

Interventions for long COVID treatments

Prepared for the OUTPOST APT, HEAL COVID and ALCAP MRFF-funded projects

October 2024 (search performed on the 7th of November 2024)

The following report provides an update of evidence syntheses activities conducted by the Living Evidence Group in October. The Bond and ALEC teams refined and finalised a search strategy for RCTs of treatments for long COVID and conducted monthly searches for RCTs on long COVID since June 2024. We have now completed full text screening of all studies published up to the end of October have included a total of 123 RCTs.

In the absence of substantial high-quality trial evidence for interventions of interest (e.g. antivirals), the Living Evidence Group has commenced a systematic review for low dose naltrexone in long COVID. Low dose naltrexone was listed as an intervention of high interest by clinicians in the clinical survey. As there are no published RCTs on this drug to date, the Living Evidence Group will identify and review research literature from pre-post studies of low dose naltrexone in long COVID. This review is underway and the results will be reported to the project team shortly.

The following table provides a summary of the currently published trials for Long COVID treatments (n=123). These trials were identified through a comprehensive systematic search on Pubmed, Cochrane and Embase, plus pre-print servers. The search is also supplemented with updates from long COVID reviews that are being conducted by EPPI-Centre and Epistemonikos. In October, 8 new RCTs on long COVID were published. These studies focused on; Physical Activity and physical therapy (n=5), Complementary and Alternative medicine(n=1), Behavioural, psychological, educational (n=1) and Diet and dietary supplements (n=1) (see Appendix A).

Table 1. Updated summary of RCTs for long COVID treatments (Most recent search conducted on 7th November 2024)

Taxonomy categories	Systematic reviews	Registered clinical trials	RCTs					
			Jun-24	Jul-24	Aug-24	Sep-24	Oct-24	Total
Pharmacological interventions			19					21
Acetylcholinesterase inhibitor			0					0
Antidepressant		3	2			1		3
Antifibrotic		1	1					1
Antihistamine		1	0					0
Antivirals	1	7	0	1				1
Beta Blockers			1					1
Corticosteroids	5		0					0
Enzyme Therapeutics			0					0
Mood stabilizer			0					0
Targeted drugs			2					2
Multiple	2		0					0
NSAIDs (*anti-inflammatory)		5	0					0
Olfactory function/anosmia			11					11
Other (BrainMax, AXA1125)			2					2

Non-pharmacological			83					102
Physical Activity and physical therapy	31		37	1		1	5	44
Therapeutic procedures	6		17	1	2	1		21
Complementary and Alternative medicine	5		6			1	1	8
Behavioural, psychological, educational	2		6	1			1	8
Diet and dietary supplements	2		17	3			1	21
Other non-drug			0					0
Both drug and non-drug interventions	2		0					0
Full texts included	56	20	102	7	2	4	8	123

*bovhyaluronidase azoximer (longidase), #Targeted drugs- includes both Leronlimab-CCR5-, and RNase

Table 2 List of studies added for long COVID treatments as of the end of October 2024

Non pharmacological interventions	
Physical Activity and Physical Therapy n=44	
<i>Digital/Telerehab n=19</i>	
Study	Date added

<p>Ahmad AM, Mohamed Awad Allah SA, Abd Elhaseeb GA, Elsharawy DE, Ahmed HS, Mohamed Abdelwahab MA. Effects of conventional versus virtual reality-simulated treadmill exercise on fatigue, cognitive function, and participant satisfaction in post-COVID-19 subjects. A randomized trial. J Exerc Sci Fit. 2024;22(4):316-21.</p>	pre July 2024
<p>Alsharidah A, Kamel F, Alanazi A, Alhawsah E, Alharbi H, Alrshedi Z, et al. A Pulmonary Telerehabilitation Program Improves Exercise Capacity and Quality of Life in Young Females Post-COVID-19 Patients. Annals of rehabilitation medicine. 2023;47:502-10.</p>	pre July 2024
<p>Berenguel Senén A, Gadella Fernández A, Godoy López J, Borrego Rodríguez J, Gallango Brejano M, Cepas Guillén P, et al. Functional rehabilitation based on therapeutic exercise training in patients with postacute COVID syndrome (RECOVER). Revista espanola de cardiologia (English ed). 2023;77:167-75.</p>	pre July 2024
<p>Bileviciute-Ljungar I, Norrefalk J, Borg K. Improved Functioning and Activity According to the International Classification of Functioning and Disability after Multidisciplinary Telerehabilitation for Post-COVID-19 Condition-A Randomized Control Study. Journal of clinical medicine. 2024;13:970-.</p>	pre July 2024
<p>Calvo-Paniagua J, Díaz-Arribas MJ, Valera-Calero JA, Ramos-Sánchez M, Fernández-de-Las-Peñas C, Navarro-Santana MJ, et al. An Educational, Exercise and Occupational Therapy-Based Telerehabilitation Program versus 'Wait-and-See' for Improving Self-Perceived Exertion in Patients with post-COVID Fatigue and Dyspnea: A Randomized Clinical Trial. Am J Phys Med Rehabil. 2024.</p>	pre July 2024
<p>Çelik Z, Kafa N, Güzel NA, Köktürk N. The effects of physical activity tele-counseling intervention on physical activity, functional performance, and quality of life in post-COVID-19 conditions: a randomized controlled trial. Expert Rev Respir Med. 2024.</p>	pre July 2024
<p>Del Corral T, Fabero-Garrido R, Plaza-Manzano G, Fernández-de-Las-Peñas C, Navarro-Santana M, López-de-Uralde-Villanueva I. Home-based respiratory muscle training on quality of life and exercise tolerance in long-term post-COVID-19: Randomized controlled trial. Ann Phys Rehabil Med. 2023;66(1):101709.</p>	pre July 2024

