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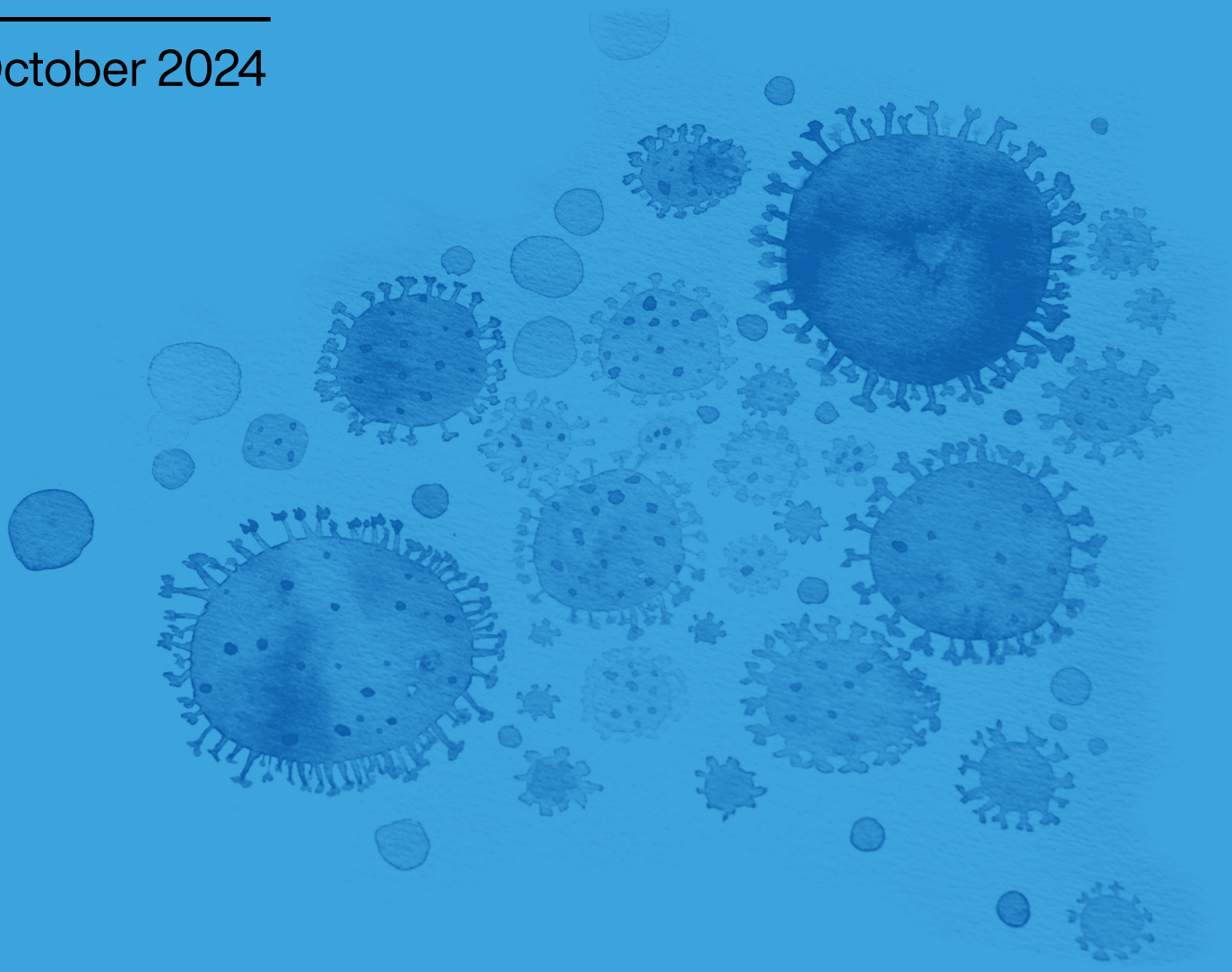
Supporting national policy development and implementation

Treatment and rehabilitation of Long COVID

A scope of the literature: update

October 2024



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Treatment and rehabilitation of Long COVID: A scope of the literature. Update October 2024

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Summary

- We identified 16 randomised controlled trials published between June and September 2024 that were focused on Long COVID treatment or rehabilitation. Across our ten reports produced to date, we have identified and assessed 156 trials published between January 2022 and September 2024.
- Eight of the 16 trials focused on treating generalised or multiple symptoms of Long COVID. Three trials focused specifically on respiratory or cardiovascular function or physical fitness, two of which also had a focus on fatigue. One other trial focused specifically on treating fatigue. Two trials focused on treating persistent problems with the sense of smell or taste (olfactory/gustatory dysfunction) and two evaluated treatments for neuropsychological sequela.
- Two trials were rated positively for 12 out of the 13 quality criteria that we assessed and three met 11 criteria. The remaining 11 trials gained a positive rating for between seven and ten criteria.

Introduction

This is the tenth report in an ongoing 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 June and September 2024.

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 2024, 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 17).

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 25).

