Appendix for report
Post covid – treatment and rehabilitation: living review
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Appendix 1 Relevant studies

Depression/Anxiety

Fan 2021

Fan Y, Shi Y, Zhang J, Sun D, Wang X, Fu G, et al. The Effects of Narrative Exposure Therapy on COVID-19 Patients with Post-Traumatic Stress Symptoms: A Randomized Controlled Trial. J Affect Disord. 2021;293:141–7. Available from https://doi.org/10.1016/j.jad.2021.06.019
Country: China
Population: 111 patients (mean age±SD: 46 ± 12.34 years) with COVID-19 who isolated for 40.72 days on average, most of them with mild symptoms, near the discharge stage with positive screening results for posttraumatic stress symptoms (PTSS).
Treatment: The intervention group received narrative Exposure Therapy (NET) and personalized psychological treatment. The NET therapy hade a duration of eight weeks with one or two sessions a week, lasting for 90-120
Aim: Screen for the prevalence of PTSS among pre-discharged COVID-19 patients and explore the effects of NET on patients experiencing PTSS.
Outcomes: Post-traumatic stress symptoms (PTSD Checklist-Civilian version), Depression (The Self-rating Depression Scale, SDS), anxiety (The Self-rating Anxiety Scale, SAS) and Sleep quality (The Pittsburg Sleep Quality Index (PQSI).
Author's conclusion: "NET likely had a positive impact on PTSS of COVID-19 patients. Clinical staff should consider applying NET to improve the psychological well-being of patients who have experienced an epidemic such as COVID-19."
Risk of bias: Moderate

Fever

No relevant studies.

Palpitations/POTS

No relevant studies.

Mental fatigue/Cognitive impairment

Palladini 2022

Palladini M, Bravi B, Colombo F, Caselani E, Di Pasquasio C, D'Orsi G, et al. Cognitive remediation therapy for post-acute persistent cognitive deficits in COVID-19 survivors: A proof-of-concept study. Neuropsychol Rehabil. 2022:1-18. Available from https://doi.org/10.1080/09602011.2022.2075016
Country: Italy
Population: 45 adults (age mean ±SD: intervention = 59.60 ± 10.00; control= 56.80 ± 7.09); COVID-19 survivors presenting cognitive impairments at one-month follow-up.
Treatment: Cognitive remediation therapy (CRT).
Aim: Our case-control study investigates the efficacy of a CRT programme administered to COVID-19 survivors in the post-acute phase of the illness.
Outcomes: Cognitive functions were evaluated with a neuropsychological screening test (Cognition in Schizophrenia (BACS)).
Author's conclusion: "Our results could pave the way to a plausible innovative treatment targeting cognitive impairments and ameliorating the quality of life of COVID-19 survivors."
Risk of bias: Moderate

Chronic obstructive pulmonary disease/Asthma

No relevant studies.

Smell/Taste

D'Ascanio 2021

D'Ascanio L, Vitelli F, Cingolani C, Maranzano M, Brenner MJ, Di Stadio A. Randomized clinical trial "olfactory dysfunction after COVID-19: olfactory rehabilitation therapy vs. intervention treatment with Palmitoylethanolamide and Luteolin": preliminary results. Eur Rev Med Pharmacol Sci. 2021;25(11):4156 – 62. Available from https://doi.org/10.26355/eurrev_202106_26059
Country: Italy
Aim: Our study investigated the efficacy of a supplement with Palmitoylethanolamide (PEA) and Luteolin to support recovery of olfaction in COVID-19 patients.
Population: 12 outpatients (mean age = 42 years), with confirmed history of COVID-19 and suffering from anosmia/hyposmia ≥ 90 days after a negative COVID-19 nasopharyngeal swab.
Treatment: The intervention was daily treatment with PEA/Luteolin oral supplement in addition to ofactory training/stimulation with Sniffin' Sticks administered twice every day (10-minute session) for 30 days. The control group did only received olfactory training.
Outcomes: Evaluation of smell function by Sniffin Sticks, follow-up after 30 days of treatment.
Author's conclusion: "Treatment combining olfactory rehabilitation with oral supplementation with PEA and Luteolin was associated with improved recovery of olfactory function, most marked in those patients with longstanding olfactory dysfunction. Further studies are necessary to replicate these findings and to determine whether early intervention including olfactory rehabilitation and PEA+Luteolin oral supplement might prevent SARS-CoV-2 associated olfactory impairment."
Risk of bias: Moderate