Espinoza-Bravo C, Arnal-Gómez A, Martínez-Arnau FM, Núñez-Cortés R, Hernández-Guillén D, Flor-Rufino C, et al. Effectiveness of Functional or Aerobic Exercise Combined With Breathing Techniques in Telerehabilitation for Patients With Long COVID: A Randomized Controlled Trial. Phys Ther. 2023;103(11).	pre July 2024
Lai CY, Lin CH, Chao TC, Chang CC, Huang CY, Chiang SL. Effectiveness of a 12-week telerehabilitation training in people with long COVID: A randomized controlled trial. Ann Phys Rehabil Med. 2024;67(5):101853.	pre July 2024
M K, A B, L D, P G, B D, P dT, et al. Feasibility of a Group-Based Telerehabilitation Intervention for Long COVID Management. ResearchSquare. 2022.	pre July 2024
McGregor G, Sandhu H, Bruce J, Sheehan B, McWilliams D, Yeung J, et al. Clinical effectiveness of an online supervised group physical and mental health rehabilitation programme for adults with post-covid-19 condition (REGAIN study): multicentre randomised controlled trial. Bmj. 2024;384:e076506.	pre July 2024
Okan F, Okan S, Duran Yücesoy F. Evaluating the Efficiency of Breathing Exercises via Telemedicine in Post-Covid-19 Patients: Randomized Controlled Study. Clin Nurs Res. 2022;31(5):771-81.	pre July 2024
Pleguezuelos E, Del Carmen A, Moreno E, Miravittles M, Serra M, Garnacho-Castaño M. Effects of a telerehabilitation program and detraining on cardiorespiratory fitness in patients with post-COVID-19 sequelae: A randomized controlled trial. Scandinavian journal of medicine & science in sports. 2023;34:e14543.	pre July 2024
Pleguezuelos E, Del Carmen A, Moreno E, Serra-Prat M, Serra-Payá N, Garnacho-Castaño MV. Telerehabilitation improves cardiorespiratory and muscular fitness and body composition in older people with post-COVID-19 syndrome. J Cachexia Sarcopenia Muscle. 2024.	pre July 2024
Samper-Pardo M, León-Herrera S, Oliván-Blázquez B, Méndez-López F, Domínguez-García M, Sánchez-Recio R. Effectiveness of a telerehabilitation intervention using ReCOVvery APP of long COVID patients: a randomized, 3-month follow-up clinical trial. Scientific reports. 2023;13:7943.	pre July 2024

Samper-Pardo M, Oliván-Blázquez B, León-Herrera S, Sánchez-Arzcuren R, Casado-Vicente V, Sánchez-Recio R. Effectiveness of ReCOVerry APP to improve the quality of life of Long COVID patients: a 6-month follow-up randomized clinical trial. 2023.	pre July 2024
Sarmiento A, Adodo R, Hodges G, Webber S, Sanchez-Ramirez D. Virtual pulmonary rehabilitation approaches in patients with post COVID syndrome: a pilot study. BMC pulmonary medicine. 2024;24:139.	pre July 2024
Stölting A, Schröder D, Müllenmeister C, Behrens GMN, Klawitter S, Klawonn F, et al. Improvement in quality of life and cognitive function in Post Covid Syndrome after online occupational therapy: results from a randomized controlled pilot study. medRxiv. 2024.	pre July 2024
Vallier JM, Simon C, Bronstein A, Dumont M, Jobic A, Paleiron N, et al. Randomized controlled trial of home-based vs. hospital-based pulmonary rehabilitation in post COVID-19 patients. Eur J Phys Rehabil Med. 2023;59(1):103-10.	pre July 2024
<i>Exercise Training/physical therapy and rehab n=25</i>	
Abo Elyazed TI, Abd El-Hakim AAE, Saleh OI, Sonbol MMF, Eid HA, Moazen E, et al. Diaphragmatic strengthening exercises for patients with post COVID-19 condition after mild-to-moderate acute COVID-19 infection: a randomized controlled study. J Rehabil Med. 2024;56:jrm25491.	pre July 2024
Bai B, Xu M, Zhou H, et al. Effects of aerobic training on cardiopulmonary fitness in patients with long COVID-19: a randomized controlled trial. Vol. 25. 2024:649.	October 2024
Besnier F, Malo J, Mohammadi H, Clavet S, Klai C, Martin N, et al. Effects of Cardiopulmonary Rehabilitation on Cardiorespiratory Fitness and Clinical Symptom Burden in Long COVID: Results from the COVID-Rehab Randomized Controlled Trial. Am J Phys Med Rehabil. 2024.	pre July 2024

