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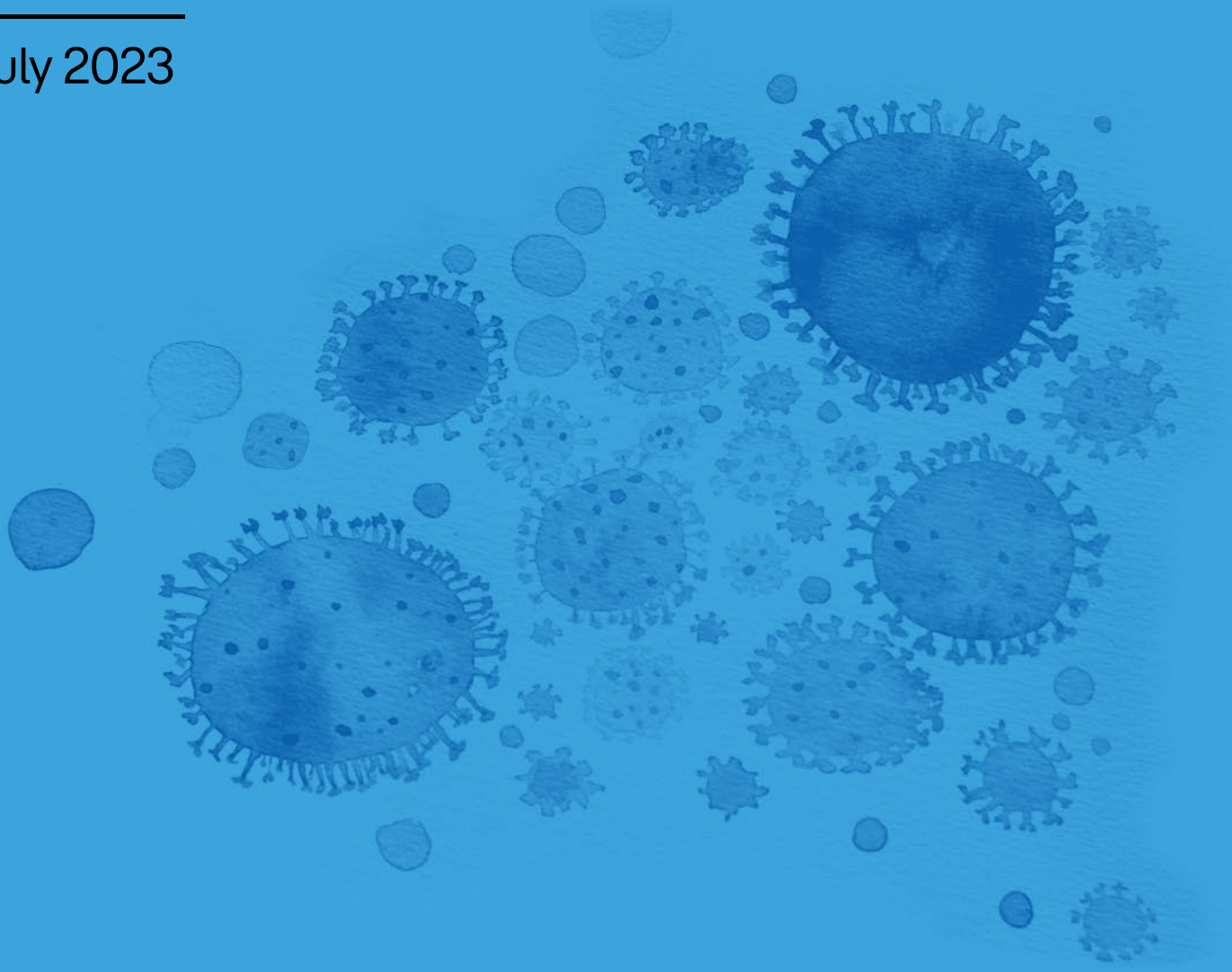
Treatment and rehabilitation of Long COVID

A scope of the literature: update

July 2023



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Treatment and rehabilitation of Long COVID: A scope of the literature. Update July 2023

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Summary

- We identified 18 randomised controlled trials published since early March 2023 that were focused on Long COVID treatment or rehabilitation. Across our five reports produced to date, we have identified and assessed 73 trials published between January 2022 and June 2023.
- Over half of the trials in the current update had a primary focus on treating persistent problems with the sense of smell or taste (olfactory/gustatory dysfunction)(n=5) or non-specific Long COVID symptoms (n=5). Other trials focused on fatigue (n=4); pulmonary/respiratory health (n=1); post COVID lung fibrosis (n=1); musculoskeletal sequelae (n=1); and erectile dysfunction (n=1).
- Five trials were rated positively for at least 11 out of the 13 criteria that we assessed. Four trials met 10 criteria and nine gained a positive rating for between five and nine criteria.

Introduction

This is the fifth 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 March and June 2023.

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.

The search strategies for CENTRAL and MEDLINE included the new MeSH heading for Long COVID "Post-Acute COVID-19 Syndrome" introduced in 2023. Searches were limited to studies added to the databases or published in 2022 or 2023, and no language restrictions were applied. 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 15).

