NIHR Policy Research Programme Reviews Facility

To support national policy development and implementation

Reviews on Long COVID

A scope of the literature: update



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Reviews on Long COVID: A scope of the literature Update April 2022

Raine G, Sutcliffe K, Sowden A

April 2022

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Aim

For this update we identified systematic reviews and review protocols focused on Long COVID that were published between November 2021 and the end of March 2022. The term Long COVID was conceptualised broadly as any symptoms/effects that persist or develop after acute COVID-19 infection.

Identification of reviews

No changes were made to the sources searched for this update, but the search strategy adopted was more comprehensive than in our original scoping exercise as we incorporated a greater number of key terms that have been used in previous research to describe symptoms persisting beyond the acute stage of COVID infection. Searches were date restricted to the time frame of interest. The three main sources we searched were:

1) PROSPERO database. (An International prospective register of systematic reviews). This was searched using the terms long COVID, post COVID, Post-acute COVID and long term COVID. Records tagged as Long COVID in the database were also screened.

2) Our living systematic map of Long COVID-19 evidence maintained by staff at the London-York NIHR Policy Reviews Facility.

3) PubMed. We first searched PubMed for key terms in the title or abstract fields and then applied the PubMed filter for 'systematic reviews' and 'meta-analysis'. A second search was also conducted to identify records with Long COVID related terms in the title or abstract fields and the words 'review' or 'meta-analysis' in the title. The PubMed search strategy is provided in Appendix 1 (page 25).

The inclusion criteria applied to reviews in this update were consistent with our original scoping work. To be included, reviews needed to have a primary focus on Long COVID (however conceptualised and defined). Reviews could focus on adults and/or children and include primary studies of any design or other reviews (i.e. reviews of reviews). We included any form of systematic review. A review was considered systematic in nature if it reported some search terms and inclusion criteria and also reported the number of references retrieved and the number of studies included. We did not apply criteria relating to the length of the time period after acute infection owing to variation in how Long COVID has been defined in the literature. Reviews were only included if the full text was readily available.

Key findings

We screened approximately 398 records and identified **54 published reviews; five other reviews that have been completed since November 2021 but not yet published; and 73 new protocols for ongoing reviews.** Table 1 (page 2) provides a summary of all reviews identified for this update by publication type and focus. The full reference and aim/research questions for all completed and ongoing reviews are provided on pages 2-24. All reviews identified from our initial scope of the literature are also listed in Appendix 2 (page 26).

Review status	Review of	Living review	Systematic
Main focus of interest	review		review
Published			
Treatment/rehabilitation		3	8
Risk factors & Pathobiology			5
Symptoms/effects	2	1	35
Completed not yet published			
Treatment/rehabilitation			1
Symptoms/effects			4
Ongoing			
Treatment/rehabilitation			17
Prevention			4
Risk factors & Pathobiology			5
Symptoms/effects	2		45

Table 1: Summary of reviews published between November 2021-March 2022

As Table 1 shows, most of the published and ongoing reviews that we identified for this update focused on prevalence and the risk of persistent symptoms/effects. However, we did also identify multiple published reviews related to treatment/rehabilitation (n=11). A sizeable number of protocols for new reviews on treatment/rehabilitation (n=17) have been registered on PROSPERO since November 2021.

Four out of the 11 published reviews related to treatment/rehabilitation focused on pulmonary rehabilitation, physiotherapy, or some form of physical activity. Another review examined best practice for GP management of Long COVID (#6 Brennan et al., 2022). Similarly, a review part funded by the Alberta Health Service and Canadian Institutes for Health Research sought to identify the best-available evidence on care models for individuals living with Long COVID (#9 Décary et al., 2021). Another review synthesised qualitative data in order to explore the lived experiences of people with Long COVID and how they perceive the healthcare services available to them (#40 Macpherson et al., 2022).

1) Reviews published between November 2021 and March 2022

Treatment & rehabilitation

Living review

1. Godbolt et al. Post COVID - treatment and rehabilitation. Living review.

Aim: To summarize published scientific articles addressing the following research question: Which treatments are effective for post COVID-19?

This living review was commissioned by the Swedish government and is published online with an accompanying evidence map. <u>https://www.sbu.se/en/publications/sbu-bereder/post-covid-19--effective-treatment-and-rehabilitation-living-review/</u>

 Andrenelli et al. International Multiprofessional Steering Committee of Cochrane Rehabilitation REH-COVER action. Rehabilitation and COVID-19: update of the rapid living systematic review by Cochrane Rehabilitation Field as of October 31st, 2021. Eur J Phys Rehabil Med. 2022; 58(1):153-156. <u>https://doi.org/10.23736/S1973-9087.22.07434-2</u> Aim: To collate, critically appraise, and synthesize current best evidence relevant to the rehabilitation of patients with COVID-19, the consequences of the disease, and its treatment.

NB: This paper was a brief update of a living systematic review that did not meet our inclusion criteria as it only reported limited methodological detail. However, as previous papers reporting on the living review met our criteria in full, we included the update.

 Negrini et al. International Multiprofessional Steering Committee of Cochrane Rehabilitation REH-COVER action. Rehabilitation and COVID-19: update of the rapid living systematic review by Cochrane Rehabilitation Field as of December 31st, 2021. Eur J Phys Rehabil Med. 2022; <u>http://doi.org/10.23736/S1973-9087.22.07497-4</u>

Aim: To collate, critically appraise, and synthesize current best evidence relevant to the rehabilitation of patients with COVID-19, the consequences of the disease, and its treatment.

NB: This paper was a brief update of a living systematic review that did not meet our inclusion criteria as it only reported limited methodological detail. However, as previous papers reporting on the living review met our criteria in full, we included the update.

Standard systematic reviews

 Ahmadi Hekmatikar et al. Functional and Psychological Changes after Exercise Training in Post-COVID-19 Patients Discharged from the Hospital: A PRISMA-Compliant Systematic Review. Int. J. Environ. Res. Public Health. 2022; 19:2290. <u>https://doi.org/10.3390/ijerph19042290</u>

Aim: To evaluate the effect of resistance or aerobic exercises in post-COVID-19 patients after hospital discharge.

 Barros et al. Atuação da fisioterapia respiratória em pacientes pós COVID-19: Uma revisão sistemática / Performance of respiratory physiotherapy in post-COVID-19 patients: A systematic review. Brazilian Journal of Health Review. 2021; 4(6):24663-24675. <u>https://doi.org/10.34119/bjhrv4n6-084</u>

Aim: To search the literature for studies on the role of respiratory physiotherapy in post COVID patients.

 Brennan et al. Enhancing the management of long COVID in general practice: a scoping review. BJGP Open. 2022; BJGPO.2021.0178. <u>https://doi.org/10.3399/BJGPO.2021.0178</u>

Aim: To provide a comprehensive account of existing research around best practice for GP management of patients with long COVID.

 Ceban et al. Registered clinical trials investigating treatment of long COVID: a scoping review and recommendations for research. Infect Dis. 2022; 14:1-11. <u>https://doi.org/10.1080/23744235.2022.2043560</u>

Aim: To provide a scope of the candidate treatments for long COVID.

 Chen et al. Effect of Pulmonary Rehabilitation for Patients with Post-COVID-19: A Systematic Review and Meta-Analysis. Front Med. 2022; 9:837420. <u>https://doi.org/10.3389/fmed.2022.837420</u>

Aim: To conduct a systematic review and meta-analysis to evaluate the effect of pulmonary rehabilitation on lung impairment for patients with post-COVID-19.

 Décary et al. Care Models for Long COVID - A Rapid Systematic Review. 2021. SPOR Evidence Alliance, COVID-END Network. https://www.medrxiv.org/content/10.1101/2021.11.17.21266404v1

Aim: To provide the best available evidence about care models for persons living with long COVID.

NB: In the PROSPERO record, this review is described as 'living' with update searches planned in one year's time. However, when published, it was only described as a living review in the abstract. There was no further detail in the main body of text and no information given about future updates. Therefore, the status of this review is currently unclear.

 Soril et al. The effectiveness of pulmonary rehabilitation for Post-COVID symptoms: A rapid review of the literature. Respir Med. 2022; 195:106782. <u>https://doi.org/10.1016/j.rmed.2022.106782</u>

Aim: To determine the clinical effectiveness of pulmonary rehabilitation for individuals with post-COVID symptoms.

11. Yelin al., ESCMID rapid guidelines for assessment and management of long COVID. Clinical Microbiology and Infection. <u>https://doi.org/10.1016/j.cmi.2022.02.018</u>

Aim: To provide evidence-based recommendations for the assessment and management of individuals with persistent symptoms after acute COVID-19 infection and to provide a definition for Long COVID.

Risk factors and Pathobiology

 Bergantini et al. Common Molecular Pathways Between Post-COVID19 Syndrome and Lung Fibrosis: A Scoping Review. Front Pharmacol. 2022; 13:748931. <u>http://doi.org/10.3389/fphar.2022.748931</u>

Aim: To identify and systematize the main pathogenetic mechanisms that are believed to be involved in post-Covid-19 pulmonary fibrosis.

NB: Review includes both empirical and non-empirical publications.

13. Maglietta et al. Prognostic Factors for Post-COVID-19 Syndrome: A Systematic Review and Meta-Analysis. J Clin Med. 2022; 11(6):1541. <u>https://doi.org/10.3390/jcm11061541</u>

Aim: To identify factors present during COVID-19 hospitalization associated with an increased risk of exhibiting new or persisting symptoms.

14. Pierce et al. Post-COVID-19 Syndrome. Nur Res. 2022; 71(2):164-174. https://doi.org/10.1097/NNR.00000000000565

Aim: To summarize and evaluate post-COVID-19 syndrome from a biological perspective.

 Pillay et al. Risk factors and preventive interventions for post Covid-19 condition: systematic reviews medRxiv. 2022; 2022.03.25.22272949. <u>https://doi.org/10.1101/2022.03.25.22272949</u>

Aim: To systematically identify and synthesize evidence around pre-existing and clinical risk factors for post COVID-19 condition (occurring ≥12 weeks after positive test/symptom onset), and interventions during the acute and post-acute phases of the illness that could potentially prevent post COVID-19 condition.

 Thongtan et al. De novo inflammatory bowel disease is a potential post-acute sequela of SARS-CoV-2 infection. The Southwest Respiratory and Critical Care Chronicles. 2021; 9(41):35-39. <u>https://doi.org/10.12746/swrccc.v9i41.913</u>

Aim: To review the current evidence on the potential pathophysiology behind the emergence of de novo IBD following acute SARS-CoV-2 infection.

Symptoms/effects

Review of reviews

 Alhumayn et al. A systematic review of the systematic review of post COVID-19 syndrome. The Journal of Medicine, Law & Public Health. 2022; 2(1):64–69. <u>https://doi.org/10.52609/jmlph.v2i1.33</u>

Aim: To explore the symptoms of post-COVID-19 and the predictors for its development.

18. Nittas et al. Long COVID Through a Public Health Lens: An Umbrella Review. Public Health Rev. 2022; 43:1604501. <u>https://doi.org/10.3389/phrs.2022.1604501</u>

Aim: To synthesize existing evidence on prevalence as well as clinical and socioeconomic aspects of long COVID.

