

The Effectiveness of Non-Pharmacological Interventions in Treating Adolescents and Young Adults with Neuropsychiatric Symptoms of Long COVID: A Systematic Review and Meta-Analysis

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Background: The management of persistent symptoms for long COVID (eg, fatigue, concentration difficulties, sleep difficulties, loss of appetite and taste, depression, and anxiety) has not been widely studied among adolescents and young adults (AYA). This systematic review and meta-analysis aimed to synthesise and review evidence on the effectiveness of non-pharmacological interventions for AYA aged 13–25 years, presenting with long COVID symptoms.

Methods: A systematic literature search was conducted in four electronic databases (PubMed, EMBASE, PsycInfo, and ProQuest) in addition to manual searches for studies from January 2020 to May 2025 (PROSPERO: CRD42024516016). The studies were screened for eligibility, and methodological quality was assessed using the Joanne Briggs Institute Critical Appraisal tool by two independent reviewers. Findings were summarised using a narrative synthesis approach, and where possible, a meta-analysis was conducted using a random effects model with standardised mean differences (SMD) and a 95% confidence interval (CI).

Results: Of the 325 screened articles, seven studies were included, which discussed six interventions. Three studies reported on the effectiveness of three multidisciplinary rehabilitation programs (eg, neuropsychological rehabilitation program, multidisciplinary post-COVID rehabilitation program, micro-choice-based concentrated group rehabilitation), three on alternative medicine practices (eg, forest bathing, traditional Thai Medicine), and one on mechanical therapy (eg, enhanced external counterpulsation). Findings suggested that interventions, although varied in duration and follow-up, were effective in improving mental health (SMD: 0.64, 95%, $p < 0.0497$). There were also non-statistical improvements in fatigue (SMD: 1.74, 95%, $p = 0.1307$), quality of life (SMD: -1.34, 95%, $p = 0.2787$), and cognitive function (SMD: 1.05, $p = 0.2989$).

Conclusion: This review's findings suggest that non-pharmacological interventions may effectively treat neuropsychiatric symptoms of long COVID in AYA, ensuring better outcomes. Nevertheless, further research must be conducted with longer-term follow-up and robust methodology to explore sustained benefits, which may better inform treatment decisions.

Trial Registration: This systematic review is registered in Prospero (CRD42024516016).

Keywords: post-acute COVID-19 syndrome, children, adolescents, non-pharmacological interventions

Background

The COVID-19 pandemic has presented a significant challenge to the health and wellbeing of everyone, and in particular adolescents and young adults (AYA).¹ AYA were reported to be particularly vulnerable to both health and financial ramifications related to COVID-19, due to the specific period of development when significant life transitions occur, such as living independently and beginning employment.² Furthermore, AYA have an increased susceptibility to the emergence of

psychological disorders, wherein approximately two-thirds of mental disorders are diagnosed before the age of 25.³ It is well documented that COVID-19 has also been detrimental to the mental health of AYA due to factors such as concerns around contamination,^{4,5} social isolation, lack of daily routine, school closures and interruption to education.^{1,4,6} This is exacerbated by the fact that adolescents have a lack of advanced emotional development, which results in less resilience and coping capabilities when compared to adults.^{4,7,8} Evidence suggests higher burdens of anxiety, depression,^{9–11} psychological distress, substance use,¹⁰ suicidal behaviour,¹² sleep disorders, and other psychosocial issues in the adolescent population in relation to COVID-19.¹⁰ In addition to the immediate burden of COVID-19, in the months following the first reported cases of COVID-19, there also began reports of persistent symptoms of the infection, often termed long COVID.¹³

Besides the health impacts of COVID-19, evidence reported an estimated 65 million people were struggling with long COVID, globally.¹⁴ Long COVID is defined by the Centers for Disease Control and Prevention as a chronic condition occurring after an initial COVID-19 infection with symptoms presenting for at least three months.¹⁵ The most common symptoms experienced by AYA include physical symptoms such as dyspnoea, anosmia, ageusia and cough,^{16,17} as well as neuropsychological symptoms¹⁸ such as fatigue, concentration difficulties, sleep difficulties, loss of appetite and taste, depression, and anxiety.¹⁶ Anxiety, low mood, and sleep problems are also reported in adults. However, older adults tend to have ongoing cough and shortness of breath, while younger people report more sensory and neuropsychiatric symptoms such as anxiety, insomnia, and palpitations.¹⁹ A 2021-review of 14 studies reported the prevalence of long COVID symptoms in children and adolescents ranging from 4% to 66%.²⁰ Many symptoms related to long COVID are subjective, self-reported symptoms which are difficult to measure in a standardised manner, which could contribute to the discrepancy observed in prevalence estimates that make service planning and management difficult. Nevertheless, as long COVID is insufficiently understood in AYA, there is a critical need to better ascertain the management of such symptoms. Moreover, persistent long COVID symptoms in AYA can interrupt their academic success, career pathways, and mental health trajectories, with possible long-term consequences into later life.²¹ Therefore, understanding the long COVID symptoms in AYA may help provide necessary data on vaccination policies, school health guidance and workforce planning.²²

Given the nature and presentations of long COVID, there is no single treatment or medication for the treatment of long COVID.²³ However, a few published guidelines outline recommended approaches,^{13,24} including one developed by the National Institute for Health and Care Excellence (NICE) based on the best available evidence at the given time. These guidelines outline that patients should be given self-management advice and support from multidisciplinary teams due to the multisystemic nature of the disease.²⁴ This could involve the use of non-pharmacological interventions in addition to pharmacological interventions. Non-pharmacological interventions are defined as any interventions aimed at improving patient health and wellbeing without the use of medicine.²⁵ In line with these recommendations, there exists some current literature that explores the efficacy of non-pharmacological interventions in treating long COVID symptoms. A recent systematic review found that rehabilitation interventions improved functional exercise capacity, dyspnoea, and quality of life (QoL).²⁶ Other systematic reviews have explored the effectiveness of both pharmacological and non-pharmacological interventions in managing long COVID symptoms predominantly focusing on older adult patients.^{27–29} Hence, there is limited understanding of the effectiveness of non-pharmacological interventions in managing long COVID symptoms in AYA.

