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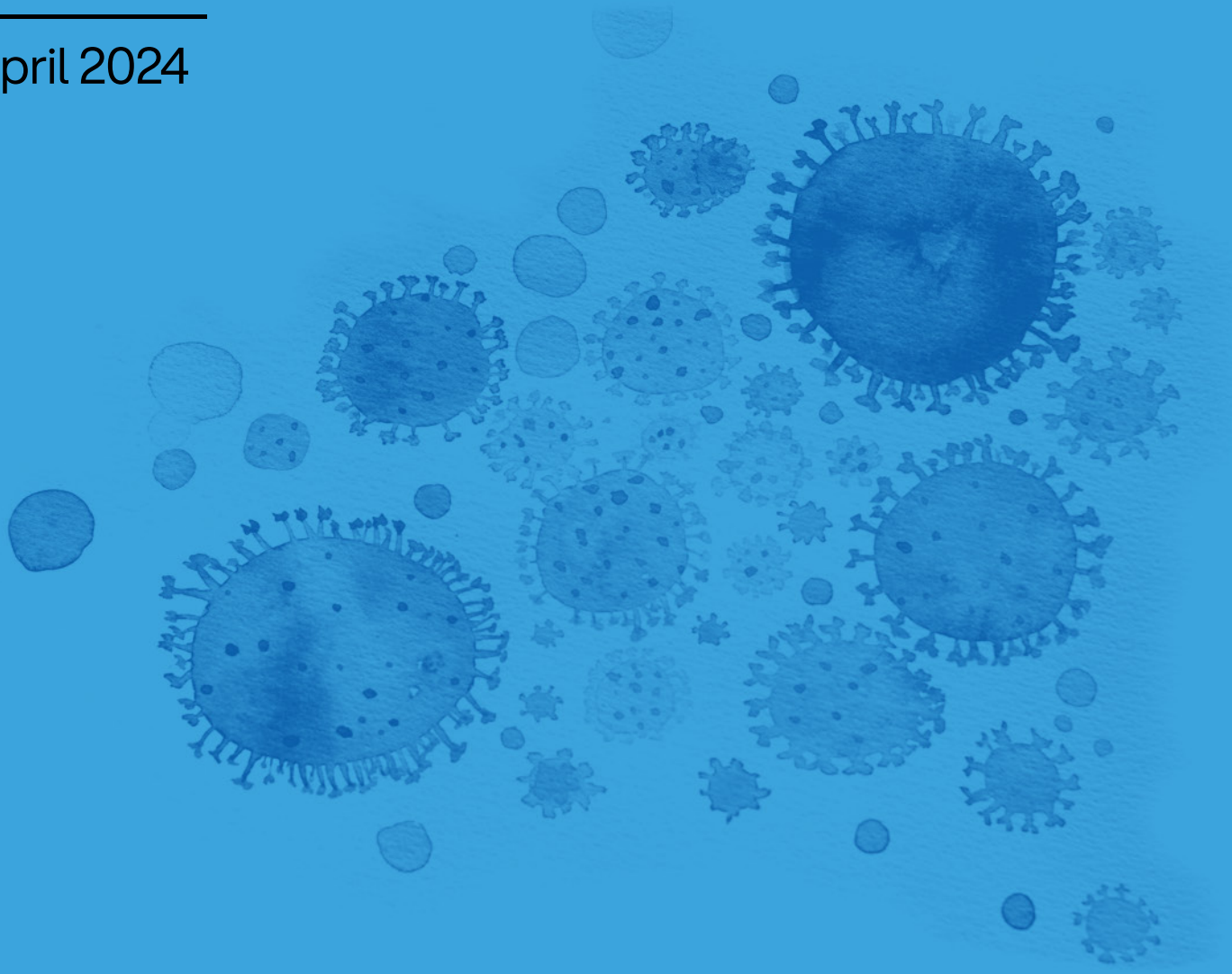
Supporting national policy development and implementation

Treatment and rehabilitation of Long COVID

A scope of the literature: update

April 2024



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

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Summary

- We identified 15 randomised controlled trials published between December 2023 and March 2024 that were focused on Long COVID treatment or rehabilitation. Across our eight reports produced to date, we have identified and assessed 121 trials published between January 2022 and March 2024.
- Seven of the 15 trials focused on treating generalised or multiple symptoms of Long COVID/Post COVID condition. Three trials evaluated treatments for fatigue, one of which also focused on individuals with other neuropsychiatric sequalae. Two trials had a focus on respiratory or cardiovascular function or physical fitness. Two other trials focused on persistent problems with the sense of smell or taste (olfactory/gustatory dysfunction). One trial focused on people with decreased functioning and participation in daily life following COVID-19.
- Two trials were rated positively for 12 out of the 13 quality criteria that we assessed. Two trials met ten criteria and 11 gained a positive rating for between six and nine criteria.

Introduction

This is the eighth 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 December 2023 and March 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. Two changes were made to the strategies for this update: the MEDLINE RCT filter sensitivity and precision-maximising version was updated with the 2023 revision; and the subject heading for randomised controlled trials on CINAHL Ultimate was exploded. Due to the rapid nature of the project, the database searches were designed to balance the need to retrieve as many relevant trials as possible against the limited time available for screening. Records were downloaded into EndNote and deduplicated against the search results from previous updates. Full search strategies can be found in Appendix 1 (page 16).