NB: This review adopted a two-stage methodology consisting of an umbrella review and a targeted evidence synthesis of the included primary studies.

Living Review

19. Li et al. Symptoms after the acute phase of COVID-19 vs in COVID-19 negative controls – a living systematic review. [Symtom efter den akuta fasen av COVID-19 vs rapporterade av covid-19 negativa controller – en levande systematisk översikt]. Centre for Assessment of Medical Technology, 2022. Örebro https://www.regionorebrolan.se/contentassets/7480ad2d4b024d4f892eea63c8cb130f/202

Aim: To map symptoms in patients after the acute phase of COVID-19 in the form of a live systematic overview and compare with COVID-19 negative controls.

NB: Report in Swedish.

Standard systematic reviews

 Ahmed et al. Post COVID-19 neurological complications; a meta-analysis. Ann Med Surg. 2022; 76:103440. <u>https://doi.org/10.1016/j.amsu.2022.103440</u>.

Aim: To present a quantitative meta-analysis of published studies regarding the post-infectious neurological complications of COVID-19.

21. Alkodaymi et al. Prevalence of post-acute COVID-19 syndrome symptoms at different followup periods: a systematic review and meta-analysis. Clin Microbiol Infect. 2022. <u>https://doi.org/10.1016/j.cmi.2022.01.014</u>

Aim: To estimate the prevalence of persistent symptoms and signs at least 12 weeks after acute COVID-19 at different follow-up periods.

22. Azab et al. Optic neuritis post-COVID-19 infection. A case report with meta-analysis. Interdiscip Neurosurg. 2021; 26:101320. <u>https://doi.org/10.1016/j.inat.2021.101320</u>

Aim: To report a case manifested with optic neuritis post-COVID-19 infection, in addition to presenting a quantitative analysis (meta-analysis) for the published similar case reports around the world.

23. Badenoch et al. Persistent neuropsychiatric symptoms after COVID-19: a systematic review and meta-analysis. Brain Commun. 2022; 4(1):fcab297 https://doi.org/10.1093/braincomms/fcab297

Aim: To estimate the prevalence of neuropsychiatric symptoms in survivors of COVID-19.

NB: Published previously as pre-print.

24. Bourmistrova et al. Long-term effects of COVID-19 on mental health: A systematic review. J Affect Disord. 2022; 299:118-125. <u>https://doi.org/10.1016/j.jad.2021.11.031</u>

Aim: To investigate the effect of COVID-19 infection on long-term mental health outcomes.

25. Boutou et al. Changes in the respiratory function of COVID-19 survivors during follow-up: A novel respiratory disorder on the rise? Int J Clin Pract. 2021; 75(10):e14301. https://doi.org/10.1111/ijcp.14301

Aim: To investigate the incidence and type of respiratory function abnormalities during the follow-up of patients who recovered from COVID-19.

26. Ceban et al. Fatigue and cognitive impairment in Post-COVID-19 Syndrome: A systematic review and meta-analysis. Brain Behav Immun. 2022; 101:93-135. https://doi.org/10.1016/j.bbj.2021.12.020

Aim: To quantify the proportion of individuals experiencing fatigue and cognitive impairment 12 or more weeks following COVID-19 diagnosis, and to characterize the inflammatory correlates and functional consequences of post-COVID-19 syndrome.

27. Cha C, Baek G. Symptoms and management of long COVID: A scoping review. J Clin Nurs. 2021. Dec 15. <u>https://doi.org/10.1111/jocn.16150</u>

Aim: To explore the extent and nature of symptoms and suggest management of long COVID.

28. Crivelli et al. Changes in cognitive functioning after COVID-19: A systematic review and metaanalysis. Alzheimers Dement. 2022; Mar 17. <u>https://doi.org/10.1002/alz.12644</u>

Aim: To assess whether there is an increased occurrence of cognitive deficits in adult patients with COVID-19 who previously had no cognitive impairment.

29. Dorri et al. Psychological problems and reduced health-related quality of life in COVID-19 survivors. J Affect Disord Rep. 2021; 6:100248. <u>https://doi.org/10.1016/j.jadr.2021.100248</u>

Aim: To summarize the available evidence on the reduced HRQoL and the prevalence of psychiatric problems, including PTSD, depression and anxiety, and HRQoL among COVID-19 survivors.

 Fabbri et al. Parenchymal lung abnormalities following hospitalisation for COVID-19 and viral pneumonitis: a systematic review and meta-analysis. Thorax. 2022 Mar 25:thoraxjnl-2021-218275. <u>https://doi.org/10.1136/thoraxjnl-2021-218275</u>

Aim: To assess the proportion of chest CT scans and pulmonary function tests consistent with parenchymal lung disease in the follow-up of people hospitalised with COVID-19 and viral pneumonitis.

31. Fajar et al. Global prevalence of persistent neuromuscular symptoms and the possible pathomechanisms in COVID-19 recovered individuals: A systematic review and metaanalysis. Narra J. 2021; 1(3): e48. <u>https://doi.org/10.52225/narra.v1i3.48</u>

Aim: To address (a) the global estimated prevalence of prolonged neuromuscular symptoms (fatigue, anosmia, headache, myalgia, and joint pain) in recovered COVID-19 patients and (b) the association of COVID-19 severity with prolonged neuromuscular symptoms.

32. Figueiredo et al. The health-related quality of life in patients with post-COVID-19 after hospitalization: a systematic review. Rev Soc Bras Med Trop. 2022; 55:e0741. https://doi.org/10.1590/0037-8682-0741-2021 Aim: To systematically discuss the main findings of HRQoL in patients post-COVID-19 that required hospitalization.

 Fiore et al. Musculoskeletal pain related to COVID-19 survivors after hospitalization: A short review. (Dolor musculoesquelético en supervivientes del COVID-19 tras la hospitalización: Una breve revision). Retos. 2022; 45:789-795. <u>https://doi.org/10.47197/retos.v44i0.90361</u>

Aim: To review the literature on the characterization and impact of musculoskeletal pain in COVID-19 survivors.

NB: paper in English.

34. Han et al. A. Long-Term Sequelae of COVID-19: A Systematic Review and Meta-Analysis of One-Year Follow-Up Studies on Post-COVID Symptoms. Pathogens. 2022; 11(2):269. <u>https://doi.org/10.3390/pathogens11020269</u>

Aim: To systematically synthesise existing evidence on long-term post-COVID symptoms. We estimated the pooled prevalence and also summarised potential risk factors of post-COVID symptoms lasting for one year after infection.

35. Hussain et al. A systematic review of acute telogen effluvium, a harrowing post-COVID-19 manifestation. J Med Virol. 2022; 94(4):1391-1401. <u>https://doi.org/10.1002/jmv.27534</u>

Aim: To compile and illustrate the clinical characteristics, physical examination findings, outcomes, and possible pathology behind acute telogen effluvium occurring in COVID-19 recovered patients.

36. Jennings et al. A Systematic Review of Persistent Symptoms and Residual Abnormal Functioning following Acute COVID-19: Ongoing Symptomatic Phase vs. Post-COVID-19 Syndrome. J Clin Med. 2021; 10(24):5913. <u>https://doi.org/10.3390/jcm10245913</u>

Aim(s): To compare the two phases of long COVID, namely ongoing symptomatic COVID-19 (signs & symptoms from 4 to 12 weeks from initial infection) and post-COVID-19 syndrome (beyond 12 weeks) with respect to symptomatology, abnormal functioning, psychological burden, and quality of life.

NB: Published previously as pre-print.

 Kanorskii SG, Post-COVID syndrome: prevalence, organ pathogenesis and routes of correction. A systematic review. [Постковидный синдром: распространенность и патогенез органных поражений, направления коррекции. Систематический обзор] КУБАНСКИЙ НАУЧНЫЙ МЕДИЦИНСКИЙ ВЕСТНИК. 2021; 28(6):90-116. <u>https://doi.org/10.25207/1608-6228-2021-28-6-90-116</u>

Aim: To collect and systematize information on the epidemiology, pathophysiology of the organspecific consequences of COVID-19 and the direction for their correction.

NB: Review in Russian.

 Khraisat et al. (2021) Meta-analysis of prevalence: the psychological sequelae among COVID-19 survivors. Int J Psychiatry Clin Pract. 2021; Oct 28:1-10 <u>https://doi.org/10.1080/13651501.2021.1993924</u>

Aim: To estimate the pooled prevalence of mental disorders among COVID-19 survivors.

39. Lopez-Leon et al. Long COVID in Children and Adolescents: A Systematic Review and Metaanalyses. medRxiv. 2022; 2022.03.10.22272237 <u>https://doi.org/10.1101/2022.03.10.2227223</u>

Aim: To estimate the prevalence of long COVID in children and adolescents and identify the full spectrum of signs and symptoms present after acute SARS-CoV-2 infection.

 Macpherson K. et al. Experiences of living with long COVID and of accessing healthcare services: a qualitative systematic review. BMJ Open. 2022; 12:e050979. <u>https://doi.org/10.1136/bmjopen-2021-050979</u>

Aim: To explore the experiences of people living with long COVID and how they perceive the healthcare services available to them.

 Middleton et al. Patient-reported respiratory outcome measures in the recovery of adults hospitalised with COVID-19: A systematic review and meta-analysis. medRxiv. 2022; 2022.03.16.22272509 <u>https://doi.org/10.1101/2022.03.16.22272509</u>

Aim: To describe patient-reported outcome measures (PROMs) in adults at least 8 weeks post hospital discharge for COVID-19.

42. Nagarajan et al. Prevalence of post-traumatic stress disorder among survivors of severe COVID-19 infections: A systematic review and meta-analysis. J Affect Disord. 2022; 299:52-59. <u>https://doi.org/10.1016/j.jad.2021.11.040</u>

Aim: To estimate the prevalence of PTSD among the severe cases of COVID-19.

NB: The follow-up/data collection time interval following discharge in included studies ranged from 4 weeks to 16 weeks.

43. Nandasena et al. Quality of life of COVID 19 patients after discharge: Systematic review. PLoS One. 2022; 17(2):e0263941. https://doi.org/10.1371/journal.pone.0263941

Aim: To pool the scientific evidence available on QOL and its factors associated with it among adult survivors of COVID 19, at different timelines.

44. Nguyen et al. Clinical patterns of somatic symptoms in patients suffering from post-acute long COVID: a systematic review. Eur J Clin Microbiol Infect Dis. 2022; 41(4):515-545. http://doi.org/10.1007/s10096-022-04417-4 Aim: To describe the prevalence of the long-term persistence of somatic clinical symptoms in discharged COVID-19 patients.

45. Patria YN, Sabirin RM. COVID-19 potentially causes long-term deterioration of lung function: a systematic review and meta-analysis. Med J Indones. 2021; 30(4):279-89. http://doi.org/10.13181/mji.oa.215660

Aim: To gather evidence on the pulmonary function of COVID-19 survivors.