Key findings

We screened 434 records and included 16 RCTs that had been published since June 2024.[4-19] This is slightly fewer than the mean number of RCTs included in the four reports that we have published in 2024 (n=18). The highest number of trials we included in a single report this year was 21[20] and the lowest was 15.[21] The total number of trials included in all four 2024 reports (n=71) is higher than in our 2023 reports (n=60). The flow of studies through the current update is shown in Appendix 3 (page 26). Table 1 (page 6) presents the aim(s) and key characteristics of the 16 trials.

Interventions

Half of the 16 trials focused on individuals experiencing generalised or multiple symptoms of Long COVID (n=8).[8, 9, 12, 13, 15-18] Three of the eight trials evaluated telerehabilitation programmes,[15, 16, 18] one of which compared two modes of programme delivery - unsupervised tele-exercise and hybrid (supervised and unsupervised).[18] Another one of the three trials focused specifically on older individuals (over 60 years old).[16] The other five trials evaluated: physical activity-focused tele-counselling;[8] high-dose vitamin D supplementation;[9] nirmatrelvir-ritonavir (combined antivirals);[12] lactoferrin treatment (an iron-binding glycoprotein);[17] and major ozone autohemotherapy (O_3-MAH).[13]

Three trials assessed treatments for individuals who primarily had problems with respiratory or cardiovascular function or physical fitness,[5, 7, 19] two of which also focused on treating

fatigue.[7, 19] Two of the three trials focused on assessing the effectiveness of exercise-based rehabilitation programmes and/or inspiratory muscle training.[5, 7] The third trial investigated the effect of intermittent hypoxia exposure (periods of hypoxia alternating with normal air).[19] One other trial focused on Astragalus root extract as a treatment for nurses with post COVID-19 chronic fatigue syndrome.[6]

Two trials focused on persistent problems with the sense of smell or taste (olfactory/gustatory dysfunction) and evaluated olfactory training with or without mometasone furoate nasal spray,[14] and forskolin (an extract from the root of the Indian Coleus plant).[4] The remaining two trials evaluated treatments for persistent neuropsychological issues. One assessed a self-directed mobile- app-delivered mindfulness intervention (Lift) for reducing post COVID psychological distress.[10] The other trial compared the effectiveness of guided imagery and Lazarus multimodal therapy for treating post COVID anxiety and feelings of hopelessness and helplessness.[11]

Across our four reports published in 2024, 42% of trials focused on interventions incorporating an exercise component and/or breathing training compared to a third of trials in our 2023 reports (32%). Approximately 17% of trials included in our reports this year had a primary focus on olfactory/gustatory dysfunction compared to 28% in our 2023 reports.

Participants

Seven trials recruited participants who had experienced persistent effects for at least four weeks after the onset of COVID symptoms or diagnosis.[7-9, 13, 16, 17, 19] In five of the seven trials, participants had persistent effects for at least 12 weeks after symptom onset or diagnosis.[7, 8, 16, 17, 19] One of the 16 trials recruited participants at least 12 weeks after COVID-19 infection,[12] and in two others, participants had experienced persistent symptoms for at least six months.[4, 6] Five trials recruited individuals at least four weeks[10, 14, 15] or 12 weeks[5, 18] after recovery or hospital discharge. In the remaining trial, individuals were recruited after recovery, but no time-related details were reported.[11]

Countries

Two trials were conducted in China;[13, 19] Egypt;[4, 5] Iran;[6, 11] and the USA.[10, 12] One trial was conducted in Canada;[7] Greece;[18] Malaysia;[14] Netherlands;[17] Spain;[16] Taiwan;[15] Thailand;[9] and Turkey.[8]

Trial quality

Assessments of the trials against the JBI criteria are provided in Table 2 (page 13). None of the trials were assessed as having a low risk of bias for all 13 appraisal criteria. We rated two trials positively for 12 out of the 13 criteria.[12, 17] In one of the two trials, it was unclear if complete follow-up information had been provided about all participants (Q8).[12] In the other trial, it was unclear if an intention-to-treat (ITT) analysis (Q9) had been used.[17]

We rated three trials positively for 11 out of the 13 criteria.[6, 9, 15] In one of these trials, there was no blinding of trial participants (Q4) and the personnel who administered the treatment (Q5). However, the nature of the intervention in this trial is likely to have precluded the use of blinding as it evaluated a telerehabilitation training programme.[15] In another trial, 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). The research team also only analysed the data of participants who completed the trial and therefore we could not give a positive rating for the use of an ITT analysis (Q9).[6] In the third trial,

it was unclear whether the personnel who administered the treatment were blinded (Q5). We also could not rate this study positively for allocation concealment (Q2) as a single researcher generated the randomisation sequence, enrolled participants, and assigned them to groups.[9]

Three trials met ten criteria[4, 5, 14] and eight trials were rated positively for between seven and nine criteria.[7, 8, 10, 11, 13, 16, 18, 19] A number of common issues were identified across the 11 trials that met ten or fewer criteria. For example, in six trials, we could not tell if an appropriate procedure had been used for allocation concealment (Q2).[7, 8, 11, 14, 18, 19] An ITT analysis was not conducted in four of the 11 trials (Q9),[7, 8, 13, 19] and in two others, we could not tell if it had been used.[4, 16]

