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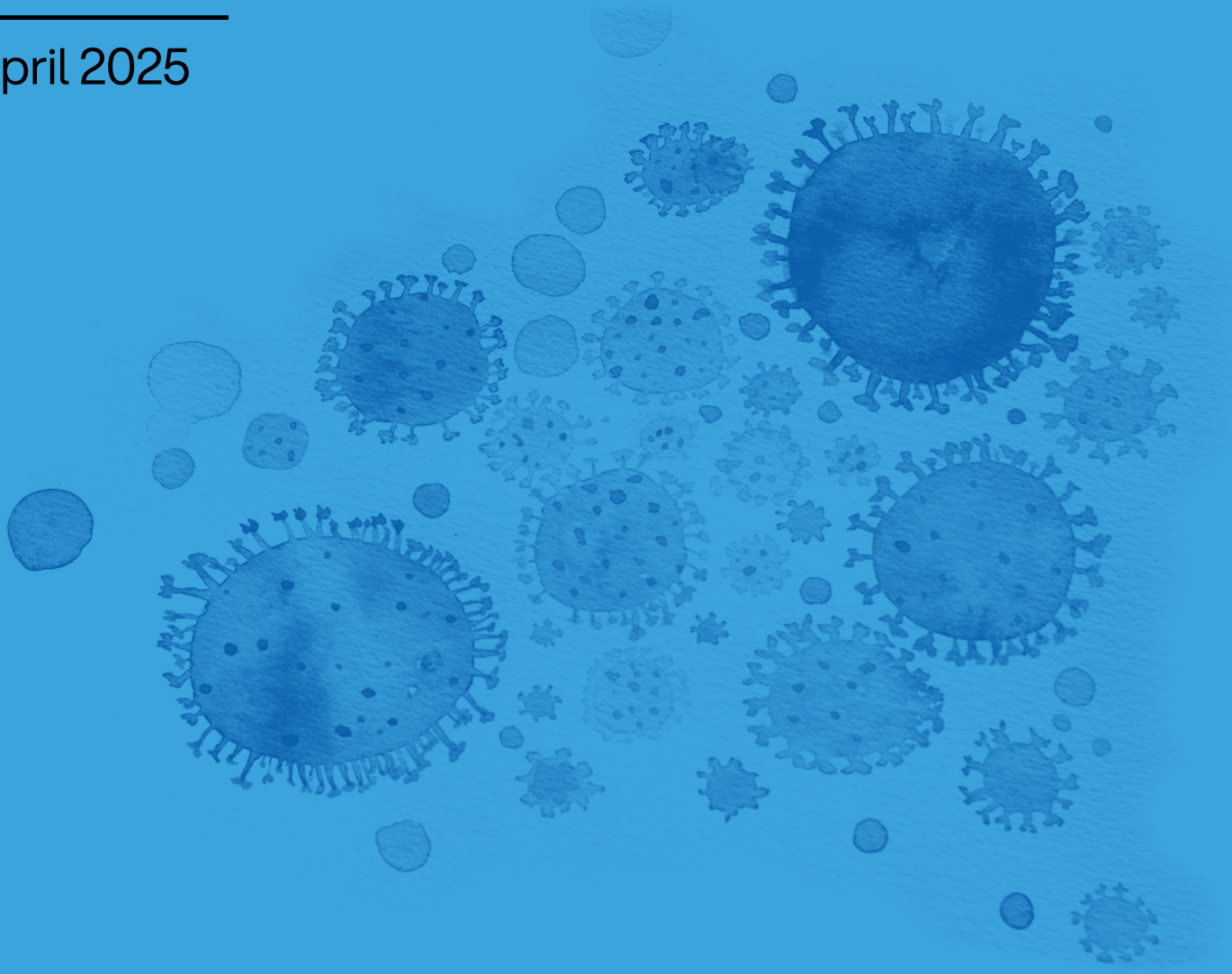
Supporting national policy development and implementation

Treatment and rehabilitation of Long COVID

A scope of the literature: Final update

April 2025



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Treatment and rehabilitation of Long COVID: A scope of the literature. Final update

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Summary

- We identified 18 randomised controlled trials published between December 2024 and March 2025 that were focused on Long COVID treatment or rehabilitation. Across all 12 of our reports produced for this programme of work, we identified and assessed 197 trials published between January 2022 and March 2025.
- Eleven of the 18 trials focused on generalised or multiple symptoms of Long COVID. Three trials focused on respiratory or cardiovascular function or physical fitness and three others evaluated treatments for neuropsychiatric issues. One trial focused on treating fatigue.
- One trial was rated positively for all 13 quality criteria that we assessed and another met 12 criteria. The remaining 16 trials gained a positive rating for between five and ten criteria.

Introduction

This is the twelfth and final report in a series of quarterly evidence scans requested by NHS England and the Department of Health and Social Care. It was conducted to identify and quality assess randomised controlled trials (RCTs) evaluating treatment or rehabilitation for Long COVID published in the three-month period between December 2024 and March 2025.

Method

Identification of studies

We searched the Cochrane Central Register of Controlled Trials (CENTRAL) using a range of key terms that have been used in the literature to describe symptoms and effects persisting beyond the acute stage of COVID-19 infection. Searches of MEDLINE, Embase, PsycINFO and CINAHL were also conducted to identify any trials that had not been incorporated into CENTRAL. We translated the CENTRAL search strategy for use in each database and used study design search filters to restrict retrieval to randomised controlled trials.

Searches were limited to studies added to the databases or published between 2022 and 2025, and no language restrictions were applied. Preprints were removed from the searches in MEDLINE and Embase. Due to the rapid nature of the project, the database searches were designed to balance the need to retrieve as many relevant trials as possible against the limited time available for screening. Records were downloaded into EndNote and deduplicated against the search results from previous updates. Full search strategies can be found in Appendix 1 (page 16).

Study selection

Studies were screened for inclusion against the following criteria:

Population - patients with Long COVID, which we conceptualised broadly as experiencing at least one symptom or effect that persists or develops after acute COVID-19 infection. No restrictions were placed on the socio-demographic characteristics of participants or COVID severity. We also did not apply criteria relating to the time period after acute infection owing to variation in how Long COVID has been defined in the literature.

Interventions - any intervention aimed at treating or rehabilitating patients with Long COVID. This could include, but was not limited to, medication, supplements, and physical therapy.

Interventions that had a primary focus on general rehabilitation from COVID-19 following hospitalisation or severe infection were excluded.

Outcomes – primary outcomes related to the effectiveness, cost-effectiveness, safety or side effects of interventions. Studies could also report outcomes related to the implementation of interventions. We excluded studies that only had a primary focus on intermediate outcomes such as blood biomarkers.

Study design - prospective trials with random allocation of participants to intervention and comparator groups. When designed and conducted to a high standard, a randomised controlled trial is often the most robust type of primary study design for investigating intervention effectiveness.[1] We excluded studies that were solely a post hoc or secondary analysis of a RCT.