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 - any outcome related to the effectiveness, cost-effectiveness, safety or side effects of interventions. Studies could also report outcomes related to the implementation of interventions.

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]

Publication type and status - any publication type, except pre-prints and conference abstracts, which report 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 23).

Key findings

We screened 392 records and identified 18 RCTs that had been published since March 2023.[4-21] This is the same number of trials as we included in our previous report in April[22] and more than we included in our other reports in January 2023 (n=12);[23] October 2022 (n=11);[24] and July 2022 (n=14).[25] The flow of studies through the current update is shown in Appendix 3 (page 24). Table 1 (page 6) presents the aim(s) and key characteristics of the 18 trials.

Interventions

Five of the 18 trials had a primary focus on persistent problems with the sense of smell or taste and investigated the effectiveness of various potential treatments – platelet-rich plasma;[4] ultramicronised palmitoylethanolamide and luteolin (umPEA-LUT) and olfactory training;[6] pentasodium diethylenetriamine pentaacetate nasal spray;[11] Omega-3 fatty acid (O3FA) supplements;[14] and the use of diode lasers.[18]

Five trials focused on non-specific Long COVID symptoms,[5, 7, 10, 15, 17] four of which evaluated exercise-based interventions: home-based training or telerehabilitation;[15, 17] Tai Chi versus aerobic training;[7] and low versus moderate intensity aerobic training.[10] The fifth trial focused on treating post-COVID symptoms using laser acupuncture.[5]

Four trials assessed various treatments for ongoing fatigue - AXA1125 (an endogenous metabolic modulator);[9] the Fit after COVID online CBT programme;[13] ImmunoSEB (systemic enzyme complex) and ProbioSEB CSC3 (probiotic complex);[16] and Brainmax (succinic acid complex with trimethylhydrazinium).[20]

One trial examined a rehabilitation programme for people with persistent problems with pulmonary/respiratory health and physical fitness.[8] One trial compared the drugs Nintedanib and Pirfenidone as treatments for post COVID lung fibrosis.[12] Another trial focused on electrical stimulation (E-stim) for treating ongoing musculoskeletal problems including atrophy, weakness,

numbness and pain.[21] The last trial evaluated the efficacy of the drug Tadalafil for treating post COVID erectile dysfunction.[19]

The proportion of included trials in the current update that assessed treatments for persistent problems with smell or taste is identical to our previous report in April (Five out of 18 trials).[22] Fewer trials in the current update focused specifically on treatments for persistent problems with pulmonary/respiratory health and physical fitness (one trial compared with six trials in April). Out of the 73 trials we have identified to date, 20 were focused on treatments for olfactory/gustatory dysfunction. Twenty-four assessed interventions with a physical therapy component and/or breathing training.

Participants

Six trials recruited participants who had persistent effects for at least 12 weeks after the onset of COVID symptoms or diagnosis.[4, 9, 12, 14, 17, 20] In eight trials, participants had ongoing effects for at least two weeks;[5] three weeks (mean);[16] four weeks;[18] eight weeks;[19] 12 weeks;[7, 11] 24 weeks;[6] and 43 weeks (mean),[21] after recovery or hospital discharge.

Two other studies also recruited participants after recovery or discharge.[8, 15] One of these trials recruited individuals with post-COVID syndrome 12 to 24 weeks after discharge from the ICU.[15] The other trial recruited individuals experiencing ongoing respiratory problems after discharge from hospital, but no further details were reported.[8] In one trial, participants were recruited three to 12 months after either diagnosis or discharge, if they had been hospitalised.[13] In the remaining trial, the population comprised individuals with symptoms of 'post-COVID' but no time related details were reported.[10]

Countries

Out of the 18 included trials, six were conducted in Egypt;[4, 5, 7, 8, 11, 18] and two in the USA.[14, 21] One trial was conducted in Brazil;[15] India;[16] Iran;[19] Italy;[6] Netherlands;[13] Russia;[20] Saudi Arabia;[10] Spain;[17] Turkey;[12] and the UK.[9]

Trial quality

Assessments of the trials against the JBI criteria are provided in Table 2 (page 11). Two trials were assessed as having a low risk of bias for all 13 appraisal criteria.[9, 16] We rated three trials positively for 11 out of the 13 criteria.[11, 13, 15] In two of the three studies, there was no blinding of either trial participants or the personnel who administered the treatment (Q4 & Q5).[13, 15] However, the nature of the interventions potentially precluded the use of blinding as one evaluated an online CBT course[13] and the other a home-based exercise programme.[15] In the third 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). It was also unclear if an appropriate statistical analysis had been conducted owing to a lack of detail about the sample size required for the study (Q12).[11]

Four trials met 10 out of the 13 criteria[10, 14, 17, 18] and nine others were rated positively for between five and nine criteria.[4-8, 12, 19-21] A number of common issues were identified across the 13 studies. For example, it was unclear if an appropriate statistical analysis had been conducted in nine of the 13 studies as no information was provided about the sample size requirements of the trial.[4-8, 12, 14, 19, 20] In nine trials, we could not tell if an appropriate procedure had been used for allocation concealment (Q2).[4-8, 18-21] It was also unclear whether an appropriate method of randomisation had been used for allocating participants to treatment groups in seven trials (Q1).[4-8, 10, 18] In seven of the