Study selection

Studies were screened for inclusion against the following criteria:

Population - patients with Long COVID, which we conceptualised broadly as experiencing at least one symptom or effect that persists or develops after acute COVID-19 infection. No restrictions were placed on the socio-demographic characteristics of participants or COVID severity. We also did not

apply criteria relating to the time period after acute infection owing to variation in how Long COVID has been defined in the literature.

Interventions - any intervention aimed at treating or rehabilitating patients with Long COVID. This could include, but was not limited to, medication, supplements, and physical therapy. Interventions that had a primary focus on general rehabilitation from COVID-19 following hospitalisation or severe infection were excluded.

Outcomes - 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 reports findings from a RCT (e.g., full papers, research letters, brief reports etc).

Quality assessment

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

Key findings

We screened 413 records and included 15 RCTs that had been published since December 2023.[(4-18)] This is a smaller number than we included in three of our seven previous reports - January 2024 (n=21);[(19)]; July 2023 (n=18);[(20)] and April 2023 (n=18).[(21)] We included more trials in the current update than in four reports - July 2022 (n=14);[(22)] October 2023 (n=12);[(23)] January 2023 (n=12);[(24)] and October 2022 (n=11).[(25)] The flow of studies through the current update is shown in Appendix 3 (page 25). Table 1 (page 6) presents the aim(s) and key characteristics of the 15 trials.

Interventions

Seven trials focused on individuals experiencing generalised or multiple symptoms of Long COVID/Post COVID syndrome.[(8, 12-15, 17, 18)] Four of the seven trials evaluated rehabilitation programmes. One evaluated a multicomponent programme combining strength, resistance and balance-focused exercises.[(8)] One trial compared the efficacy of continuous and interval training,[(14)] and another focused on an exercise-based programme with inspiratory muscle training.[(17)] The fourth trial evaluated an online supervised group physical and mental health rehabilitation programme (REGAIN - rehabilitation exercise and psychological support after COVID-19 infection).[(13)] Of the remaining three trials, one evaluated the effect of a synbiotic preparation (SIM01), which contained three strains of bacteria as well as prebiotics to promote bacterial growth.[(12)] The other two trials assessed internet-based group psychotherapy,[(18)] and a therapeutic intervention based on self-adjustment strategies.[(15)]

Three of the 15 trials assessed treatments primarily for fatigue. One evaluated the drug Amantadine;[(9)] another assessed an app-based physical activity intervention;[(10)] whilst the third trial

evaluated transcranial direct current stimulation in individuals with fatigue and other neuropsychiatric sequelae.[11]

Two trials assessed treatments for individuals who had problems with respiratory or cardiovascular function or physical fitness. One trial evaluated a telerehabilitation exercise programme;[7] the other focused on symptom management and compared the effect of using automatically titrating oxygen systems and constant-flow oxygen systems during walking on the oxygenation levels of recovered COVID-19 patients who were still experiencing hypoxaemia.[5]

Two trials focused on persistent problems with the sense of smell or taste and investigated the effectiveness of local and systemic photobiomodulation therapy (use of low-powered lasers)[16] and a sodium phytate nasal spray.[4] The final trial focused on multidisciplinary group telerehabilitation for people with decreased functioning and participation in daily life following COVID-19.[6]

Seven of the 15 RCTs in the current update evaluated interventions incorporating an exercise component, which is the highest proportion in any of our eight reports to date. The proportion of included trials in the current update that focused on the treatment of olfactory/gustatory dysfunction (two out of 15 RCTs) is the lowest since our first report in July 2022 (one out of 14 RCTs).[22]

Participants

Six trials recruited participants who had experienced persistent effects for at least four weeks after the onset of COVID symptoms or diagnosis.[4, 9, 11, 14, 15, 18] In four of the six trials, participants had persistent effects, on average, for at least 12 weeks after symptom onset or diagnosis.[4, 14, 15, 18] In another study, the reported time since diagnosis was approximately 17 days.[16]

Three trials recruited individuals with persisting symptoms at least four weeks[12] or 12 weeks after COVID-19 infection.[6, 10] In one trial, participants had experienced persistent symptoms for more than 12 months.[7] Another three trials recruited individuals after acute infection but no time related details were reported.[5, 8, 17] In the remaining trial, participants had persistent effects for at least three months after hospital discharge.[13]

Countries

Three trials were conducted in Germany,[5, 10, 14] and two in Brazil[8, 16] and Spain.[7, 15] One trial was conducted in the Czech Republic;[11] Hong Kong;[12] Indonesia;[18] Iran;[9] Poland;[17] Saudi Arabia;[4] Sweden;[6] and the UK.[13]

Trial quality

Assessments of the trials against the JBI criteria are provided in Table 2 (page 11). 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.[4, 12] In one of these trials, we could not tell if an appropriate procedure had been used to prevent researchers from knowing whether the next patient would be allocated to the treatment or comparator group (allocation concealment) (Q2).[4] In the other trial, insufficient information had been provided about why people dropped out of the study (Q8).[12]