Publication type and status - any publication type, except pre-prints and conference abstracts, which reports findings from a RCT (e.g., full papers, research letters, brief reports etc).

Quality assessment

Each study was appraised according to the Joanna Briggs Institute (JBI) Checklist for Randomized Controlled Trials.[2] In contrast to the Cochrane Risk of Bias Tool,[3] the JBI checklist does not require an assessment of bias for specific outcomes. It provides instead a general appraisal of each trial as a whole, which was needed in this piece of work as we were not seeking to extract and synthesise outcome data. Assessments were conducted by one reviewer and checked by another. The appraisal identified potential sources of bias and threats to the validity and reliability of study findings. The full checklist is provided in Appendix 2 (page 24).

Key findings

We screened 374 records and included 18 RCTs that had been published since December 2024[1].[4-21] This is identical to the mean number of RCTs included in our four previous reports published between April 2024 and January 2025 (n=18). The flow of studies through the current update is shown in Appendix 3 (page 25). Table 1 (page 6) presents the aim(s) and key characteristics of the 18 trials.

Interventions

Eleven of the 18 trials focused on individuals experiencing generalised or multiple symptoms of Long COVID.[4, 7-10, 12-14, 16-18] Three of the 11 trials evaluated the effectiveness of programmes based primarily on aerobic exercise, breathing training, and/or strength/resistance training.[8, 9, 17] Of these, one compared two modes of delivering exercise-based rehabilitation and education (face-to-face and remote);[8] another compared two different types of training (endurance only and combined endurance and resistance training);[17] and the third assessed

[1] We also identified the following paper which reported additional outcomes from a trial that we included and assessed in our April 2024 report. Bileviciute-Ljungar I, Apelman A, et al. A first randomized eight-week multidisciplinary telerehabilitation study for the post-COVID-19 condition: improvements in health- and pain-related parameters. Journal of Clinical Medicine. 2025 Jan 14;14(2):486

the impact of supplementing an aerobic exercise training programme with inspiratory and expiratory muscle training.[9]

Three of the 11 trials evaluated oral supplementation with vitamins K2 and D3;[4] thiamine (vitamin B1);[18] and omega-3,[16] one of which focused specifically on healthcare workers and assessed feasibility as the primary outcome. Improvement in persistent symptoms and safety/tolerability were assessed as secondary outcomes.[16] The remaining five trials on generalised/multiple symptoms of Long COVID evaluated: a transdiagnostic programme based on a cognitive and behavioural approach;[12] the impact of a remotely delivered weight management programme (Counterweight) on Long COVID symptoms in people with excess body weight;[7] Balneotherapy (bathing and exercising in thermal mineral water);[13] the safety of plasma exchange therapy;[10] and the acceptability, feasibility, and implementation of auricular vagus nerve stimulation in female Long COVID patients.[14]

Three of the 18 trials in the current update assessed treatments for individuals who primarily had problems with respiratory or cardiovascular function or physical fitness.[19-21] Two of these trials evaluated the effectiveness of multicomponent telerehabilitation,[19, 21] one of which compared two modes of programme delivery - fully remote and hybrid (remote and face-to-face delivery).[19] The third trial investigated the effects of auricular vagus nerve stimulation in people with postural orthostatic tachycardia syndrome (POTS) after COVID-19.[20]

Three of the 18 trials focused on treating neuropsychiatric sequelae,[6, 11, 15] one of which assessed vascular photobiomodulation (use of a low intensity laser to irradiate blood vessels) as a treatment for post COVID tension headache and other forms of head, face and neck pain.[6] Another evaluated pressing needle therapy for treating persistent symptoms of anxiety, depression and insomnia.[11] The third trial evaluated the use of oral supplements containing magnesium and vitamin D to treat individuals with post COVID depression and low levels of magnesium and vitamin D.[15]

One of the 18 trials focused on treating people with persistent post COVID fatigue. It evaluated the effectiveness of an individualised and symptom-titrated resistance and aerobic training programme.[5]

Six of the 18 trials in the current update (33%) evaluated interventions based primarily on physical activity, strength/resistance training and/or breathing training. This is less than the mean percentage of such trials included in our four previous reports (April 2024 to January 2025) (44%). For the second consecutive report, we did not identify any recently published trials of interventions for COVID-19 induced olfactory dysfunction.

Participants

Twelve trials recruited participants who had experienced persistent effects for at least twelve weeks after the onset of COVID symptoms or diagnosis.[4-10, 13, 15, 17, 20, 21] In another trial, participants had experienced persistent effects for at least three weeks after the onset of COVID symptoms or diagnosis.[18]

In two trials participants were recruited after testing negative [11] and between four and eight weeks after hospital discharge.[19] In two other trials, participants had persistent symptoms for at least 12 weeks after COVID-19 infection, but it was unclear if this related to time since symptom onset, diagnosis or recovery/discharge.[12, 16] The remaining trial recruited individuals who had a confirmed diagnosis of Long COVID, but no time-related details were reported.[14]

Countries

Three trials were conducted in Spain [9, 10, 13] and two trials were conducted in Austria;[14, 17] Brazil;[6, 19] China;[11, 20] UK;[7, 8] and the USA.[4, 16] One trial was conducted in Germany;[5] Iran;[18] Mexico;[15] Norway;[12] and Turkey.[21]

Trial quality

Assessments of the trials against the JBI criteria are provided in Table 2 (page 12). We assessed one trial as having a low risk of bias for all 13 appraisal criteria.[9] We assessed another trial positively for 12 out of the 13 criteria.[11] There was no blinding of the personnel who administered the treatment in this trial (Q5) owing to the nature of the intervention.

Four trials met ten criteria[10, 12, 13, 21] and 12 trials were rated positively for between five and nine criteria.[4-8, 14-20] A number of common issues were identified across the 16 trials that met ten or fewer criteria. For example, an intention-to-treat (ITT) analysis was not conducted in ten of the 16 trials (Q9).[5-7, 13-17, 19, 21] We were unable to tell if an appropriate statistical analysis had been conducted in ten trials as there was insufficient information reported about the sample size requirements of the study or because it was unclear if the number of trial participants had been sufficient to produce a robust analysis (Q12).[4-6, 10, 14-16, 18-20] In eight of the 16 trials, we could not tell if an appropriate procedure had been used to prevent researchers from knowing whether the next patient would be allocated to the treatment or comparator group (allocation concealment) (Q2).[5, 7, 10, 14-16, 18, 20]

In four trials that we rated positively for nine[7, 8] or ten[12, 13] criteria, there was no blinding of trial participants (Q4) and the personnel who administered the treatment (Q5). However, the nature of the intervention in these trials is likely to have precluded the use of blinding. In another study that we rated positively for ten criteria, there was no blinding of the personnel who administered the treatment owing to the nature of the intervention (Q5).[21]

In seven of the other 11 trials rated positively for fewer than 11 criteria, we could not tell if there was blinding of outcome assessors (Q6).[4, 5, 10, 14, 15, 19, 20] In four of the 11 trials, there was no blinding of participants (Q4) and the personnel who administered the treatment (Q5).[4, 5, 15, 19] There was no blinding of trial participants, the personnel who administered the treatment nor outcome assessors in two other trials.[17, 18] In three trials, there was no blinding of the personnel who administered the treatment (Q5)[6, 14, 20] and in another trial, we could not tell if they were blinded.[16] The nature of the intervention in some of these 11 trials may have prevented the use of blinding.

