38.80%) | 0.365 |
| Married or in a relationship | 87 (64.93%) | 46 (68.66%) | 41 (61.20%) | |
| *Educational Level (%) | | | | |
| No studies or primary studies | 6 (4.47%) | 3 (4.47%) | 3 (4.47%) | 1.000 |
| Secondary or university studies | 128 (95.53%) | 64 (95.53%) | 64 (95.53%) | |
| *Living area (%) | | | | |
| Rural area | 32 (23.88%) | 16 (23.88%) | 16 (23.88%) | 1.000 |
| Urban area | 102 (76.12%) | 51 (76.12%) | 51 (76.12%) | |
| *Occupational status (%) | | | | |
| Employed | 61 (45.52%) | 29 (43.28%) | 32 (47.76%) | 0.537 |
| Unemployed | 7 (5.22%) | 3 (4.47%) | 4 (5.97%) | |
| TWD | 47 (35.07%) | 24 (35.82%) | 23 (34.32%) | |
| PWD | 9 (6.71%) | 5 (7.46%) | 4 (5.97%) | |
| Retired | 4 (2.98%) | 1 (1.49%) | 3 (4.47%) | |
| Others | 6 (4.47%) | 5 (7.46%) | 1 (1.49%) | |
| Time since infection (months) | 23.77 (7.87) | 22.91 (8.06) | 24.63 (7.63) | 0.208 |
| Number of symptoms | 17.07 (6.28) | 18.34 (6.27) | 15.81 (6.08) | 0.019 |
| SF-36 | | | | |
| SF-36 Physical health | 30.33 (8.13) | 29.29 (8.20) | 31.37 (7.98) | 0.140 |
| SF-36 Mental health | 33.55 (11.46) | 32.95 (11.22) | 34.14 (11.76) | 0.551 |
| Cognitive state (MoCA) | 24.37 (3.64) | 24.57 (3.88) | 24.16 (3.40) | 0.525 |
| Physical Functioning (Sit-to-Stand test) | 9.93 (4.69) | 9.12 (3.58) | 10.75 (5.50) | 0.045 |
| Affective state (HADS) | 18.73 (8.52) | 19.21 (8.47) | 18.25 (8.60) | 0.519 |
| Insomnia Severity Index (ISI) | 14.23 (6.71) | 14.67 (6.78) | 13.79 (6.66) | 0.450 |
| Self-efficacy | 41.35 (9.30) | 41.37 (9.53) | 41.33 (9.14) | 0.978 |
| Health literacy | 11.49 (3.57) | 11.43 (3.51) | 11.55 (3.64) | 0.847 |
| Patient activation | 38.63 (6.30) | 38.49 (6.67) | 38.76 (5.95) | 0.806 |

Notes Statistics used: Mean and standard deviation except for variables with *, for which frequencies and percentages have been used. For comparison, Student's t test was used except for the variables with *, for which chi-squared has been used. Abbreviations TWD: Temporary work disability; PWD: Permanent work disability; SF-36: 36-Item Short Form Health Survey; MoCA: Montreal Cognitive Assessment; HADS: Hospital Anxiety and Depression Scale; ISI: Insomnia Severity Index