In seven of the 11 trials, there was no blinding of trial participants (Q4) and the personnel who administered the treatment (Q5).[5, 7, 8, 10, 13, 16, 18] In an eighth study, there was no blinding of participants, and it was unclear whether the personnel who administered the treatment were also blinded.[14] However, the nature of the intervention in these eight trials is likely to have precluded the blinding of both groups of individuals. The personnel who administered the treatment (Q5) and those who assessed outcomes (Q6) were not blinded in another study, potentially owing to the nature of the intervention.[19] We were unable to tell if the outcome assessors were blinded in four trials.[8, 10, 13, 18] In one study, it was unclear if there was blinding of trial participants, the personnel who administered the treatment or outcome assessors.[11]

Conclusion

To conclude, in this evidence scan, we identified 16 RCTs published between June and September 2024 that examined interventions for the treatment or rehabilitation of people with Long COVID. Across our ten reports produced to date, we have identified and assessed 156 trials published since January 2022. Eight trials in the current update focused on treating generalised or multiple symptoms of Long COVID. Three trials focused on respiratory or cardiovascular function or physical fitness, two of which also had a focus on fatigue; one other trial evaluated a treatment for fatigue. The remaining four trials focused on treating olfactory/gustatory dysfunction (n=2) and neuropsychological sequela (n=2). Two trials were rated positively for 12 out of 13 quality criteria and three met 11 criteria. The remaining 11 trials gained positive ratings for between seven and ten criteria.

Table 1: Study characteristics (n=16)

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
Abdelazim (2024)[4] Egypt	To demonstrate the efficacy of oral forskolin for the treatment of olfactory dysfunction following COVID-19, compared with a placebo	Olfactory and/or gustatory dysfunction	Unclear/not stated: symptoms for at least six months	Mixed (285; 255 completed) 51% female (145/285)	Olfactory and/or gustatory function: "Sniffin' Sticks" (TDI score), and Clinical Global Impression - Severity (CGI-S) and - Improvement (CGI-I) scales	Placebo: capsules
Abo Elyazed (2024)[5] Egypt	To assess the clinical effects of incentive spirometry and diaphragmatic breathing in patients with post COVID-19 condition and diaphragmatic dysfunction compared with standard care alone	Respiratory or cardiovascular function or physical fitness: diaphragmatic excursion of < 10 mm or paradoxical diaphragmatic movement and/or diaphragm thickening fractions < 20%	After recovery: symptoms three months after seroconversion of acute COVID-19 infection	Mixed (60) 43% female (26/60)	Pulmonary/respiratory or cardiovascular function: modified Medical Research Council (mMRC) dyspnoea scale	Standard care
Banihashemi (2024)[6] Iran	To evaluate the effect of Astragalus root extract on nurses suffering from post-COVID-	Fatigue/lack of energy: CFS	Unclear/not stated: history of infection, and chronic fatigue (lasting over six months)	Mixed (64, 58 completed; 59 analysed) 49% female (29/59)	Fatigue: self-report scale for assessing CFS based on the DePaul Symptom Questionnaire	Placebo: corn starch

	19 chronic fatigue syndrome (CFS)					
Besnier (2024)[7] Canada	To investigate the effectiveness of an eight-week individualised cardiopulmonary rehabilitation programme on cardiorespiratory fitness in individuals with Long COVID	Respiratory or cardiovascular function or physical fitness: dyspnoea Fatigue/lack of energy	After symptom onset or diagnosis: symptoms for more than three months after initial positive test	Mixed (40, 35 completed) 69% female (24/35)	Pulmonary/respiratory or cardiovascular function: VO_2peak (cycle ergometer)	Usual daily activities
Celik (2024)[8] Turkey	To investigate the effectiveness of tele-counselling to promote physical activity in COVID-19 survivors at the persistent phase	General/multiple: Long COVID	After symptom onset or diagnosis: symptoms for more than 12 weeks	Mixed (28, 27 analysed) 81% female (22/27)	Pulmonary/respiratory or cardiovascular function: Modified Borg Scale, and Numeric Rating Scale Physical fitness: daily energy expenditure, step counts and physical activity intensity; 4m gait speed (4-MGS), sit-to-stand test Quality of life: SF-36 Psychological: Mental Health Continuum Short Form Fatigue: Fatigue Severity Scale (FSS) Other: Exercise Stages of Change Scale (intention to exercise), and Exercise	Brief information about being physically active