To address this knowledge gap, this study aimed to systematically synthesize the most up to date evidence regarding the effectiveness of non-pharmacological interventions for neuropsychiatric symptoms of long COVID in AYA. These findings may guide clinical applications and support future research on non-pharmacological interventions for managing long COVID in AYA.

Materials and Methods

This review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.³⁰ The protocol was registered in PROSPERO (CRD42024516016).³¹

Information Sources and Search Strategy

For this systematic review, four electronic databases (PubMed, EMBASE, PsycInfo, and ProQuest) were used to search for studies. Cross references were also searched for further relevant articles. We searched for peer-reviewed studies written in English over the past 5 years (January 2020 – May 2024). A final manual search on Google Scholar was conducted in May 2025. Studies within the last 5 years were chosen due to the emergence of COVID-19 in early 2020,³² following the first reports of the conditions in late December 2019.³³ The full search strategy, including the search terms, is included in [Appendix 1](#). Duplicates were removed in EndNote and again in the Rayyan tool for systematic reviews for any that were missed.

Eligibility Criteria

Inclusion criteria included studies reporting on: (1) the effectiveness of a non-pharmacological intervention (interventions that do not use medicine for the treatment of patients) in managing long COVID symptoms; (2) study designs (eg, randomised control trials (RCTs), quasi-experimental studies, cohort studies, or observational studies) with either a control group or comparison with baseline and a post-intervention follow-up timepoint (pre-post design); (3) participants' age ranged between or included 13 to 25 years, and they presented with long COVID; (4) published in a peer-reviewed journal; and (5) in English language.

Studies were excluded if (1) population did not include the age group of our interest; (2) primary outcome was other than neuropsychiatric symptoms of long COVID; (3) the study described acute COVID symptoms rather than long COVID; (4) the study described pharmacological interventions rather than non-pharmacological; (5) no evaluation of intervention; (6) the study focused on animals; and (7) the study did not contain a control group or baseline comparison.

Study Selection and Screening

Two reviewers (SC and MNH) independently performed initial title and abstract screening using the Rayyan software. They independently conducted a screening of the full texts and compared results. A third reviewer (JRJ) was involved as needed to resolve any disagreements on included articles and reach consensus.

Data Extraction

Two reviewers (SC and MNH) completed data extraction ([Appendix 4](#)) from the included articles. Study ID (author and year), study design, country, sample size, characteristics of the study population (age, gender, diagnoses, co-existing conditions) and long COVID signs or symptoms were identified. Type of intervention, duration, and the outcome of interest were also extracted. Data relevant to AYA (13–25 years) was extracted.

Methodological Quality and Risk of Bias Assessment

Methodological quality and risk of bias of included studies were assessed using the Joanne Briggs Institute (JBI) critical appraisal tools as per the study design.^{34,35} The primary author (SC) assessed risk of bias for the included studies and were reviewed by two reviewers (MNH, JRJ).

Data Analysis and Synthesis

Given the considerable heterogeneity across intervention approaches, duration, outcomes, measurement tools and timing of outcome assessments, an overall narrative synthesis was conducted. Studies were narratively synthesized to integrate findings from included studies by the main reviewer (SC), then checked by two other independent reviewers (MNH and JRJ). The results were synthesized with appropriate emphasis on studies that were more methodologically robust using the National Health and Medical Research Council (NHMRC) levels of evidence and grade guidelines tool. The NHMRC levels of evidence have four levels of quality, which make up the evidence hierarchy. “Higher” level scores, which provide greater confidence in evidence include Level I (systematic reviews of RCTs), level II (RCTs) and III-1 (pseudorandomised control trials). “Moderate” level scores include level III-2 (comparative studies with concurrent controls: non-randomised experimental trials, cohort studies, case-control studies, or interrupted time series with

a control group). “Lower” level scores include III-3 (comparative studies without controls: historical control study, two or more single arm study, or interrupted time series without a parallel control group) and level IV (case series studies with either post-test or pre- and post-test outcomes).³⁶

Where sufficient data was available, meta-analyses were performed using Meta-Mar 3.5.1³⁷ using a random effects model, and Cohen’s d was calculated using the standardised mean differences (SMD) and confidence intervals (CI) to account for the heterogeneity among the studies. These were reported using forest plots and stratified by outcomes (mental health; fatigue; QoL; cognitive function) and I² estimates were used to report the levels of heterogeneity.³⁸ Given the number of studies included in the meta-analyses, tests for publication biases were not conducted.³⁹

Results

Search Results

The study selection process was described in the PRISMA flow diagram,³⁰ shown in Figure 1. Findings of the four electronic databases yielded a total of 464 articles. After removing 144 duplicates, we completed title and abstract screening on the remaining 320 papers. This resulted in the exclusion of 287 papers. Report retrieval was then conducted, with 17 articles being excluded due to the unavailability of full texts. Of the 16 texts after full-text screening, 13 were excluded. We also reviewed five full texts identified through manual searching on Google Scholar and bibliographies of sentinel articles. Of the five texts after full-text screening, we excluded one. Overall, two were excluded for the wrong intervention type, ten for the wrong population, one for not including an intervention, and one for the wrong study design. Finally, all seven studies were included in our narrative review and six in our meta-analysis.