Cunha ACR, Silva JC, Garcês CP, et al. Online and Face-to-Face Mat Pilates Training for Long COVID-19 Patients: A Randomized Controlled Trial on Health Outcomes. Vol. 21. International journal of environmental research and public health. 2024 Oct 19.	October 2024
Dwiputra B, Ambari A, Triangto K, et al. The home-based breathing and chest mobility exercise improves cardiorespiratory functional capacity in long COVID with cardiovascular comorbidities: a randomized study. Vol. 24. 2024:574.	October 2024
Gaudreau-Majeau F, Gagnon C, Djedaa S, Bérubé B, Malo J, Iglesias-Grau J, et al. Cardiopulmonary rehabilitation's influence on cognitive functions, psychological state, and sleep quality in long COVID-19 patients: A randomized controlled trial. Neuropsychological rehabilitation. 2024:1-17.	pre July 2024
Gomes Dos Santos EG, Vieira da Costa K, Cordeiro de Souza IT, Victor Dos Santos Felix J, Furtado Brandão CB, Michelle de Souza Fernandes V, et al. Effects of a cardiopulmonary rehabilitation protocol on functional capacity, dyspnea, fatigue, and body composition in individuals with post-COVID-19 syndrome: A randomized controlled trial. Physiother Res Int. 2024;29(2):e2086.	pre July 2024
Jimeno-Almazán A, Buendía-Romero Á, Martínez-Cava A, Franco-López F, Sánchez-Alcaraz BJ, Courel-Ibáñez J, et al. Effects of a concurrent training, respiratory muscle exercise, and self-management recommendations on recovery from post-COVID-19 conditions: the RECOVE trial. J Appl Physiol (1985). 2023;134(1):95-104.	pre July 2024
Jimeno-Almazán A, Franco-López F, Buendía-Romero Á, Martínez-Cava A, Sánchez-Agar JA, Sánchez-Alcaraz Martínez BJ, et al. Rehabilitation for post-COVID-19 condition through a supervised exercise intervention: A randomized controlled trial. Scand J Med Sci Sports. 2022;32(12):1791-801.	pre July 2024
Kaczmarczyk K, Matharu Y, Bobowik P, Gajewski J, Maciejewska-Skrendo A, Kulig K. Resistance Exercise Program Is Feasible and Effective in Improving Functional Strength in Post-COVID Survivors. Journal of clinical medicine. 2024;13:1712-.	pre July 2024
Kaddoussi R, Rejeb H, Kalai A, et al. Effects of a cardiopulmonary rehabilitation programme on submaximal exercise in Tunisian patients with long-COVID19: a randomized clinical trial. Vol. 41. 2024:197-217.	October 2024

<p>Kerling A, Beyer S, Dirks M, Scharbau M, Hennemann A, Dopfer-Jablonka A, et al. Effects of a randomized-controlled and online-supported physical activity intervention on exercise capacity, fatigue and health related quality of life in patients with post-COVID-19 syndrome. BMC sports science, medicine & rehabilitation. 2024;16:33.</p>	<p>pre July 2024</p>
<p>Kogel A, Machatschek M, Scharschmidt R, Wollny C, Lordick F, Ghanem M, et al. Physical exercise as a treatment for persisting symptoms post-COVID infection: review of ongoing studies and prospective randomized controlled training study. Clin Res Cardiol. 2023;112(11):1699-709.</p>	<p>pre July 2024</p>
<p>Leon-Herrera S, Olivan-Blazquez B, Sanchez-Recio R, Mendez-Lopez F, Magallon-Botaya R, Sanchez-Arizcuren R. Effectiveness of an online multimodal rehabilitation program in long COVID patients: a randomized clinical trial. Arch Public Health. 2024;82(1):159.</p>	<p>September 2024</p>
<p>Maritescu A, Crisan AF, Pescaru CC, Stoicescu ER, Oancea C, Iacob D. Effectiveness of Combined Pulmonary Rehabilitation and Progressive Muscle Relaxation in Treating Long-Term COVID-19 Symptoms: A Randomized Controlled Trial. Vol. 13. Journal of clinical medicine. 2024 Oct 18.</p>	<p>October 2024</p>
<p>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. Eur Respir J. 2022;60(4).</p>	<p>pre July 2024</p>
<p>Mooren J, Garbsch R, Schäfer H, Kotewitsch M, Waranski M, Teschler M, et al. Medical Rehabilitation of Patients with Post-COVID-19 Syndrome-A Comparison of Aerobic Interval and Continuous Training. Journal of clinical medicine. 2023;12:6739-.</p>	<p>pre July 2024</p>
<p>Palau P, Domínguez E, Gonzalez C, Bondía E, Albiach C, Sastre C, et al. Effect of a home-based inspiratory muscle training programme on functional capacity in postdischarged patients with long COVID: the InsCOVID trial. BMJ Open Respir Res. 2022;9(1).</p>	<p>pre July 2024</p>