					Processes of Change Scale (process of change)	
Charoenporn (2024)[9] Thailand	To evaluate the effectiveness of high-dose vitamin D supplementation in alleviating fatigue and neuro-psychiatric symptoms in post-COVID syndrome	General/multiple: at least one of the following symptoms - fatigue, anxiety, depression, sleep disturbances, and cognitive impairment	After symptom onset or diagnosis: within three months of the onset of COVID-19 and persisting for a minimum of one month	Mixed (80) 78% female (62/80)	Psychological: DASS-21 (Depression, Anxiety and Stress Scale) Fatigue: CFQ-11 - Chalder Fatigue Scale Cognitive: Addenbrooke's Cognitive Examination III (ACE-III) Trail Making Test A and B (TMT-A and TMT-B) (speed processing test) Other: Pittsburgh Sleep Quality Index (PSQI)	Placebo: starch powder capsule
Cox (2024)[10] USA	To determine the feasibility and clinical effect of a self-directed mobile app-based mindfulness intervention (Lift) on symptoms of psychological distress	Neuropsychiatric: a score of five or higher on the Patient Health Questionnaire (PHQ-9) (depression)	After discharge: one month after discharge	Mixed (56, 45 completed) 68% female (38/56)	Psychological: PHQ-9	Usual care
Farzin (2024)[11] Iran	To examine the effectiveness of guided imagery and Lazarus multimodal therapy on COVID-19 anxiety syndrome	Neuropsychiatric: anxiety and hopelessness or helplessness (life expectancy)	Unclear/not stated: recovered from COVID-19	Mixed (45) 67% female (30/45)	Psychological: anxiety (COVID-19 Anxiety Questionnaire - CDAS)	No intervention

	and life expectancy in individuals who have recovered from COVID-19				Other: Miller's life expectancy questionnaire (MLEQ)	
Geng (2024)[12] USA	To assess the efficacy of a 15-day course of nirmatrelvir-ritonavir in reducing the severity of select post-acute sequelae of SARS-CoV-2 infection (PASC) symptoms	General/multiple: PASC - at least two self-reported moderate or severe core symptoms or symptom clusters defined as fatigue, brain fog, body aches, cardiovascular symptoms shortness of breath, and gastrointestinal symptoms	Unclear/not stated: PASC for three or more months, 90 days since COVID-19 infection	Mixed (155, 143 completed) 59% female (92/155)	General or multiple symptoms/clinical outcomes: core symptom severity (Likert scale)	Placebo with ritonavir
He (2024)[13] China	To assess the therapeutic effects of major ozone autohaemotherapy (O_3-MAH) in patients with post-acute sequelae of COVID-19	General/multiple: PASC	After symptom onset or diagnosis: ongoing for at least four weeks	Mixed (77, 73 analysed) 36% female (26/73)	Pulmonary/respiratory or cardiovascular function: forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), and tidal volume (VT), and the FEV_1/FVC ratio Physical fitness: six-minute walk distance (6MWD) General or multiple symptoms/clinical outcomes: difference in symptom score	Standard care