Two trials met ten criteria;[10, 13] and 11 were rated positively for between six and nine criteria.[5-9, 11, 14-18] A number of common issues were identified across the 13 trials that met ten or fewer criteria. For example, an Intention to treat (ITT) analysis was not conducted in seven trials (Q9),[5, 6, 9-11, 17, 18] and in another study, we could not tell if it had been used.[8]

In eight of the 13 trials we could not tell if an appropriate procedure had been used for allocation concealment (Q2).[5, 7, 9, 11, 14-16, 18] We were also unable to tell if an appropriate method of randomisation had been used for allocating participants to treatment groups in five trials (Q1).[5, 9, 11, 15, 18] It was unclear if an appropriate statistical analysis had been conducted in five trials as no information was provided about the sample size requirements of the study (Q12).[5, 6, 11, 17, 18]

In five trials that we rated positively for nine[7, 8, 15] or ten[10, 13] criteria, there was no blinding of trial participants (Q4) and the personnel who administered the treatment (Q5). However, the nature of the intervention in these trials is likely to have precluded the use of blinding. Four of the trials evaluated rehabilitation programmes with an exercise-based component and the fifth assessed a therapeutic intervention based on self-adjustment strategies. In one of the five trials, we could not determine whether or not the personnel who assessed outcomes were blinded.[7]

It was unclear whether trial participants were blinded in two of the remaining eight trials (Q4).[14, 18] In five trials, we could not tell if there was blinding of the personnel who administered the treatment (Q5)[11] and/or the outcome assessors (Q6).[5, 6, 14, 18]

In three of the eight trials, there was no blinding of participants (Q4) and/or the personnel who administered the treatment (Q5).[6, 15, 17, 18] Neither the personnel who administered the treatment nor those who assessed outcomes were blinded in one trial.[16] In another trial, there was no blinding of trial participants, the personnel who administered the treatment or outcome assessors.[9] Again, the nature of the intervention in some of these trials may have prevented the use of blinding.

Conclusion

To conclude, in this evidence scan, we identified 15 RCTs published between December 2023 and March 2024 that examined interventions for the treatment or rehabilitation of people with Long COVID. Across our eight reports produced to date, we have identified and assessed 121 trials published since January 2022. Seven trials in the current update focused on treating generalised or multiple symptoms of Long COVID/Post COVID condition. Three trials evaluated treatments for fatigue (n=3), one of which also had a focus on other neuropsychiatric symptoms. Four trials focused on cardiovascular function/physical fitness (n=2) or olfactory/gustatory dysfunction (n=2). The remaining trial focused on people with decreased functioning and participation in daily life following COVID-19. Trial quality varied, with two rated positively for 12 out of the 13 criteria. Two trials met ten criteria and 11 gained positive ratings for between six and nine criteria.

Table 1: Study characteristics (n=15)

First author Country	Aim of study	Main symptom or effect experienced	Post COVID time	Participants' gender (n) and % female	Primary outcome(s) of interest	Comparator
Altemani (2024)[4] Saudi Arabia	To investigate the efficacy of sodium phytate as a natural chelating agent in reducing elevated calcium levels in nasal mucus among individuals experiencing olfactory dysfunction following COVID-19	Olfactory and/or gustatory dysfunction	After symptom onset or diagnosis: positive test for COVID-19 and olfactory dysfunction for more than 90 days	Mixed (52) 54% female (28/52)	Olfactory and/or gustatory function: Sniffin' Sticks test; calcium in nasal secretions	Placebo: sodium chloride nasal spray
Berkel (2023)[5] Germany	To examine the effect of constant-flow oxygen systems compared with automatically titrating oxygen systems on oxygenation during walking in hypoxaemic patients with post-acute sequelae of COVID-19	Respiratory or cardiovascular function or physical fitness: hypoxaemia (pO2 under 55mmHg or SpO2 less than 88% at rest or exercise)	After recovery: recovered from SARS-CoV-2 infection (confirmed by PCR-test)	Mixed (17; 15 completed) 27% female (4/15)	Pulmonary/respiratory or cardiovascular function: blood oxygen level (SpO2)	Constant-flow oxygen systems
Bileviciute-Ljungar (2024)[6] Sweden	To investigate the short- and long-term outcomes, appropriateness, and feasibility of multidisciplinary telerehabilitation conducted in groups for people with symptoms that remain after a SARS-CoV-2 infection (post-COVID-19 condition)	Decreased ability to perform daily activities: at least 50% reduced functioning and activity or participation in daily life	Unclear/not stated: at least 12 weeks after acute infection	Mixed (116; 109 completed eight weeks, 81 at six months) 82% female (89/109) at eight weeks 83% female	General or multiple: Functional Compass COVID-19 questionnaire (38 of 47 questions)	Waiting list