Pietranis KA, Izdebska WM, Kuryliszyn-Moskal A, Dakowicz A, Ciotkiewicz M, Kaniewska K, et al. Effects of Pulmonary Rehabilitation on Respiratory Function and Thickness of the Diaphragm in Patients with Post-COVID-19 Syndrome: A Randomized Clinical Trial. J Clin Med. 2024;13(2).	pre July 2024
Romanet C, Wormser J, Fels A, Lucas P, Prudat C, Sacco E, et al. Effectiveness of exercise training on the dyspnoea of individuals with long COVID: A randomised controlled multicentre trial. Ann Phys Rehabil Med. 2023;66(5):101765.	pre July 2024
Sánchez Milá Z, Rodríguez Sanz D, Martín Nieto A, Jiménez Lobo A, Ramos Hernández M, Campón Chekroun A, et al. Effects of a respiratory and neurological rehabilitation treatment plan in post Covid-19 affected university students. Randomized clinical study. Chronic Respiratory Disease. 2024;21.	pre July 2024
Sánchez-Milá Z, Abuín-Porras V, Romero-Morales C, Almazán-Polo J, Velázquez Saornil J. Effectiveness of a respiratory rehabilitation program including an inspiration training device versus traditional respiratory rehabilitation: a randomized controlled trial. PeerJ. 2023;11:e16360-e.	pre July 2024
Spiesshoefer J, Regmi B, Senol M, Jörn B, Gorol O, Elfeturi M, et al. Potential Diaphragm Muscle Weakness-related Dyspnea Persists Two Years after COVID-19 and Could Be Improved by Inspiratory Muscle Training: Results of an Observational and an Interventional Trial. Am J Respir Crit Care Med. 2024.	pre July 2024
Stavrou VT, Vavougiou GD, Astara K, Mysiris DS, Tsirimona G, Papayianni E, et al. The Impact of Different Exercise Modes in Fitness and Cognitive Indicators: Hybrid versus Tele-Exercise in Patients with Long Post-COVID-19 Syndrome. Brain Sci. 2024;14(7).	July 2024
Tryfonos A, Pourhamidi K, Jörnåker G, Engvall M, Eriksson L, Elhallos S, et al. Functional Limitations and Exercise Intolerance in Patients With Post-COVID Condition: A Randomized Crossover Clinical Trial. JAMA Netw Open. 2024;7(4):e244386.	pre July 2024
Therapeutic n=21	

Abo El Naga H, El Zaiat R, Hamdan A. The potential therapeutic effect of platelet-rich plasma in the treatment of post-COVID-19 parosmia. The Egyptian Journal of Otolaryngology. 2022;38.	pre July 2024
Amorim NTS, Cavalcanti FCB, Moura E, Sobral Filho D, Leitão CCS, Almeida MM, et al. Does whole-body vibration improve risk of falls, balance, and heart rate variability in post-COVID-19 patients? A randomized clinical trial. J Bodyw Mov Ther. 2024;39:518-24.	pre July 2024
Badran B, Huffman S, Dancy M, Austelle C, Bikson M, Kautz S, et al. A pilot randomized controlled trial of supervised, at-home, self-administered transcutaneous auricular vagus nerve stimulation (taVNS) to manage long COVID symptoms. Bioelectronic medicine. 2022;8:13.	pre July 2024
Bowen R, Arany P. Use of either transcranial or whole-body photobiomodulation treatments improves COVID-19 brain fog. Journal of biophotonics. 2023;16:e202200391.	pre July 2024
Cardoso Soares P, de Freitas P, Eduardo C, Azevedo L. Photobiomodulation, Transmucosal Laser Irradiation of Blood, or B complex as alternatives to treat Covid-19 Related Long-Term Taste Impairment: double-blind randomized clinical trial. Lasers in medical science. 2023;38:261.	pre July 2024
Catalogna M, Sasson E, Hadanny A, Parag Y, Zilberman-Itskovich S, Efrati S. Effects of hyperbaric oxygen therapy on functional and structural connectivity in post-COVID-19 condition patients: A randomized, sham-controlled trial. NeuroImage Clinical. 2022;36:103218-.	pre July 2024
Duffy A, Naimi B, Garvey E, Hunter S, Kumar A, Kahn C, et al. Topical platelet-rich plasma as a possible treatment for olfactory dysfunction—A randomized controlled trial. International Forum of Allergy & Rhinology. 2024.	pre July 2024
Evman M, Cetin Z. Effectiveness of platelet-rich plasma on post-COVID chronic olfactory dysfunction. Revista da Associacao Medica Brasileira (1992). 2023;69:e20230666.	pre July 2024