Conclusion

To conclude, in this evidence scan, we identified 18 RCTs published between December 2024 and March 2025 that examined interventions for the treatment or rehabilitation of people with Long COVID. Eleven trials in the current update focused on treating generalised or multiple symptoms of Long COVID. Three trials focused on improving respiratory or cardiovascular function or physical fitness, and three others addressed neuropsychiatric sequalae. The remaining trial focused on treating post COVID fatigue. One trial was rated positively for all 13 quality criteria that we assessed and another met 12 criteria. Sixteen trials gained a positive rating for between five and ten criteria.

Table 1: Study characteristics (n=18)

First author (year) Country	Aim of study	Main symptom or effect experienced	Post COVID time	Participants' gender (n) and % female	Primary outcome(s) of interest	Comparator
Atieh (2025)[4] USA	To investigate the effects of vitamins K2/D3 on Long COVID symptoms, as well as gut and inflammatory markers, in people with established Long COVID	General/multiple: at least two moderate-intensity symptoms (affecting daily life) attributable to Long COVID	After onset or diagnosis: at least three months following confirmed COVID-19 infection	Mixed (151; 123 completed) 71% female (107/151)	General or multiple: RECOVER Long COVID Research Index Score; number and type of LC symptoms Blood parameters: metabolic biomarkers - markers of immune activation and gut function	No intervention (usual care)
Barz (2024)[5] Germany	To investigate the effectiveness of an individualised and symptom-titrated exercise programme on fatigue in people with post-COVID condition	Fatigue/lack of energy	After onset or diagnosis: at least 12 weeks after positive test	Mixed (224; 118 completed) 69% female (81/118)	Fatigue: Fatigue Severity Scale (FSS)	Waiting list
Campos (2024)[6] Brazil	To assess the impact of vascular photo-biomodulation on post-COVID-19 patients experiencing tension-type headache, orofacial pain, or both, persisting for more than three months	Neuropsychiatric: orofacial pain or tension-type headache	After onset or diagnosis: more than three months from infection	Mixed (40; 34 analysed; 28 completed) 85% female (29/34)	Performing daily activities: Headache Impact Test (HIT-6) Other: Brief Pain Inventory (BPI); Visual Analog Scale (VAS); and analgesic intake (from medication reminders)	Sham vascular photo-biomodulation
Combet (2025)[7]	To assess whether a remotely delivered	General/multiple: most important self-reported	After onset or diagnosis:	Mixed (235; 214 analysed;	General or multiple: symptom score for the most important	Waiting list

UK	structured weight management programme could improve Long COVID symptoms in people living with overweight	Long COVID symptoms (fatigue, breathlessness, pain, anxiety/depression or other)	symptoms for more than 12 weeks	205 completed) 85% female (198/234)	symptom self-selected by participants (fatigue, breathlessness, pain, anxiety/ depression or other). Fatigue (Chalder fatigue scale); breathlessness (mMRC, Medical Research Council dyspnoea scale); pain (P4 pain rating scale); anxiety and depression (Hospital Anxiety and Depression Scale, HADS); or other symptoms scored on a 10-point VAS	
Daynes (2025)[8] UK	To determine the efficacy of exercise-based rehabilitation interventions, either face-to-face or remote, compared to usual care, in individuals experiencing post-COVID syndrome following a hospitalisation for acute COVID-19	General/multiple: confirmed diagnosis of post-COVID syndrome, with ongoing symptoms resulting in self-reported functional impairment	After onset or diagnosis: ongoing symptoms for more than 12 weeks	Mixed: (181; number completing unclear 45% female (82/181)	Physical fitness: Incremental Shuttle Walking Test (ISWT)	Both face-to-face and remote rehabilitation with usual care, were compared to usual care alone
del Corral (2025)[9] Spain	To assess the effects of adding inspiratory and expiratory muscle training to an aerobic exercise training programme for health-related quality of life (HRQoL) and exercise tolerance in individuals with long-term post-COVID-19 symptoms	General/multiple: long-term post-COVID-19 symptoms, including fatigue and dyspnoea	After onset or diagnosis: at least three months before enrolment	Mixed (64; 59 completed) 64% female (41/64)	Physical fitness: exercise tolerance on a cycle ergometer (electrocardiogram, heart rate, blood pressure; and peak VO_2) Quality of life: health-related quality of life (EQ-5D-5L)	Sham respiratory muscle training with aerobic exercise

España-Cueto (2025)[10] Spain	To assess the safety and efficacy of therapeutic plasma exchange in patients with post-COVID-19 condition	General/multiple: PCC diagnosis, with symptoms that hindered their daily activities	After onset or diagnosis: at least 90 days since testing positive	Mixed (50) 66% female (33/50)	Feasibility, tolerability and/or safety: safety Secondary outcomes included functional status, symptomology, quality of life, fatigue, neurocognitive symptoms, anxiety and depression	Placebo - sham plasma exchange
Liang (2024)[11] China	To evaluate the effect of pressing needle therapy on depression, anxiety, and sleep in patients recovering from COVID-19, and to provide a more effective and convenient treatment for the sequelae of COVID-19	Neuropsychiatric: depression, anxiety and insomnia	After recovery or discharge: after negative test	Mixed (136) 45% female (61/136)	Psychological: depression (Patient Health Questionnaire, PHQ-9); anxiety (Generalized Anxiety Disorder Scale, GAD-7) and insomnia (Insomnia Severity Index, ISI)	Sham needle pressing
Nerli (2024)[12] Norway	To assess the effectiveness of a brief outpatient rehabilitation programme based on a cognitive and behavioural approach for patients with post–COVID-19 condition	General/multiple: post-COVID condition with functional disability that interrupts all or most normal activities	Unclear/not stated: at least three months after acute infection	Mixed (314; 253 completed; 227 at 12 months) 72% female (225/314)	Physical fitness: participant-reported physical function - SF-36 Physical Function Subscale (SF-36-PFS)	Usual care
Ovejero (2025)[13] Spain	To evaluate the effects of Balneotherapy on post-acute COVID syndrome symptoms	General/multiple: Post-Acute COVID Syndrome (PACS)	After onset or diagnosis: three months from symptom onset	Mixed (98; 90 analysed) 86% female (84/98)	General or multiple: breathlessness (mMRC Dyspnoea Scale); quality of life (Short Form-36 Health Survey, SF-36); functional status (Post-COVID-19 Functional Status scale, PCFS); Psychological (HADS); Memory	Usual care and regular daily activities