 Premraj et al. Mid and long-term neurological and neuropsychiatric manifestations of post-COVID-19 syndrome: A meta-analysis. J Neurol Sci. 2022; 434:120162. <u>https://doi:10.1016/j.jns.2022.120162</u>

Aim: To determine the prevalence of neurological and neuropsychiatric symptoms reported 12 weeks or more after acute COVID-19 onset in adults.

47. Ramzi ZS. Hospital readmissions and post-discharge all-cause mortality in COVID-19 recovered patients: A systematic review and meta-analysis. Am J Emerg Med. 2022; 51:267-279. <u>https://doi.org/10.1016/j.ajem.2021.10.059</u>

Aim: To investigate the prevalence of one year hospital readmissions and post-discharge all-cause mortality in recovered COVID-19 patients.

 Rungjirajittranon et al. Thrombotic and Hemorrhagic Incidences in Patients After Discharge from COVID-19 Infection: A Systematic Review and Meta-Analysis. Clin Appl Thromb Hemost. 2021; 27:10760296211069082. <u>https://doi.org/10.1177/10760296211069082</u>

Aim: To better understand the incidence of thrombosis, bleeding, and mortality rates among patients discharged after COVID-19 hospitalization.

49. SeyedAlinaghi et al. Late Complications of COVID-19; a Systematic Review of Current Evidence. Arch Acad Emerg Med. 2021; 9(1):e14. <u>https://doi.org/10.22037/aaem.v9i1.1058</u>

Aim: To investigate the available evidence for long-term complications of COVID-19.

 Shafiabadi Hassani et al. Cardiac Magnetic Resonance Imaging Findings in 2954 COVID-19 Adult Survivors: A Comprehensive Systematic Review. J Magn Reson Imaging. 2022; 55(3):866-880. <u>https://doi.org/10.1002/jmri.27852</u>

Aim: To systematically review the main cardiac MRI findings in COVID-19 adult survivors.

51. Stefanou et al. Neurological manifestations of long-COVID syndrome: a narrative review. Ther Adv Chronic Dis. 2022 Feb 17. <u>https://doi.org/10.1177/20406223221076890</u> Aim: To provide a comprehensive overview of our current understanding of the long-term neurological sequelae of COVID-19, along with a methodological framework for a systematic diagnostic approach and management of patients with neurological manifestations of Long-COVID syndrome.

52. Tucci V, Saary J. Persistent and emergent clinical sequelae of mild COVID-19. Aerosp Med Hum Perform. 2021; 92(12):962–969. https://doi.org/10.3357/AMHP.5892.2021

Aim: To better characterize the persistent and emergent sequelae of asymptomatic and relatively mild COVID-19.

53. Wu et al. Persistence of Symptoms After Discharge of Patients Hospitalized Due to COVID-19. Front Med. 2021; 8:761314. <u>http://doi.org/10.3389/fmed.2021.761314</u>

Aim: To summarize primary research evidence on symptom prevalence, complications, and management of long COVID.

54. Yusuf et al. Global prevalence of prolonged gastrointestinal symptoms in COVID-19 survivors and potential pathogenesis: A systematic review and meta-analysis. F1000Res. 2021; 10:301. https://doi.org/10.12688/f1000research.52216.1

Aim: (a) To determine the global prevalence of prolonged GI symptoms including nausea, vomiting, diarrhea, lack of appetite, abdominal pain, and dysgeusia in those who had recovered from mild and severe COVID-19 and (b) to determine the association of COVID-19 severity with prolonged GI symptoms.

2) Reviews completed since November 2021, but not yet published

Treatment and rehabilitation

 Marshall-Andon et al. A Systematic Review of Post-COVID-19 Rehabilitation Guidelines. PROSPERO 2021 CRD42021236049 Available from: <u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021236049</u>

Review question(s): What do available clinical guidelines recommend for the rehabilitation of patients following COVID-19?

Symptoms/effects

 Ávila Cabral et al. Long-term impact of Covid-19 on executive functions: A systematic review and meta-analysis. PROSPERO 2021 CRD42021262961 Available from: <u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021262961</u>

Review question(s): 1)What is the prevalence of neurocognitive disorders and neurologic manifestations that affect executive functions in post-Covid-19 syndrome patients? 2) How does neurologic manifestations during ongoing symptomatic Covid-19 correlates with executive functions impairment in post-Covid-19 syndrome?

3. Di Matteo et al. Post Covid syndrome: symptoms and stratified follow up. A systematic review and meta-analysis. PROSPERO 2021 CRD42021283689 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021283689 Review question(s): How many studies have considered post Covid 19 follow-up and what symptoms and timing have they investigated?

Tan et al. Prognosis & persistence of smell & taste dysfunction in COVID-19: a meta-analysis with parametric cure modelling of recovery curves. PROSPERO 2021 CRD42021283922. Available from:

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021283922

Review question(s): 1) What is the percentage of COVID-19 patients with olfactory/gustatory dysfunction who recover their sense of smell/taste? 2) What percentage of patients develop persistent olfactory/gustatory dysfunction? 3) What is the time-to-recovery of smell/taste? 4) What are the prognostic factors in association with time-to-recovery or extent of recovery of smell/taste?

5. Zakia et al. Systematic review and meta-analysis of prevalence and risk factors for psychiatric symptoms in long COVID patients. PROSPERO 2021 CRD42021240776 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021240776

Review question(s): 1) What is the prevalence of psychiatric symptoms (depression, anxiety, PTSD, and others) in long COVID patients? 2) What are the risk factors of psychiatric symptoms (depression, anxiety, PTSD, and others) in long COVID patients?

3) Protocols of ongoing reviews related to Long COVID published between November 2021 and March 2022

Treatment & rehabilitation

 Al-Mhanna et al. Effectiveness of physical activity and rehabilitation on physical function and quality of life of COVID-19 survivor: a systematic review. PROSPERO 2021 CRD42021283087 Available from:

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021283087

Review question(s): To determine the effectiveness of physical activity on quality of life and physical function in COVID-19 survivor.

 Bailly et al. Systematic review of the programs of physical activity used in COVID-19 rehabilitations. PROSPERO 2022 CRD42022289219 Available from: <u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022289219</u>

Review question(s): Are physical activity programs beneficial for post-COVID-19 rehabilitation?

3. Barbosa et al. Influence of pulmonary rehabilitation in post-Covid patients. Systematic review with metaanalysis. PROSPERO 2021 CRD42021289747 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021289747

Review question(s): Does pulmonary rehabilitation contribute to patients' recovery?

 Benzakour et al. Update of the potential treatments for psychiatric post-COVID-19 symptoms: still a lot of suffering and many more things to learn. PROSPERO 2022 CRD42022311416 Available from:

<u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022311416</u> Review question(s): 1) What are the treatments which are the most efficient and available for the treatments of the psychiatric post-COVID symptoms, according to WHO's definition of post-COVID syndrome.

 Bezerra et al. Treatment options for patients who develop post-COVID acute kidney injury. PROSPERO 2021 CRD42021297821 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021297821

Review question(s): 1) What kidney problems are caused by COVID-19? 2) What are the best treatment options for post-COVID-19 acute kidney injury?

6. Esseroukh et al. Rehabilitation interventions for patients with post-acute COVID-19 syndrome: a systematic review. PROSPERO 2022 CRD42022304254 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022304254

Review question(s): To evaluate the efficacy of rehabilitation interventions for patients with PACS and to analyse the main changes in long-term outcomes after the interventions.

 Fernandez et al. How does regular physical activity affect recovery from the after-effects of Covid-19?. PROSPERO 2022 CRD42022306323 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022306323

Review question(s): How does regular physical activity affect recovery from the after-effects of Covid-19?

 Ghadirzadeh et al. Treating post-COVID-19 anosmia: a systematic review and meta-analysis. PROSPERO 2022 CRD42022314114 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022314114

Review question(s): Which treatment strategies have shown promising results in treating post-COVID-19 anosmia?

 Hoang et al. Topical steroid and olfactory training for persistent post-COVID-19 olfactory dysfunction: a systematic review and network meta-analysis. PROSPERO 2021 CRD42021292686 Available from:

<u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021292686</u> Review question(s): In patients with persistent post-COVID-19 olfactory dysfunction, what are the benefits and harms of different interventions for treatment?

10. Kim et al. Complementary and alternative medicine (CAM) for Long-COVID: a systematic review. PROSPERO 2021 CRD42021281526 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021281526 Review question: To identify evidence of various complementary and alternative medicine interventions for postviral syndrome.

11. Marcelino et al. Exercise in post COVID-19 rehabilitation. PROSPERO 2022 CRD42022301572 Available from:

<u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022301572</u> Review question(s): Can physical exercise help with the recovery of physical fitness in patients with

post-COVID-19 persistent complaints/symptoms?

 Neto et al. Effects of physical rehabilitation interventions on functioning and health-related quality of life in people with and post-COVID-19 infection: systematic review and metaanalysis. PROSPERO 2022 CRD42022316491 Available from: <u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022316491</u>

Review question: Are physical rehabilitation interventions effective on functioning and healthrelated quality of life in people with and after COVID-19 infection?

 Njøten et al. Rehabilitation for patients with long-COVID and the impact on health and everyday functioning: a systematic review and meta-analysis. PROSPERO 2021 CRD42021295878 Available from:

<u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021295878</u> Review question(s): Does outpatient rehabilitation for patients with persistent symptoms more than 12 weeks after COVID-19 infection improve health status and everyday functioning?

 Oliveira et al. Effect of pulmonary rehabilitation on dyspnea, fatigue, peripheral muscle strength and exercise capacity in Post-Covid patients: a systematic review and meta-analysis. PROSPERO 2022 CRD42022310788 Available from: <u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022310788</u>

Review question(s): Is a pulmonary rehabilitation program effective to reduce dyspnea and fatigue, and to improve peripheral muscle strength and exercise capacity in Post-Covid-19 patients?

 Vandebroek et al. Treatment modalities for COVID-19 associated olfactory dysfunction: a systematic review. PROSPERO 2022 CRD42022300627 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022300627

Review question(s): 1) What is the effect of the studied treatments on the recovery rate of COVID-19 associated olfactory dysfunction? 2) What is the effect of the studied treatments on the olfactory function test scores (objectively: smell testscore; subjectively: VAS-score, quality of life) in COVID-19 associated olfactory dysfunction? 3) What are the adverse effects of the different treatment modalities for COVID-19 associated olfactory dysfunction?

16. Westby et al. The effectiveness and safety of pharmacological and non-pharmacological interventions against symptoms of Long COVID: a systematic review. PROSPERO 2022

CRD42022304493 Available from:

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022304493

Review question(s): 1) What is the effectiveness and safety of pharmacological and non-pharmacological interventions against Long COVID? 2) Are there effective targeted treatments for people with Long COVID (e.g. corticosteroids for interstitial lung disease; bronchodilators in people with asthma-like symptoms), including test-and-treat trials of alternative strategies?

17. Wilkinson et al. Nutrition to assist immune function during post-acute SARS-CoV infections in adults: a systematic review. PROSPERO 2022 CRD42022306051 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022306051

Review question(s): 1) What nutritional interventions are safe and effective for symptoms associated with post-acute SARS-CoV infection? 2) What is known about how nutritional interventions impact or assist the immune function(s) in post-acute SARS-CoV infection?