He Y, Liu X, Zha S, Wang Y, Zhang J, Zhang Q, et al. A pilot randomized controlled trial of major ozone autohemotherapy for patients with post-acute sequelae of COVID-19. 2024;139.	July 2024
Klířová M, Adamová A, Biačková N, Laskov O, Renková V, Stuchlířková Z, et al. Transcranial direct current stimulation (tDCS) in the treatment of neuropsychiatric symptoms of long COVID. Sci Rep. 2024;14(1):2193.	pre July 2024
Lee M, Zulbaran-Rojas A, Bargas-Ochoa M, Martinez-Leal B, Bara R, Flores-Camargo A, et al. Gastrocnemius electrical stimulation increases ankle dorsiflexion strength in patients with post-acute sequelae of SARS-COV-2 (PASC): a double-blind randomized controlled trial. Sci Rep. 2024;14(1):17939.	August 2024
Leitman M, Fuchs S, Tyomkin V, Hadanny A, Zilberman-Itskovich S, Efrati S. The effect of hyperbaric oxygen therapy on myocardial function in post-COVID-19 syndrome patients: a randomized controlled trial. Scientific reports. 2023;13:9473.	pre July 2024
Oliver-Mas S, Delgado-Alonso C, Delgado-Álvarez A, Díez-Cirarda M, Cuevas C, Fernández-Romero L, et al. Transcranial direct current stimulation for post-COVID fatigue: a randomized, double-blind, controlled pilot study. Brain Commun. 2023;5(2):fcad117.	pre July 2024
Orlova EV, Lyamina NP, Skorobogatyth NV, Pogonchenkova IV. Clinical Efficacy of Individually Dosed Intermittent Hypoxia-Hyperoxic Therapy in Osteoarthritis Patients with Post-Covid Syndrome. Bulletin of Rehabilitation Medicine. 2022;21(2):6-16.	pre July 2024
Santana K, França E, Sato J, Silva A, Queiroz M, de Farias J, et al. Non-invasive brain stimulation for fatigue in post-acute sequelae of SARS-CoV-2 (PASC). Brain Stimul. 2023;16(1):100-7.	pre July 2024
Shogenova LV, Truong TT, Kryukova NO, Yusupkhodzhaeva KA, Pozdnyakova DD, Kim TG, et al. Hydrogen inhalation in rehabilitation program of the medical staff recovered from COVID-19. Cardiovascular Therapy and Prevention. 2021;20(6).	pre July 2024
Soldatenko AA, Gumenyuk LN, Berdieva DM, Ponomarchuk EI. Effectiveness of enriching drug treatment with systemic ozone therapy in patients with post-COVID asthenic syndrome. Bulletin of Russian State Medical University. 2024(2024(4)).	September 2024

Yan CH, Jang SS, Lin HC, Ma Y, Khanwalkar AR, Thai A, et al. Use of platelet-rich plasma for COVID-19-related olfactory loss: a randomized controlled trial. Int Forum Allergy Rhinol. 2023;13(6):989-97.	pre July 2024
Zha S, Liu X, Yao Y, He Y, Wang Y, Zhang Q, et al. Short-term intermittent hypoxia exposure for dyspnea and fatigue in post-acute sequelae of COVID-19: A randomized controlled study. Respir Med. 2024;232:107763.	August 2024
Zilberman-Itskovich S, Catalogna M, Sasson E, Elman-Shina K, Hadanny A, Lang E, et al. Hyperbaric oxygen therapy improves neurocognitive functions and symptoms of post-COVID condition: randomized controlled trial. Sci Rep. 2022;12(1):11252.	pre July 2024
Zulbaran-Rojas A, Lee M, Bara R, Flores-Camargo A, Spitz G, Finco M, et al. Electrical stimulation to regain lower extremity muscle perfusion and endurance in patients with post-acute sequelae of SARS CoV-2: A randomized controlled trial. Physiological reports. 2023;11:e15636.	pre July 2024
Complementary n=8	
Bérubé S, Demers C, Bussière N, Cloutier F, Pek V, Chen A, et al. Olfactory Training Impacts Olfactory Dysfunction Induced by COVID-19: A Pilot Study. ORL J Otorhinolaryngol Relat Spec. 2023;85(2):57-66.	pre July 2024
Bhandari R. Online Yoga and Ayurveda Intervention as Tertiary Prevention of Psychological Comorbidities in COVID-19 Survivors: A Randomized Controlled Trial. Annals of neurosciences. 2022;29:233-44.	pre July 2024
Crucianelli S, Mariano A, Valeriani F, et al. Effects of sulphur thermal water inhalations in long-COVID syndrome: Spa-centred, double-blinded, randomised case-control pilot study. Vol. 24.100251. Clinical medicine (London, England). 2024 Oct 5.	October 2024psychia
Hawkins J, Hires C, Keenan L, Dunne E. Aromatherapy blend of thyme, orange, clove bud, and frankincense boosts energy levels in post-COVID-19 female patients: A randomized, double-blinded, placebo controlled clinical trial. Complement Ther Med. 2022;67:102823.	pre July 2024

<p>Khan AM, Piccirillo J, Kallogjeri D, Piccirillo JF. Efficacy of Combined Visual-Olfactory Training With Patient-Preferred Scents as Treatment for Patients With COVID-19 Resultant Olfactory Loss: A Randomized Clinical Trial. JAMA Otolaryngol Head Neck Surg. 2023;149(2):141-9.</p>	<p>pre July 2024</p>
<p>Rana A, Bhattacharya P, Ganguly S, Saha S, Naskar S, Ghosh S, et al. Individualized Homeopathic Medicinal Products in the Treatment of Post-COVID-19 Conditions: A Double-Blind, Randomized, Placebo-Controlled, Feasibility Trial. J Integr Complement Med. 2024.</p>	<p>September 2024</p>
<p>Saha S, Singh R, Mani I, Chakraborty K, Sarkar P, Rana A, et al. Individualized Homeopathic Medicines in the Treatment of Post-COVID-19 Fatigue in Adults: Single-Blind, Randomized, Placebo-Controlled Trial. Complement Med Res. 2024;31(1):1-9.</p>	<p>pre July 2024</p>
<p>Sumbalová Z, Kucharská J, Rausová Z, Palacka P, Kovalčíková E, Takácsová T, et al. Reduced platelet mitochondrial respiration and oxidative phosphorylation in patients with post COVID-19 syndrome are regenerated after spa rehabilitation and targeted ubiquinol therapy. Front Mol Biosci. 2022;9:1016352</p>	<p>pre July 2024</p>
<p>Behavioural n=8</p>	
<p>Armstrong M, Owen R, Van Niekerk KS, Saynor ZL. Personalised Health Behaviour Support Programme in Adults With Post-COVID Syndrome: A Randomised, Controlled Pilot Feasibility Trial. Vol. 27.e70079. Health expectations : an international journal of public participation in health care and health policy. 2024 Oct.</p>	<p>October 2024</p>
<p>González-Moreno J, Pozuelo C, Manos D, Gómez-Martínez S, Cantero-García M. A third generation therapies approach in long covid patients: Efficacy of an intervention program with spanish adults. Current Psychology: A Journal for Diverse Perspectives on Diverse Psychological Issues. 2024.</p>	<p>pre July 2024</p>