13 trials, an ITT analysis was not conducted,[5, 10, 14, 17, 19-21] and in one other, we could not tell if it had been used (Q9).[6]

In four studies, we could not tell if there was blinding of trial participants and the personnel who administered the treatment (Q4 & Q5).[5-7, 12] It was also unclear whether the personnel who assessed outcomes of interest were blinded in seven studies (Q6).[4, 5, 7, 8, 14, 19, 20] In five trials, there was no blinding of participants[4, 8, 17] and/or the personnel who administered the treatment,[4, 8, 10, 17, 18] and in another trial, there was no blinding of outcome assessors.[21] Again, the nature of the intervention in some of these studies, particularly those that evaluated physical therapy-based programmes, could have prevented the use of blinding.

To conclude, this evidence scan identified 18 RCTs published between March and June 2023 that examined interventions for the treatment or rehabilitation of people with Long COVID. Across our five reports produced to date, we have now identified and assessed 73 trials published since January 2022. Most of the trials in the current update had a primary focus on treating persistent problems with the sense of smell or taste (n=5) or non-specific Long COVID symptoms (n=5). Trial quality varied, but five were rated positively for at least 11 out of the 13 criteria, and four met 10 criteria. The other nine trials gained positive ratings for between five and nine 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
Abo El Nago (2022)[4] [a] Egypt	To assess the potential therapeutic effect of platelet-rich plasma in the treatment of post-COVID olfactory dysfunction	Olfactory and/or gustatory dysfunction	After positive test: more than 3 months after test	Mixed (60) 67% female (40/60)	Olfactory and/or gustatory function: parosmia assessed on a visual analogue scale from 0 to 10	Continued with pre-study treatment protocol (including olfactory training, topical corticosteroids, omega-three, vitamin B12, and zinc supplementation)
Alghitany (2023)[5] Egypt	To evaluate the potential benefits of laser acupuncture on immunomodulation and dyspnoea in post-COVID patients	General/multiple symptoms: post-COVID symptoms including cough, fatigue, and dyspnoea	After recovery: two weeks after recovery	Mixed (80; 75 analysed) % female not reported	Pulmonary/respiratory or cardiovascular function: dyspnoea (mMRC dyspnoea scale) Blood parameters: Total lymphocyte count and Interleukin 6	Sham laser acupuncture (laser off - no light)
Di Stadio (2023)[6] [b] Italy	To evaluate the efficacy of ultramicronised palmitoylethanolamide and luteolin (umPEA-LUT) and olfactory training (OT) compared to OT alone for the treatment of smell disorders in an Italian post-COVID population	Olfactory and/or gustatory dysfunction	After recovery: more than 180 days (6 months) after recovery (negative test)	Mixed (130) 54% female (70/130)	Olfactory and/or gustatory function: Sniffin' Sticks test; parosmia (distorted smell); and cacosmia (aversive smell) assessed via validated questionnaire	Conventional therapy: olfactory training and daily treatment with placebo supplement (multivitamin, vitamin D and/or alpha-lipoic acid)
Elhamrawy (2023)[7] Egypt	To understand the impact of Tai Chi versus aerobic training on hand grip strength, fatigue,	General/multiple symptoms: mild-to-moderate post-COVID-19 symptoms	After recovery: at least 3 months post-recovery (negative test)	Mixed (54) 35% female (19/54)	Physical fitness: hand grip strength; four tests from the Senior Fitness Test (SFT): 30-second arm curls; 30-second	Control group performed activities of daily living

	and functional performance in the elderly post-COVID-19				chair stands; 8-Foot up and go exercise test (balance); and 2-minute step test (cardiopulmonary fitness) Fatigue: Fatigue Severity Scale (FSS)	
Fares (2023)[8] Egypt	To determine the effectiveness of a pulmonary rehabilitation program on severe post-COVID19 patients regarding pulmonary function and dyspnoea	Respiratory or cardiovascular function or physical fitness	After discharge: post hospitalisation - no further details reported	Mixed (100) 31% female (31/100)	Pulmonary/respiratory or cardiovascular function: dyspnoea (mMRC scale); oxygen saturation; forced vital capacity (FVC), FEV1 and FEV1/FVC ratio Physical fitness: Six-minute walk test (6MWT)	No intervention
Finnigan (2023)[9] UK	To assess the efficacy, safety, and tolerability of AXA1125 (an endogenous metabolic modulator) in patients with fatigue-predominant Long COVID	Fatigue/lack of energy	After diagnosis: mean time from diagnosis to randomisation about 500 days; range 99 to 795 days	Mixed (41) 68% female (28/41)	Physical fitness: post-exercise skeletal muscle (phosphocreatine) recovery rate time constant, determined from Phosphorus Magnetic Resonance Spectroscopy (P-MRS) using the gastrocnemius medialis muscle of the calf	Placebo
Ibrahim (2023)[10] Saudi Arabia	To compare the impact of 10 weeks of low- vs moderate-intensity aerobic training on physical fitness, psychological status, and quality of life of post-COVID-19 elderly patients	General/multiple symptoms: post-COVID symptoms including pain, fatigue, muscle weakness, breathlessness, and reduced quality of life	Unclear/not stated: post COVID (no further details)	Mixed (73; 72 analysed) 57% female (41/72)	Physical fitness: Six-minute walk test; Post-COVID-19 Functional Scale (PCFS)	Medical care and advice
Imam (2023)[11]	To investigate the effect of pentasodium	Olfactory and/or gustatory dysfunction	After recovery: at least three	Mixed (66)	Olfactory and/or gustatory function: Burghart Sniffin'	Placebo - 0.9% sodium chloride nasal spray