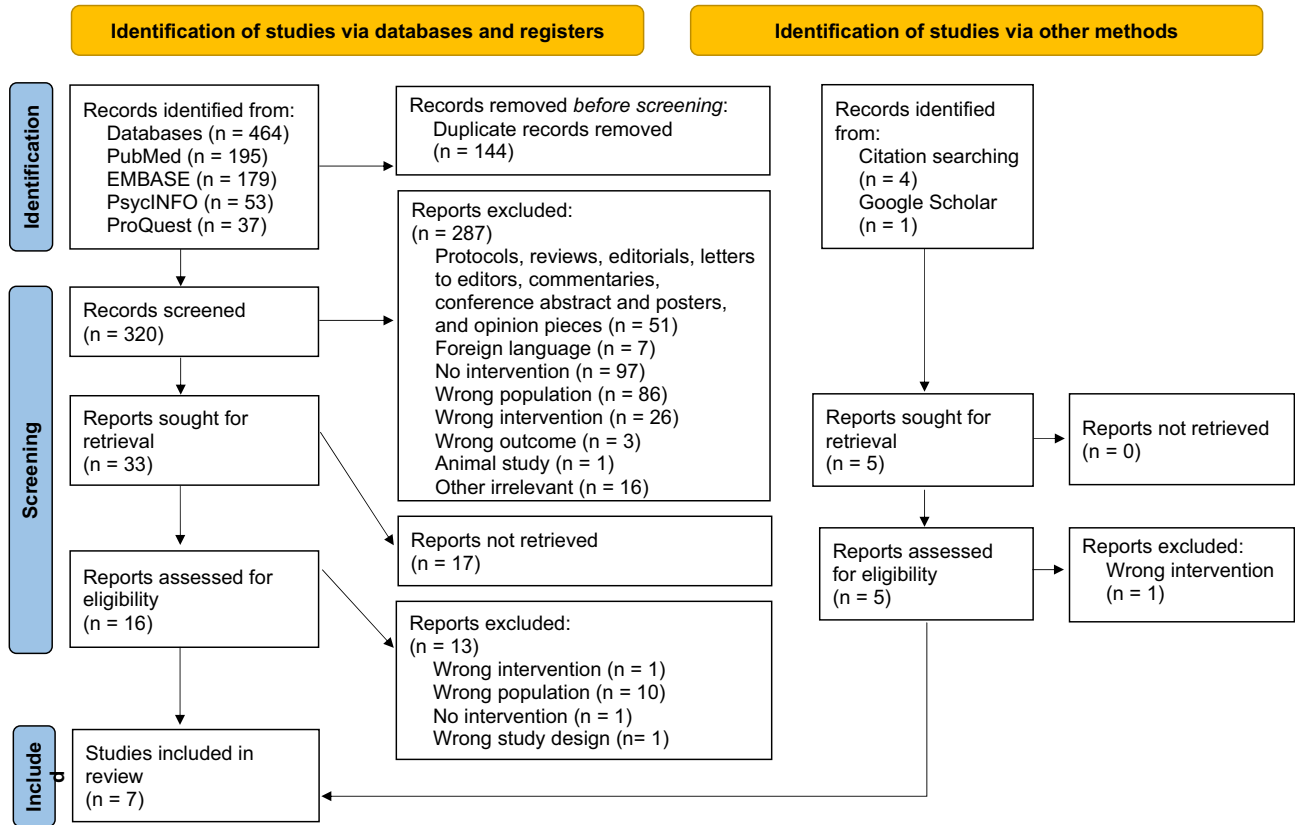


Figure 1 PRISMA flow diagram of the literature search and screening process.

Characteristics of Included Studies

Among the seven studies, two were retrospective medical record review of patient cohort studies,^{40,41} two were longitudinal studies,^{42,43} one was a waitlist controlled before-after design,⁴⁴ one was an open non-randomised control trial,⁴⁵ and one was a pilot study using a pre-post design.⁴⁶ Five of the studies were conducted in Europe (Germany, Switzerland, Norway and the UK),^{41,43–46} one in South East Asia (Thailand)⁴⁰ and one in South America (Brazil).⁴² Five of the studies included males and females^{41–43,45,46} and two studies only included females.^{40,44} The number of participants ranged from 16 to 239. All of the studies included participants within the ages of 19–25. However, none of the studies included participants aged 13–18. Detailed participant characteristics are included in [Table 1](#).

Effectiveness of the Interventions

Details of each study and the interventions are shown in [Table 2](#). The main interventions were forest bathing, traditional Thai medicine (TTM), neuropsychological rehabilitation program, multidisciplinary post-COVID rehabilitation program, micro-choice based concentrated group rehabilitation and enhanced external counterpulsation (EECP). The duration of interventions ranged from one week to four weeks. The primary outcomes included the fatigue, headache, sleep difficulty, anxiety, depression and cognitive functions.