Kuut T, Müller F, Csorba I, Braamse A, Aldenkamp A, Appelman B, et al. Efficacy of Cognitive-Behavioral Therapy Targeting Severe Fatigue Following Coronavirus Disease 2019: Results of a Randomized Controlled Trial. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2023;77:687-95.	pre July 2024
Navas-Otero A, Calvache-Mateo A, Calles-Plata I, Valenza-Peña G, Hernández-Hernández S, Ortiz-Rubio A, et al. A lifestyle adjustments program in long COVID-19 improves symptomatic severity and quality of life. A randomized control trial. Patient Educ Couns. 2024;122:108180.	pre July 2024
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. Lancet Respir Med. 2022;10(9):851-62.	pre July 2024
Shatri H, Sinulingga DI, Rumende CM, Setiati S, Putranto R, Ginanjar E, et al. Effectiveness of Internet-Based Group Supportive Psychotherapy on Psychic and Somatic Symptoms, Neutrophil-Lymphocyte Ratio, and Heart Rate Variability in Post COVID-19 Syndrome Patients. Acta Med Indones. 2023;55(4):411-20.	pre July 2024
Toussaint LL, Bratty AJ. Amygdala and Insula Retraining (AIR) Significantly Reduces Fatigue and Increases Energy in People with Long COVID. Evid Based Complement Alternat Med. 2023;2023:7068326.	pre July 2024
Uswatte G, Taub E, Ball K, Mitchell BS, Blake JA, McKay S, et al. Long COVID Brain Fog Treatment: findings from a Pilot Randomized Controlled Trial of Constraint-Induced Cognitive Therapy. 2024.	July 2024
Diet and Dietary n=21	
Abdelazim MH, Alsenani F, Alnuhait M, Alshammari AS, Altemani AH, Althagafi EA, et al. Efficacy of forskolin as a promising therapy for chronic olfactory dysfunction post COVID-19. 2024.	July 2024

<p>Brichetti V, Rubilar T, Tejada JV, Montecino P, Crespi-Abril AC, Barbieri ES, et al. EuroQol-5D-3L in Long Covid patients After Supplementation with Echa Marine, a Sea Urchin Eggs Extract: a double-blinded, multicentric study. medRxiv. 2023.</p>	<p>pre July 2024</p>
<p>Cantone E, D'Ascanio L, De Luca P, Roccamatisi D, La La Mantia I, Brenner M, et al. Persistent COVID-19 parosmia and olfactory loss post olfactory training: randomized clinical trial comparing central and peripheral-acting therapeutics. European archives of oto-rhino-laryngology : official journal of the European Federation of Oto-Rhino-Laryngological Societies (EUFOS) : affiliated with the German Society for Oto-Rhino-Laryngology - Head and Neck Surgery. 2024.</p>	<p>pre July 2024</p>
<p>Charoenporn V, Tungasukruthai P, Teacharushatakit P, Hanvivattanakul S, Sriyakul K, Sukprasert S, et al. Effects of an 8-week high-dose vitamin D supplementation on fatigue and neuropsychiatric manifestations in post-COVID syndrome: A randomized controlled trial. Psychiatry and Clinical Neurosciences. 2024</p>	<p>July 2024</p>
<p>Chung T, Zhang H, Wong F, Sridhar S, Lee T, Leung G, et al. A Pilot Study of Short-Course Oral Vitamin A and Aerosolised Diffuser Olfactory Training for the Treatment of Smell Loss in Long COVID. Brain sciences. 2023;13:1014-.</p>	<p>pre July 2024</p>
<p>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.</p>	<p>pre July 2024</p>
<p>De Luca P, Camaioni A, Marra P, Salzano G, Carriere G, Ricciardi L, et al. Effect of Ultra-Micronized Palmitoylethanolamide and Luteolin on Olfaction and Memory in Patients with Long COVID: Results of a Longitudinal Study. Cells. 2022;11(16):2552-.</p>	<p>pre July 2024</p>
<p>Di Stadio A, Cantone E, De Luca P, Di Nola C, Massimilla E, Motta G, et al. Parosmia COVID-19 Related Treated by a Combination of Olfactory Training and Ultramicronized PEA-LUT: A Prospective Randomized Controlled Trial. Biomedicines. 2023;11:1109-.</p>	<p>pre July 2024</p>
<p>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;20(10):2001-12.</p>	<p>pre July 2024</p>