Egypt	diethylenetriamine pentaacetate (DTPA) nasal spray on post-COVID-19 anosmia		months after testing negative for SARS-CoV-2 infection	58% female (38/66)	Sticks; threshold (T), discrimination (D), identification (I), and global score (sum TDI score)	
Kerget (2023)[12] Turkey	To compare the effects of treatment with Nintedanib and Pirfenidone in patients with COVID-19-related fibrosis	Lung abnormalities: chronic COVID-19 symptoms, and fibrosis secondary to COVID-19	After diagnosis: diagnosed at least 3 months ago	Mixed (30) 60% female (18/30)	Pulmonary/respiratory or cardiovascular function: spirometry (FVC, FEV, DLCO); Six-minute walk test with oxygen saturation; and contrast lung CT	Two treatments compared; no other comparator
Kuut (2023)[13] The Netherlands	To investigate the efficacy of online CBT (Fit after COVID) for severe fatigue following COVID-19, compared with care as usual	Fatigue/lack of energy	Both: three to 12 months after either diagnosis or hospital discharge, if hospitalised	Mixed (114) 73% female (83/114)	Fatigue: 8-item fatigue subscale of the 20-item Checklist Individual Strength (CIS-fatigue)	Usual care. No access to the 'Fit after COVID' CBT programme
Lerner (2023)[14] USA	To evaluate the efficacy of omega-3 fatty acid (O3FA) supplementation in the treatment of COVID-related olfactory dysfunction	Olfactory and/or gustatory dysfunction	After symptom onset: approximately 200 days on average from symptom onset	Mixed (139; 117 analysed) 79% female (92/117)	Olfactory and/or gustatory function: Brief Smell Identification Test (BSIT)	Placebo
Longobardi (2023)[15] Brazil	To investigate the effects of a 16-week home-based exercise training programme on HRQoL and health-related outcomes in survivors of severe/critical COVID-19	General/multiple symptoms: all met the criteria for post-COVID syndrome	After discharge: between 3 months and 6 months after discharge from ICU; mean about 158 days	Mixed (50; 41 completed) 25/50 female (50%)	Physical fitness: SF-36 physical health	Usual care included general advice for a healthy lifestyle; patients were contacted by phone or text every 2 months
Rathi (2021)[16] India	To evaluate the efficacy and safety of the health supplements ImmunoSEB (systemic enzyme complex)	Fatigue/lack of energy	After recovery: about 19.5 days on average from	Mixed (200) 37% female (73/200)	Fatigue: physical and mental fatigue (Chronic Fatigue Questionnaire, CFQ-11)	Placebo - maltodextrin

	and ProbioSEB CSC3 (probiotic complex) in patients suffering from COVID-19 induced fatigue		negative test (range 2-87 days)			
Samper-Pardo (2023)[17] Spain	To analyse the clinical efficacy of telerehabilitation in the recovery of Long COVID patients through the ReCOVery app	General/multiple symptoms: persistent symptoms	After diagnosis: 12 or more weeks since diagnosis	Mixed (100; 87 completed) 80% female (80/100)	Quality of life: SF-36 physical and mental health	Usual care by the primary health care GP, without the app
Shabaan (2023)[18] Egypt	To evaluate the effectiveness of the diode laser in managing loss of taste sensation in patients with post-COVID syndrome	Olfactory and/or gustatory dysfunction	After recovery: at least four weeks after recovery	Mixed (36) 78% female (28/36)	Olfactory and/or gustatory function: gustatory function - a standardised and validated test that assessed ability to perceive four primary tastes (sweet, salty, sour, and bitter)	Placebo - light emitted from the therapy handpiece
Shamohammadi (2023)[19] Iran	To investigate the efficacy of Tadalafil on improvement of men with erectile dysfunction caused by COVID-19	Reproductive disorders	After recovery: two months after recovery of COVID-19 (negative test)	Male only (70; 62 completed)	Erectile function: International Index of Erectile Function (IIEF-5)	Placebo - sugar capsules
Tanashyan (2022)[20] [c] Russia	To study the efficacy and safety of Brainmax (a succinic acid complex with trimethylhydrazinium) used to treat patients with asthenic syndrome after COVID-19 infection	Fatigue/lack of energy	After diagnosis: from 12 to 16 weeks, up to 12 months, since diagnosis	Mixed (160) 75% female (120/160)	Fatigue: Multidimensional Fatigue Inventory (MFI-20)	Placebo
Zulbaran-Rojas (2023)[21] USA	To investigate the potential benefits of electrical stimulation (E-stim) in improving the recovery of individuals with	Musculoskeletal: persistent leg symptoms such as atrophy, weakness, numbness, and/or pain	After recovery: approximately 300 days after clearance of acute infection	Mixed (19; 18 analysed; 36 legs) 72% female (13/18)	Physical fitness: muscle recovery and endurance (including muscle perfusion and oxyhaemoglobin level)	Sham stimulation