				(67/81) at six months		
Calvo-Paniagua (2024)[7] Spain	To compare the effectiveness of a tele-rehabilitation exercise programme versus 'wait-and-see' on physical exertion, quality of life, dyspnoea severity, heart rate and oxygen saturation in patients with post-COVID fatigue and dyspnoea	Respiratory or cardiovascular function or physical fitness: moderate respiratory and/or functional impairment starting after acute SARS-CoV-2 infection	Unclear/not stated: patients with long-lasting symptoms (more than 12 months)	Mixed (64) 63% female (40/64)	Physical fitness: Modified Borg Dyspnea Scale (MBDS)	No intervention
de Oliveira (2023)[8] Brazil	To evaluate whether multicomponent rehabilitation is effective in improving functional mobility and quality of life in individuals with post-COVID-19 syndrome	General/multiple: post-COVID-19 syndrome	Unclear/not stated: with post-COVID-19 syndrome	Mixed (59; 26 completed) 58% female (34/59)	Physical fitness: six-minute walk test (6MWT), and Berg balance scale Quality of life: SF-36	No training: educational orientation and usual daily life
Harandi (2024)[9] Iran	To assess the impact of Amantadine on patients with post-COVID-19 fatigue	Fatigue/lack of energy	After symptom onset or diagnosis: 30 to 60 days after the onset of COVID-19	Mixed (66; 62 completed) 63% female (39/62)	Fatigue: Fatigue Severity Scale (FSS), and Visual Analog Fatigue Scale (VAFS)	No treatment
Kerling (2024)[10] Germany	To assess the impact of an online-guided intervention intended to facilitate physical activity, on the mental and physical capability of post-COVID syndrome patients	Fatigue/lack of energy: Fatigue Assessment Scale score of 22 points or higher	Unclear/not stated: persisting symptoms three or more months after SARS-CoV-2 infection	Mixed (72; 62 analysed) 68% female (42/62)	Pulmonary/respiratory or cardiovascular function: change in V̇O2peak during an exercise test	No intervention: continued daily activities

Klirova (2024)[11] Czech Republic	To assess the efficacy of transcranial direct current stimulation in the treatment of neuropsychiatric symptoms of post-acute sequelae of SARS-CoV-2 infection (PASC)	Fatigue/lack of energy: Patients with neuropsychiatric symptoms of PASC presenting with chronic fatigue	After symptom onset or diagnosis: symptoms more than one month after detection of COVID-19	Mixed (35; 33 analysed) 70% female (23/33)	Fatigue: Fatigue Impact Scale (FIS) total score	Sham tDCS
Lau (2024)[12] Hong Kong	To assess a synbiotic preparation (SIM01) for the alleviation of post-acute COVID-19 syndrome (PACS) symptoms	General/multiple: one or more of 14 PACS symptoms	Unclear/not stated: four weeks or more after SARS-CoV-2 infection	Mixed (463; 403 completed six months) 65% female (303/463)	General/multiple: post-acute COVID-19 syndrome 14-item improvement questionnaire (PACSQ-14)	Placebo: Vitamin C
McGregor (2024)[13] UK	To evaluate whether a structured online supervised group physical and mental health rehabilitation programme can improve health-related quality of life compared with usual care in adults with post-COVID-19 condition	General/multiple: physical and/or mental health sequelae	After discharge: at least three months after hospital discharge	Mixed (585; 442 completed 12 months) 52% female (305/585)	Quality of life: PROMIS preference (PROPr) score	Best practice usual care (one 30-minute, online, one-to-one consultation of advice and support from a trained practitioner)
Mooren (2023)[14] Germany	To compare moderate-intensity continuous training and interval training for the medical rehabilitation of post-COVID syndrome patients	General/multiple: Post COVID syndrome	After symptom onset or diagnosis: at least one COVID-19 infection (with positive PCR test), and performance deficits lasting for at least three months. (Mean time from infection to	Mixed (139; 110 completed) 38% female (42/110)	Physical fitness: Peak oxygen uptake (VO2peak)	Two interventions: interval (60% then 30% maximal workload) versus continuous (50%) ergometer training A matched non-randomised non-COVID group of coronary artery