Alternative Practices

Three of the studies evaluated alternative practices.^{40,44,46} McEwan et al (2022) assessed a four-week waitlist control period followed by four weekly online forest bathing sessions. Patients were informed on the history and purpose of forest bathing, followed by engagement with sensory activities and sharing circles to learn and interact with others. The

Table 1 Characteristics of Included Studies

References	Study Design	Population Gender	Age	Country	Sample Size	Long COVID Description
Chokpaisam et al 2024 ⁴⁰	A retrospective clinical study	Females only	Mean age: 41.12. This study included a case study of a 19-year-old participant.	Thailand	17	There was an average long COVID duration time of 25.76. The main neuropsychological symptoms were tiredness, insomnia, and headache.
Sathymoorthy et al 2022 ⁴¹	Retrospective analysis of a contemporary, consecutive patient cohort	Males and females	Mean age: 53.81 Age range: 21-79	Switzerland	16	The time from an acute COVID-19 diagnosis to the start of treatment was approximately 8.33 ± 3.57 months. Patients all had neuropsychological symptoms of long COVID.
Braga et al 2023 ⁴²	Longitudinal study	Males and females	Mean age: 48.8 Age range: 22-77	Brazil	208	The study included participants who had been referred to the long COVID program at the Sarah Network of Rehabilitation Hospitals. The patients presented with cognitive issues such as problems with attention, concentration and memory.
Müller et al 2023 ⁴³	Longitudinal observational study	Males and females	Mean age: 50.62 Age range: 21-69	Germany	124	The participants had acute COVID-19 at an average of 408.81 days prior to the beginning of treatment.
McEwan et al 2022 ⁴⁴	Waitlist controlled, repeated measures design	Females only	Mean age: 37.13 Age range: 24-61	UK	22	The most prevalent neuropsychological long COVID symptoms were tiredness, brain-fog, poor sleep quality, depression, and anxiety.
Kvale et al 2024 ⁴⁵	Open non-randomised pilot study	Males and females	Mean age: 48 Age range: 19-84	Norway	239	The participants had to have long COVID symptoms at least two months after an initial COVID-19 infection. Common neuropsychological symptoms included fatigue, concentration difficulties, and insomnia.
Torner et al 2024 ⁴⁶	Pilot study using a pre-post design	Males and females	Mean age: 41.85 Age range: 20–71	Germany	36	The symptoms participants had included cognitive impairment, depression, and anxiety.

Table 2 Characteristics of Interventions and Their Outcomes, Effectiveness

Reference	Intervention	Description of Interventions	Duration	Outcomes and Measurement Tools
McEwan et al 2022 ⁴⁴	Forest bathing	Intervention started with four weeks of a waitlist period. This was followed by a slow mindful nature walk involving sensory activities. This included visual activities such as noticing colours, shapes, and movements in nature, listening activities, smell activities such as smelling leaf-litter and soil and touch activities where participants feel the texture of bark. Participants also were invited to a 'sit-spot' to observe nature and also participated in sharing circles to share and gain insight from each other. An at home option was available to patients who were guided through the use of photographs, videos and objects found in their own homes. The therapy was guided by forest therapy guides who underwent six to 12 months of training.	Four-week waitlist period and four-week forest bathing period.	Anxiety: tension subscale of POMS Fatigue: long COVID symptom survey Headache and sleep difficulty: long COVID symptom survey
Torner et al 2024 ⁴⁶	Forest bathing	The intervention consisted of two weeks of audio-guided and mindfulness-based forest bathing. The sessions were performed independently by participants in forests near them. They were guided by the audio files providing standardised instructions and exercises for an immersive sensory experience. These audio files were developed by a trained forest therapy guide and trained forest therapist. Sessions involved breathing exercises, stimulation of all five senses, mindfulness exercises and a 'sit-spot' for meditation.	Two weeks with four 60-minute sessions.	Anxiety and depression/mental health: SF-36 and C19-YRS Fatigue: FAQ Cognitive function: C19-YRS
Chokpaisam et al 2024 ⁴⁰	TTM	Traditional Thai massage with aromatic herbal oil, herbal compresses, herbal hot steam, lung acupressure massage and breathing exercises were administered by traditional Thai doctors.	Maximum seven days. Mean: 4.65 days	Mental health: SF-36 Fatigue: SF-36 QoL: SF-36 Headache and sleep difficulty: qualitative methods
Braga et al 2023 ⁴²	Neuropsychological rehabilitation program	The program involved receiving information about cognitive functions and strategies to compensate for and manage their neuropsychological deficits. Patients then are able to identify their strengths and weaknesses, utilising these strategies in their own lives. Physicians (neurologists and geriatricians), nurses, nutritionists, speech pathologists, psychologists, and educators specialising in physical education and dance were involved.	Four weeks, with weekly two-hour group meetings.	Anxiety and depression: HADS QoL: WHOQoL-Bref Cognitive function: BNIS and NEUPSILIN subtests
Müller et al 2023 ⁴³	Multidisciplinary post-COVID rehabilitation program	The program involved psychological therapy, physiotherapy, sports therapy, respiratory therapy and health promotion interventions. Cognitive training using a computer-based program "Fresh Minder 2, 3 and 4" (Version 2.7.7, Version 3.5.5 and Version 4.0.8). Physicians, physiotherapists, sport therapists, psychologists, social professionals, nutritionists, nurses, and medical laboratory assistants were involved.	Mean: 28.77 (9–42) days	Anxiety and depression: HADS Fatigue: BFI and FIS Cognitive function: MoCA version 8.1 and 8.2
Kvale et al 2024 ⁴⁵	Micro-choice based concentrated group rehabilitation	The program consisted of a three-phase intervention. Phase one: preparing for change through one or two consultations with a member of the multidisciplinary team, consisting of patient education and identification of micro-habits. Phase two: treatment stage involving patient education, practical sessions where patients could practise what they learnt and discussion sessions. Towards the end of phase two, patients were required to develop concrete follow-up plans. Phase three: follow-up through online reporting and a call by the group leader. Medical doctors, nurses, physical therapists, chiropractors, pharmacists, psychologists, and clinical nutritionists were involved.	Phase one: two weeks Phase two: three to four days Phase three: three weeks	Anxiety and depression: EQ-5D-5L QoL: EQ-5D-5L
Sathymoorthy et al 2022 ⁴¹	EECP	Non-invasive outpatient therapy where the EECP device delivers shear stress to improve cerebral blood flow were performed at Flow Therapy treatment centres.	15-35 sessions	Fatigue: PROMIS fatigue score QoL: SAQ-QOL Cognitive function: qualitative methods