					failures in everyday life following severe head injury (MFE-30); pain (VAS); sleep (Pittsburgh Sleep Quality Index PSQI)	
Pfoser-Poschacher (2025)[14] Austria	To investigate the acceptability, feasibility, and implementation of a three-month vagus nerve stimulation treatment with two different frequencies (10Hz, 25Hz) in female Long COVID patients, compared with a control frequency	General/multiple: Long COVID	Unclear/not stated: Long COVID diagnosis	Female only (36; 35 completed)	Feasibility, tolerability and/or safety: acceptability, feasibility, (Austrian school grading system: 1: very good, 2: good, 3: satisfactory, 4: sufficient, 5: not sufficient), and adherence (duration and frequency of VNS sessions, reasons for adherence or nonadherence and participants' subjective perceptions of the treatment effects) Secondary outcomes included impact on symptoms, heart rate variability, heart rate, blood pressure and rate pressure, cortisol in saliva at 8am, fatigue, quality of life, dyspnoea, insomnia, and adverse events	Two intervention groups - VNS at 10Hz or 25Hz; compared with control VNS at 2Hz
Rodríguez-Morán (2024)[15] Mexico	To evaluate the efficacy and safety of oral supplementation with magnesium chloride plus vitamin D in alleviating depressive symptoms related to Long COVID	Neuropsychiatric: mild-to-moderate depression (with hypomagnesaemia and vitamin D deficiency)	After onset or diagnosis: persisting symptoms for more than 12 weeks	Mixed (60; 59 completed) 65% female (39/60)	Psychological: Beck Depression Inventory (BDI)	Vitamin D alone

Sarkar (2024)[16] USA	To explore the feasibility of using omega-3 supplements versus placebo among healthcare workers with long-term symptoms of COVID-19	General/multiple: more than one ongoing symptom of shortness of breath, cough, fatigue, loss of taste, or loss of smell	Unclear/not stated: more than 12 weeks after infection	Mixed (32; 18 completed) 91% female (29/32)	Feasibility, tolerability and/or safety: feasibility (enrolment and compliance with the study protocol) Secondary outcomes: improvement of Long COVID symptoms and safety/tolerability	Placebo
Sick (2024)[17] Austria	To investigate the effects of endurance versus concurrent exercise on physical function, symptoms and quality of life in individuals with Post-COVID Syndrome (PCS), that did not need hospital admission during acute COVID-19	General/multiple: at least one symptom of PCS	After onset or diagnosis: at least 12 weeks after diagnosis	Mixed (66; 42 completed) 79% female (33/42)	Physical fitness: VO_2 peak on the cardiopulmonary exercise test (CPET)	Two intervention groups (endurance or concurrent exercise); compared with control (usual level of exercise)
Tehrani (2024)[18] Iran	To investigate the efficacy of Thiamine (vitamin B1) in alleviating symptoms of post-acute COVID-19 syndrome	General/multiple: diagnosis of post-acute COVID-19 syndrome and persistent symptoms such as fatigue, sleep disturbances, anosmia, ageusia, chest pain, cough, arthralgia, hair loss, or skin rashes	After onset or diagnosis: three weeks after symptom onset	Mixed (66) 47% female (31/66)	General or multiple: frequency and severity of symptoms (Visual assessment tool); sleep quality (PSQI)	Supportive therapy alone
Vian (2024)[19] Brazil	To evaluate and compare the effectiveness of a pulmonary telerehabilitation	Respiratory or cardiovascular function or physical fitness: patients with persistent respiratory	After recovery or discharge: 30 or more days after	Mixed (49; 30 completed)	Physical fitness: Six-Minute Walk Test (6MWT) distance	Fully remote supervision was compared with

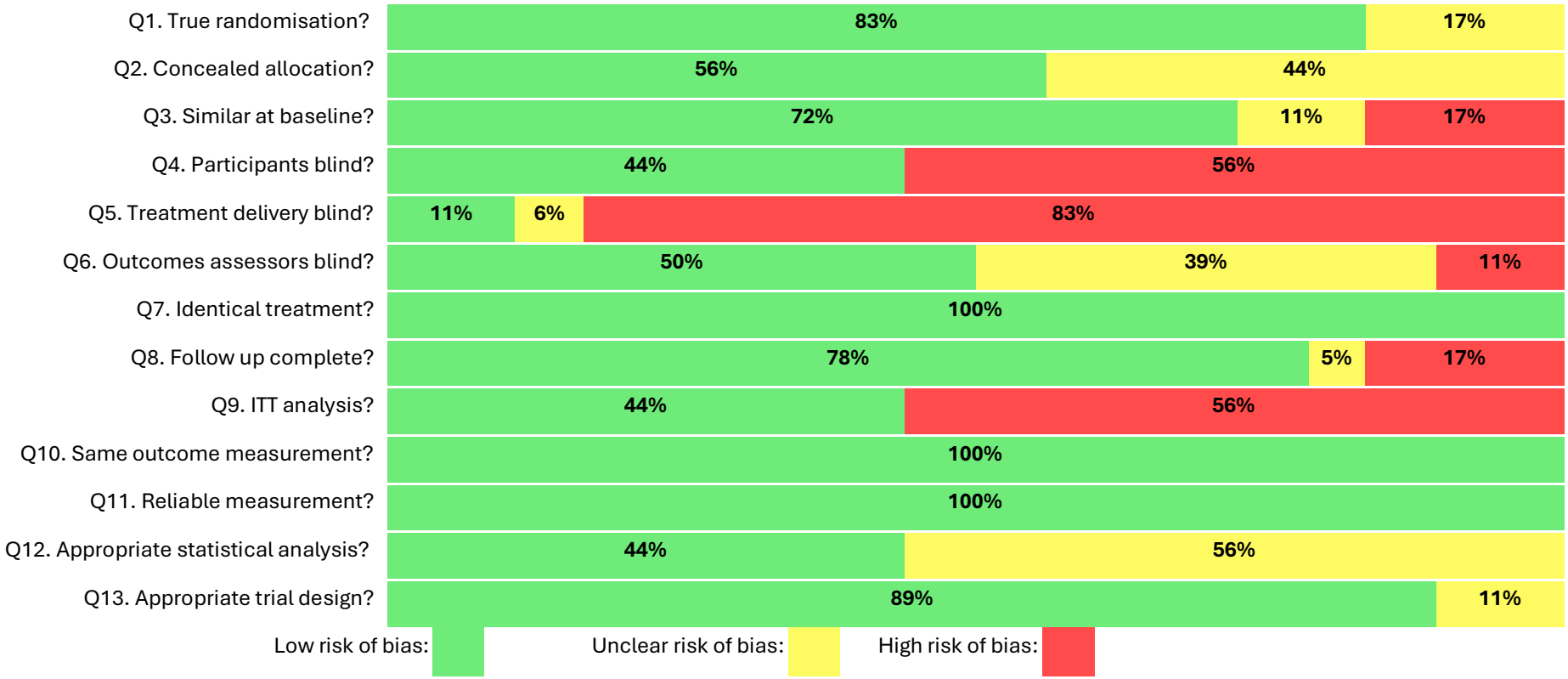
	programme in the exclusively remote modality versus the hybrid modality (remote and face-to-face) in patients with persistent respiratory dysfunction following hospitalisation for COVID-19 pneumonia	dysfunction and reduced functional capacity	discharge (max 60 days)	50% female (15/30)		hybrid (remote and face-to-face) [Patients were also allocated (not randomly) to a non-intervention group]
Wang (2025)[20] China	To explore the potential therapeutic benefits of low-level tragus stimulation in patients with postural orthostatic tachycardia syndrome (POTS) following COVID-19 infection	Respiratory or cardiovascular function or physical fitness: POTS - increase in heart rate of > 30 bpm within 10 min of standing from lying face-up, without orthostatic hypotension (drop in blood pressure > 20/10 mmHg)	After onset or diagnosis: symptoms for more than three months	Mixed (57) 61% female (35/57)	Pulmonary/respiratory or cardiovascular function: heart rate; heart rate variability analysis (electrocardiogram); blood pressure Blood parameters: plasma neuropeptide Y (NPY)	Sham stimulation
Yasaci (2025)[21] Turkey	To evaluate the effects of a structured telerehabilitation programme on dyspnoea, pain, functional capacity, sleep quality, anxiety, and depression in individuals with post-COVID-19 syndrome	Respiratory or cardiovascular function or physical fitness: diagnosed with PCS with dyspnoea	After onset or diagnosis: more than three months after diagnosis	Mixed (64; 60 completed) 52% female (31/60)	Pulmonary/respiratory or cardiovascular function: mMRC (Modified Medical Research Council) Dyspnoea Scale Physical fitness: five times sit-to-stand test (5-STS) Psychological: Hospital Anxiety and Depression Scale (HADS) Other: pain (numerical pain rating scale (NPRS); sleep quality (PSQI)	Brochure detailing an unsupervised home exercise programme (same exercises as in the treatment group protocol)