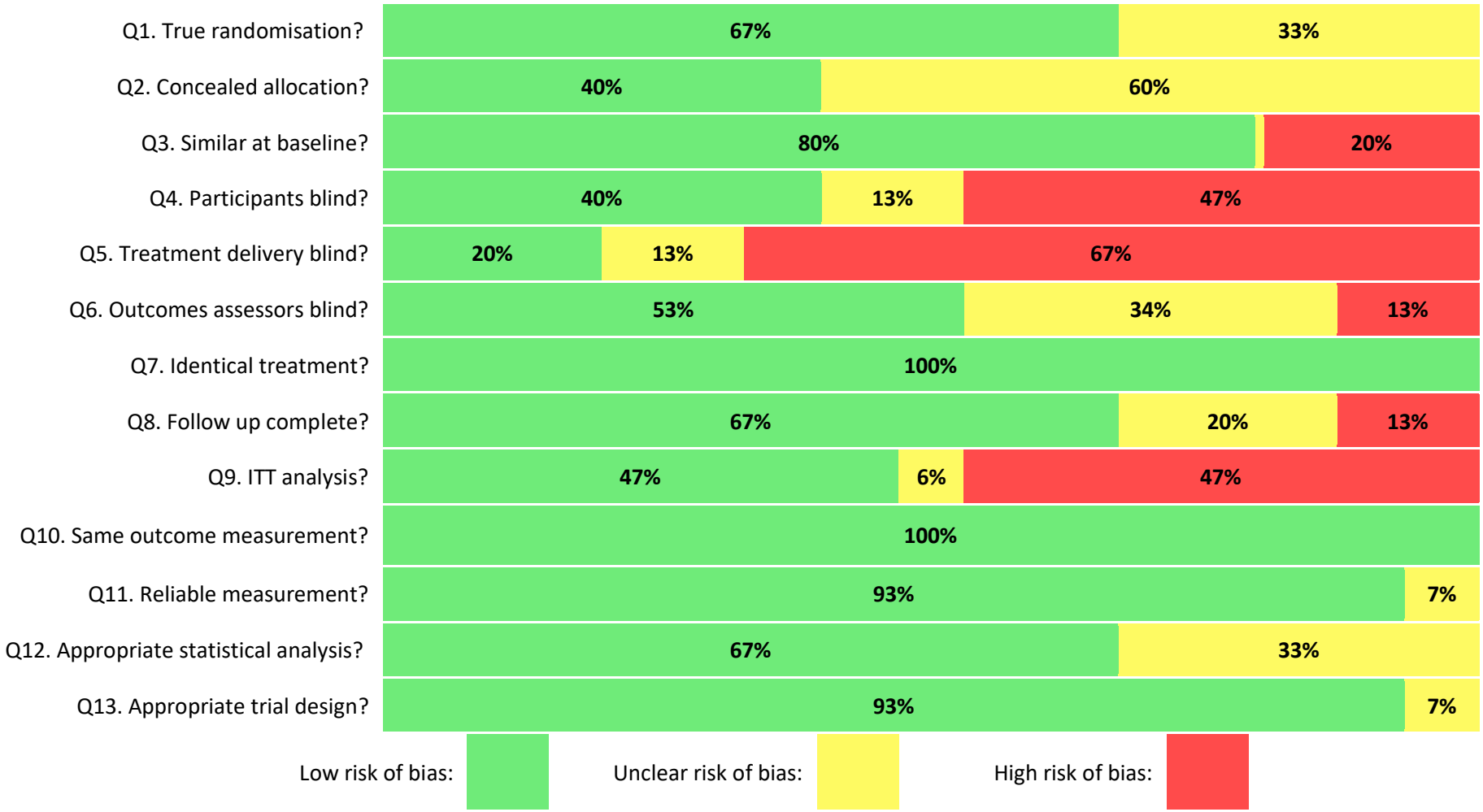
			rehabilitation was 260 days)			disease patients (n = 96) on continuous (50%) training was also compared
Navas-Otero (2024)[15] Spain	To evaluate the efficacy of a therapeutic intervention based on lifestyle self-adjustment strategies for improving symptomatic severity and quality of life of people with Long COVID	General/multiple: Long COVID-19 syndrome	After symptom onset or diagnosis: mean time from diagnosis approximately 19 months	Mixed (54) 81% female (44/54)	Quality of life: EQ-5D Disability/functional impairment: World Health Organization Disability Assessment Schedule, WHODAS 2.0 tool) Performing daily activities: Work and Social Adjustment Scale (WSAS)	Usual care, plus a leaflet about the main Long COVID symptoms
Parreira (2024)[16] Brazil	To evaluate local and systemic photobiomodulation in patients with COVID-19-related dysgeusia with the expectation of improving taste dysfunction	Olfactory and/or gustatory dysfunction: Dysgeusia	After symptom onset or diagnosis: Individuals no longer in the stage of disease transmission (15 days after the beginning of the study). Mean time since diagnosis approximately 17 days	Mixed (70) 77% female (54/70)	Olfactory and/or gustatory function: change in dysgeusia assessed using taste tests and questionnaires developed by the study authors	Sham photobiomodulation and guidance on olfactory therapy
Pietranis (2024)[17] Poland	To assess the effectiveness of a six-week rehabilitation programme on respiratory function in post-COVID-19 patients	General/multiple: scores of 1 to 4 on the Post-COVID-19 Functional Status (PCFS) scale and the modified Medical Research Council (mMRC) dyspnoea scale	Unclear/not stated: a confirmed history of COVID-19	Mixed (83; 61 or 59 number completed unclear) 64% female (39/61)	Pulmonary/respiratory or cardiovascular function: maximum inspiratory pressure (PImax)	Placebo: the same programme of physiotherapy with the mechanism to provide resistance removed from the respiratory muscle trainer

Shatri (2023)[18] Indonesia	To identify the effectiveness of supportive group psychotherapy delivered via internet-based teleconsultation in post-COVID-19 syndrome patients	General/multiple: post-COVID syndrome	After symptom onset or diagnosis: tested positive three months before recruitment	Mixed (77; 71 completed) 77% female (59/77)	Pulmonary/respiratory or cardiovascular function: heart rate variability - standard deviation normal to normal (SDNN) index Psychological: Symptom Checklist-90 (SCL90) Blood parameters: Neutrophil Lymphocyte Ratio	Education