<p>Di Stadio A, Gallina S, Cocuzza S, De Luca P, Ingrassia A, Oliva S, et al. Treatment of COVID-19 olfactory dysfunction with olfactory training, palmitoylethanolamide with luteolin, or combined therapy: a blinded controlled multicenter randomized trial. European archives of oto-rhino-laryngology : official journal of the European Federation of Oto-Rhino-Laryngological Societies (EUFOS) : affiliated with the German Society for Oto-Rhino-Laryngology - Head and Neck Surgery. 2023;280:4949-61.</p>	pre July 2024
<p>Figueiredo L, Paim P, Cerqueira-Silva T, Barreto C, Lessa M. Alpha-lipoic acid does not improve olfactory training results in olfactory loss due to COVID-19: a double-blind randomized trial. Brazilian journal of otorhinolaryngology. 2023;90:101356-.</p>	pre July 2024
<p>Finnigan LEM, Cassar MP, Koziel MJ, Pradines J, Lamum H, Azer K, et al. Efficacy and tolerability of an endogenous metabolic modulator (AXA1125) in fatigue-predominant long COVID: a single-centre, double-blind, randomised controlled phase 2a pilot study. EClinicalMedicine. 2023;59:101946.</p>	pre July 2024
<p>Hansen KS, Mogensen TH, Agergaard J, Schiøttz-Christensen B, Østergaard L, Vibholm LK, et al. High-dose coenzyme Q10 therapy versus placebo in patients with post COVID-19 condition: a randomized, phase 2, crossover trial. Lancet Reg Health Eur. 2023;24:100539.</p>	pre July 2024
<p>Lau RI, Su Q, Lau ISF, Ching JYL, Wong MCS, Lau LHS, et al. A synbiotic preparation (SIM01) for post-acute COVID-19 syndrome in Hong Kong (RECOVERY): a randomised, double-blind, placebo-controlled trial. Lancet Infect Dis. 2024;24(3):256-65.</p>	pre July 2024
<p>Lerner D, Garvey K, Arrighi-Allisan A, Kominsky E, Filimonov A, Al-Awady A, et al. Omega-3 Fatty Acid Supplementation for the Treatment of Persistent COVID-Related Olfactory Dysfunction. American journal of rhinology & allergy. 2023;37:531-40.</p>	pre July 2024
<p>Lukkunaprasit T, Satapornpong P, Kulchanawichien P, et al. Impact of combined plant extracts on long COVID: An exploratory randomized controlled trial.:103107. Complementary therapies in medicine. 2024 Oct 31.</p>	October 2024
<p>Marinoni B, Rimondi A, Bottaro F, Ciafardini C, Amoroso C, Muià M, et al. The Role of VSL#3® in the Treatment of Fatigue and Other Symptoms in Long Covid-19 Syndrome: a Randomized, Double-blind, Placebo-controlled Pilot Study (DELong#3). 2023.</p>	pre July 2024

<p>Redel AL, Miry F, Hellemons ME, Oswald LMA, Braunstahl GJ. Effect of lactoferrin treatment on symptoms and physical performance in long COVID patients: a randomised, double-blind, placebo-controlled trial. ERJ Open Res. 2024;10(4).</p>	<p>July 2024</p>
<p>Slankamenac J, Ranisavljev M, Todorovic N, Ostojic J, Stajer V, Ostojic SM. Creatine supplementation combined with breathing exercises reduces respiratory discomfort and improves creatine status in patients with long-COVID. J Postgrad Med. 2024;70(2):101-104. doi:10.4103/jpgm.jpgm_650_23</p>	<p>pre July 2024</p>
<p>Tosato M, Calvani R, Picca A, Ciciarello F, Galluzzo V, Coelho-Júnior HJ, et al. Effects of L-Arginine Plus Vitamin C Supplementation on Physical Performance, Endothelial Function, and Persistent Fatigue in Adults with Long COVID: A Single-Blind Randomized Controlled Trial. Nutrients. 2022;14(23).</p>	<p>pre July 2024</p>
<p>Versace V, Ortelli P, Dezi S, Ferrazzoli D, Alibardi A, Bonini I, et al. Co-ultramicrosized palmitoylethanolamide/luteolin normalizes GABA(B)-ergic activity and cortical plasticity in long COVID-19 syndrome. Clin Neurophysiol. 2023;145:81-8.</p>	<p>pre July 2024</p>
<p>Pharmacological interventions n=21</p>	
<p>Abdelazim MH, Abdelazim AH. Effect of Sodium Gluconate on Decreasing Elevated Nasal Calcium and Improving Olfactory Function Post COVID-19 Infection. Am J Rhinol Allergy. 2022;36(6):841-8.</p>	<p>pre July 2024</p>
<p>Abdelazim MH, Abdelazim AH, Moneir W. The effect of intra-nasal tetra sodium pyrophosphate on decreasing elevated nasal calcium and improving olfactory function post COVID-19: a randomized controlled trial. Allergy Asthma Clin Immunol. 2022;18(1):67.</p>	<p>pre July 2024</p>