Table 2: JBI risk of bias assessment

First author (year)	Q1. True randomisation?	Q2. Concealed allocation?	Q3. Similar at baseline?	Q4. Participants blind?	Q5. Treatment delivery blind?	Q6. Outcomes assessors blind?	Q7. Identical treatment?	Q8. Follow up complete?	Q9. ITT analysis?	Q10. Same outcome measurement?	Q11. Reliable measurement?	Q12. Appropriate statistical analysis?	Q13. Appropriate trial design?
Atieh (2025)	?	+	?	-	-	?	+	+	+	+	+	?	?
Barz (2024)	?	?	+	-	-	?	+	?	-	+	+	?	+
Campos (2024)	+	+	+	+	-	+	+	-	-	+	+	?	+
Combet (2025)	+	?	+	-	-	+	+	+	-	+	+	+	+
Daynes (2025)	+	+	?	-	-	+	+	+	+	+	+	+	?
del Corral (2025)	+	+	+	+	+	+	+	+	+	+	+	+	+
España-Cueto (2025)	+	?	+	+	+	?	+	+	+	+	+	?	+
Liang (2024)	+	+	+	+	-	+	+	+	+	+	+	+	+
Nerli (2024)	+	+	-	-	-	+	+	+	+	+	+	+	+
Ovejero (2025)	+	+	+	-	-	+	+	+	-	+	+	+	+
Pfoser-Poschacher (2025)	?	?	+	+	-	?	+	+	-	+	+	?	+
Rodríguez-Morán (2024)	+	?	+	-	-	?	+	+	-	+	+	?	+
Sarkar (2024)	+	?	+	+	?	+	+	-	-	+	+	?	+
Sick (2024)	+	+	-	-	-	-	+	+	-	+	+	+	+
Tehrani (2024)	+	?	-	-	-	-	+	+	+	+	+	?	+
Vian (2024)	+	+	+	-	-	?	+	+	-	+	+	?	+

Wang (2025)	+	?	+	+	-	?	+	+	+	+	+	?	+
Yasaci (2025)	+	+	+	+	-	+	+	-	-	+	+	+	+

Low risk of bias: + Unclear risk of bias: ? High risk of bias: -



NB: figures may not add up to 100% due to rounding. In our reports, we adopt a 'once randomised, always analysed' approach to assessing the use of an ITT analysis (Q9), which is consistent with previous research and guidance.[22-24]

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21. Yasaci Z, Mustafaoglu R, Ozgur O, Kuveloglu B, Esen Y, Ozmen O, et al. Virtual recovery: efficacy of telerehabilitation on dyspnea, pain, and functional capacity in post-COVID-19 syndrome. Irish Journal of Medical Science. 2025;194(2):631-40.

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23. Bondemark L, Abdulraheem S. Intention to treat (ITT) analysis as reported in orthodontic randomized controlled trials-evaluations of methodology and recommendations for the accurate use of ITT analysis and handling dropouts. Eur J Orthod. 2018;40(4):409-13.

24. Cochrane Australia. Intention-to-treat (ITT) and other forms of data analysis [Video]. 2022 Available from: https://www.youtube.com/watch?v=mZp2KomA3Ws.

Appendix 1 – search strategies

Cochrane Controlled Register of Trials (CENTRAL)
via Wiley http://onlinelibrary.wiley.com/
Issue: Issue 2 of 12, February 2025
Date searched: 3rd March 2025
Records retrieved: 2446

Although 2446 records were identified overall in CENTRAL, trial register records were removed from this set, leaving a total of 2099 records downloaded for this update.

#1 MeSH descriptor: [Post-Acute COVID-19 Syndrome] this term only 322
#2 MeSH descriptor: [COVID-19] this term only and with qualifier(s): [complications - CO] 420
#3 MeSH descriptor: [COVID-19] this term only 8229
#4 MeSH descriptor: [SARS-CoV-2] this term only 3551
#5 MeSH descriptor: [Syndrome] this term only 6926
#6 MeSH descriptor: [Survivors] this term only 1767
#7 #3 or #4 8462
#8 #5 or #6 8687
#9 #7 and #8 109
#10 #1 or #2 or #9 769
#11 (long next (covid* or covid-19 or covid19 or coronavirus) or longcovid*):ti,ab,kw 639
#12 (post next (covid* or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2) or postcovid*):ti,ab,kw 996
#13 ((post acute or postacute) near/2 (covid* or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)):ti,ab,kw 1751
#14 PASC:ti,ab,kw 86
#15 (sequela* near/6 (covid* or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)):ti,ab,kw 210
#16 (chronic near/2 (covid* or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)):ti,ab,kw 46
#17 (ongoing next (covid* or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)):ti,ab,kw 115
#18 ((long* term or longterm) near/3 (covid* or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)):ti,ab,kw 1062
#19 (persist* near/6 (covid* or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)):ti,ab,kw 343
#20 ((post discharg* or postdischarg*) near/4 (covid* or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)):ti,ab,kw1623
#21 ((long haul* or longhaul*) near/6 (covid* or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)):ti,ab,kw 875
#22 (surviv* near/3 (covid* or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)):ti,ab,kw 228
#23 (after next (covid* or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)):ti,ab,kw 374
#24 ((ongoing or lasting or prolonged or fluctuat* or residual* or continu* or linger*) near/6 (symptom* or effect* or complication* or sequela* or syndrome or illness* or disorder$ or dysfunction* or impair* or impact* or consequence*) near/6 (covid* or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)):ti,ab,kw 211