Prevention

 Bhandari et al. Online yoga interventions in the tertiary prevention of psychological comorbidities in Covid-19 survivors: a systematic review. PROSPERO 2022 CRD42022311443 Available from:

<u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022311443</u> Review question(s): Can online yoga interventions be used in the tertiary prevention of psychological co-morbidities in COVID-19 survivors?

19. Bhandari et al. Ayurvedic herbal formulations as tertiary prevention of psychological comorbidities in Covid-19 survivors. PROSPERO 2022 CRD42022310252 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022310252

Review question: Does Ayurvedic herbal concoction help in the tertiary prevention of psychological co-morbidities in COVID-19 survivors?

20. Ceban et al. Efficacy of COVID-19 vaccination in the prevention and treatment of Long Covid: a systematic review and meta-analysis. PROSPERO 2022 CRD42022307220 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022307220

Review question(s): 1) Does prior SARS-CoV-2 vaccination affect the incidence and presentation of long COVID in breakthrough cases? 2) Does SARS-CoV-2 vaccination post factum affect pre-existing long COVID?

21. Marra et al. The COVID-19 vaccine effectiveness in post-COVID-19 conditions: a systematic review and meta-analysis. PROSPERO 2022 CRD42022318686 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022318686

Review question(s): To evaluate the COVID-19 vaccine effectiveness among individuals in general population studying the COVID-19 post-conditions.

Risk factors and pathobiology

22. Ceban et al. Neuroimaging findings in long COVID: a systematic review. PROSPERO 2021 CRD42021292720 Available from:

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021292720

Review question(s): Is there a neurobiological signature of long COVID? [i.e., compared to healthy or non-COVID-19 controls, and/or compared to individuals who have fully recovered from COVID-19 and do not exhibit persistent symptoms]

23. Kaleem et al. Synthesizing the pathophysiology of post-acute COVID-19 syndrome: a systematic review. PROSPERO 2022 CRD42022281496 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022281496

Review question: (1) What pathophysiological processes are associated with post-acute COVID-19 syndrome? (2) What biomarkers are associated with post-acute COVID-19 syndrome? (NB: Protocol indicates that both primary research studies and systematic reviews will be included).

26. Ni Sim et al. Risk factors for developing post COVID-19 condition of fatigue and dyspnoea in adults: a systematic review. PROSPERO 2022 CRD42022318597 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022318597

Review question(s): 1) To identify common factors that predict the development of post COVID-19 condition specifically fatigue and dyspnoea among adult population with COVID-19. 2) To explore whether vaccination has any influence on developing post COVID-19 condition after a breakthrough infection.

24. Simadibrata et al. Gut microbiota profile in patients with COVID-19 and postacute COVID-19 syndrome: a systematic review. PROSPERO 2022 CRD42022309856 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022309856

Review question(s): 1) What is the gut microbiota profile in COVID-19 and long COVID/post-acute COVID-19 syndrome? 2) Is COVID-19 and long COVID characterized by a pathological gut microbial profile and whether the severity of COVID-19 and long COVID is associated with the gut microbial profile?

25. Udeh et al. Immunological drivers of persistent symptoms in long COVID: a systematic review and meta-analysis. PROSPERO 2021 CRD42021291732 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021291732

Review question(s): What is the difference in the immunological profile [I] of COVID-19 convalescent patients [P] with and without persistent symptoms [C] 2 months post-COVID infection [T], and what is their role as a marker of disease progression as well as an outcome predictor [O]?

Symptoms/effects

Review of Reviews

27. Bennett et al. Long-term clinical and health outcomes following COVID-19 disease: an umbrella review. PROSPERO 2022 CRD42022303557 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022303557 Review question(s): What evidence is provided in systematic reviews about the long-term clinical and health outcomes of COVID-19 and what can be synthesized using an umbrella review approach?

28. Mazza et al. Epidemiology of depression in COVID-19 survivors: an umbrella review of metaanalyses. PROSPERO 2022 CRD42022310693 Available from:

<u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022310693</u> Review question(s): To investigate the prevalence of depression among COVID-19 survivors providing a robust synthesis of current published evidence on this topic that can inform further research in understanding post-COVID depression and its associated risk factors.

Standard reviews

29. Al-Oraibi et al. Prevalence of long-COVID among healthcare workers: a systematic review and meta-analysis. PROSPERO 2022 CRD42022312781 Available from:

<u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022312781</u> Review question(s): 1) What is the pooled prevalence of long-COVID among healthcare workers (HCWs) infected with SARSCoV-2 virus globally? 2) What is the prevalence of long-COVID among healthcare workers (HCWs) infected with SARS-CoV-2 virus globally when stratified by age, gender, country, ethnicity, and vaccination status? 3) What are the symptoms (and their clustering) among healthcare workers (HCWs) with long-COVID?

30. Ambrosino et al. Clinical assessment of endothelial function in convalescent COVID-19 patients: a meta-analysis with meta-regressions. PROSPERO 2021 CRD42021289684 Available from:

<u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021289684</u> Review question(s): Does COVID-19 have a relevant impact on clinical markers of endothelial function during convalescence?

31. Arana et al. Physical performance and respiratory function measures in the evaluation of post COVID-19 syndrome: systematic review. PROSPERO 2021 CRD42021287040 Available from:

<u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021287040</u> Review question(s): What are the clinical measures and outcomes of physical performance and respiratory function in the evaluation of adults with post COVID-19 syndrome?

32. Bazdar et al. A systematic review of chest imaging findings in long COVID patients. PROSPERO 2021 CRD42021292358 Available from:

https://www.crd.york.ac.uk/prospero/display record.php?ID=CRD42021292358 Review question(s): What is currently known about the chest imaging findings in Long COVID patients and on which aspects of this topic is further study needed?

33. Bianco et al. Signs of myocardial involvement in athletes recovering from COVID-19: a systematic review and meta-analysis. PROSPERO 2022 CRD42022300819 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022300819 Review question(s): The primary objective of the study was to assess the presence of signs of myocarditis and/or myocardial involvement post COVID-19 infection.

34. Bonnechère et al. The impact of COVID-19 infection on cognitive function in healthy individuals: a systematic review and meta-analysis. PROSPERO 2022 CRD42022303425 Available from:

https://www.crd.york.ac.uk/prospero/display record.php?ID=CRD42022303425 Review question(s): What is the extent of the increased risk of developing cognitive impairment and cognitive decline after COVID-19 infection?

35. Buechner et al. Prevalence rates of comorbid depression in patients suffering from (long-/post-) COVID-19 or chronic fatigue syndrome (ME/CFS) in dependence of diagnostic approach: a systematic review. PROSPERO 2022 CRD42022308498 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022308498

Review question(s): What prevalence rates of depressive disorders can be found in patients with a history of COVID-19 disease or chronic fatigue syndrome depending on the method used to diagnose depression (clinical interview, screening questionnaire or other)?

 36. Chang et al. Psychiatric and neuropsychiatric complications in the post-acute phase of Covid-19 infection: a systematic review and meta-analysis. PROSPERO 2022 CRD42022313396 Available from:

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022313396

Review question(s): 1) What is the risk of psychiatric complications in post-acute phase of COVID-19 infection? 2) What is the risk of neuropsychiatric complications in post-acute phase of COVID-19 infection?

37. Chen et al. Systematic Review of the Neurological Symptoms and Proposed Causes of Long Covid Syndrome. PROSPERO 2022 CRD42022288403 Available from:

<u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022288403</u> Review question(s): 1) What are the neurological manifestations of long-COVID? 2) Is there any positive evidence suggestive of the presence of functional neurological symptoms in long-COVID? 3) What are the proposed causes of long-COVID?

38. Cunha et al. Post-COVID-19 syndrome and quality of life after hospitalization: a systematic review. PROSPERO 2022 CRD42022309487 Available from:

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022309487

Review question(s): What factors in the post-COVID-19 syndrome are associated with health-related changes in quality of life?

39. de Sena et al. COVID-19: assessment of neurocognitive impacts. PROSPERO 2022 CRD42022309257 Available from:

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022309257

Review question(s): To verify which neurocognitive skills are most compromised in the post-COVID-19 period. Do people infected by COVID-19 present neurocognitive impairment in cognitive skills such as attention, memory, executive functions, visuoconstructive, praxic, gnostic skills, and others cognitive abilities?

40. Dos Santos et al. Clinical manifestations in patients with and without post-COVID-19 comorbidities: a systematic review. PROSPERO 2021 CRD42021290739 Available from: https://www.crd.york.ac.uk/prospero/display record.php?ID=CRD42021290739

Review question(s): (1) Do patients with comorbidities present more symptoms/clinical manifestations in the post-COVID period when compared to patients without comorbidities? (2) What impact of comorbidity on the quality of life of patients who had COVID-19?

 Durstenfeld et al. Cardiopulmonary exercise testing to evaluate post-acute sequelae of COVID-19 (Long COVID): a systematic review and meta-analysis. PROSPERO 2021 CRD42021299842 Available from:

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021299842 Review question(s): 1) Is exercise capacity as measured by peak oxygen consumption during cardiopulmonary exercise testing reduced among adults with prior SARS-CoV-2 infection in the post-

acute phase of COVID-19? 2) Are there differences in exercise capacity between those reporting cardiopulmonary symptoms ("Cardiopulmonary Long COVID") and those who have fully recovered?

42. Effiong et al. Post-acute sequelae of COVID-19 and adverse psychiatric outcomes: an etiology and risk systematic review protocol. PROSPERO 2022 CRD42022308737 Available from: https://www.crd.york.ac.uk/prospero/display record.php?ID=CRD42022308737

Review question(s): 1) Are people with post-acute sequelae of COVID-19 (PASC) at greater risk of an adverse psychiatric outcome (depression, anxiety, substance use disorder, posttraumatic stress disorder, psychosis, dementia, self-harm, suicide) than those without PASC? 2) Does the association between PASC and an adverse psychiatric outcome vary with age, sex, the severity of COVID-19 (mild, moderate, severe, critical), and duration of PASC (short-term (1 month), intermediate term (2-5 months), and long-term (? 6 months) following COVID-19 diagnosis)? 3) Is PASC an independent risk factor for an adverse psychiatric outcome?

 Florez et al. Post COVID-19 syndrome related to cardiovascular, pulmonary, neurological, mental health disease, and quality of life: systematic review from December 2019 to October 2021. PROSPERO 2022 CRD42022293152 Available from: <u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022293152</u>

Review question(s): What are the sequelae of Post COVID-19 Syndrome related to cardiovascular, pulmonary, neurological, mental health, and quality of life following 4 weeks of the active phase in patients who had COVID-19 with severe versus mild disease or healthy patients in the period December 2019 to October 2021?

44. Giffoni et al. Neurocognitive disorder and "brain fog" as a long-term syndrome or sequelae in non-severe COVID-19 survivors: a systematic review and meta-analysis. PROSPERO 2021 CRD42021296698 Available from:

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021296698

Review question(s): What is the prevalence and incidence of long-term neurocognitive impairment and "brain fog" in patients recovered from asymptomatic, mild and moderate COVID-19 infection?