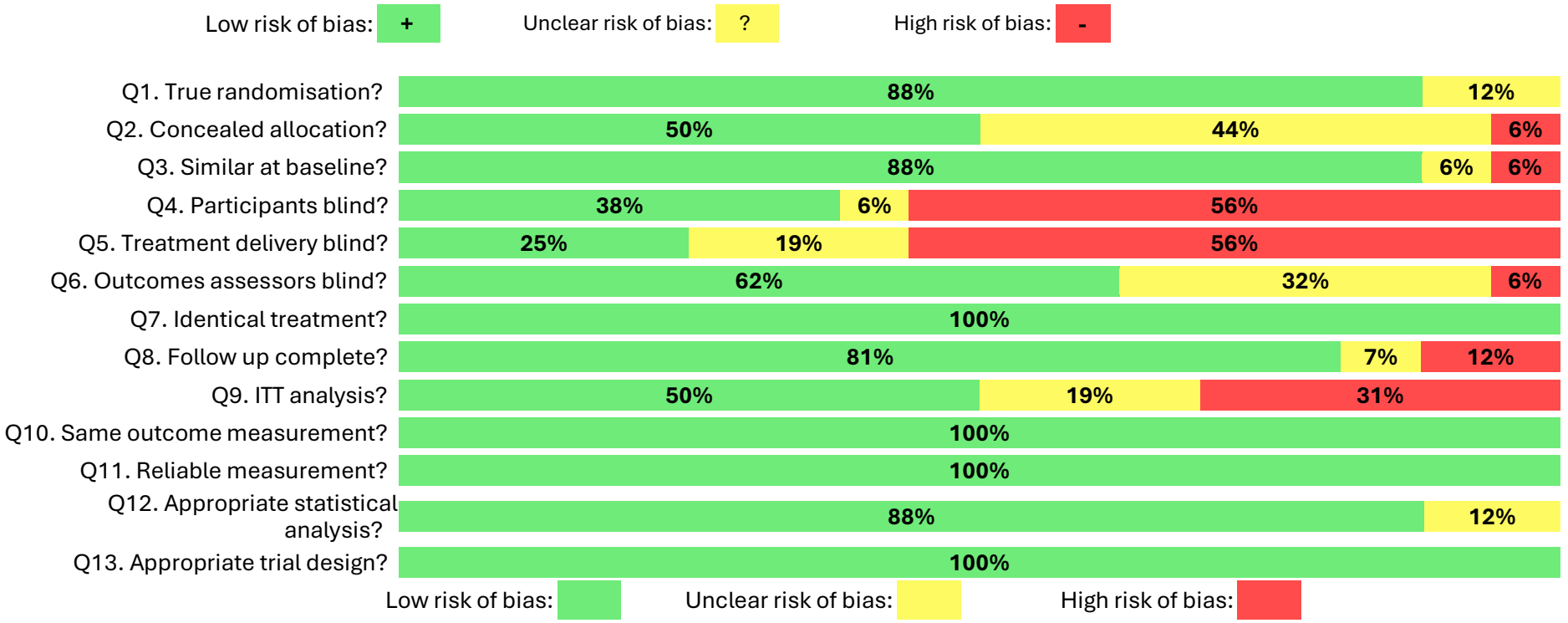
Ho (2024)[14] Malaysia	To investigate and compare the effectiveness of olfactory training and combined treatment (topical corticosteroids/ olfactory training) in improving residual smell disturbances among patients after recovery from COVID-19 infection	Olfactory and/or gustatory dysfunction	After recovery: symptoms for more than four weeks after recovery	Mixed (31) 68% female (21/31)	Olfactory and/or gustatory function: Top International Biotech Smell Identification Test (TIBSIT), and English Olfactory Disorder Questionnaire (eODQ)	Control - no further details reported
Lai (2024)[15] Taiwan	To investigate the effectiveness of a 12-week telerehabilitation training programme in participants with Long COVID	General/multiple: symptoms such as dyspnoea, persistent cough, easily fatigued, headache, or joint pain	After recovery: at least four weeks after a negative test	Mixed (182, 122 completed) 38% female (70/182)	Pulmonary/respiratory or cardiovascular function: cardiopulmonary exercise testing including VO_2peak, workload, anaerobic threshold, O_2 pulse, forced vital capacity (FVC, L/min), forced expiratory volume in 1 sec (FEV_1, L/min), FEV_1/FVC ratio (%), heart rate recovery (HRR) at 1 and 2 min, and ventilatory efficiency (VE/VCO_2 slope)	Usual care or usual lifestyle
Pleguezuelos (2024)[16] Spain	To evaluate the effects of a 12-week telerehabilitation programme on cardiorespiratory and muscular	General/multiple: post-COVID-19 syndrome - mainly dyspnoea, persistent fatigue, and muscle weakness	After symptom onset or diagnosis: over three months from symptom onset	Mixed (120, 106 analysed) 39% female (41/106)	Pulmonary/respiratory or cardiovascular function: cardiopulmonary exercise testing (CPET), relative and absolute VO_2peak, minute ventilation (VE), ventilatory	Usual lifestyle

	fitness and body composition in older patients with post-COVID-19 syndrome				equivalent for oxygen ($VE{\cdot}VO_2$), ventilatory equivalent for carbon dioxide ($VE{\cdot}VCO_2$), respiratory exchange ratio (RER), and end-tidal partial pressure of oxygen and carbon dioxide ($PetO_2$ and $PetCO_2$) Physical fitness: isokinetic knee flexor and extensor muscle strength Other: body composition bioelectrical impedance analysis (BIA), including body mass, body fat mass, fat free mass, soft lean mass, and skeletal muscle mass	
Redel (2024)[17] The Netherlands	To investigate the effect of lactoferrin on various Long COVID domains, including fatigue, anxiety, depression, cognitive failure and muscle strength	General/multiple: at least two symptoms of Long COVID	After symptom onset or diagnosis: symptoms for three months from onset, lasting between two and 12 months	Mixed (72, 65 completed) 63% female (45/72)	Fatigue: Fatigue Assessment Scale (FAS)	Placebo: cellulose
Stavrou (2024)[18] Greece	To obtain evidence whether an unsupervised tele-exercise programme via an online platform is a feasible alternative	General/multiple: Long COVID	After recovery: three months after discharge	Mixed (49) 20% female (14/69)	Pulmonary/respiratory or cardiovascular function: pulmonary function testing (spirometry) Physical fitness: oxidative stress (reactive oxygen	Compared modes of delivery Hybrid (two of three weekly sessions in

	to a hybrid mode of supervised and unsupervised exercise sessions for improving clinical outcomes in patients recovering from COVID-19				metabolites - d-ROMs test, and plasma antioxidant capacity - PAT test), 6MWT, handgrip strength, and 30-s sit-to-stand test Cognitive: Montreal Cognitive Assessment (MoCA) Other: body composition including muscle mass, percentage of body fat, visceral fat, and lean body mass	person, one remote)
Zha (2024)[19] China	To investigate the effect of intermittent hypoxia exposure (5-min hypoxia alternating with 5-min normal air, repeated five times) on dyspnoea and fatigue in patients with post-acute sequelae of COVID-19	Respiratory or cardiovascular function or physical fitness: dyspnoea Fatigue/lack of energy	After symptom onset or diagnosis: persistent symptoms for 12 or more weeks	Mixed (98, 95 completed) 65% female (62/95)	Pulmonary/respiratory or cardiovascular function: spirometry - including tidal volume (VT), forced vital capacity (FVC), FVC %pred (predicted), forced expiratory volume in 1s (FEV_1), FEV_1 %pred, and FEV_1/FVC; Borg Dyspnea Scale; mMRC scale Physical fitness: 6MWD - six-minute walk distance Fatigue: FAS; CFQ-11	Normoxia - compressed air through a mask with the same flow of nitrogen as in intermittent hypoxia exposure Both groups received usual care, including inhaled bronchodilators and nebulisation therapy