Table 2 Outcome data at baseline and 3-month follow-up

| Variables | Intervention group N=62 Mean (SD) | Control group N=62 Mean (SD) | Significance p-value |
|---|-----------------------------------|------------------------------|----------------------|
| Primary outcomes | | | |
| SF-36 Physical Health | | | |
| Baseline (T0) | 29.29 (8.20) | 31.37 (7.98) | 0.140 |
| 3 months (T1) | 31.08 (9.76) | 32.83 (8.65) | 0.295 |
| T1-T0 | 1.97 (8.77) | 1.38 (6.83) | 0.678 |
| SF-36 Mental Health | | | |
| Baseline (T0) | 32.95 (11.22) | 34.14 (11.76) | 0.551 |
| 3 months (T1) | 35.05 (11.78) | 32.14 (9.86) | 0.138 |
| T1-T0 | 1.98 (8.87) | -1.26 (8.99) | 0.046 |
| Secondary outcomes | | | |
| Number of persistent symptoms | | | |
| Baseline (T0) | 18.34 (6.27) | 15.81 (6.08) | 0.019 |
| 3 months (T1) | 17.95 (7.02) | 15.79 (6.22) | 0.072 |
| T1-T0 | -0.73 (4.41) | -0.27 (3.17) | 0.514 |
| Cognitive state (MoCA) | | | |
| Baseline (T0) | 24.57 (3.88) | 24.16 (3.40) | 0.525 |
| 3 months (T1) | 25.44 (2.93) | 24.40 (3.81) | 0.094 |
| T1-T0 | 0.53 (2.26) | 0.42 (2.83) | 0.807 |
| Physical Functioning (Sit-to-Stand Test) | | | |
| Baseline (T0) | 9.12 (3.58) | 10.75 (5.50) | 0.045 |
| 3 months (T1) | 9.58 (4.77) | 10.35 (4.47) | 0.353 |
| T1-T0 | 0.58 (2.76) | -0.29 (2.98) | 0.094 |
| Affective state (HADS) | | | |
| Baseline (T0) | 19.21 (8.47) | 18.25 (8.60) | 0.519 |
| 3 months (T1) | 17.21 (8.93) | 18.69 (8.38) | 0.342 |
| T1-T0 | -1.87 (6.24) | -0.10 (5.59) | 0.098 |
| Insomnia Severity Index (ISI) | | | |
| Baseline (T0) | 14.67 (6.78) | 13.79 (6.66) | 0.450 |
| 3 months (T1) | 13.42 (7.00) | 13.85 (6.40) | 0.718 |
| T1-T0 | -1.19 (5.82) | -0.52 (5.20) | 0.496 |
| Self-Efficacy | | | |
| Baseline (T0) | 41.37 (9.53) | 41.33 (9.14) | 0.978 |
| 3 months (T1) | 41.06 (9.30) | 40.13 (9.25) | 0.576 |
| T1-T0 | -0.85 (8.85) | -0.77 (6.19) | 0.953 |
| Health Literacy | | | |
| Baseline (T0) | 11.43 (3.51) | 11.55 (3.64) | 0.847 |
| 3 months (T1) | 11.76 (4.01) | 11.68 (3.76) | 0.908 |
| T1-T0 | 0.45 (3.14) | 0.35 (3.51) | 0.872 |
| Patient Activation | | | |
| Baseline (T0) | 38.49 (6.67) | 38.76 (5.95) | 0.806 |
| 3 months (T1) | 39.03 (6.50) | 38.02 (6.61) | 0.390 |
| T1-T0 | 0.63 (5.77) | -0.56 (4.86) | 0.216 |

Abbreviations SF36: 36-Item Short Form Health Survey; MoCA: Montreal Cognitive Assessment; HADS: Hospital Anxiety and Depression Scale; ISI: Insomnia Severity Index

the extent possible, of the quality of life prior to the disease [59, 60].

In the present study, linear regression analyses initially revealed a significant relationship between self-efficacy and mental health-related quality of life. Self-efficacy—defined as an individual's self-perceived ability and

Table 3 Linear regression model for improvement in SF-36 Mental Health (SF-36 Mental Health T1-T0) scores in relation to intervention/control group, gender, age, occupational status, improvement in cognitive state (MoCA), improvement in physical functioning (sit-to-stand test), improvement in Insomnia Severity Index (ISI), improvement in personal constructs (self-efficacy, health literacy, and patient activation)

| SF-36 Mental Health (T1-T0) | Coefficient | p-value | CI below 95% | | Collinearity Statistics | |
|--|--------------|--------------|--------------|-----------|-------------------------|-------|
| | | | CI above 95% | Tolerance | VIF | |
| Group (intervention/control) | 3.193 | 0.044 | 0.088 | 6.297 | 0.939 | 1.064 |
| Gender (male/female) | 2.515 | 0.269 | -1.974 | 7.003 | 0.950 | 1.053 |
| Age | 0.002 | 0.988 | -0.211 | 0.215 | 0.906 | 1.104 |
| Occupational status (employed/non-employed) | 2.028 | 0.213 | -1.181 | 5.236 | 0.898 | 1.113 |
| Cognitive state T1-T0 (MoCA) | 0.413 | 0.190 | -0.208 | 1.034 | 0.907 | 1.102 |
| Physical Functioning T1-T0 (Sit-to-Stand Test) | -0.038 | 0.889 | -0.570 | 0.495 | 0.958 | 1.044 |
| Insomnia Severity Index T1-T0 (ISI) | -0.048 | 0.741 | -0.337 | 0.241 | 0.899 | 1.112 |
| Self-efficacy T1-T0 | 0.298 | 0.009 | 0.078 | 0.519 | 0.807 | 1.239 |
| Health Literacy T1-T0 | 0.407 | 0.108 | -0.090 | 0.904 | 0.838 | 1.193 |
| Patient Activation T1-T0 | 0.143 | 0.379 | -0.177 | 0.463 | 0.778 | 1.286 |
| R2 | 0.197 | | | | | |
| R2adj | 0.126 | | | | | |
| p-value | 0.004 | | | | | |