#25 (OR #11-#24) 3319
#26 #10 or #25 with Cochrane Library publication date Between Jan 2022 and Mar 2025, in Trials 2430
#27 #10 or #25 with Publication Year from 2022 to 2025, in Trials 2291
#28 #26 or #27 2446

MEDLINE ALL
(includes: Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE Daily and Ovid MEDLINE)
via Ovid http://ovidsp.ovid.com/
Date range: 1946 to February 28, 2025
Date searched: 3rd March 2025
Records retrieved: 1487

The MEDLINE strategy below includes a search filter to limit retrieval to RCTs using the Cochrane Highly Sensitive Search Strategy for identifying randomized trials in MEDLINE: sensitivity and precision-maximizing version (2023 revision); Ovid format.

Lefebvre C, Glanville J, Briscoe S, Littlewood A, Marshall C, Metzendorf M-I, Noel-Storr A, Rader T, Shokraneh F, Thomas J, Wieland LS. Technical Supplement to Chapter 4: Searching for and selecting studies. In: Higgins JPT, Thomas J, Chandler J, Cumpston MS, Li T, Page MJ, Welch VA (eds). Cochrane Handbook for Systematic Reviews of Interventions Version 6.4 (updated October 2023). Cochrane, 2023. Available from: www.training.cochrane.org/handbook.

1 Post-Acute COVID-19 Syndrome/ (4202)
2 COVID-19 post-intensive care syndrome.mp. (6)
3 COVID-19/co [Complications] (20374)
4 COVID-19/ or SARS-CoV-2/ (294346)
5 Syndrome/ (124997)
6 Survivors/ (32378)
7 5 or 6 (157250)
8 4 and 7 (1261)
9 1 or 2 or 3 or 8 (23464)
10 ((long adj (covid$ or covid-19 or covid19 or coronavirus)) or longcovid$).ti,ab,kf,ot,bt. (6987)
11 ((post adj (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)) or postcovid$).ti,ab,kf,ot,bt. (13379)
12 ((post acute or postacute) adj2 (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)).ti,ab,kf,ot,bt. (1369)
13 PASC.ti,ab,kf,ot,bt. (1236)
14 (sequela$ adj6 (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)).ti,ab,kf,ot,bt. (3606)
15 (chronic adj2 (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)).ti,ab,kf,ot,bt. (436)
16 (ongoing adj (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)).ti,ab,kf,ot,bt. (3591)
17 ((long$ term or longterm) adj3 (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)).ti,ab,kf,ot,bt. (2930)
18 (persist$ adj6 (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)).ti,ab,kf,ot,bt. (5419)

19 ((post discharg$ or postdischarg$) adj4 (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)).ti,ab,kf,ot,bt. (106)
20 ((long haul$ or longhaul$) adj6 (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)).ti,ab,kf,ot,bt. (301)
21 (surviv$ adj3 (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)).ti,ab,kf,ot,bt. (3708)
22 (after adj (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)).ti,ab,kf,ot,bt. (11746)
23 ((ongoing or lasting or prolonged or fluctuat$ or residual$ or continu$ or linger$) adj6 (symptom$ or effect$ or complication$ or sequela$ or syndrome or illness$ or disorder$ or dysfunction$ or impair$ or impact$ or consequence$) adj6 (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)).ti,ab,kf,ot,bt. (3632)
24 or/10-23 (42087)
25 9 or 24 (57433)
26 exp randomized controlled trial/ (634458)
27 controlled clinical trial.pt. (95682)
28 randomi#ed.ab. (812723)
29 placebo.ab. (256363)
30 clinical trials as topic.sh. (204457)
31 randomly.ab. (454166)
32 trial.ti. (329943)
33 26 or 27 or 28 or 29 or 30 or 31 or 32 (1716775)
34 exp animals/ not humans.sh. (5311502)
35 33 not 34 (1585310)
36 25 and 35 (2016)
37 limit 36 to yr="2022 -Current" (1494)
38 (2022* or 2023* or 2024* or 2025*).dt. (5010901)
39 36 and 38 (1456)
40 37 or 39 (1503)
41 preprint.pt. (36674)
42 40 not 41 (1487)

Embase
via Ovid http://ovidsp.ovid.com/
Date range: 1974 to 2025 February 28
Date searched: 3rd March 2025
Records retrieved: 2248

The Embase strategy below includes a search filter to limit retrieval to RCTs:

Lefebvre C, Eisinga A, McDonald S, Paul N. Enhancing access to reports of clinical trials published world-wide - the contribution of EMBASE records to the Cochrane Central Register of Controlled Trials (CENTRAL) in The Cochrane Library. *Emerg Themes Epidemiol* 2008;5:13

1 long COVID/ (9834)
2 ((long adj (covid$ or covid-19 or covid19 or coronavirus)) or longcovid$).ti,ab,kw,ot. (7354)
3 ((post adj (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)) or postcovid$).ti,ab,kw,ot. (17094)
4 ((post acute or postacute) adj2 (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)).ti,ab,kw,ot. (1196)
5 PASC.ti,ab,kw,ot. (1534)

6 (sequela$ adj6 (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)).ti,ab,kw,ot. (4423)
7 (chronic adj2 (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)).ti,ab,kw,ot. (547)
8 (ongoing adj (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)).ti,ab,kw,ot. (3738)
9 ((long$ term or longterm) adj3 (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)).ti,ab,kw,ot. (3661)
10 (persist$ adj6 (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)).ti,ab,kw,ot. (6917)
11 ((post discharg$ or postdischarg$) adj4 (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)).ti,ab,kw,ot. (200)
12 ((long haul$ or longhaul$) adj6 (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)).ti,ab,kw,ot. (318)
13 (surviv$ adj3 (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)).ti,ab,kw,ot. (5414)
14 (after adj (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)).ti,ab,kw,ot. (15964)
15 ((ongoing or lasting or prolonged or fluctuat$ or residual$ or continu$ or linger$) adj6 (symptom$ or effect$ or complication$ or sequela$ or syndrome or illness$ or disorder$ or dysfunction$ or impair$ or impact$ or consequence$) adj6 (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)).ti,ab,kw,ot. (4468)
16 or/2-15 (53366)
17 1 or 16 (54216)
18 random$.ti,ab. (2172541)
19 factorial$.ti,ab. (51415)
20 crossover$.ti,ab. (97243)
21 cross-over$.ti,ab. (39811)
22 placebo$.ti,ab. (391076)
23 (doubl$ adj blind$).ti,ab. (259383)
24 (singl$ adj blind$).ti,ab. (34864)
25 assign$.ti,ab. (535075)
26 allocat$.ti,ab. (226090)
27 volunteer$.ti,ab. (309508)
28 Crossover Procedure/ (81324)
29 double blind procedure/ (228902)
30 Randomized Controlled Trial/ (867095)
31 single blind procedure/ (58211)
32 controlled clinical trial/ (445043)
33 or/18-32 (3322752)
34 (animal/ or animal experiment/ or animal model/ or animal tissue/ or nonhuman/) not exp human/ (7200282)
35 33 not 34 (2966332)
36 17 and 35 (3825)
37 limit 36 to yr="2022 -Current" (3004)
38 (2022$ or 2023$ or 2024$ or 2025$).dd. (6213272)
39 36 and 38 (3132)
40 37 or 39 (3177)
41 (conference abstract or "conference review").pt. (5397936)
42 40 not 41 (2414)
43 limit 42 to "remove preprint records" (2248)