Abdelazim MH, Mandour Z, Abdelazim AH, Ismaiel WF, Gamal M, Abourehab MAS, et al. Intra Nasal Use of Ethylene Diamine Tetra Acetic Acid for Improving Olfactory Dysfunction Post COVID-19. Am J Rhinol Allergy. 2023;37(6):630-7.	pre July 2024
Altemani A, Alanazi M, Altemani A, Alharbi A, Alsaahli S, Alotaib N, et al. 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: A Prospective Randomized Double-Controlled Clinical Trial. American journal of rhinology & allergy. 2023;38:116-22.	pre July 2024
Andrews JS, Boonyaratanakornkit JB, Krusinska E, Allen S, Posada JA. Assessment of the Impact of RNase in Patients With Severe Fatigue Related to Post-Acute Sequelae of SARS-CoV-2 Infection (PASC): A Randomized Phase 2 Trial of RSLV-132. Clin Infect Dis. 2024.	pre July 2024
Dal Negro R, Turco P, Povero M. Nebivolol: an effective option against long-lasting dyspnoea following COVID-19 pneumonia - a pivotal double-blind, cross-over controlled study. Multidisciplinary respiratory medicine. 2022;17:886.	pre July 2024
Gaylis NB, Ritter A, Kelly SA, Pourhassan NZ, Tiwary M, Sacha JB, et al. Reduced Cell Surface Levels of C-C Chemokine Receptor 5 and Immunosuppression in Long Coronavirus Disease 2019 Syndrome. Clin Infect Dis. 2022;75(7):1232-4.	pre July 2024
Geng LN, Bonilla H, Hedlin H, Jacobson KB, Tian L, Jagannathan P, et al. Nirmatrelvir-Ritonavir and Symptoms in Adults With Postacute Sequelae of SARS-CoV-2 Infection: The STOP-PASC Randomized Clinical Trial. JAMA Intern Med. 2024.	July 2024
Gupta S, Lee JJ, Perrin A, Khan A, Smith HJ, Farrell N, et al. Efficacy and Safety of Saline Nasal Irrigation Plus Theophylline for Treatment of COVID-19-Related Olfactory Dysfunction: The SCENT2 Phase 2 Randomized Clinical Trial. JAMA Otolaryngol Head Neck Surg. 2022;148(9):830-7.	pre July 2024
Guttuso T, Jr., Zhu J, Wilding GE. Lithium Aspartate for Long COVID Fatigue and Cognitive Dysfunction: A Randomized Clinical Trial. JAMA Netw Open. 2024;7(10):e2436874.	September 2024

Hamed S, Ahmed M. The effectiveness of cerebrolysin, a multi-modal neurotrophic factor, for treatment of post-covid-19 persistent olfactory, gustatory and trigeminal chemosensory dysfunctions: a randomized clinical trial. Expert review of clinical pharmacology. 2023;16:1261-76.	pre July 2024
Hintschich CA, Dietz M, Haehner A, Hummel T. Topical Administration of Mometasone Is Not Helpful in Post-COVID-19 Olfactory Dysfunction. Life (Basel). 2022;12(10).	pre July 2024
Imam MS, Abdelazim MH, Abdelazim AH, Ismaiel WF, Gamal M, Abourehab MAS, et al. Efficacy of pentasodium diethylenetriamine pentaacetate in ameliorating anosmia post COVID-19. Am J Otolaryngol. 2023;44(4):103871.	pre July 2024
Kerget B, Çil G, Araz Ö, Alper F, Akgün M. Comparison of two antifibrotic treatments for lung fibrosis in post-COVID-19 syndrome: A randomized, prospective study. Medicina clinica (English ed). 2023;160:525-30.	pre July 2024
Kwan ATH, Guo Z, Ceban F, Le GH, Wong S, Teopiz KM, et al. Assessing the Effects of Metabolic Disruption, Body Mass Index and Inflammation on Depressive Symptoms in Post-COVID-19 Condition: A Randomized Controlled Trial on Vortioxetine. Adv Ther. 2024;41(5):1983-94.	pre July 2024
Lasheen H, Abou-Zeid M. Olfactory mucosa steroid injection in treatment of post-COVID-19 olfactory dysfunction: a randomized control trial. The Egyptian Journal of Otolaryngology. 2023;39.	pre July 2024
Mahadev A, Hentati F, Miller B, Bao J, Perrin A, Kallogjeri D, et al. Efficacy of Gabapentin For Post-COVID-19 Olfactory Dysfunction: The GRACE Randomized Clinical Trial. JAMA otolaryngology-- head & neck surgery. 2023;149:1111-.	pre July 2024
McIntyre RS, Phan L, Kwan ATH, Mansur RB, Rosenblat JD, Guo Z, et al. Vortioxetine for the treatment of post-COVID-19 condition: a randomized controlled trial. Brain. 2024;147(3):849-57.	pre July 2024

<p>Schmidt F, Azar C, Goektas O. Treatment of Olfactory Disorders After SARS - CoViD 2 Virus Infection. Ear, nose, & throat journal. 2023;1455613231168487-014556132311684.</p>	<p>pre July 2024</p>
<p>Tanashyan M, Morozova S, Raskurazhev A, Kuznetsova P. A prospective randomized, double-blind placebo-controlled study to evaluate the effectiveness of neuroprotective therapy using functional brain MRI in patients with post-covid chronic fatigue syndrome. Biomed Pharmacother. 2023;168:115723.</p>	<p>pre July 2024</p>
<p>Tanashyan MM, Raskurazhev AA, Kuznetsova PI, Bely PA, Zaslavskaya KI. [Prospects and possibilities for the treatment of patients with long COVID-19 syndrome]. Ter Arkh. 2022;94(11):1285-93.</p>	<p>pre July 2024</p>