Notes Significant differences ($p \leq 0.05$) are highlighted in bold. Dependent variable: SF-36 Mental Health (T1-T0). Abbreviations SF-36: Short Form Health Survey; MoCA: Montreal Cognitive Assessment; ISI: Insomnia Severity Index; VIF: variance inflation factor

confidence to undertake behaviors that can lead to desired outcomes [61] is an important factor influencing patients' ability to self-manage their symptoms. Existing evidence indicates that patients with high self-efficacy have a perceived ability to manage the challenges related to their illnesses, a lower personal burden, and a greater quality of life, which is consistent with our results [62, 63]. Although self-efficacy was a contributing variable, no significant difference in changes were observed between the groups or timepoints. This observation suggests that the intervention may be more beneficial for individuals with initially high self-efficacy, which could be considered as part of the selection process in future studies or practical applications of the intervention. It might also be valuable to implement a preliminary intervention aimed at improving self-efficacy. This approach could optimize resources by directing the intervention towards those most likely to benefit significantly. However, it would be prudent to further explore how self-efficacy and other factors may influence the outcomes of the intervention, which could guide more personalized and effective strategies.

Furthermore, the fact of having received the intervention also predicted better results in mental health-related quality of life. Therefore, it seems worthwhile to discuss those content features and methodologies used that could have benefited the achievement of these outcomes. The telerehabilitation program tested in this study has addressed numerous symptoms of Long COVID. During eight group sessions, physical, cognitive, and respiratory rehabilitation exercises were provided, as well as recommendations on nutrition, sleep hygiene, emotional management, or useful community resources for this disease.

The published guidelines on the management of Long COVID [31, 32, 64] recommend an interdisciplinary approach such as the one provided.

Although the results were not significant compared to those of the control group, greater improvements were observed withing the group that received the telerehabilitation program in some symptoms related to cognitive and affective state, physical functioning, and sleep disorders. These symptoms are severely disabling, limiting the performance of activities of daily living and deteriorating quality of life [65–68], so it is important to address them in those programs intended to recover the quality of life of these patients.

In addition to holistic and interdisciplinary content, the group methodology may have been a key factor in achieving these results. Wright et al. [69]. confirmed that the group format is preferred among patients with Long COVID, as it strengthens the sense of belonging, prevents social isolation, and promotes support among members, which is a crucial aspect for recovery. Some research has already proposed different group interventions (meditation, yoga, psychoeducational programs, singing) with positive results obtained in the management of the specific symptoms of Long COVID [25, 26, 69–74].

Most of these interventions employed digital media, with videoconferencing being a prominent feature [25, 26, 69–72, 74]. This digital tool was also used in the present study, supported by an online platform where all the content viewed during the session was uploaded. The use of videoconferencing allowed continuous monitoring by the professional leading the sessions, as well as direct contact among the group members. Group digital

interventions produce positive results in emotional well-being and quality of life, since the social support from a peer group offers the opportunity to share common experiences and successes, in addition to obtaining mutual reinforcement and collective problems-solving [75]. Both online professional monitoring and group support may have favored adherence to the intervention, an important element of the effectiveness of an intervention and the achievement of its results [76]. With other technological tools—such as mobile applications—, this adherence would present a challenge to this population due to the lack of continuous monitoring by a professional as well as the absence of opportunities to contact and be mutually supported by individuals facing similar circumstances [21].

This study sheds light on new intervention tools and methodologies for a recently emerged disease that still faces a large gap in clinical practice. COVID-19 has had a considerable impact throughout the world, causing a health crisis from its beginning [77, 78]. Considering that the COVID-19 pandemic has weakened most health systems around the world, collapsing them and exhausting available healthcare resources—plus the fact that at least 10% of people with COVID-19 develop persistent symptoms— finding cost-effective resources to address this situation should be considered a priority [79, 80]. The application of group interventions is essential [81], since it enables professionals to assist a greater number of people, reducing both time and the costs of social and health services [82].