45. Guinto et al. Long COVID and lung imaging abnormalities: a systematic review and metaanalysis. PROSPERO 2021 CRD42021291415 Available from: <u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021291415</u>

Review question(s): Do the majority of adult long-COVID patients show lung imaging abnormalities?

- 46. Gupta et al. Characterizing the clinical features of long-term COVID-19 in previously hospitalized individuals: a systematic review. PROSPERO 2022 CRD42022306931 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022306931
 Review question(s): To conduct a de novo, clinically focused systematic review to identify long-term symptoms that appear following COVID-19 in patients that required hospitalization, and to understand the frequency and temporal nature of these symptoms and develop a definition for long-term COVID-19 for use in future analytical work.
 - 47. Huang et al. The prevalence and variety of post-acute COVID-19 symptoms at different follow-up time points and in different countries. PROSPERO 2022 CRD42022300274 Available from:

https://www.crd.york.ac.uk/prospero/display record.php?ID=CRD42022300274 Review question(s): What is the prevalence and variety of post-acute COVID-19 symptoms at different follow-up time points and in different countries?

48. Jödicke et al. An updated systematic review to characterise Long COVID symptoms as recorded in real world data vs. self-reported data. PROSPERO 2021 CRD42021292122 Available from:

<u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021292122</u> Review question(s): To summarise symptoms and diagnoses characterising long COVID based on the current literature as of September 2021.

49. Kwan et al. A Systematic Review and Meta-Analysis to Investigate the Association between Pre-Existing Depression and Susceptibility to Long COVID-19. PROSPERO 2021 CRD42021293383 Available from:

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021293383

Review question(s): To provide a comprehensive review of the association between pre-existing depression and susceptibility to Long COVID-19 (i.e., post-COVID-19 syndrome).

50. Lemes et al. A Systematic Review on Acute and Post-acute COVID-19 Presentation in Athletes. PROSPERO 2022 CRD42022301817 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022301817

Review question: What are the acute and post-acute COVID-19 symptoms presentation in athletes?

51. Jiang et al. A systematic review and meta-analysis of the long-term outcomes after SARS-CoV-2 infection in neonates, children and adolescents. PROSPERO 2022 CRD42022309815 Available from:

<u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022309815</u> Review question(s): What are the characteristics of the long-term outcomes of SARS-CoV-2 infection in neonates, children and adolescents, including those with multisystem inflammatory syndrome in children and adolescents (MIS-C)?

52. Liu et al. Long-term consequences of COVID-19 at 6 months and above: a systematic review and meta-analysis. PROSPERO 2022 CRD42022309720 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022309720

Review question: What are the long-term consequences of COVID-19 at 6 months and above, and how severe are they?

53. Loro et al. Neurological and neuropsychiatric symptoms in long-COVID 19 syndrome: a systematic review. PROSPERO 2021 CRD42021272151 Available from: <u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021272151</u>

Review question(s): What is the presence, prevalence and clinical manifestations of neurological and neuropsychiatric symptoms in patients with a clinical history of symptomatic SARS-CoV-2 infection?

54. Madhavan et al. Effect of COVID-19 on semen parameters beyond 3 months of infectionmeta analysis and systematic review.. PROSPERO 2021 CRD42021293442 Available from: https://www.crd.york.ac.uk/prospero/display record.php?ID=CRD42021293442

Review question(s): What is the effect of COVID-19 on semen parameters beyond 3 months of infection?

55. Moreno-Martínez et al. Comparative analysis of clinical features of pain in post-COVID and chronic obstructive pulmonary disease. A systematic review. PROSPERO 2022 CRD42022292617 Available from:

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022292617

Review question(s): In patients infected with SARS-CoV-2 (P) and suffering from persistent COVID (E), what are the clinical characteristics of pain (O) compared to people suffering from COPD (C)?

56. Moussa et al. Incidence of post-COVID-19 vascular access thrombosis among hemodialysis patients: a systematic review and meta-analysis. PROSPERO 2022 CRD42022313400.

Available from:

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022313400

Review question(s): The objectives of this systematic review are to assess the incidence, and the independent risk factors of vascular access complications (e.g. vascular access thrombosis) post COVID-19 infection among end-stage kidney disease patients on chronic hemodialysis.

57. Patel et al. Gastrointestinal manifestations, investigations and treatments of COVID-19 in children: a systematic review. PROSPERO 2022 CRD42022297877 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022297877

Review question(s): To summarise 1) what are the gastrointestinal manifestations of long COVID in children and young people; 2) what investigations have been studied in the diagnosis of gastrointestinal complications of long COVID in children and young people; What treatments have been studied in response to gastrointestinal complications of long COVID in children and young people.

58. Pires et al. Impact of long COVID on workers: a systematic review. PROSPERO 2021 CRD42021288120 Available from:

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021288120 Review question(s): To assess the effects of long COVID among workers and its impact on their health status and working life.

59. Ramael et al. What is the effect of long COVID on the exercise capacity/functional activity level/movement behaviour? PROSPERO 2022 CRD42022293532 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022293532

Review question(s): What is the effect of long COVID on the exercise capacity/functional activity/movement behaviour?

60. Rocha et al. Implications of glycemic control on the risk of developing post acute COVID-19 syndrome in patients with diabetes mellitus: a systematic review. PROSPERO 2021 CRD42021298257 Available from:

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021298257

Review question(s): Do patients with diabetes mellitus (DM) and blood glucose control, infected with SARS-CoV-2, have a lower chance of developing long COVID than patients with diabetes mellitus without adequate blood glucose control?

61. Sahimi et al. Systematic review and meta-analysis on brain fog as post-COVID-19 sequelae. PROSPERO 2021 CRD42021292266 Available from: <u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021292266</u>

Review question(s): 1) What is the prevalence of brain fog in patients with post COVID-19 infection? 2) What cognitive domains are involved in brain fogs in post COVID-19 infection? 3) What are the interventions used for brain fogs in post COVID-19 infection? 62. Saini et al. Developing trends in patterns of cognitive subdomain impairment in post COVID-19 patients. PROSPERO 2022 CRD42022318721 Available from:

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022318721

Review question(s): In patients previously diagnosed with or treated for COVID-19 this review aims to: 1) Characterise the patterns and prevalence of impaired and preserved function across specific cognition domains 2) Investigate the association between patient, disease and treatment factors and subsequent cognitive impairment across specific domains.

63. Santos et al. Clinical profile of pain in post-COVID-19 patients: a systematic review. PROSPERO 2021 CRD42021290734 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021290734

Review question(s): What is the clinical profile of pain in post-COVID patients?

64. Serafini et al. Psychiatric symptoms in post-COVID patients: a systematic review and metaanalysis. PROSPERO 2022 CRD42022299408 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022299408

Review question(s): 1) What are the main psychiatric manifestations of long-COVID syndrome? 2) Are they different to other post-acute medical/infectious conditions? 3) What are the prevalence and factors associated with psychiatric disorders among long-COVID patients?

65. Smith et al. Is COVID-19 infection associated with loss of muscle strength? A systematic review of the literature. PROSPERO 2022 CRD42022307014 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022307014

Review question(s): Is COVID-19 infection associated with the loss of muscle strength?

66. Tilwani et al. Lung function test in post-infection patients by COVID-19: A Systematic review and Meta-analysis. PROSPERO 2021 CRD42021291998 Available from: <u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021291998</u>

Review question(s): To determine the prevalence of restrictive pattern, obstructive pattern and altered diffusion in post-COVID-19 infection patients.

67. Trott et al. Sensory symptoms of long-COVID: a systematic review. PROSPERO 2021 CRD42021292804 Available from:

<u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021292804</u> Review question(s): What sensory symptoms (including taste, hearing, smell, vision) are associated with long-COVID?

68. Utomo et al. Impaired olfaction post coronavirus disease-2019: a systematic review of smell recovery predictive factors. PROSPERO 2022 CRD42022318412 Available from: <u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022318412</u> Review question(s): 1) What is the prevalence of olfactory dysfunction and its recovery in patients with post COVID-19? 2) What are the predictive factors of olfactory function recovery in patients with olfactory impairment with post-COVID-19 if any?

69. Zheng et al. Persistent symptoms and risk factors among pediatric patients with COVID-19: a systematic review and meta-analysis. PROSPERO 2021 CRD42021293614 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021293614

Review question(s): What is the prevalence and risk factors of long-term sequelae in pediatric patients with COVID-19?

70. Watanabe et al. One-year follow-up CT findings in COVID-19 patients: a systematic review and meta-analysis. PROSPERO 2022 CRD42022313149 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022313149

Review question(s): what is the evidence on 1-year follow-up of pulmonary sequelae

71. Winoto et al. Hypertension and diabetes mellitus as risk factors for post Covid-19 syndrome: meta-analysis. PROSPERO 2022 CRD42022299589 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022299589

Review question(s): Do hypertension and diabetes mellitus increase the risk of post-COVID syndrome incidence?

72. Yang et al. Sequelae of COVID-19 patients up to 1 year after discharge: a systematic review and meta-analysis. PROSPERO 2022 CRD42022314319 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022314319

Review question(s): What are the long-term sequelae in discharged COVID-19 patients and which of them will persist in one year follow-up?

73. Yi et al. COVID-19 survivors and long-term kidney outcomes: a systematic review and metaanalysis. PROSPERO 2021 CRD42021290341 Available from: <u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021290341</u>

Review question(s): 1) To determine whether post-acute COVID-19 patients/COVID-19 survivors have an increased long-term risk of acute kidney injury (AKI) and other kidney impairments compared with patients without COVID-19 infection. 2) To determine whether post-acute COVID-19 patients/COVID-19 survivors with chronic kidney disease, acute kidney injury and other kidney diseases have an increased risk of mortality and clinical outcomes compared with those without kidney impairments.

Appendix 1: PubMed search strategy

Search 1

#6 #1 OR #4 Filters: Systematic Reviews, Meta-analysis

#5 #1 OR #4

#4 #2 AND #3

#3 COVID [ti] OR COVID-19 [ti] OR SARS-CoV-2 [ti]

#2 long term symptom* [tiab] OR long term effect* [tiab] OR persisting symptom*[tiab] OR persistent symptom*[tiab] OR long term sequelae [tiab] OR post discharge [tiab] OR postdischarge [tiab]

#1 Long covid [tiab] OR post covid [tiab] OR post acute covid [tiab] OR PASC [tiab] OR long term covid [tiab] OR ongoing covid [tiab] OR chronic covid [tiab] OR Long haul* [tiab]

Search 2 #8 #5 AND #6 Filters from 5/11/2021 – 21/04/2022

#7 #5 AND #6

#6 review [ti] OR meta-analysis [ti]

#5 #1 OR #4

#4 #2 AND #3

#3 COVID [ti] OR COVID-19 [ti] OR SARS-CoV-2 [ti]

#2 long term symptom* [tiab] OR long term effect* [tiab] OR persisting symptom*[tiab] OR persistent symptom*[tiab] OR long term sequelae [tiab] OR post discharge [tiab] OR postdischarge [tiab]

1 Long covid [tiab] OR post covid [tiab] OR post acute covid [tiab] OR PASC [tiab] OR long term covid [tiab] OR ongoing covid [tiab] OR chronic covid [tiab] OR Long haul* [tiab]

Appendix 2: Key findings from our initial scoping work

For the initial scope of the literature, we searched three main sources: PROSPERO database; our living systematic map of Long COVID-19 evidence and PUBMED. However, we only used a small number of key search terms. The PROSPERO database was searched using the term long COVID, and records tagged as long COVID in the database were also screened. We first searched PUBMED for the terms long COVID or post COVID in the title or abstract fields and then applied the PUBMED filter for 'systematic reviews' and 'meta-analysis'. A second search was also conducted to identify records with the terms long COVID or post COVID in the title or abstract fields and the words 'review' or 'meta-analysis' in the title.