study reported improvements in anxiety (3.37 ± 0.95 vs 1.73 ± 0.62 , $p < 0.001$), measured through the tension subscale of the Profiles of Mood States (POMS). Improvements in fatigue, memory and concentration, headaches and difficulty sleeping were accounted for under long-COVID symptoms (3.99 ± 1.16 vs 3.11 ± 1.15 , $p < 0.01$), measured using a long COVID symptom survey created by the authors.

Another study by Torner et al (2024) evaluated a two-week audio-guided and mindfulness-based forest bathing, in which participants engaged in individual sessions guided by 60-minute audio recording that included various sensory activities. There were improvements in overall mental health (40.18 ± 1.92 vs 42.74 ± 1.86 , $p < 0.05$) measured through SF-36 and the COVID-19 Yorkshire Rehabilitation Scale (C19-YRS) (2.64 ± 0.46 vs 2.17 ± 0.48 , $p < 0.05$). C19-YRS also evidenced improvements in depression (2.36 ± 0.44 vs 1.97 ± 0.42 , $p < 0.05$) and anxiety (2.92 ± 0.44 vs 2.36 ± 0.44 , $p < 0.05$). Improvements in fatigue were also identified, separated into cognitive (0.62 ± 0.06 vs 0.42 ± 0.05 , $p < 0.001$), and affective fatigue (0.42 ± 0.04 vs 0.31 ± 0.04 , $p < 0.01$), measured by the Fatigue Assessment Questionnaire (FAQ). Furthermore, cognitive impairment improved (4.39 ± 0.44 vs 3.31 ± 0.39 , $p < 0.001$), as measured by C19-YRS.

The Chokpaisarn et al (2024) study followed TTM guidelines, incorporating traditional Thai massage with aromatic herbal oil, herbal compresses, herbal hot steam, lung acupressure massage, and breathing exercises. Patients received treatment for up to seven days, with the mean duration being 4.65 days. There was an improvement in emotional well-being measured through the SF-36 questionnaire (78.35 ± 17.44 vs 81.18 ± 17.99 , $p = 0.336$). However, the mean difference was not statistically significant. Changes in SF-36 scores also showed improvements in energy/fatigue (65.59 ± 21.50 vs 75.29 ± 19.48 , $p = 0.031$) and overall QoL (65.41 ± 27.40 vs 75.93 ± 24.57). The study also reported its effects on headaches and insomnia, measured through numbers and percentages of patients presenting with such symptoms at day zero, three, five, and seven of the intervention. For headaches, two patients (11.76%) presented with headaches on day zero and decreased to zero patients for the remainder of the intervention. Six patients (35.29%) presented with insomnia on day zero, which decreased to two patients (11.76%) by day 3 and zero for the remainder of the intervention.

Multidisciplinary Rehabilitation

Three studies assessed multidisciplinary rehabilitation.^{42,43,45} Braga et al (2023) utilised a multidisciplinary team following the Sarah Network of Rehabilitation Hospitals' neuropsychological rehabilitation program, which implemented a psychoeducational focus on cognitive and emotional function. Patients participated in the program for four consecutive weeks, with two-hour weekly group sessions which could be attended virtually or in person. There were improvements in depression (8.73 ± 3.57 vs 7.25 ± 3.88 , $p < 0.001$) and anxiety (9.89 ± 4.14 vs 8.34 ± 3.93 , $p < 0.001$) measured using Hospital Anxiety and Depression Scale (HADS). The study also found significant improvements in the QoL measured using WHOQoL-Bref (3.25 ± 0.63 vs 3.51 ± 0.63 , $p < 0.001$). Furthermore, significant improvements in cognitive function were seen measured using the Barrow Neurological Institute Screen for Higher Cerebral Functions (BNIS) (-1.23 ± 1.27 vs -0.79 ± 1.35 , $p < 0.001$), NEUPSILIN subtests of Phonemic Verbal Fluency Test (-0.55 ± 1.06 vs -0.16 ± 1.02 , $p < 0.001$) and Clock drawing test for executive functions (3.21 ± 1.41 vs 3.44 ± 1.23 , $p = 0.017$).

The study by Müller et al (2023) involved physical and psychological rehabilitation and was also conducted by a multidisciplinary team. Patients participated in the rehabilitation program for a mean duration of 28.77 (9–42) days. The study found significant improvements in mental health, measured through improved HADS depression scores (7.33 ± 5.25 vs 6.33 ± 5.25 , $p < 0.001$) and HADS anxiety scores (7.33 ± 5.25 vs 6.00 ± 5.25 , $p < 0.001$). The rehabilitation also showed improvement in fatigue through improved Brief Fatigue Inventory (BFI) scores (5.63 ± 1.58 vs 5.27 ± 2.03 , $p = 0.004$) and Fatigue Impact Scale (FIS) scores (94.33 ± 30.01 vs 87.42 ± 35.08 , $p = 0.001$). Participants also had improved cognitive function with improvements in Montreal Cognitive Assessment (MoCA) version 8.1 and 8.2 test scores (26.67 ± 2.25 vs 27.33 ± 2.25 , $p = 0.015$) and Digital Symbol Substitution Test (DSST) scores (45.33 ± 12.00 vs 49.00 ± 12.75 , $p < 0.001$).