PsycINFO
via Ovid http://ovidsp.ovid.com/
Date range: 1806 to February 2025 Week 4
Date searched: 3rd March 2025
Records retrieved: 655

The PsycINFO strategy below includes a search filter to limit retrieval to RCTs developed by the information specialist at the Cochrane Common Mental Disorders Group.

1 post-covid-19 conditions/ (406)
2 covid-19/ (44601)
3 coronavirus/ (6233)
4 syndromes/ (18747)
5 sequelae/ (4134)
6 2 or 3 (47107)
7 4 or 5 (22812)
8 6 and 7 (411)
9 1 or 8 (775)
10 ((long adj (covid$ or covid-19 or covid19 or coronavirus)) or longcovid$).ti,ab,id,ot. (517)
11 ((post adj (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)) or postcovid$).ti,ab,id,ot. (1647)
12 ((post acute or postacute) adj2 (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)).ti,ab,id,ot. (88)
13 PASC.ti,ab,id,ot. (72)
14 (sequela$ adj6 (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)).ti,ab,id,ot. (287)
15 (chronic adj2 (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)).ti,ab,id,ot. (32)
16 (ongoing adj (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)).ti,ab,id,ot. (439)
17 ((long$ term or longterm) adj3 (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)).ti,ab,id,ot. (269)
18 (persist$ adj6 (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)).ti,ab,id,ot. (417)
19 ((post discharg$ or postdischarg$) adj4 (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)).ti,ab,id,ot. (9)
20 ((long haul$ or longhaul$) adj6 (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)).ti,ab,id,ot. (29)
21 (surviv$ adj3 (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)).ti,ab,id,ot. (410)
22 (after adj (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)).ti,ab,id,ot. (827)
23 ((ongoing or lasting or prolonged or fluctuat$ or residual$ or continu$ or linger$) adj6 (symptom$ or effect$ or complication$ or sequela$ or syndrome or illness$ or disorder$ or dysfunction$ or impair$ or impact$ or consequence$) adj6 (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)).ti,ab,id,ot. (480)
24 or/10-23 (4192)
25 randomized clinical trials/ (606)
26 randomized controlled trials/ (1143)
27 clinical trials/ (12485)
28 clinical trial.md. (45705)

29 (randomi#ed or randomi#ation or randomi#ing).ti,ab,id. (121747)
30 randomly.ti,ab,id. (89782)
31 (RCT or "at random" or (random* adj3 (administ* or allocat* or assign* or class* or cluster* or control* or crossover or cross over or pragmatic or quasi or determine* or divide* or division or distribut* or expose* or fashion or number* or place* or recruit* or split or substitut* or treat*))).ti,ab,id. (141772)
32 (groups or (control* adj3 group*)).ab. (653919)
33 ((control* or trial or study or group*) and (waitlist* or wait* list* or ((treatment or care) adj2 usual))).ti,ab,id,hw. (21179)
34 ((single or double or triple or treble) adj2 (blind* or mask* or dummy)).ti,ab,id. (30744)
35 trial.ti. (42765)
36 (placebo or sham).ti,ab,id,hw. (61232)
37 treatment outcome.md. (25891)
38 treatment effectiveness evaluation/ (31037)
39 mental health program evaluation/ (2551)
40 or/25-39 (869709)
41 9 or 24 (4388)
42 40 and 41 (726)
43 limit 42 to yr="2022 -Current" (587)
44 (2022$ or 2023$ or 2024$ or 2025$).up. (609615)
45 42 and 44 (641)
46 43 or 45 (655)

CINAHL Complete
via Ebsco https://www.ebsco.com/
Date range: Inception to 20250303
Date searched: 3rd March 2025
Records retrieved: 1151

The CINAHL strategy below includes a search filter to limit retrieval to RCTs developed by Glanville et al.:

Glanville J, Dooley G, Wisniewski S, Foxlee R, Noel-Storr A. Development of a search filter to identify reports of controlled clinical trials within CINAHL Plus. *Health Info Libr J* 2019;36:73-90.

S1 (MH "Post-Acute COVID-19 Syndrome") 1,779
S2 TI (long N1 (covid* or covid-19 or covid19 or coronavirus) or longcovid*) OR AB (long N1 (covid* or covid-19 or covid19 or coronavirus) or longcovid*) 2,113
S3 TI (post N1 (covid* or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2) or postcovid*) OR AB (post N1 (covid* or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2) or postcovid*) 2,190
S4 TI (("post acute" or post-acute or postacute) N3 (covid* or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)) OR AB (("post acute" or post-acute or postacute) N3 (covid* or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)) 464
S5 TI PASC OR AB PASC 138
S6 TI (sequela* N6 (covid* or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)) OR AB (sequela* N6 (covid* or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)) 732

S7 TI (chronic N2 (covid* or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)) OR AB (chronic N2 (covid* or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)) 319
S8 TI (ongoing N1 (covid* or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)) OR AB (ongoing N1 (covid* or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)) 770
S9 TI ((long* N1 term or long-term or longterm) N3 (covid* or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)) OR AB ((long* N1 term or long-term or longterm) N3 (covid* or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)) 1,283
S10 TI (persist* N6 (covid* or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)) OR AB (persist* N6 (covid* or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)) 1,177
S11 TI ((post N1 discharg* or post-discharg* or postdischarg*) N4 (covid* or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)) OR AB ((post N1 discharg* or post-discharg* or postdischarg*) N4 (covid* or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)) 59
S12 TI ((long N1 haul* or long-haul* or longhaul*) N6 (covid* or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)) OR AB ((long N1 haul* or long-haul* or longhaul*) N6 (covid* or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)) 89
S13 TI (surviv* N3 (covid* or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)) OR AB (surviv* N3 (covid* or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)) 1,239
S14 TI (after N1 (covid* or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)) OR AB (after N1 (covid* or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)) 5,196
S15 TI ((ongoing or lasting or prolonged or fluctuat* or residual* or continu* or linger*) N6 (symptom* or effect* or complication* or sequela* or syndrome or illness* or disorder$ or dysfunction* or impair* or impact* or consequence*) N6 (covid* or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)) OR AB ((ongoing or lasting or prolonged or fluctuat* or residual* or continu* or linger*) N6 (symptom* or effect* or complication* or sequela* or syndrome or illness* or disorder$ or dysfunction* or impair* or impact* or consequence*) N6 (covid* or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)) 1,069
S16 (MH "Randomized Controlled Trials") 149,628
S17 (MH "Double-Blind Studies") 54,772
S18 (MH "Single-Blind Studies") 16,284
S19 (MH "Random Assignment") 90,466
S20 (MH "Pretest-Posttest Design") 58,408
S21 (MH "Cluster Sample") 5,938
S22 TI (randomised OR randomized) 159,279
S23 AB random* 414,520
S24 TI trial 204,195
S25 MH (sample size) AND AB (assigned OR allocated OR control) 4,514
S26 MH (placebos) 14,624
S27 PT (randomized controlled trial) 162,083
S28 AB (control W5 group) 153,769
S29 MH (crossover design) OR MH (comparative studies) 514,079
S30 AB (cluster W3 RCT) 526
S31 MH animals+ 102,172