Overall, we identified 51 published reviews (including six pre-print papers and one conference abstract); nine completed reviews that were yet to be published; and 77 protocols for ongoing reviews. Table A below provides a summary of all reviews identified from our initial scoping work by publication type and main focus.

/		0		
Review status	Review of review	Living review	Systematic review	
Main focus				
Published				
Symptoms/effects and/or risk factors	1	3	43	
Treatment/rehabilitation		1	2	
Prevention		1		
Completed not yet published				
Symptoms/effects			7	
Treatment/rehabilitation			1	
Lived experience			1	
Ongoing			·	
Symptoms/effects and/or risk factors	1	3	55	
Treatment/rehabilitation		2	13	
Health & economics			3	
•			_	

Table A: Summary of reviews identified from scoping exercise

Published reviews

Primary focus: Treatment/Rehabilitation

Living reviews

 O'Byrne et al. Interventions for the treatment of persistent post-COVID-19 olfactory dysfunction. Cochrane Database Syst Rev 2021; 7(7) https://doi.org/10.1002/14651858.CD013876.pub2

Aim: To assess the effects (benefits and harms) of interventions that have been used, or proposed, to treat persisting olfactory dysfunction (4 weeks or more) due to COVID-19 infection

Standard reviews

 Lindsay et al. What are the recommendations for returning athletes who have experienced long term COVID-19 symptoms? Ann Med 2021; 53(1):1935-1944. <u>https://doi.org/10.1080/07853890.2021.1992496</u>

Aim: To synthesise the recommendations for returning athletes who have experienced long COVID symptoms

 Webber et al. Apparent discordance between the epidemiology of COVID-19 and recommended outcomes and treatments: A scoping review. Phys Ther 2021; 101(11):pzab115. <u>http://doi.org/10.1093/ptj/pzab155</u>

Aim: To synthesize outpatient rehabilitation assessment and treatment recommendations for adults in post-acute COVID-19 stages

Primary focus: Prevention

Living reviews

 Webster, K. E., O'Byrne, L., et al. (2021). Interventions for the prevention of persistent post-COVID-19 olfactory dysfunction. *Cochrane Database Syst Rev, 7*(7), <u>https://doi.org/10.1002/14651858.CD013877.pub2</u>

Aim: To assess the effects (benefits and harms) of interventions that have been used, or proposed, to prevent persisting olfactory dysfunction due to COVID-19 infection.

Primary focus: Symptoms/effects & risk factors

Review of reviews

 de Araújo et al. (2021). Manifestações clínicas e laboratoriais pós-covid Quais são as manifestações clínicas persistentes, sequelas ou complicações da COVID-19? <u>https://www.researchgate.net/publication/355752133 Manifestacoes_clinicas_e_laboratoriais_pos-covid_-_Revisao_rapida</u>

Aim: To identify the persistent clinical manifestations, sequelae or complications of COVID-19.

Living reviews

 Domingo, F.R. et al. Prevalence of long-term effects in individuals diagnosed with COVID-19: an updated living systematic review. medRxiv. 2021: 2021.06.03.21258317. <u>https://doi.org/10.1101/2021.06.03.21258317</u>

Aim: To summarise studies reporting the frequency of symptoms, sequelae, and difficulties in conducting usual activities experienced by individuals living with post COVID-19 condition at four weeks or more after initial COVID-19 diagnosis.

 Hoshijima et al. Incidence of Long-term Post-acute Sequelae of SARS-CoV-2 Infection Related to Pain and Other Symptoms: A Living Systematic Review and Meta-analysis. medRxiv. 2021; 2021.04.08.21255109. <u>https://doi.org/10.1101/2021.04.08.21255109</u>

Aim: To determine long-term symptoms in COVID-19 survivors after infection.

8. Michelen et al. Characterising long COVID: A living systematic review. *BMJ Glob Health 2021;* 6(9). <u>https://doi.org/10.1136/bmjgh-2021-005427</u>

Aim: To regularly synthesise evidence on long COVID characteristics, to help inform clinical management, rehabilitation strategies and interventional studies to improve long-term outcomes.

Standard reviews

9. Ahmad et al. LONG COVID: An insight. Eur Rev Med Pharmacol Sci 2021; 25(17):5561-5577. https://doi.org/10.26355/eurrev_202109_26669

Aim: To analyse and review the currently available published literature related to long COVID, understanding its pattern, and predicting the long-term effects on survivors.

10. Aiyegbusi et al. Symptoms, complications and management of long COVID: A review. J R Soc Med 2021; 114(9):428-442. <u>https://doi.org/:10.1177/01410768211032850</u>

Aim: To summarise the current evidence on symptom prevalence complications & management of long COVID & highlight priority areas for research.

11. Akbarialiabad et al. Long COVID, a comprehensive systematic scoping review. Infection 2021; 49:1163–1186. <u>https://doi.org/10.1007/s15010-021-01666-x</u>

Aim: To synthesize what is known about persistent COVID-19, its signs and symptoms, its pathophysiology, and the current management recommendations.

 Amdal et al. Health-related quality of life issues, including symptoms, in patients with active COVID-19 or post COVID-19; a systematic literature review. Qual Life Res 2021; 30(12):3367-3381. <u>https://doi.org/10.1007/s11136-021-02908-z</u>

Aim: To identify all relevant health-related quality of life (HRQoL) issues associated with COVID-19.

13. Anaya et al. Post-COVID syndrome. A case series and comprehensive review. Autoimmun Rev 2021; 20(11):102947. https://doi.org/10.1016/j.autrev.2021.102947

Aim: To report a case series of patients with Post COVID syndrome and conduct a systematic review and meta-analysis on the topic.

14. Badenoch et al. Persistent neuropsychiatric symptoms after COVID-19: a systematic review and meta-analysis. medRxiv. 2021; 2021.04.30.21256413; https://doi.org/10.1101/2021.04.30.21256413

Aim: To estimate the prevalence of neuropsychiatric symptoms in survivors of COVID-19.

15. Behnood et al. Persistent symptoms following SARS-COV-2 infection among children and young people: A meta-analysis of controlled and uncontrolled studies. Journal of Infection 2021; https://doi.org/10.1016/j.jinf.2021.11.011

Aim: To assess evidence on long-term post-COVID symptoms in children and young people examining prevalence, risk factors, type and duration.

 Cabrera Martimbianco et al. Frequency, signs and symptoms, and criteria adopted for long COVID-19: A systematic review. Int J Clin Pract 2021; 75(10):e14357. <u>https://doi.org/10.1111/ijcp.14357</u>

Aim: To assess evidence on long-term post-COVID symptoms in children and young people examining prevalence, risk factors, type and duration.

17. Cares-Marambio et al. Prevalence of potential respiratory symptoms in survivors of hospital admission after coronavirus disease 2019 (COVID-19): A systematic review and metaanalysis. Chron Respir Dis 2021; 18:14799731211002240. https://doi.org/10.1177/14799731211002240 Aim: To critically evaluate the available information on the frequency of long COVID-19 and the characteristics of its clinical manifestations.

 Chakraborty et al. A review of prolonged post-COVID-19 symptoms and their implications on dental management. Int J Environ Res Public Health 2021; 18(10). <u>https://doi.org/10.3390/ijerph18105131</u>

Aim: To describe the prevalence of prolonged symptoms of COVID-19 post-recovery.

19. Daroische et al. Cognitive impairment after COVID-19-a review on objective test data. Front Neurol 2021; 12:699582. <u>https://doi.org/10.3389/fneur.2021.699582</u>

Aim: To review the literature on cognitive impairment after COVID-19 infection.

20. d'Ettorre et al. (2021). COVID-19 sequelae in working age patients: A systematic review. J Med Virol 2021; 94:858- 868. <u>https://doi.org/10.1002/jmv.27399</u>

Aim: To assess both occurrence and risk factors for sequelae of COVID in recovered patients.

 De-la-Rosa-Martinez et al. Long-term manifestations and modifiers of prevalence estimates of the post-COVID-19 syndrome: A systematic review and meta-analysis. medRxiv. 2021; 2021.10.17.21265123. <u>https://doi.org/10.1101/2021.10.17.21265123</u>

Aim: To summarize published data on Post-acute COVID-19 syndrome characterizing the clinical presentation, prevalence, and modifiers of prevalence estimates.

 Fahriani et al. (2021). Persistence of long COVID symptoms in COVID-19 survivors worldwide and its potential pathogenesis - A systematic review and meta-analysis. Narra J 2021; 1(2): e36. <u>http://doi.org/10.52225/narraj.v1i2.36</u>

Aim: To estimate the prevalence of persistent long COVID symptoms among COVID-19 survivors and to discuss the potential pathogeneses.

 Fernández-de-Las-Peñas et al. Prevalence of post-COVID-19 symptoms in hospitalized and non-hospitalized COVID-19 survivors: A systematic review and meta-analysis. Eur J Intern Med 2021; 92:55-70. <u>https://doi.org/10.1016/j.ejim.2021.06.009</u>

Aim: To analyse the prevalence of post-COVID-19 symptoms in hospitalized and non-hospitalized patients recovered from COVID-19.

24. Fernández-de-Las-Peñas et al. Headache as an acute and post-COVID-19 symptom in COVID-19 survivors: A meta-analysis of the current literature. Eur J Neurol 2021; 28(11):3820-3825. https://doi.org/10.1111/ene.15040

Aim: To synthesize the prevalence of post-COVID headache in hospitalized and non-hospitalized patients recovering from SARS-CoV-2 infection.

 Fernández-de-Las-Peñas et al. Time course prevalence of post-COVID pain symptoms of musculoskeletal origin in patients who had survived to severe acute respiratory syndrome coronavirus 2 infection: A systematic review and meta-analysis. Pain 2021; <u>https://doi.org/10.1097/j.pain.00000000002496</u> Aim: To synthesize the prevalence of post-coronavirus disease (COVID) pain symptoms of musculoskeletal origin in hospitalized or nonhospitalized patients recovered from SARS-CoV-2 infection.

26. Groff, D et al. Short-term and long-term rates of postacute sequelae of SARS-CoV-2 infection: A systematic review. JAMA Netw Open 2021; 4(10):e2128568. https://doi.org/10.1001/jamanetworkopen.2021.28568

Aim: To estimate the overall and organ system—specific frequency of post-acute sequelae of COVID-19.