Similarly, the study by Kvale et al (2024) involved physical and functional rehabilitation, guided by a multidisciplinary team. The program targeted micro-choices that were used to manage their health challenges and explored new strategies to better regulate their symptoms. The process was split into three phases, with an initial preparation for change stage, the concentrated intervention stage, followed by an integrating change into every life stage.

The concentrated intervention lasted three to four days. The study found an improvement in anxiety and depression measured through improved EQ-5D-5L anxiety and depression dimension distribution across participants presenting with “no problem” (27.3% vs 38.2%, $p = 0.210$) but the difference was not statistically significant. Overall, QoL improved, as measured by EQ-5D-5L index scores (0.748 ± 0.01 vs 0.796 ± 0.02 , $p = 0.014$).

Mechanical Therapy

One study evaluated physical therapy assessed EECF to promote blood flow and reduce vascular inflammation and endothelial dysfunction.⁴¹ Patients were treated with either 35 sessions lasting one hour or a modified regimen consisting of 15 sessions. The study found an improvement on fatigue measured through the mean difference of the PROMIS fatigue score when compared to baseline (-4.63 ± 3.42 , $p < 0.001$). Improvement in QoL was also seen in Seattle Angina Questionnaire – Quality of Life (SAQ-QOL) scores (23.80 ± 31.02 , $p = 0.004$) and six patients (38%) also reported improved cognition (memory recall, focus and concentration), described as brain fog.

Findings of the Meta-Analysis

Findings of the meta-analysis revealed high heterogeneity among the included studies, indicating substantial variability in outcomes. Therefore, the results should be interpreted with caution.

Mental Health Symptoms

Five studies^{40,42–44,46} with a total of 407 participants were included in a meta-analysis evaluating reductions in mental health symptoms in patients with long COVID. The pooled effect size measured using SMD was 0.64 (95% CI: 0.0012 to 1.2692, $p < 0.0497$), indicating a statistically significant moderate effect of reducing mental health symptoms. The heterogeneity among the studies was considerable, with an I^2 statistic of 84%.

Fatigue

Our meta-analysis on the reduction of fatigue included three studies^{40,43,46} with a total of 177 participants. The pooled effect size was 1.74 (95% CI: -0.9416 to 4.4262 , $p = 0.1307$), indicating a large effect on reducing fatigue. However, this was not statistically significant, and heterogeneity was high with an I^2 statistic of 97%.

Quality of Life

Three studies^{40,42,45} with a total of 464 participants were included in a meta-analysis evaluating improvement in QoL. The pooled effect size was -1.34 (95% CI: -5.2620 to 2.5784 , $p = 0.2787$), indicating a substantial effect on improving QoL. However, this result was not statistically significant, and heterogeneity was considerable with an I^2 statistic of 98%.

Cognitive Functioning

Our meta-analysis on reductions in cognitive difficulties included three studies with a total of 332 participants. The pooled effect size was 1.05 (95% CI: -2.1961 to 4.2934 , $p = 0.2989$), indicating a significant effect on improving cognitive function. However, this was not statistically significant, and heterogeneity was high with an I^2 statistic of 96%. A detailed forest plot is shown in [Figure 2](#).

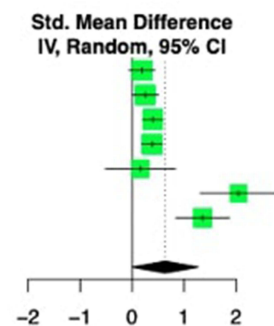
Risk of Bias of Included Studies

The risk of bias is shown in [Appendix 2](#) and [Appendix 3](#). Studies were considered high quality if 60% of the criteria were answered with “YES”. Five studies were considered high quality, and two studies were considered moderate quality. The assessment of the studies revealed that there was a low percentage score (<50% of studies were compliant) for the following items within the JBI critical appraisal tool for Case Series:³⁵ three (“Were valid methods used for identification of the condition for all participants included in the case series?”) and nine (“Was there clear reporting of the presenting sites'/clinics' demographic information?”).³⁵ One study⁴⁴ was considered to provide moderate quality evidence, being a level III-2 study on the NHMRC evidence hierarchy,³⁶ while the other six^{40–43,45,46} were all considered to provide low-quality evidence, being a level IV study on the hierarchy.³⁶

Mental health

Study	Pre-intervention			Post-intervention			Weight	Std. Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total		
Muller et al. (depression) ⁴³	7.33	5.2500	122	6.33	5.2500	122	15.5%	0.19 [-0.06; 0.44]
Muller et al. (anxiety) ⁴³	7.33	5.2500	122	6.00	5.2500	122	15.5%	0.25 [0.00; 0.51]
Braga et al. (depression) ⁴²	8.73	3.5700	208	7.25	3.8800	208	15.7%	0.40 [0.20; 0.59]
Braga et al. (anxiety) ⁴²	9.89	4.1400	208	8.34	3.9300	208	15.7%	0.38 [0.19; 0.58]
Chokpaisarn et al. ⁴⁰	-78.35	17.4400	17	-81.18	17.9900	17	12.3%	0.16 [-0.51; 0.83]
McEwan et al. (anxiety) ⁴⁴	3.37	0.9500	22	1.73	0.6200	22	11.7%	2.04 [1.31; 2.78]
Torner et al. ⁴⁶	-40.18	1.9200	36	-42.74	1.8600	36	13.6%	1.35 [0.84; 1.87]
Total (95% CI)			735			735	100.0%	0.64 [0.00; 1.27]