	musculoskeletal post-acute sequelae of SARS-CoV-2					

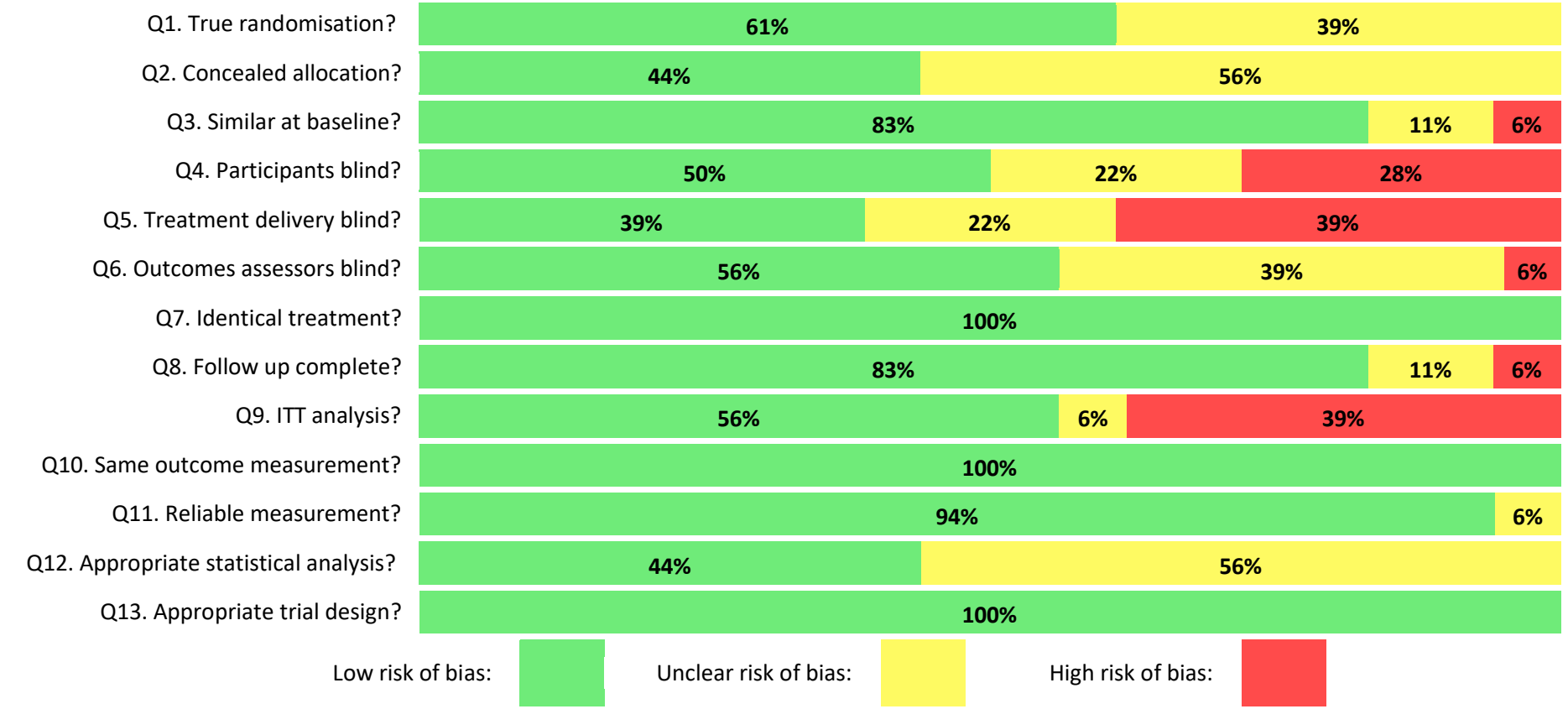
[a] Described as a pilot study. The journal website indicates that the paper was first published in October 2022, but it was not identified from any of our previous searches. [b] This trial has the same aim and protocol identification number as one included in our first report in July 2022. However, the study reported in the current update was conducted later and with fewer participants than the trial included in the July report. [C] Machine translated from Russian.

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?
Abo (2022)	?	?	+	-	-	?	+	+	+	+	+	?	+
Alghitany (2023)	?	?	+	?	?	?	+	+	-	+	+	?	+
Di Stadio (2023)	?	?	?	?	?	+	+	?	?	+	+	?	+
Elhamrawy (2023)	?	?	+	?	?	?	+	+	+	+	+	?	+
Fares (2023)	?	?	+	-	-	?	+	+	+	+	+	?	+
Finnigan (2023)	+	+	+	+	+	+	+	+	+	+	+	+	+
Ibrahim (2023)	?	+	+	+	-	+	+	+	-	+	+	+	+
Imam (2023)	+	?	+	+	+	+	+	+	+	+	+	?	+
Kerget (2023)	+	+	+	?	?	+	+	+	+	+	?	?	+
Kuut (2023)	+	+	+	-	-	+	+	+	+	+	+	+	+
Lerner (2023)	+	+	+	+	+	?	+	+	-	+	+	?	+
Longobardi (2023)	+	+	+	-	-	+	+	+	+	+	+	+	+
Rathi (2021)	+	+	+	+	+	+	+	+	+	+	+	+	+
Samper-Pardo (2023)	+	+	+	-	-	+	+	+	-	+	+	+	+