The pragmatic approach adopted in this intervention is crucial for evaluating its applicability in real-world contexts [83]. The choice of this approach is based on the urgent need for intervention tools that can be readily integrated into the routine care of Long COVID patients [84]. Conversely, multimodal online interventions allow for easy implementation across a variety of clinical and community settings [85].

In this study, a significant improvement in mental health-related quality of life was observed in the intervention group. Furthermore, participants in this group showed improvements in several other health parameters, suggesting that the program had a broadly positive impact. However, it is crucial to consider that residual confounding may have influenced these results [86]. The random assignment of participants to the two groups helped minimize the influence of confounding variables. Despite these efforts, the authors of this study acknowledge the possibility of residual confounding due to significant initial differences in some parameters, such as the number of persistent symptoms and the Sit-to-Stand test score. These differences could have influenced the magnitude of improvements and are considered a limitation of this study.

Another potential source of internal confounding could have been the variability in adherence to the rehabilitation program. Due to the nature of our study, measuring adherence was challenging because, although session attendance was recorded, we were unable to quantify the time each patient spent on autonomous work at home. Differences in commitment to the intervention could have influenced the outcomes. Adherence to the program should be considered in future studies to better understand its impact on the observed results.

This study also has other limitations. First, due to the nature of the study intervention, participants were not blinded to allocation, as they were informed of the group assignment in the trial. This is a common limitation among studies on medical, rehabilitative, or psychological interventions. However, blind evaluation by independent researchers was possible. On the other hand, in a novel disease such as Long COVID, marked by a high degree of uncertainty, it is difficult to prevent patients in the control group from seeking answers (sociohealth resources, other studies, health assets, etc.) and from acting on their impulse to get ahead, master their symptoms and recover their quality of life prior to the disease [87]. In addition, the large difference in the sex ratio of the participants precluded an analysis from a gender perspective. Finally, the reinfections, outbreaks and relapses among some patients throughout the telerehabilitation program, prevented them from attending some of the sessions, or even completing the entire program.

Future directions

To build on these findings, future research should include qualitative studies to gain deeper insights into participants' experiences and perceptions of the intervention. Such studies could explore how different aspects of the multimodal telerehabilitation program impacted participants' engagement and satisfaction. The research team is currently conducting qualitative analysis using data collected from discussion forums on the rehabilitation platform. This forthcoming study will explore participants' perceptions and experiences, contributing to a better understanding of the intervention's impact and helping to refine future approaches. Additionally, future studies could investigate how factors such as self-efficacy and adherence specifically affect the outcomes of the intervention, leading to more personalized and targeted strategies for managing Long COVID.

Conclusions

In conclusion, this multimodal telerehabilitation program, composed of eight group videoconferences, shows promising effectiveness in enhancing mental health-related quality of life for Long COVID patients.

The findings indicate the potential for this approach to enhance psychological well-being within this population.

Abbreviations

| | |
|-----------|--|
| ADLs | Activities of Daily Living |
| TAU | Treatment as usual |
| SF-36 | 36-Item Short Form Health Survey Questionnaire |
| SD | Standard deviation |
| RA | Research Assistant |
| GP | General Practitioner |
| PHC | Primary Health Care |
| MoCA | Montreal Cognitive Assessment |
| HADS | Hospital Anxiety and Depression Scale |
| ISI | Insomnia Severity Index |
| HLS-EUQ16 | Health Literacy Europe Questionnaire |
| PAM | Patient Activation Measure |
| TWD | Temporary Work Disability |
| PWD | Permanent Work Disability |
| VIF | Variance Inflation Factor |

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s13690-024-01354-w>.

Supplementary Material 1

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Author contributions

SL-H, BO-B and RM-B drew up the research design. SL-H and BO-B developed the study and coordinated the fieldwork. RS-R, FM-L and RS-A made the analyses. SL-H and BO-B wrote the manuscript. BO-B is the principal investigator of the project. All authors reviewed the manuscript content and approved the final version for submission.

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Data availability

The datasets used and/or analysed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

Ethical approval was granted by the Clinical Research Ethics Committee of Aragón (PI22/482). The procedures carried out to produce this work were adjusted to the ethical standards of the aforementioned committee and to the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. Study participants received written information about the voluntary participation, the conditions of the study, the right to quit at any time, the data security, and the publication of anonymized results. All subjects signed a written informed consent form; their data were anonymized and

used only for research purposes. The protocol was followed as approved by the Ethics Committee, so no changes had to be reported to it.

Competing interests

The authors declare no competing interests.

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