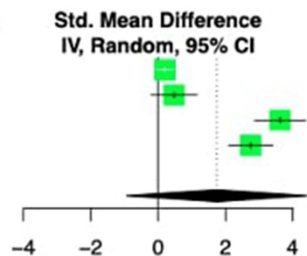
Heterogeneity: $\tau^2 = 0.3725$; $\chi^2 = 36.92$, $df = 6$ ($P < 0.01$); $I^2 = 84\%$



Fatigue

Study	Pre-intervention			Post-intervention			Weight	Std. Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total		
Muller et al. ⁴³	5.63	1.5800	122	5.27	2.0300	122	25.7%	0.20 [-0.05; 0.45]
Chokpaisarn et al. ⁴⁰	-65.59	21.5000	17	-75.29	19.4800	17	24.8%	0.47 [-0.21; 1.16]
Torner et al. (cognitive) ⁴⁶	0.62	0.0600	36	0.42	0.0500	36	24.6%	3.62 [2.86; 4.38]
Torner et al. (affect) ⁴⁶	0.42	0.0400	36	0.31	0.0400	36	24.9%	2.75 [2.10; 3.40]
Total (95% CI)			211			211	100.0%	1.74 [-0.94; 4.43]

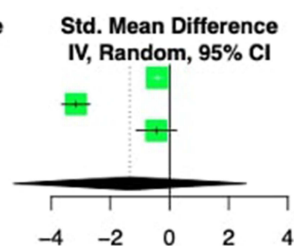
Heterogeneity: $\tau^2 = 2.7450$; $\chi^2 = 110.67$, $df = 3$ ($P < 0.01$); $I^2 = 97\%$



Quality of life

Study	Pre-intervention			Post-intervention			Weight	Std. Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total		
Braga et al. ⁴²	3.25	0.6300	208	3.51	0.6300	208	34.1%	-0.41 [-0.61; -0.22]
Kvale et al. ⁴⁵	0.75	0.0100	76	0.80	0.0200	76	33.4%	-3.16 [-3.64; -2.68]
Chokpaisarn et al. ⁴⁰	65.59	21.5000	17	75.93	24.5700	17	32.6%	-0.45 [-1.13; 0.23]
Total (95% CI)			301			301	100.0%	-1.34 [-5.26; 2.58]

Heterogeneity: $\tau^2 = 2.4308$; $\chi^2 = 109.70$, $df = 2$ ($P < 0.01$); $I^2 = 98\%$



Cognitive function

Study	Pre-intervention			Post-intervention			Weight	Std. Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total		
Muller et al. ⁴³	-26.67	2.2500	122	-27.33	2.2500	122	33.9%	0.29 [0.04; 0.55]
Braga et al. ⁴²	1.23	1.2700	208	0.79	1.3500	208	34.0%	0.34 [0.14; 0.53]
Torner et al. ⁴⁶	4.39	0.4400	36	3.31	0.3900	36	32.2%	2.60 [1.97; 3.23]
Total (95% CI)			366			366	100.0%	1.05 [-2.20; 4.29]

Heterogeneity: $\tau^2 = 1.6329$; $\chi^2 = 47.20$, $df = 2$ ($P < 0.01$); $I^2 = 96\%$

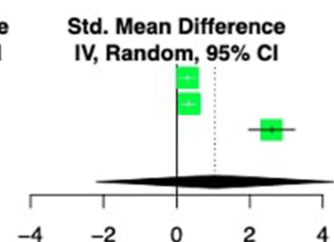


Figure 2 A forest plot showing the findings of meta-analysis.

Discussion

This systematic review and meta-analysis provided up-to-date evidence on the effectiveness of non-pharmacological interventions in managing neuropsychiatric long COVID symptoms in AYA. The findings of our review indicate that non-pharmacological interventions, including alternative practices, multidisciplinary rehabilitation, and physical therapy, can be effective in improving symptoms of long COVID in AYA, particularly for improving mental health symptoms. Non-statistically significant improvements were also observed in fatigue, QoL, and cognitive function.

Despite growing interest in alternative therapies, scarce systematic reviews and original research are investigating the effectiveness of TTM or forest bathing in managing neuropsychiatric long COVID symptoms. Our systematic review highlights the potential benefit of using alternative therapies to reduce mental health symptoms and fatigue for individuals with long COVID, whilst also demonstrating the lack of available methodologically sound research and good quality evidence

on this topic. This finding is consistent with existing literature on sensory-based interventions, such as aromatherapy, which have been reported to increase energy levels in different populations experiencing fatigue, a common symptom of long COVID,^{47,48} due to activation of the limbic system.⁴⁷ It is also consistent with literature, which has found alternative practices to effectively reduce mental health symptoms in different populations, as a result of stress reduction and affect regulation.⁴⁸ However, these findings should be interpreted with caution due to the high levels of heterogeneity, which might be influenced by factors such as small sample sizes, high variability in follow-up times, differences in measurement tools for the same outcome and variety in the interventions. This variability is reflected in another systematic review, which examined adult populations.⁴⁹ Hence, there is a need for further research to explore the potential benefits for mental health, fatigue, QoL, and cognitive function.