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?
Abdelazim (2024)	+	+	+	+	+	+	+	-	?	+	+	?	+
Abo Elyazed (2024)	+	+	+	-	-	+	+	+	+	+	+	?	+
Banihashemi (2024)	+	?	+	+	+	+	+	+	-	+	+	+	+
Besnier (2024)	+	?	+	-	-	+	+	+	-	+	+	+	+
Celik (2024)	+	?	?	-	-	?	+	+	-	+	+	+	+
Charoenporn (2024)	+	-	+	+	?	+	+	+	+	+	+	+	+
Cox (2024)	+	+	+	-	-	?	+	-	+	+	+	+	+
Farzin (2024)	?	?	+	?	?	?	+	+	+	+	+	+	+
Geng (2024)	+	+	+	+	+	+	+	?	+	+	+	+	+
He (2024)	+	+	+	-	-	?	+	+	-	+	+	+	+
Ho (2024)	+	?	+	-	?	+	+	+	+	+	+	+	+
Lai (2024)	+	+	+	-	-	+	+	+	+	+	+	+	+
Pleguezuelos (2024)	+	+	-	-	-	+	+	+	?	+	+	+	+
Redel (2024)	+	+	+	+	+	+	+	+	?	+	+	+	+
Stavrou (2024)	?	?	+	-	-	?	+	+	+	+	+	+	+
Zha (2024)	+	?	+	+	-	-	+	+	-	+	+	+	+



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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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 8 of 12, August 2024
Date searched: 3rd September 2024
Records retrieved: 1860

Although 2156 records were identified overall in CENTRAL, trial register records were removed from this set, leaving a total of 1860 records downloaded for this update.

#1 MeSH descriptor: [Post-Acute COVID-19 Syndrome] this term only 267
#2 MeSH descriptor: [COVID-19] this term only and with qualifier(s): [complications - CO] 354
#3 MeSH descriptor: [COVID-19] this term only 8006
#4 MeSH descriptor: [SARS-CoV-2] this term only 3401
#5 MeSH descriptor: [Syndrome] this term only 6723
#6 MeSH descriptor: [Survivors] this term only 1814
#7 #3 or #4 8265
#8 #5 or #6 8531
#9 #7 and #8 106
#10 #1 or #2 or #9 665
#11 (long next (covid* or covid-19 or covid19 or coronavirus) or longcovid*):ti,ab,kw 536
#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 870
#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 1584
#14 PASC:ti,ab,kw 75
#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 189
#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 44
#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 113
#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 938
#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 309
#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,kw1443
#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 750
#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 215
#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 351
#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 200
#25 (OR #11-#24) 3063

#26 #10 or #25 with Cochrane Library publication date Between Jan 2022 and Sep 2024, in Trials 2140
#27 #10 or #25 with Publication Year from 2022 to 2024, in Trials 1999
#28 #26 or #27 2156

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 August 29, 2024
Date searched: 3rd September 2024
Records retrieved: 1243

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/ (3647)
2 COVID-19 post-intensive care syndrome.mp. (6)
3 COVID-19/co [Complications] (18732)
4 COVID-19/ or SARS-CoV-2/ (279376)
5 Syndrome/ (124401)
6 Survivors/ (31821)
7 5 or 6 (156098)
8 4 and 7 (1175)
9 1 or 2 or 3 or 8 (21465)
10 ((long adj (covid$ or covid-19 or covid19 or coronavirus)) or longcovid$).ti,ab,kf,ot,bt. (5966)
11 ((post adj (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)) or postcovid$).ti,ab,kf,ot,bt. (11824)
12 ((post acute or postacute) adj2 (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)).ti,ab,kf,ot,bt. (1195)
13 PASC.ti,ab,kf,ot,bt. (1072)
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. (3234)
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. (385)
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. (3528)
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. (2667)
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. (4926)
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. (100)

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. (291)
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. (3479)
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. (10883)
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. (3362)
24 or/10-23 (38516)
25 9 or 24 (52854)
26 exp randomized controlled trial/ (621846)
27 controlled clinical trial.pt. (95595)
28 randomi#ed.ab. (785394)
29 placebo.ab. (251215)
30 clinical trials as topic.sh. (203186)
31 randomly.ab. (440818)
32 trial.ti. (316673)
33 26 or 27 or 28 or 29 or 30 or 31 or 32 (1672975)
34 exp animals/ not humans.sh. (5253348)
35 33 not 34 (1543931)
36 25 and 35 (1772)
37 limit 36 to yr="2022 -Current" (1251)
38 (2022* or 2023* or 2024*).dt. (4206591)
39 36 and 38 (1212)
40 37 or 39 (1259)
41 preprint.pt. (28525)
42 40 not 41 (1243)