Shabaan (2023)	?	?	+	+	-	+	+	+	+	+	+	+	+
Shamohammadi (2023)	+	?	+	+	+	?	+	-	-	+	+	?	+
Tanashyan (2022)	+	?	?	+	+	?	+	?	-	+	+	?	+
Zulbaran-Rojas (2023)	+	?	-	+	+	-	+	+	-	+	+	+	+

+ = low risk of bias; - = high risk of bias; and ? = unclear risk of bias



NB: figures may not add up to 100% due to rounding

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23. Raine G, Khouja C, Khatwa M, Harden M, Sutcliffe K, Sowden A. Treatment and rehabilitation of Long COVID: A scope of the literature. Update January 2023. London: EPPI Centre, UCL Social Research Institute, UCL Institute of Education, University College London; 2023.

24. Raine G, Khouja C, Harden M, Sutcliffe K, Sowden A. Treatment and rehabilitation of Long COVID: A scope of the literature. Update October 2022. London: EPPI Centre, UCL Social Research Institute, UCL Institute of Education, University College London; 2022.

25. Raine G, Khouja C, Khatwa M, Sutcliffe K, Sowden A. Treatment and rehabilitation of Long COVID: A scope of the literature. London: EPPI Centre, UCL Social Research Institute, UCL Institute of Education, University College London; 2022.

Appendix 1 – search strategies

Cochrane Controlled Register of Trials (CENTRAL)
via Wiley http://onlinelibrary.wiley.com/
Issue: Issue 6 of 12, June 2023
Date searched: 5th June 2023
Records retrieved: 948

Although 1174 records were identified overall in CENTRAL, trial register records were removed from this set, leaving a total of 948 records downloaded for this update.

#1 MeSH descriptor: [Post-Acute COVID-19 Syndrome] this term only 31
#2 MeSH descriptor: [COVID-19] this term only and with qualifier(s): [complications - CO] 210
#3 MeSH descriptor: [COVID-19] this term only 4372
#4 MeSH descriptor: [SARS-CoV-2] this term only 2282
#5 MeSH descriptor: [Syndrome] this term only 6142
#6 MeSH descriptor: [Survivors] this term only 1526
#7 #3 or #4 4585
#8 #5 or #6 7663
#9 #7 and #8 46
#10 #1 or #2 or #9 268
#11 (long next (covid* or covid-19 or covid19 or coronavirus) or longcovid*):ti,ab,kw 257
#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 517
#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 950
#14 PASC:ti,ab,kw 49
#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 124
#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 29
#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 91
#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 603
#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 195
#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,kw 851
#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 414
#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 168
#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 239
#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 131
#25 {OR #11-#24} 2127
#26 #10 or #25 with Cochrane Library publication date Between Jan 2022 and Jun 2023, in Trials 1165

#27 #10 or #25 with Publication Year from 2022 to 2023, in Trials 1051
#28 #26 or #27 1178

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 June 01, 2023
Date searched: 5th June 2023
Records retrieved: 662

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 (2008 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 6.2 (updated February 2021). Cochrane, 2021. Available from: www.training.cochrane.org/handbook.

1 Post-Acute COVID-19 Syndrome/ (2039)
2 COVID-19 post-intensive care syndrome.mp. (5)
3 COVID-19/co [Complications] (14552)
4 COVID-19/ or SARS-CoV-2/ (231057)
5 Syndrome/ (122467)
6 Survivors/ (30234)
7 5 or 6 (152581)
8 4 and 7 (979)
9 1 or 2 or 3 or 8 (15936)
10 ((long adj (covid$ or covid-19 or covid19 or coronavirus)) or longcovid$).ti,ab,kf,ot,bt. (3293)
11 ((post adj (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)) or postcovid$).ti,ab,kf,ot,bt. (7768)
12 ((post acute or postacute) adj2 (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)).ti,ab,kf,ot,bt. (748)
13 PASC.ti,ab,kf,ot,bt. (639)
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. (2220)
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. (290)
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. (3185)
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. (1922)
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. (3475)
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. (84)
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. (234)

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. (2747)
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. (7927)
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. (2508)
24 or/10-23 (28113)
25 9 or 24 (39675)
26 randomized controlled trial.pt. (593679)
27 controlled clinical trial.pt. (95319)
28 randomi#ed.ab. (722655)
29 placebo.ab. (238686)
30 clinical trials as topic.sh. (200986)
31 randomly.ab. (409517)
32 trial.ti. (286241)
33 26 or 27 or 28 or 29 or 30 or 31 or 32 (1572065)
34 exp animals/ not humans.sh. (5126093)
35 33 not 34 (1449130)
36 25 and 35 (1180)
37 limit 36 to yr="2022 -Current" (661)
38 (2022* or 2023*).dt. (2280682)
39 36 and 38 (623)
40 37 or 39 (669)
41 preprint.pt. (9083)
42 40 not 41 (662)