Di Stadio 2022

Di Stadio A, D'Ascanio L, Vaira LA, Cantone E, De Luca P, Cingolani C, et al. Ultramicronized Palmitoylethanolamide and Luteolin Supplement Combined with Olfactory Training to Treat Post-COVID-19 Olfactory Impairment: A Multi-Center Double-Blinded Randomized Placebo-Controlled Clinical Trial. Curr Neuropharmacol. 2022. Available from https://doi.org/10.2174/1570159X20666220420113513
Country: Italy
Population: 185 adults (43.5 + 14.6 years; 65% female); prior COVID-19; persistent olfactory impairment >6 months after negative SARS-CoV-2 testing; without prior history of olfactory dysfunction sinonasal disorders.
Treatment: Ultramicronized PEA-LUT 770 mg oral supplements plus olfactory training for 90 days.
Aim: To investigate recovery of olfactory function in patients treated with PEA-LUT oral supplements plus olfactory training versus olfactory training plus placebo.
Outcomes: Sniffin'Sticks assessments were used to test the patients at baseline and 90 days.
Author's conclusion: "Among individuals with olfactory dysfunction post-COVID-19, combining PEA-LUT with olfactory training resulted in greater recovery of smell than olfactory training alone."
Risk of bias: Moderate

Le Bon 2021

Le Bon SD, Konopnicki D, Pisarski N, Prunier L, Lechien JR, Horoi M. Efficacy and safety of oral corticosteroids and olfactory training in the management of COVID-19-related loss of smell. Eur Arch Otorhinolaryngol. 2021. Available from https://doi.org/10.1007/s00405-020-06520-8
Country: Belgium
Population: 27 participants (age mean ±SD: intervention = 42 ± 14, control = 44 ± 14), nonhospitalized patients with loss of smell due to COVID-19 and still dysosmic 5 weeks after having lost their sense of smell.
Treatment: Oral corticosteroids (10-day course of 32 mg of methylprednisolone once daily) and olfactory training (sniffing four odours from 'Smell Training. Kit' for approximately 10 s each twice daily, for 10 weeks).
Aim: In this pilot study, we investigated the efficacy and the safety of oral corticosteroids and olfactory training as a treatment for patients with persistent olfactory dysfunction as a result of COVID-19.
Outcomes: "The 'Sniffin' Sticks' battery test"
Author's conclusion: "This pilot study may suggest the combination of a short course of oral corticosteroids and olfactory training is safe and may be beneficial in helping patients with enduring dysosmia recover from olfactory loss due to COVID-19. There is a crucial need for further investigation with larger cohorts to corroborate these findings."
Risk of bias: Moderate

Lung function/Breathing

Li 2021

Li Ja, Xia W, Zhan C, Liu S, Yin Z, Wang J, et al. A telerehabilitation programme in post-discharge COVID-19 patients (TERECO): a randomised controlled trial. Thorax. 2021. Available from https://doi.org/10.1136/thoraxjnl-2021-217382
Country: China
Population: 120 participants (age range = 18–74, mean±SD = 50.61±10.98) discharged after inpatient treatment for COVID-19, with remaining dyspnoea complaints.
Treatment: Telerehabilitation programme for COVID-19 (TERECO), unsupervised home-based for 6-weeks, comprising breathing control and thoracic expansion, aerobic exercise and LMS exercise, delivered via smartphone, and remotely monitored with heart rate telemetry.
Aim: To investigate superiority of a telerehabilitation programme for COVID-19 (TERECO) over no rehabilitation with regard to exercise capacity, lower limb muscle strength (LMS), pulmonary function, health-related quality of life (HRQOL) and dyspnoea.
Outcomes: Primary outcome: 6 min walking distance (6MWD). Secondary outcomes: squat time, pulmonary function, HRQOL, mMRC-dyspnoea. Assessed at 6 weeks (posttreatment) and 24 weeks (follow-up).
Author's conclusion: "This trial demonstrated superiority of TERECO over no rehabilitation for 6MWD, LMS, and physical HRQOL."
Risk of bias: Moderate

McNarry 2021

McNarry MA, Berg RMG, Shelley J, Hudson J, Saynor ZL, Duckers J, et al. Inspiratory Muscle Training Enhances Recovery Post COVID-19: A Randomised Controlled Trial. The European respiratory journal. 2022. Available from https://doi.org/10.1183/13993003.03101-2021
Country: UK
Population: 281 adults (46.6 ± 12.2 years; 88% female) recovering from self-reported COVID-19 (9.0 ± 4.2 months post-acute infection), primary symptom of breathlessness.
Treatment: Inspiratory Muscle Training, 3 unsupervised sessions/week for 8 weeks, with a handheld inspiratory flow resistive device that wirelessly syncs to a mobile device via an App to provide graphical biofeedback.
Aim: The aim of the current study was to investigate the potential rehabilitative role of inspiratory muscle training (IMT).
Outcomes: Health-related quality of life and breathlessness questionnaires, respiratory muscle strength and fitness; pre and post intervention.
Author's conclusion: "IMT may represent an important home-based rehabilitation strategy for wider implementation as part of COVID-19 rehabilitative strategies. Given the diverse nature of long-COVID, further research is warranted on the individual responses to rehabilitation - the withdrawal rate herein highlights that no one strategy is likely to be appropriate for all."
Risk of bias: Moderate