27. Hayes et al. More than 100 persistent symptoms of SARS-CoV-2 (long COVID): A scoping review. Front Med 2021; 8:750378. <u>https://doi.org/10.3389/fmed.2021.750378</u>

Aim: To conduct a systematic search of the published literature concerning long COVID symptoms and their prevalence

28. Huntley, C. C., & Patel, K. Respiratory sequelae following SARS, MERS, and COVID-19: A systematic review and meta-analysis of pulmonary function tests and CT features (PRE-PRINT). SSRN 2021; <u>https://dx.doi.org/10.2139/ssrn.3844876</u>

Aim: To define respiratory physiological and thoracic radiological sequelae / complications following SARS, MERS & COVID-19 infection.

29. Iqbal et al. Characteristics and predictors of acute and chronic post-COVID syndrome: A systematic review and meta-analysis. EClinicalMedicine 2021; 36:100899. https://doi.org/10.1016/j.eclinm.2021.100899

Aim: To detail the prevalence of clinical features and identify potential predictors for acute and chronic post-COVID syndrome.

30. Iwu et al. (2021). The occurrence of long COVID: A rapid review. Pan Afr Med J, 38, 65. https://doi.org/10.11604/pamj.2021.38.65.27366

Aim: To synthesise evidence on the long-term effects of the SARS-CoV-2 infection among survivors.

 Jennings, G et al. (2021). A systematic review of persistent symptoms and residual abnormal functioning following acute COVID-19: Ongoing symptomatic phase vs. post-COVID-19 syndrome. medRxiv. 2021; 2021.06.25.21259372. <u>https://doi.org/10.1101/2021.06.25.21259372</u>

Aim: To compare the two phases of long COVID, namely ongoing symptomatic COVID-19 (signs & symptoms from 4 to 12 weeks from initial infection) and post-COVID-19 syndrome (beyond 12 weeks) with respect to symptomatology, abnormal functioning, psychological burden, and quality of life.

32. Long et al. Follow-ups on persistent symptoms and pulmonary function among post-acute COVID-19 patients: A systematic review and meta-analysis. Front Med 2021; 8; 702635. https://doi.org/10.3389/fmed.2021.702635 Aim: To explore existing data about post-acute COVID-19 Syndrome.

33. Lopez-Leon et al. More than 50 long-term effects of COVID-19: A systematic review and meta-analysis. Sci Rep 2021; 11(1):16144. <u>https://doi.org/10.1038/s41598-021-95565-8</u>

Aim: To estimate the frequency of symptoms, signs or abnormal laboratory parameters extending beyond the acute phase of COVID-19.

34. Malik et al. Post-acute COVID-19 syndrome (PCS) and health-related quality of life (HRQoL)-a systematic review and meta-analysis. J Med Virol 2022; 94(1):253-262. https://doi.org/10.1002/jmv.27309

Aim: To evaluate the pooled prevalence of poor quality of life in patients post COVID-19. Also, to conduct a meta-regression to evaluate the effects of persistent symptoms and intensive care unit (ICU) admission on the poor quality of life.

35. Mejía-Zambrano. Radiological and functional pulmonary complications in patients recovered from COVID-19. Microbes, Infection and Chemotherapy 2021; 1:e1217. https://doi.org/10.54034/mic.e1217

Aim: To determine radiological and functional pulmonary complications in patients recovered from COVID-19.

36. Nasserie et al. Assessment of the frequency and variety of persistent symptoms among patients with COVID-19: A systematic review. JAMA Netw Open 2021; 4(5):e2111417. http://doi.org/10.1001/jamanetworkopen.2021.11417

Aim: To examine the frequency and nature of persistent symptoms after COVID-19 infection.

37. Poudel et al. Impact of COVID-19 on health-related quality of life of patients: A structured review. PLoS One 2021; 16(10):e0259164. <u>http://doi.org/10.1371/journal.pone.0259164</u>

Aim: To assess the impacts of COVID-19 on health-related quality of life and explore the risk factors for reduced HRQoL of COVID-19 patients.

 Ramadan et al. Cardiac sequelae after coronavirus disease 2019 recovery: A systematic review. Clin Microbiol Infect 2021; 27(9):1250-1261. <u>https://doi.org/10.1016/j.cmi.2021.06.015</u>

Aim: To assess the range of cardiac sequelae after COVID-19 recovery.

39. Rao et al. Fatigue symptoms associated with COVID-19 in convalescent or recovered COVID-19 patients; a systematic review and meta-analysis. Ann Behav Med 2021; 56(3):219-234. https://doi.org/10.1093/abm/kaab081

Aim: To evaluate the prevalence of fatigue in post-recovery from SARS-CoV-2 infection.

40. Renaud-Charest et al. Onset and frequency of depression in post-COVID-19 syndrome: A systematic review. J Psychiatr Res 2021; 144:129-137. https://doi.org/10.1016/j.jpsychires.2021.09.054 Aim: To determine the frequency of depressive symptoms and clinically significant depression more than 12 weeks following SARS-CoV-2 infection.

41. Salamanna et al. Post-COVID-19 syndrome: The persistent symptoms at the post-viral stage of the disease. A systematic review of the current data. Front Med 2021; 8:653516. https://doi.org/10.3389/fmed.2021.653516

Aim: To assess the current evidence on the long-term symptoms in COVID-19 patients.

42. Sanchez-Ramirez et al. Long-term impact of COVID-19: A systematic review of the literature and meta-analysis. Biomedicines 2021; 9(8). https://doi.org/10.3390/biomedicines9080900

Aim: To explore post COVID-19 effects on patients.

43. Sandler et al. Long COVID and post-infective fatigue syndrome: A review. Open Forum Infect Dis 2021; 8(10):ofab440. <u>https://doi.org/10.1093/ofid/ofab440</u>

Aim: To conduct a systematic review on the emerging data on the epidemiology of fatigue after COVID-19 infection.

44. Schou et al. Psychiatric and neuropsychiatric sequelae of COVID-19 - a systematic review. Brain Behav Immun 2021; 97:328-348. <u>https://doi.org/10.1016/j.bbi.2021.07.018</u>

Aim: 1) To provide an overview of the current evidence of psychiatric complications in long-COVID after primary symptoms of acute COVID-19 have ceased. 2) To identify risk factors and molecular mechanisms which could give rise to psychiatric symptoms.

 Shanbehzadeh et al. Physical and mental health complications post-COVID-19: Scoping review. J Psychosom Res 2021; 147:110525. https://doi.org/10.1016/j.jpsychores.2021.110525

Aim: To review studies that evaluated physical and mental health problems post-COVID-19.

46. So et al. Radiological and functional lung sequelae of COVID-19: A systematic review and meta-analysis. BMC Pulm Med 2021; 21(1):97. <u>https://doi.org/10.1186/s12890-021-01463-0</u>

Aim: To clarify the characteristics of radiological and functional lung sequelae of COVID-19 patients described in the follow-up period after COVID-19.

47. Soriano-Moreno et al. A systematic review of the frequency of persistent constitutional and respiratory symptoms related to COVID-19: A new long COVID syndrome? American Journal Of Respiratory And Critical Care Medicine 2021; 203:9. https://www.atsjournals.org/doi/abs/10.1164/ajrccm-conference.2021.203.1 MeetingAbstracts.A3795

Aim: To summarize what is known about long term sequelae among patients who were hospitalized for severe COVID-19 pneumonia.

 Torres-Castro et al. Respiratory function in patients post-infection by COVID-19: A systematic review and meta-analysis. Pulmonology 2021; 27(4):328-337. https://doi.org/10.1016/j.pulmoe.2020.10.013

Aim: To determine the prevalence of restrictive pattern, obstructive pattern and altered diffusion in patients post-COVID-19 infection and to describe the different evaluations of respiratory function used with these patients.

49. Van Kessel et al. Post-acute and long-COVID-19 symptoms in patients with mild diseases: A systematic review. Fam Pract 2021; 39(1):159-167 <u>https://doi.org/10.1093/fampra/cmab076</u>

Aim: To create an overview of the nature and frequency of persistent symptoms experienced by patients after mild COVID-19 infection.

50. Willi et al. (2021). COVID-19 sequelae in adults aged less than 50 years: A systematic review. Travel Med Infect Dis 2021; 40:101995. <u>https://doi.org/10.1016/j.tmaid.2021.101995</u>

Aim: To evaluate the available evidence of all intermediate and long-term COVID-19 sequelae affecting formerly healthy adults.

 Wong, T. & Weitzer, D. Long COVID and Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS)-a systematic review and comparison of clinical presentation and symptomatology. Medicina 2021; 57(5) <u>https://doi.org/10.3390/medicina57050418</u>

Aim(s): To conduct a systematic review of the research available into the symptomatology of long COVID, and compared them with known symptoms of myalgic encephalomyelitis/ chronic fatigue syndrome (ME/CFS).

Reviews Completed, but not yet published

* Identified as now published from update searches

Primary focus: Symptoms/effects & risk factors

- Macdonald et al. Exploring people's lived experience of Long COVID: a systematic review. PROSPERO 2021 CRD42021271392 Available from: <u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021271392</u> Review question(s): What are people's lived experiences of long COVID symptoms?
- Bal et al. COVID-19 disease severity to predict persistent symptoms: A systematic review and meta-analysis. PROSPERO 2021 CRD42021272990 Available from: <u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021272990</u> Review question(s): 1) How does disease severity affect the prevalence rates and risk of persistent symptoms amongst COVID-19 patients. 2) Does the severity of the disease change the risk of symptoms for up to 12 weeks post-COVID-19 infection and beyond?
- *Ceban et al. Fatigue and cognitive impairment in post-COVID-19 syndrome: a systematic review and meta-analysis. PROSPERO 2021 CRD42021256965 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021256965
Research question(s): 1) What is the incidence of fatigue and cognitive impairment following COVID-19 infection? 2) Do individuals exhibit elevated markers of inflammation 12+ weeks following COVID-19 infection? 3) Do individuals exhibit functional impairment 12+ weeks following COVID-19 infection?

- Curtivo dos Passos et al, The Long Term Loss of Smell and Taste in COVID-19 Patients A Systematic Review and Meta-Analysis. PROSPERO 2020 CRD42020216612 Available from: <u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020216612</u> Research question(s): What is the profile of patients with COVID-19 who have lasting symptoms of loss of smell and taste?
- 5. Jones et al. Physical activity in long-haulers. A systematic review of the prevalence of long-term symptoms and clinical manifestations that may impact (return to) physical activity in people following active COVID-19 infection. PROSPERO 2020 CRD42020206245 Available from: <u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020206245</u> Research question(s): To quantify the prevalence of long-term symptoms and clinical manifestations of COVID-19 that have the potential to impact (return to) physical activity.
- Kim et al. Usage of complementary and alternative medicine for COVID-19: a systematic review of observational studies. PROSPERO 2021 CRD42021278452 Available from: <u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021278452</u> Research question(s): To assess usage of complementary and alternative medicine (CAM) interventions for COVID-19 patients worldwide.
- Park et al. Lung function and chest CT findings after recovery from COVID-19: systematic review and meta-anslysis. PROSPERO 2021 CRD42021234357 Available from: <u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021234357</u> Research question(s): How common are sequelae after recovery from COVID-19, demonstrated by pulmonary function tests or chest CT scans?
- *Premraj et al. Neurological and neuropsychiatric manifestations of post-COVID-19 syndrome: a meta-analysis. PROSPERO 2021 CRD42021254647 Available from: <u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021254647</u> Research question(s): What are the symptoms of neurological/neuropsychiatric symptoms of post-COVID-19 syndrome and their prevalence in hospital and community cohorts?
- *Rungjirajittranon et al. Thrombotic and hemorrhagic incidences in patients after discharge from COVID-19 infection: a systematic review and meta-analysis. PROSPERO 2021 CRD42021278161 Available from: <u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021278161</u> Research question(s): To assess thrombotic and hemorrhagic incidences in patients after discharge from COVID-19 infection.