Embase
via Ovid http://ovidsp.ovid.com/
Date range: 1974 to 2023 June 02
Date searched: 5th June 2023
Records retrieved: 1065

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/ (4549)
2 ((long adj (covid$ or covid-19 or covid19 or coronavirus)) or longcovid$).ti,ab,kw,ot. (3508)
3 ((post adj (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)) or postcovid$).ti,ab,kw,ot. (10277)
4 ((post acute or postacute) adj2 (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)).ti,ab,kw,ot. (729)
5 PASC.ti,ab,kw,ot. (830)
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. (2890)
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. (377)

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. (3543)
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. (2494)
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. (4712)
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. (161)
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. (264)
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. (4203)
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. (11161)
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. (3238)
16 or/2-15 (37073)
17 1 or 16 (37522)
18 random$.ti,ab. (1973251)
19 factorial$.ti,ab. (47377)
20 crossover$.ti,ab. (90963)
21 cross-over$.ti,ab. (37858)
22 placebo$.ti,ab. (368904)
23 (doubl$ adj blind$).ti,ab. (245828)
24 (singl$ adj blind$).ti,ab. (31830)
25 assign$.ti,ab. (491200)
26 allocat$.ti,ab. (202386)
27 volunteer$.ti,ab. (295256)
28 Crossover Procedure/ (75366)
29 double blind procedure/ (210936)
30 Randomized Controlled Trial/ (787571)
31 single blind procedure/ (52041)
32 controlled clinical trial/ (469363)
33 or/18-32 (3059682)
34 (animal/ or animal experiment/ or animal model/ or animal tissue/ or nonhuman/) not exp human/ (6817178)
35 33 not 34 (2731827)
36 17 and 35 (2310)
37 limit 36 to yr="2022 -Current" (1420)
38 (2022$ or 2023$).dd. (1015950)
39 36 and 38 (589)
40 37 or 39 (1521)
41 (conference abstract or "conference review").pt. (4791541)
42 40 not 41 (1151)
43 limit 42 to "remove preprint records" (1065)

PsycINFO
via Ovid http://ovidsp.ovid.com/
Date range: 1806 to May Week 5 2023
Date searched: 5th June 2023
Records retrieved: 219

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 covid-19/ (21807)
2 coronavirus/ (5703)
3 syndromes/ (17399)
4 sequelae/ (3941)
5 1 or 2 (24181)
6 3 or 4 (21273)
7 5 and 6 (271)
8 ((long adj (covid$ or covid-19 or covid19 or coronavirus)) or longcovid$).ti,ab,id,ot. (164)
9 ((post adj (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)) or postcovid$).ti,ab,id,ot. (649)
10 ((post acute or postacute) adj2 (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)).ti,ab,id,ot. (31)
11 PASC.ti,ab,id,ot. (32)
12 (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. (159)
13 (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. (21)
14 (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. (309)
15 ((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. (150)
16 (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. (188)
17 ((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. (7)
18 ((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. (15)
19 (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. (230)
20 (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. (400)
21 ((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. (252)
22 or/8-21 (2064)
23 randomized clinical trials/ (467)
24 randomized controlled trials/ (981)
25 clinical trials/ (12196)
26 clinical trial.md. (37420)
27 (randomi#ed or randomi#ation or randomi#ing).ti,ab,id. (107347)
28 randomly.ti,ab,id. (83139)

29 (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. (126883)
30 (groups or (control* adj3 group*)).ab. (606404)
31 ((control* or trial or study or group*) and (waitlist* or wait* list* or ((treatment or care) adj2 usual))).ti,ab,id,hw. (18650)
32 ((single or double or triple or treble) adj2 (blind* or mask* or dummy)).ti,ab,id. (29029)
33 trial.ti. (37606)
34 (placebo or sham).ti,ab,id,hw. (57969)
35 treatment outcome.md. (23528)
36 treatment effectiveness evaluation/ (27957)
37 mental health program evaluation/ (2347)
38 or/23-37 (803493)
39 7 or 22 (2199)
40 38 and 39 (295)
41 limit 40 to yr="2022 -Current" (171)
42 (2022$ or 2023$).up. (263939)
43 40 and 42 (211)
44 41 or 43 (219)

CINAHL Ultimate
via Ebsco https://www.ebsco.com/
Date range: Inception to 20230602
Date searched: 5th June 2023
Records retrieved: 502

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.