Embase
via Ovid http://ovidsp.ovid.com/
Date range: 1974 to 2024 August 30
Date searched: 3rd September 2024
Records retrieved: 1881

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/ (8410)
2 ((long adj (covid$ or covid-19 or covid19 or coronavirus)) or longcovid$).ti,ab,kw,ot. (6247)
3 ((post adj (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)) or postcovid$).ti,ab,kw,ot. (15207)
4 ((post acute or postacute) adj2 (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)).ti,ab,kw,ot. (1100)
5 PASC.ti,ab,kw,ot. (1354)
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. (4051)

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. (510)
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. (3739)
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. (3371)
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. (6369)
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. (193)
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. (314)
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. (5148)
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. (14921)
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. (4197)
16 or/2-15 (49345)
17 1 or 16 (50134)
18 random$.ti,ab. (2114586)
19 factorial$.ti,ab. (50252)
20 crossover$.ti,ab. (95370)
21 cross-over$.ti,ab. (39255)
22 placebo$.ti,ab. (384981)
23 (doubl$ adj blind$).ti,ab. (255612)
24 (singl$ adj blind$).ti,ab. (33878)
25 assign$.ti,ab. (522439)
26 allocat$.ti,ab. (218760)
27 volunteer$.ti,ab. (305689)
28 Crossover Procedure/ (79471)
29 double blind procedure/ (223108)
30 Randomized Controlled Trial/ (840845)
31 single blind procedure/ (56123)
32 controlled clinical trial/ (473843)
33 or/18-32 (3254676)
34 (animal/ or animal experiment/ or animal model/ or animal tissue/ or nonhuman/) not exp human/ (7071347)
35 33 not 34 (2906948)
36 17 and 35 (3384)
37 limit 36 to yr="2022 -Current" (2531)
38 (2022$ or 2023$ or 2024$).dd. (1626035)
39 36 and 38 (907)
40 37 or 39 (2655)
41 (conference abstract or "conference review").pt. (5237880)
42 40 not 41 (2012)
43 limit 42 to "remove preprint records" (1881)

PsycINFO
via Ovid http://ovidsp.ovid.com/
Date range: 1806 to August 2024 Week 5
Date searched: 3rd September 2024
Records retrieved: 544

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/ (301)
2 covid-19/ (39226)
3 coronavirus/ (6134)
4 syndromes/ (18397)
5 sequelae/ (4081)
6 2 or 3 (41704)
7 4 or 5 (22409)
8 6 and 7 (387)
9 1 or 8 (652)
10 ((long adj (covid$ or covid-19 or covid19 or coronavirus)) or longcovid$).ti,ab,id,ot. (422)
11 ((post adj (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)) or postcovid$).ti,ab,id,ot. (1346)
12 ((post acute or postacute) adj2 (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)).ti,ab,id,ot. (70)
13 PASC.ti,ab,id,ot. (65)
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. (257)
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. (31)
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. (417)
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. (239)
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. (365)
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. (8)
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. (28)
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. (373)
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. (716)
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. (425)
24 or/10-23 (3608)
25 randomized clinical trials/ (563)
26 randomized controlled trials/ (1099)
27 clinical trials/ (12387)
28 clinical trial.md. (43530)

29 (randomi#ed or randomi#ation or randomi#ing).ti,ab,id. (117967)
30 randomly.ti,ab,id. (88033)
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. (137882)
32 (groups or (control* adj3 group*)).ab. (641157)
33 ((control* or trial or study or group*) and (waitlist* or wait* list* or ((treatment or care) adj2 usual))).ti,ab,id,hw. (20526)
34 ((single or double or triple or treble) adj2 (blind* or mask* or dummy)).ti,ab,id. (30273)
35 trial.ti. (41457)
36 (placebo or sham).ti,ab,id,hw. (60388)
37 treatment outcome.md. (25312)
38 treatment effectiveness evaluation/ (30133)
39 mental health program evaluation/ (2518)
40 or/25-39 (852002)
41 9 or 24 (3794)
42 40 and 41 (617)
43 limit 42 to yr="2022 -Current" (476)
44 (2022$ or 2023$ or 2024$).up. (516554)
45 42 and 44 (533)
46 43 or 45 (544)

CINAHL Ultimate
via Ebsco https://www.ebsco.com/
Date range: Inception to 20240903
Date searched: 3rd September 2024
Records retrieved: 982

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") 1,507
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*) 1,775
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*) 1,965
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)) 414
S5 TI PASC OR AB PASC 123
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)) 673