S32 MH (animal studies) 154,233
S33 TI (animal model*) 3,940
S34 S31 OR S32 OR S33 247,515
S35 MH (human) 2,881,189
S36 S34 NOT S35 212,862
S37 S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 1,087,821
S38 S37 NOT S36 1,039,480
S39 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 13,849
S40 S38 AND S39 1,474
S41 S38 AND S39 Limiters - Publication Date: 20220101-20250331 1,134
S42 (ZD 2022* or 2023* or 2024* or 2025*) 386,257
S43 S40 AND S42 308
S44 S41 OR S43 1,151

Appendix 2

The Joanna Briggs Institute Critical Appraisal Checklist for Randomized Controlled Trials

Q1 Was true randomization used for assignment of participants to treatment groups? Yes, No, Unclear, NA

Q2 Was allocation to treatment groups concealed? Yes, No, Unclear, NA

Q3 Were treatment groups similar at the baseline? Yes, No, Unclear, NA

Q4 Were participants blind to treatment assignment? Yes, No, Unclear, NA

Q5 Were those delivering treatment blind to treatment assignment? Yes, No, Unclear, NA

Q6 Were outcomes assessors blind to treatment assignment? Yes, No, Unclear, NA

Q7 Were treatment groups treated identically other than the intervention of interest? Yes, No, Unclear, NA

Q8 Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analyzed? Yes, No, Unclear, NA

Q9 Were participants analyzed in the groups to which they were randomized? Yes, No, Unclear, NA

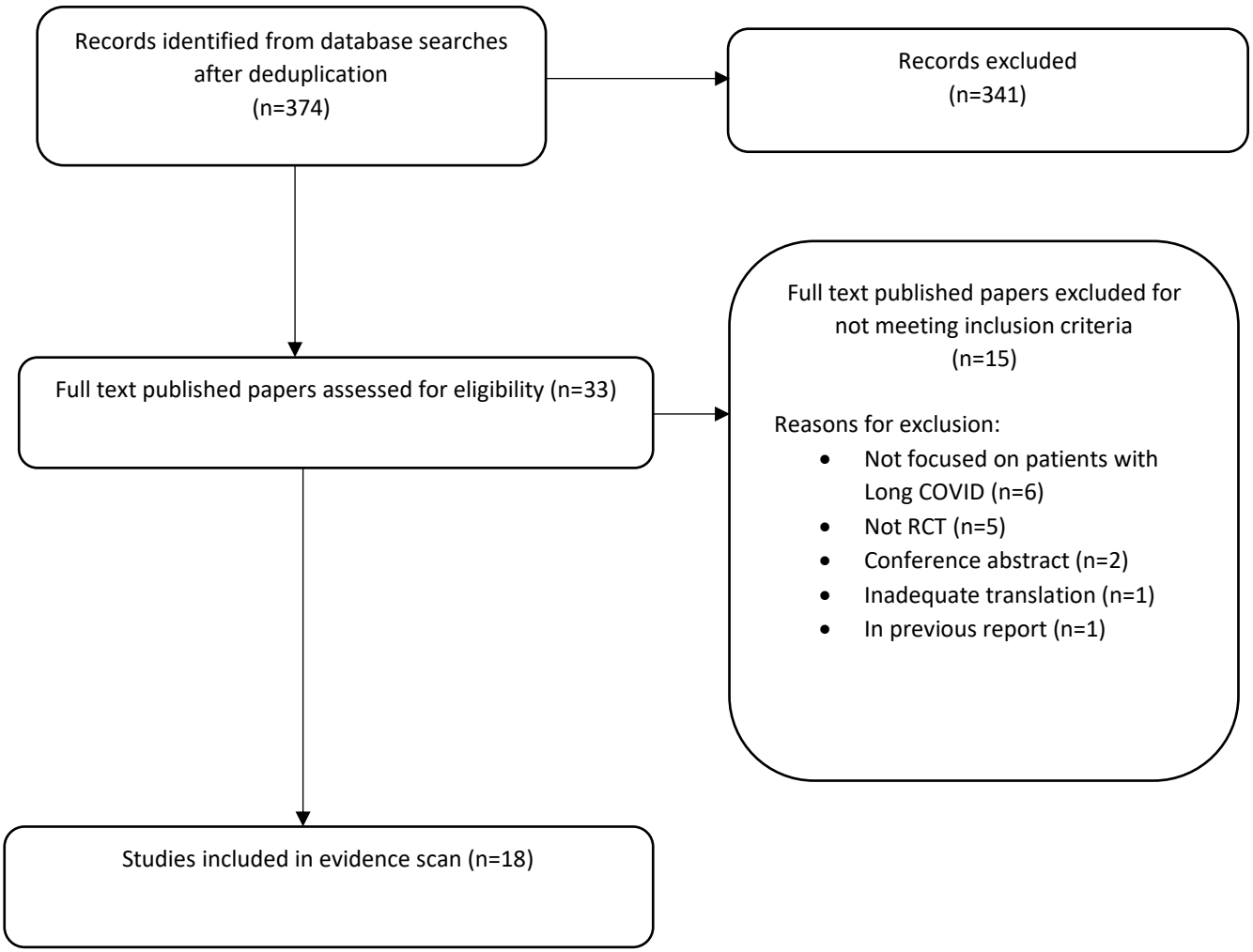
Q10 Were outcomes measured in the same way for treatment groups? Yes, No, Unclear, NA

Q11 Were outcomes measured in a reliable way? Yes, No, Unclear, NA

Q12 Was appropriate statistical analysis used? Yes, No, Unclear, NA

Q13 Was the trial design appropriate, and any deviations from the standard RCT design (individual randomization, parallel groups) accounted for in the conduct and analysis of the trial? Yes, No, Unclear, NA

Appendix 3: Flow of studies through the review



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