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?
Altemani (2024)	+	?	+	+	+	+	+	+	+	+	+	+	+
Berkel (2023)	?	?	+	+	+	?	+	+	-	+	+	?	?
Bileviciute-Ljungar (2024)	+	+	+	-	-	?	+	?	-	+	+	?	+
Calvo-Paniagua (2024)	+	?	+	-	-	?	+	+	+	+	+	+	+
de Oliveira (2023)	+	+	+	-	-	+	+	?	?	+	+	+	+
Harandi (2024)	?	?	-	-	-	-	+	+	-	+	+	+	+
Kerling (2024)	+	+	+	-	-	+	+	+	-	+	+	+	+
Klirova (2024)	?	?	-	+	?	+	+	+	-	+	+	?	+
Lau (2024)	+	+	+	+	+	+	+	-	+	+	+	+	+
McGregor (2024)	+	+	+	-	-	+	+	-	+	+	+	+	+
Mooren (2023)	+	?	+	?	?	?	+	+	+	+	+	+	+
Navas-Otero (2024)	?	?	+	-	-	+	+	+	+	+	+	+	+
Parreira (2024)	+	?	+	+	-	-	+	+	+	+	?	+	+
Pietranis (2024)	+	+	-	+	-	+	+	?	-	+	+	?	+
Shatri (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. 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.[26-28]

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22. 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. Available from: https://eppi.ioe.ac.uk/cms/Default.aspx?tabid=3860.

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 October 2023. London: EPPI Centre, UCL Social Research Institute, UCL Institute of Education, University College London 2023. Available from: https://eppi.ioe.ac.uk/cms/Default.aspx?tabid=3860.

24. Raine G, Khouja C, Khatwa 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. Available from: https://eppi.ioe.ac.uk/cms/Default.aspx?tabid=3860.

25. 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. Available from: https://eppi.ioe.ac.uk/cms/Default.aspx?tabid=3860.

26. Barretto Dos Santos Lopes Batista K, Thiruvenkatachari B, O'Brien K. Intention-to-treat analysis: Are we managing dropouts and missing data properly in research on orthodontic treatment? A systematic review. Am J Orthod Dentofacial Orthop. 2019;155(1):19-27.e3.

27. 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.

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

Appendix 1 – search strategies

Cochrane Controlled Register of Trials (CENTRAL)
via Wiley http://onlinelibrary.wiley.com/
Issue: Issue 2 of 12, February 2024
Date searched: 11th March 2024
Records retrieved: 801

Although 801 records were identified overall in CENTRAL, trial register records were removed from this set, leaving a total of 661 records downloaded for this update.

#1 [mh ^"Post-Acute COVID-19 Syndrome"] 187
#2 [mh ^COVID-19/co] 309
#3 [mh ^COVID-19] 7483
#4 [mh ^SARS-CoV-2] 3126
#5 [mh ^Syndrome] 6478
#6 [mh ^Survivors] 1792
#7 #3 or #4 7741
#8 #5 or #6 8265
#9 #7 and #8 101
#10 #1 or #2 or #9 551
#11 (long next (covid* or "covid-19" or covid19 or coronavirus) or longcovid*):ti,ab,kw 394
#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 725
#13 ((post next 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 243
#14 PASC:ti,ab,kw 59
#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 159
#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 34
#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 107
#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 775
#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 264
#20 ((post next 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 17
#21 ((long next 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 17
#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 195
#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 321
#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 183
#25 {OR #11-#24} 2036
#26 #10 or #25 with Publication Year from 2023 to 2024, in Trials 674

#27 #10 or #25 with Cochrane Library publication date Between Jan 2023 and Mar 2024, in Trials 773
#28 #26 or #27 801

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 March 08, 2024
Date searched: 11th March 2024
Records retrieved: 575

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/ (3108)
2 COVID-19 post-intensive care syndrome.mp. (6)
3 COVID-19/co (16979)
4 COVID-19/ or SARS-CoV-2/ (262493)
5 Syndrome/ (123703)
6 Survivors/ (31316)
7 5 or 6 (154895)
8 4 and 7 (1113)
9 1 or 2 or 3 or 8 (19322)
10 ((long adj (covid$ or covid-19 or covid19 or coronavirus)) or longcovid$).ti,ab,kf,ot,bt. (4942)
11 ((post adj (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)) or postcovid$).ti,ab,kf,ot,bt. (10330)
12 ((post acute or postacute) adj2 (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)).ti,ab,kf,ot,bt. (1026)
13 PASC.ti,ab,kf,ot,bt. (910)
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. (2899)
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. (347)
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. (3449)
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. (2393)
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. (4423)
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. (95)
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. (266)

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. (3214)
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. (9890)
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. (3087)
24 or/10-23 (34853)
25 9 or 24 (48030)
26 exp randomized controlled trial/ (611279)
27 randomized controlled trial.pt. (609689)
28 controlled clinical trial.pt. (95577)
29 randomi?ed.ab. (761022)
30 placebo.ab. (246389)
31 clinical trials as topic.sh. (201840)
32 randomly.ab. (428766)
33 trial.ti. (304559)
34 or/26-33 (1633393)
35 exp animals/ not humans.sh. (5201238)
36 34 not 35 (1506705)
37 25 and 36 (1527)
38 limit 37 to yr="2023-Current" (570)
39 (2023* or 2024*).dt. (1884355)
40 37 and 39 (527)
41 38 or 40 (594)
42 preprint.pt. (20605)
43 41 not 42 (586)
44 remove duplicates from 43 (575)