Okan 2022

Okan F, Okan S, Duran Yucesoy F. Evaluating the Efficiency of Breathing Exercises via Telemedicine in Post-Covid-19 Patients: Randomized Controlled Study. Clin Nurs Res. 2022:10547738221097241. Available from https://doi.org/10.1177/10547738221097241
Country: Turkey
Population: 52 adults (age mean ±SD: intervention = 48.85 ± 10.85 , control = 52.19 ± 14.84); after Covid-19 pneumonia; presented to the Chest Diseases Outpatient Clinic with dyspnea.
Treatment: Breathing exercise (respiratory control, pursed lip breathing, and diaphragmatic breathing exercises) 3 times a day for 5 weeks (one session performed via telemedicine each week).
Aim: The aim of the study was to evaluate the effectiveness of breathing exercises given by telemedicine in post-Covid-19 dyspneic individuals.
Outcomes: Primary: Spirometry (FVC, FEV1, FEV1/FVC Ratio, and MVV) and six-minute walk test (6MWT); Secondary: St George's Respiratory Questionnaire (SGRQ) score.
Author's conclusion: "With breathing exercise training applied through telemedicine, improvements were observed in the pulmonary functions, quality of life, and exercise capacities of dyspneic post-Covid-19 individuals."
Risk of bias: Moderate

Philip 2022

Philip KEJ, Owles H, McVey S, Pagnuco T, Bruce K, Brunjes H, et al. An online breathing and wellbeing programme (ENO Breathe) for people with persistent symptoms following COVID-19: a parallel-group, single-blind, randomised controlled trial. The Lancet Respiratory medicine. 2022. Available from https://doi.org/10.1016/S2213-2600(22)00125-4
Country: UK
Population: 150 adults (age mean ±SD: intervention = 49 ± 12 , control = 50 ± 12); recovering from COVID-19, with ongoing breathlessness.
Treatment: The English National Opera Breathe programme, breathing retraining using singing techniques (6 weeks, online).
Aim: We assessed whether an online breathing and wellbeing programme improves health related quality-of-life (HRQoL) in people with persisting breathlessness following COVID-19.
Outcomes: Health related quality-of-life (assessed using the RAND 36-item short form survey instrument mental health composite (MHC) and physical health composite (PHC) scores).
Author's conclusion: "Our findings suggest that an online breathing and wellbeing programme can improve the mental component of HRQoL and elements of breathlessness in people with persisting symptoms after COVID-19".
Risk of bias: Moderate

Neurological difficulties

No relevant studies.

Kidney problems

No relevant studies.

Pneumonia

No relevant studies.

Pain

Scaturro 2022

Scaturro D, Vitagliani F, Di Bella VE, Falco V, Tomasello S, Lauricella L, et al. The Role of Acetyl-Carnitine and Rehabilitation in the Management of Patients with Post-COVID Syndrome: Case-Control Study. Applied Sciences. 2022;12(8):4084-. Available from https://doi.org/10.3390/app12084084
Country: Italy
Population: 60 adults (age mean ±SD= 58.7 ±5.4); after Covid-19 pneumonia; with clinical characteristics similar to fibromyalgia.
Treatment: L-acetyl-carnitine (ALC 500 mg) therapy and rehabilitation protocol for 10 days.
Aim: We evaluated the effectiveness of physical exercise, in association with L-acetylcarnitine (ALC) therapy, in patients with Post-COVID syndrome, on musculoskeletal pain, dyspnea, functional capacity, quality of life, and depression.
Outcomes: "Perceived musculoskeletal pain and degree of dyspnea".
Author's conclusion: "We believe that the combination of physical exercise with ALC intake is a promising and effective treatment in the management of post-COVID syndrome, especially for the management of musculoskeletal pain and depression, as well as for improving quality of life."
Risk of bias: Moderate

Sleeping problems

No relevant studies.

Dizziness/Nausea

No relevant studies.

Other

Chen 2021

Chen Y, Liu C, Wang T, Qi J, Jia X, Zeng X, et al. Efficacy and safety of Bufei Huoxue capsules in the management of convalescent patients with COVID-19 infection: A multicentre, double-blind, and randomised controlled trial. J Ethnopharmacol. 2021:114830. Available from https://doi.org/10.1016/j.jep.2021.114830
Country: China
Population: 131 patients (age mean ±SD: intervention = 54.16 ± 12.11 , control = 52.51 ± 12.31) hospitalized; meeting discharge standards; in the rehabilitation period after COVID-19 infection; with qi deficiency in the lung and spleen.
Treatment: Chinese medicine Bufei Huoxue capsules.
Aim: The present study aimed to evaluate the efficacy and safety of Bufei Huoxue in restoring the functional status and exercise tolerance of patients recovering from COVID-19.
Outcomes: Primary : Chest CT, 6-min Walk Distance. Secondary: Fatigue, St George's Respiratory Questionnaire, Dyspnea, Chinese medicine symptom complex score.
Author's conclusion: "Bufei Huoxue may exert strong rehabilitative effects on physiological activity in patients recovering from COVID-19, which may in turn attenuate symptoms of fatigue and improve exercise tolerance."
Risk of bias: Moderate