Furthermore, our systematic review supports the effectiveness of multidisciplinary rehabilitation programs in improving depression and anxiety in long COVID patients, highlighting its effectiveness in AYA. Although non-significant, the pooled effect size for fatigue and QoL showed some positive findings. Similar findings were reported in other systematic reviews by Dillen et al,⁵⁰ who reported beneficial effects on all four outcomes and Torres & Gradidge⁵¹ who found improvements in psychological recovery and QoL. These systematic reviews, however, looked at older adult populations, rather than AYA. Furthermore, Pouliopoulou et al²⁶ conducted a systematic review assessing rehabilitation programs in adults and reported limited evidence supporting improvements in fatigue, outlining that exercise-induced fatigue could counteract the intended benefits. Our findings align with these findings, suggesting that the exercise-induced fatigue could be a potential barrier to the effectiveness of rehabilitation programs. Nevertheless, as long as COVID is a multisystemic condition, multidisciplinary rehabilitation programs may be effective in providing holistic, patient-centred care that targets different body systems. This idea is supported by Alhumayn et al,⁵² who suggest that the variability in the manifestation of long COVID mandates a multidisciplinary team approach to assist in individual patients' needs. Collectively, the evidence suggests potential benefits of utilising multidisciplinary rehabilitation as a primary intervention in improving mental health symptoms of long COVID in AYA. Still, more research must be conducted to further establish the potential benefits of multidisciplinary rehabilitation in reducing fatigue and improving QoL in AYA with long COVID.

Our study also examined the potential benefits of mechanical therapy in improving neuropsychiatric symptoms of long COVID, including fatigue, QoL and cognitive function. While other cohort studies^{53,54} on older adult populations found a reduction in fatigue from EECF, the pooled results for these outcomes in our meta-analysis were not statistically significant. The mechanisms, including EECF's pulsatile shear stress improving cerebral blood flow⁴¹ and systemic endothelial function,⁵⁴ may still be plausible in improving symptoms of long COVID as these processes are theorised as a pathological process present in long COVID.⁵⁵ However, further research must be conducted to validate these strategies. Similarly, a systematic review found that other mechanical therapy methods, such as massage, improved fatigue and cognitive function in older adults.⁵⁰ However, there was very low certainty of evidence supporting this. Together, the evidence underscores the need for more rigorous research to investigate the potential role of mechanical therapy in improving the symptom burden of long COVID in AYA.

Strengths and Limitations

To our knowledge, this study is the first to systematically review the effectiveness of non-pharmacological interventions in the treatment of AYA presenting with neuropsychiatric symptoms of long COVID. A significant strength of this systematic review is its rigorous methodology, including the use of a comprehensive search strategy within four databases and manual searching in relevant sources to retrieve eligible studies. The screening process was also conducted independently by two reviewers reaching a consensus, thereby contributing to the robustness of our methodology.

However, there are a few limitations to our study. The robustness of the underlying studies limits the certainty of our analysis of the supporting evidence. All the studies, excluding one, were cohort studies with no comparison group. There was also no age-based sub-group analyses conducted in the studies, making it difficult to ascertain the effectiveness of the interventions in the AYA participants alone, rather than in the general participant group. Furthermore, the small sample sizes and inadequate information on outcomes for specific demographics in some studies contribute to the limitations of the review. Additionally, the meta-analyses revealed significant heterogeneity ranging from 84 to 98% on

the four outcomes that were measured which may yield unreliable estimates. These limitations make it challenging to make unified recommendations on which interventions in particular are specifically beneficial for AYA.

Implications for Practice and Directions for Future Research

Although the COVID-19 pandemic has decreased, its long-term effects continue to affect people, including AYA, and there must also be substantial consideration of the risk of future pandemic-like situations. Non-pharmacological interventions can potentially be valuable tools for managing neuropsychiatric symptoms in vulnerable populations during future pandemic-like situations,⁵⁶ offering effective alternatives to or supplementing pharmacological management. Additionally, a combination of several of these interventions could also prove beneficial, which should be examined in future studies.

Our systematic review also highlights the need for further research addressing the effectiveness of non-pharmacological interventions relative to control groups in treating long COVID symptoms in AYA. In particular, robust study designs, such as RCTs with large sample sizes and extended follow-ups, should be conducted to support the above findings. Moreover, evidence is particularly limited for the adolescent population (13–17), and significant research should be undertaken to enable optimal care for that population group. Finally, more research is required to determine the symptoms of long COVID most affecting AYA, as well as the underlying pathophysiology to allow for more standardised diagnostic criteria and measurement tools, which will subsequently strengthen the evidence of future research. Better research will also allow for further insight into which management strategies are most effective in managing specific symptoms and their outcomes, allowing for a more tailored approach for AYA.

Conclusions

This systematic review focused on examining the effectiveness of non-pharmacological interventions in managing neuropsychiatric symptoms of long COVID among AYA. The findings highlight the potential benefits of non-pharmacological interventions in managing symptoms to inform the development of multifaceted interventions for AYA suffering from long COVID. Our results showcase that multidisciplinary rehabilitation, alternative practices, and mechanical therapies show some promise in reducing neuropsychiatric symptoms of long COVID in AYA, particularly mental health symptoms. However, the full efficacy of these interventions in AYA requires further research using robust methodology such as RCTs and larger sample size. Additional studies with comparison groups are integral to determining the effectiveness of these interventions in reducing specific symptomatology across various age groups and across both sexes. To reduce the symptom burden of long COVID in AYA, further research should be conducted to allow for a more tailored approach to specific symptoms and the integration of several different intervention types.

Data Sharing Statement

The data used to support the findings of this study are included within the article. [Appendix 4](#) contained the supporting information on which the results were built upon. For further inquiries, please contact the corresponding author, Professor Valsamma Eapen.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

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