#	Query	Results
S1	(MH "Post-Acute COVID-19 Syndrome")	762
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*)	1,147
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*)	1,457
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))	304
S5	TI PASC OR AB PASC	96
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))	523
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))	253

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)) 701
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)) 964
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)) 856
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)) 49
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)) 94
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)) 1,010
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)) 3,793
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)) 858
S16 (MH "Randomized Controlled Trials") 137,956
S17 (MH "Double-Blind Studies") 54,283
S18 (MH "Single-Blind Studies") 16,001
S19 (MH "Random Assignment") 79,397
S20 (MH "Pretest-Posttest Design") 53,199
S21 (MH "Cluster Sample") 5,274
S22 TI randomised OR randomized 140,685
S23 AB random* 397,852
S24 TI trial 181,640
S25 MH (sample size) AND AB (assigned OR allocated OR control) 4,410
S26 MH (placebos) 14,051
S27 PT (randomized controlled trial) 150,746
S28 AB (control W5 group) 143,738
S29 MH (crossover design) OR MH (comparative studies) 480,201
S30 AB (cluster W3 RCT) 494
S31 MH animals+ 105,284
S32 MH (animal studies) 152,576
S33 TI (animal model*) 3,790
S34 S31 OR S32 OR S33 248,957

S35 MH (human) 2,694,960
S36 S34 NOT S35 214,821
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 1,018,164
S38 S37 NOT S36 970,538
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 9,865
S40 S38 AND S39 823
S41 S38 AND S39 Limiters - Published Date: 20220101-20230531 480
S42 (ZD 2022* OR 2023*) 384,754
S43 S40 AND S42 299
S44 S41 OR S43 502

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

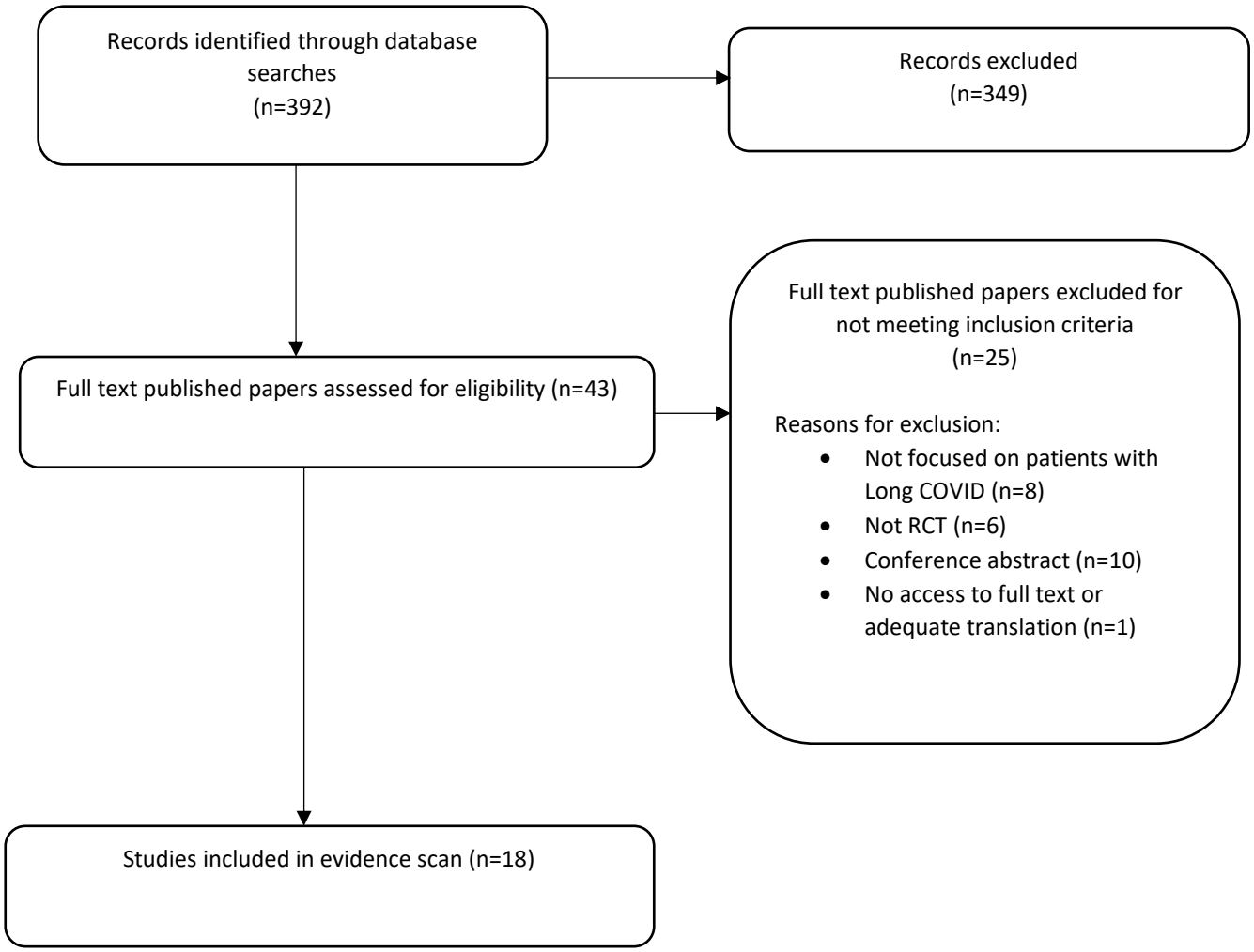
Q10 Were outcomes measured in the same way for treatment groups? Yes, No, Unclear, NA

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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- Undertaking policy-relevant systematic reviews of health and social care research
- Developing capacity for undertaking and using reviews
- Producing new and improved methods for undertaking reviews
- Promoting global awareness and use of systematic reviews in decision-making

The Reviews Facility is a collaboration between the following centres:
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