Embase
via Ovid http://ovidsp.ovid.com/
Date range: 1974 to 2024 March 08
Date searched: 11th March 2024
Records retrieved: 849

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/ (7051)
2 ((long adj (covid$ or covid-19 or covid19 or coronavirus)) or longcovid$).ti,ab,kw,ot. (5160)
3 ((post adj (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)) or postcovid$).ti,ab,kw,ot. (13305)
4 ((post acute or postacute) adj2 (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)).ti,ab,kw,ot. (945)
5 PASC.ti,ab,kw,ot. (1143)
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. (3598)

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. (441)
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. (3560)
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. (2986)
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. (5607)
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. (182)
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. (292)
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. (4733)
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. (13406)
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. (3792)
16 or/2-15 (44081)
17 1 or 16 (44768)
18 random$.ti,ab. (2041673)
19 factorial$.ti,ab. (48871)
20 crossover$.ti,ab. (92908)
21 cross-over$.ti,ab. (38525)
22 placebo$.ti,ab. (376039)
23 (doubl$ adj blind$).ti,ab. (250163)
24 (singl$ adj blind$).ti,ab. (32750)
25 assign$.ti,ab. (506496)
26 allocat$.ti,ab. (210284)
27 volunteer$.ti,ab. (300591)
28 Crossover Procedure/ (77215)
29 double blind procedure/ (216701)
30 Randomized Controlled Trial/ (810875)
31 single blind procedure/ (53877)
32 controlled clinical trial/ (472555)
33 or/18-32 (3155873)
34 (animal/ or animal experiment/ or animal model/ or animal tissue/ or nonhuman/) not exp human/ (6934182)
35 33 not 34 (2817413)
36 17 and 35 (2934)
37 limit 36 to yr="2023 -Current" (1092)
38 (2023$ or 2024$).dd. (815950)
39 36 and 38 (422)
40 37 or 39 (1186)
41 (conference abstract or "conference review").pt. (5088192)
42 40 not 41 (903)
43 limit 42 to "remove preprint records" (854)
44 remove duplicates from 43 (849)

PsycINFO
via Ovid http://ovidsp.ovid.com/
Date range: 1806 to March Week 2 2024
Date searched: 11th March 2024
Records retrieved: 267

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/ (185)
2 covid-19/ (32953)
3 coronavirus/ (6008)
4 syndromes/ (18023)
5 sequelae/ (4022)
6 2 or 3 (35401)
7 4 or 5 (21977)
8 6 and 7 (348)
9 1 or 8 (502)
10 Long COVID/ or ((long adj (covid$ or covid-19 or covid19 or coronavirus)) or longcovid$).ti,ab,id,ot. (333)
11 ((post adj (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)) or postcovid$).ti,ab,id,ot. (1052)
12 ((post acute or postacute) adj2 (covid$ or covid-19 or covid19 or coronavirus or SARS-CoV-2 or SARS-CoV2 or SARSCoV2 or SARSCoV-2)).ti,ab,id,ot. (53)
13 PASC.ti,ab,id,ot. (53)
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. (221)
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. (25)
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. (384)
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. (202)
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. (303)
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. (7)
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. (22)
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. (322)
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. (584)
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. (359)
24 or/10-23 (2978)
25 Randomized Clinical Trials/ (523)
26 randomized controlled trials/ (1060)
27 clinical trials/ (12310)

28 clinical trial.md. (41130)
29 (randomi#ed or randomi#ation or randomi#ing).ti,ab,id. (113627)
30 randomly.ti,ab,id. (86120)
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. (133407)
32 (groups or (control* adj3 group*)).ab. (627250)
33 ((control* or trial or study or group*) and (waitlist* or wait* list* or ((treatment or care) adj2 usual))).ti,ab,id,hw. (19753)
34 ((single or double or triple or treble) adj2 (blind* or mask* or dummy)).ti,ab,id. (29779)
35 trial.ti. (39824)
36 (placebo or sham).ti,ab,id,hw. (59431)
37 treatment outcome.md. (24598)
38 treatment effectiveness evaluation/ (29302)
39 mental health program evaluation/ (2468)
40 or/25-39 (832660)
41 9 or 24 (3146)
42 40 and 41 (479)
43 limit 42 to yr="2023 -Current" (179)
44 (2023$ or 2024$).up. (229949)
45 42 and 44 (255)
46 43 or 45 (268)
47 remove duplicates from 46 (267)

CINAHL Ultimate
via Ebsco https://www.ebsco.com/
Date range: Inception to 20241231
Date searched: 11th March 2024
Records retrieved: 460

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") (1,243)
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*) (1,538)
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*) (1,739)
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)) (374)
S5 TI PASC OR AB PASC (110)
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)) (611)

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)) (278)

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)) (734)

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)) (1,102)

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)) (969)

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)) (51)

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)) (1,093)

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)) (4,413)

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)) (932)

S16 (MH "Randomized Controlled Trials+") (143,706)

S17 (MH "Double-Blind Studies") (54,902)

S18 (MH "Single-Blind Studies") (16,200)