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)) 303
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)) 755
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)) 1,180
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)) 1,077
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)) 53
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)) 90
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)) 1,157
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)) 4,803
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)) 995
S16 (MH "Randomized Controlled Trials+") 147,140
S17 (MH "Double-Blind Studies") 54,588
S18 (MH "Single-Blind Studies") 16,175
S19 (MH "Random Assignment") 87,440
S20 (MH "Pretest-Posttest Design") 57,096
S21 (MH "Cluster Sample") 5,639
S22 TI (randomised OR randomized) 154,559
S23 AB random* 407,645
S24 TI trial 198,571
S25 MH (sample size) AND AB (assigned OR allocated OR control) 4,490
S26 MH (placebos) 14,581
S27 PT (randomized controlled trial) 159,363
S28 AB (control W5 group) 151,519
S29 MH (crossover design) OR MH (comparative studies) 507,617
S30 AB (cluster W3 RCT) 511
S31 MH animals+ 102,472

S32 MH (animal studies) 157,736
S33 TI (animal model*) 4,001
S34 S31 OR S32 OR S33 251,222
S35 MH (human) 2,823,703
S36 S34 NOT S35 216,472
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 1,070,443
S38 S37 NOT S36 1,021,319
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 12,654
S40 S38 AND S39 1,306
S41 S38 AND S39 Limiters - Publication Date: 20220101-20240931 965
S42 (ZD 2022* or 2023* or 2024*) 370,200
S43 S40 AND S42 276
S44 S41 OR S43 982

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

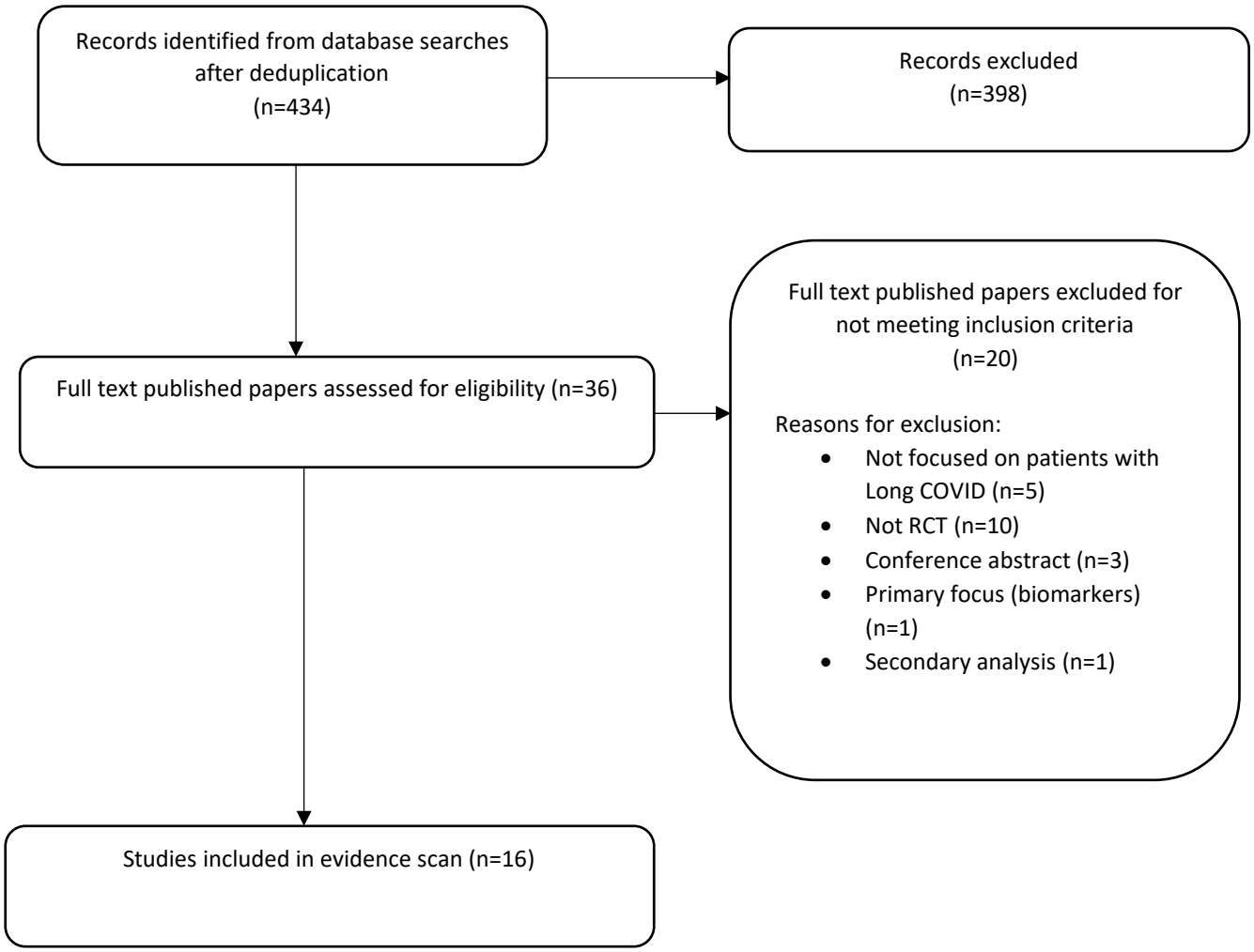
Q10 Were outcomes measured in the same way for treatment groups? Yes, No, Unclear, NA

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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