S19 (MH "Random Assignment") (84,340)

S20 (MH "Pretest-Posttest Design") (55,511)

S21 (MH "Cluster Sample") (5,503)

S22 TI randomised OR randomized (333,506)

S23 AB random* (402,218)

S24 TI trial (192,520)

S25 MH (sample size) AND AB (assigned OR allocated OR control) (4,476)

S26 MH (placebos) (14,409)

S27 PT (randomized controlled trial) (157,034)

S28 AB (control W5 group) (148,564)

S29 MH (crossover design) OR MH (comparative studies) (498,527)

S30 AB (cluster W3 RCT) (508)

S31 MH animals+ (104,729)

S32 MH (animal studies) (157,478)
S33 TI (animal model*) (3,965)
S34 S31 OR S32 OR S33 (253,144)
S35 MH (human) (2,796,567)
S36 S34 NOT S35 (218,311)
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 (1,051,525)
S38 S37 NOT S36 (1,002,654)
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 (11,530)
S40 S38 AND S39 (1,128)
S41 S38 AND S39 Limiters - Publication Date: 20230101-20241231(422)
S42 (ZD 2023* or 2024*) (254,612)
S43 S40 AND S42 (338)
S44 S41 OR S43 (460)

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

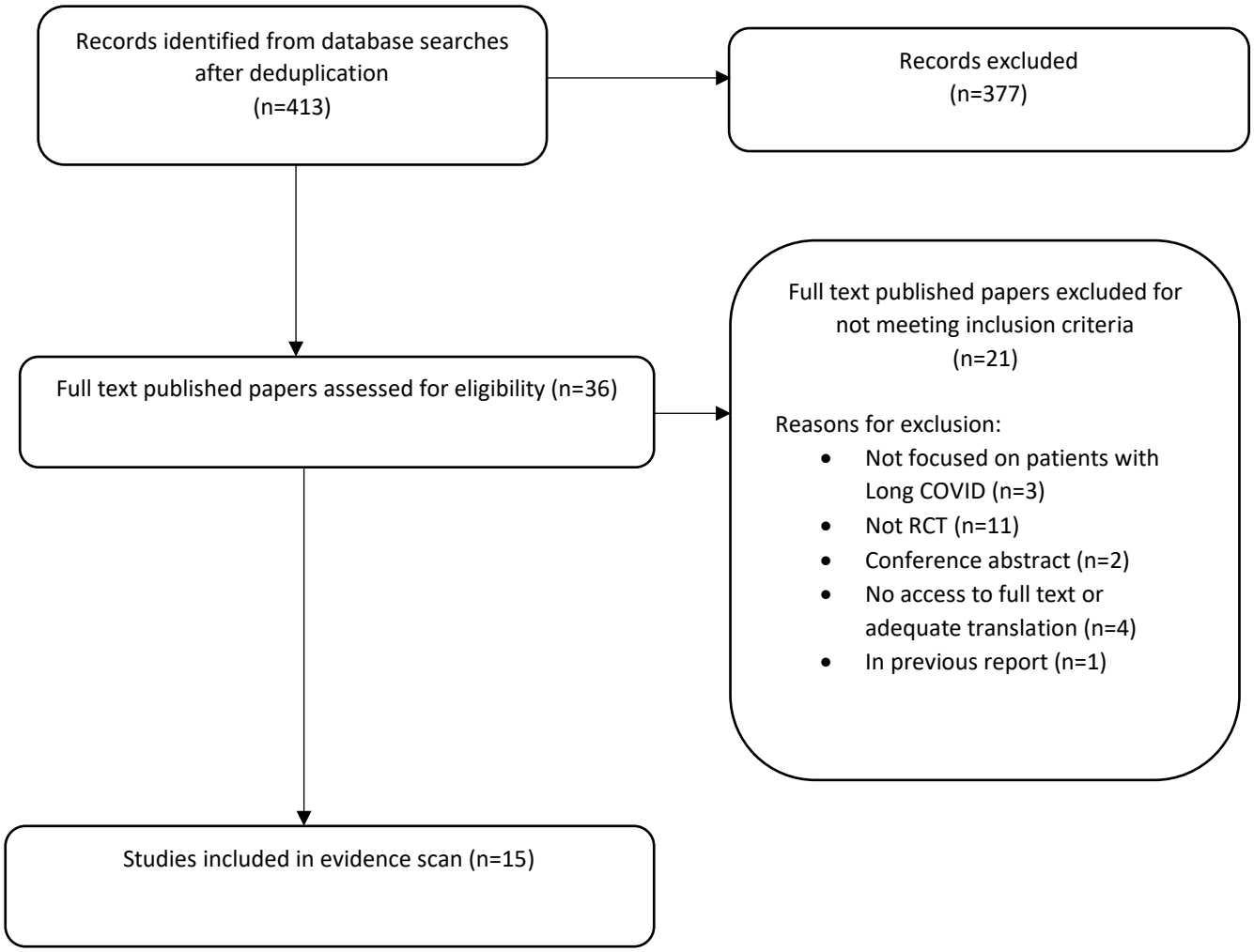
Q10 Were outcomes measured in the same way for treatment groups? Yes, No, Unclear, NA

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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