Protocols of ongoing reviews related to Long COVID

* Identified as now published from update searches

Treatment & rehabilitation

Living reviews

1. *Décary et al. A living systematic review of care models for long COVID/post COVID-19 condition. <u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021282266</u>

Review question(s): What is the best-available evidence about care models for long COVID (e.g. care pathways, structured clinics)?

2. *Godbolt et al. Post COVID - treatment and rehabilitation. Living review. https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021276717

Review question(s): What treatment and rehabilitation are effective for symptoms of post COVID?

Standard systematic reviews

 Cardoso da Silva et al. Physical exercise with post-COVID-19 syndrome in older adults: systematic review and meta-analysis. <u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021270400</u>

Review question(s): What are the effects of physical exercise on older adults affected by COVID-19?

4. Chandan et al. Post-viral syndromes: a systematic review of symptoms, health impacts, treatments and their implications for the management of Long COVID. https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021282074

Review question(s): This systematic review will (1) summarise the symptoms and health impacts (clinical complications and impacts on quality of life and work capability) of previous post-viral syndromes that follow acute infections (2) summarise evidence on non-pharmacological treatments for previous post-viral syndromes and long COVID.

NB: Protocol indicates that both primary research studies and secondary analyses including systematic reviews will be included.

5. Lopes Sauers et al. Rehabilitation outcome measures used in patients with post COVID-19 syndrome: a systematic review and meta-analysis.

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021286714

Review question(s): a) What rehabilitation outcome measures have been used in the literature in patients with post COVID-19 syndrome? b) Are the outcome measures used in these studies consistent with the American Physical Therapy Association (APTA) COVID-19 core outcome measures recommendations? c) What are the measurement properties of the outcome measures used in patients who underwent rehabilitation for post COVID-19 syndrome?

6. Mandini et al. Physical activity for the management of anxiety and depression in adults and elderly subjects: systematic review and meta-analysis for the application in long COVID-19 patients. <u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021254823</u>

Review question(s): Could a physical activity program be effective in reducing anxiety and depression in long-COVID-19 affected individuals?

 Marotta et al. Effects of rehabilitation on reduction of post-COVID-19 fatigue: a systematic review. <u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021284058</u>
 Review question(s): Not stated.

8. *Marshall-Andon et al. A Systematic Review of Post-COVID-19 Rehabilitation Guidelines. https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021236049

Review question(s): What do available clinical guidelines recommend for the rehabilitation of patients following COVID-19?

 Nna et al. Long COVID: A protocol for systematic review and meta-analysis of symptomatology and treatment approaches. https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021236457

Review question(s): a) What are the pooled prevalences of various symptoms of long COVID? b) What are the various reported treatment approaches to long COVID? c) How do factors such as geographic location, race, age, social class, and gender influence symptoms of and treatments to long COVID?

Ruberti et al. Recommendations for the respiratory rehabilitation of discharged COVID-19 patients. <u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021254192</u>
 Review question(s): What are the recommendations and best respiratory rehabilitation treatment for post COVID-19 patients? What is the gold standard of respiratory rehabilitation in patients with pulmonary sequela?

11. Sepúlveda-Loyola et al. Physical rehabilitation in adults with post-COVID syndrome on important clinical outcomes: systematic review and metanalysis. <u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021259740</u>

Review question(s): What is the effect of physical rehabilitation in patients with Post-COVID syndrome on important clinical outcomes?

12. Servais et al. Systematic review on the role of physical therapy and rehabilitation management for patients with COVID-19.

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021245320 Review question(s): What is the role of physical therapy and rehabilitation management in patients with COVID-19 ?

NB: Population of interest is COVID-19 patients at any stage of the disease.

13. Sharma et al. Recent advances in chest rehabilitation among individuals with COVID-19: a systematic review.

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021284940

Review question(s): Are chest rehabilitation techniques effective in managing COVID-19?

NB: Population of interest is individuals with COVID-19.

14. Silva et al. Effects of inspiratory muscle training on Post-COVID-19 syndrome.

<u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021261507</u> Review question(s): Is inspiratory muscle training effective compared to placebo for increasing ventilatory muscle strength, functional capacity, and quality of life in patients with Post-COVID-19 syndrome?

15. Zhang et al. The effectiveness of respiratory rehabilitation for patients with coronavirusrelated pneumonia (COVID-19, SARS, MERS): a systematic review and meta-analysis. <u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020202011</u>

Review question(s): Which respiratory rehabilitation approaches are effective in improving the health status of COVID-19 patients?

Health & economics

16. Campbell et al. Predictors of COVID-19 outcomes: an individual participant meta-analysis: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020224323

Review question(s): 1) What are the long-term outcomes of people after COVID-19 in relation to the ICF (International Classification of Functioning, Disability and Health)? 2) What are the predictors of long-term outcomes? 3) What are the direct and indirect costs associated with long-COVID-19?

17. Ceban et al. The global economic burden of COVID-19: a systematic review and metaanalysis of national DALYs.

https://www.crd.york.ac.uk/prospero/display record.php?ID=CRD42021274063 Review question(s): (1) What is the pooled global disability-adjusted life years (DALYs) estimate of COVID-19? (2) What are the most notable socioeconomic implications and productivity losses

NB: Population of interest is individuals with symptoms persisting beyond the resolution of the acute phase, defined as at least 4 weeks following initial diagnosis (long COVID).

18. Thompson et al. The burden of long COVID: a systematic review.

associated with COVID-19 sequelae in different regions of the world?

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021288753

Review question(s): This systematic review aims to identify and summarise available evidence on the burden of long COVID. This aim is to understand the prevalence, morbidity and mortality associated with long COVID, including the economic impact and indirect costs.

Risk factors; risk factors & prevalence

19. Bachion et al. Fatigue predictors in adults and elderly after the acute phase of COVID-19: systematic review and meta-analysis.

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021272377

Review question(s) What factors predict fatigue in adults and elderly individuals after the acute phase of COVID-19?

20. *Caminiti et al. Prognostic factors for persistent symptoms and quality of life after hospitalization for COVID-19: a systematic review and meta-analysis. https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021253467

Review question(s): In patients hospitalized for COVID-19, which factors, already present or emerging during hospitalization, are associated with an increased risk of exhibiting new or persisting symptoms, worse quality of life and worse psychosocial health beyond 12 weeks?

21. Hahne et al. Pre-existing autoimmune and allergic diseases as risk factors for Long-COVID symptoms: protocol for a rapid review.

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021247612 Review question(s): Are pre-existing autoimmune and allergic diseases risk factors for Long-COVID symptoms?

22. Hamada et al. Risk of admission among COVID-19 patients after initial acute episode of COVID-19: a systematic review and meta-analysis.

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021244348

Review question(s): 1) What are the rates and risk of admission among COVID-19 patients after the index episode of COVID-19? 2) What are the risk factors for admission after recovery from the index episode?

23. Hu et al. Risk factors for hospital readmission among discharge patients with COVID-19: a systematic review and meta-analysis.

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021272310

Review question(s): 1) What are the estimates for readmission rate following hospitalisation for COVID-19? 2) What are the characteristics and risk factors for those participants who are readmitted compared to those who are not readmitted?

NB: Discharge duration of interest is within 14, 30, 60 and 60+ days.

24. Narain et al Characterizing the relationship between long COVID, inflammation and mood disorders: a systematic review

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021257503

Review question(s): What is the relationship of Long COVID to mood disorders and inflammation?

25. *Pillay et al. Risk factors and preventive interventions for post-COVID-19 condition: protocol for systematic reviews.

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021270354

Review question(s): 1) Among people who have had COVID-19, what are the associations between pre-existing and clinical risk factors and development of post-COVID-19 condition? 2) Among people in the acute (symptom onset to 4 weeks) or early post-acute phase (4-8 weeks) of COVID-19 what are the effects of interventions to prevent post-COVID-19 condition?

26. Thung Sen et al. Systematic review and meta-analysis of post-acute COVID-19 symptoms and risk based on infection severity.

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021241778

Review question(s): 1) What are the rates of post-acute COVID-19 symptoms and pathological changes? 2) How does the risk differ between mild-moderate COVID-19 cases to severe-critical cases? 3) Are there difference across the life-span/age spectrum, i.e., children vs adults vs elderly?

27. Zakia et al. Systematic review and meta-analysis of prevalence and risk factors for psychiatric symptoms in long COVID patients https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021240776

Review question(s) 1) What is the prevalence of psychiatric symptoms (depression, anxiety, PTSD, and others) in long COVID patients? 2) What are the risk factors of psychiatric symptoms (depression, anxiety, PTSD, and others) in long COVID patients?

28. Zhang et al. The prevalence, incidence, risk factors and clinical outcome of neuropsychiatric complications associated with SARS-CoV-2: systematic review and meta-analysis. <u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021245371</u>

Review question(s): 1) What is the prevalence and incidence of neuropsychiatric complications following SARS-CoV-2? 2) What are the main risk factors associated with neuropsychiatric complications following SARS-CoV-2? 3) What is the clinical outcome of neuropsychiatric complications following SARS-CoV-2?

29. Zheng et al. Prevalence of and risk factors for post-COVID breathlessness in COVID-19 survivors: a systematic review and meta-analysis.

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021285733

Review question(s): 1) To determine the prevalence of post-COVID breathlessness in COVID-19 survivors by different follow-up lengths, population characteristics and methodological approaches. 2) To determine the risk factors or mechanisms of post-COVID breathlessness. 3) To investigate the therapies for the prevention or treatment of post-COVID breathlessness.

Symptoms, effects & prevalence

Review of Reviews

30. Paterson et al. What are the longer-term holistic health consequences of COVID-19 among survivors? An umbrella systematic review protocol.

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021284508

Review question(s): Among COVID-19 survivors, what are the physical, psychological, social, and spiritual impacts of the illness which extend beyond the acute phase?

Living reviews

31. O'Mahoney et al. A living systematic review of the prevalence and long-term health effects of ongoing symptomatic COVID 19 and post COVID 19 syndrome among hospitalised and non-hospitalised patients by age, sex, ethnicity and deprivation. https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021238247 Review question(s): 1) What is the overall prevalence of ongoing symptomatic COVID 19 and post COVID 19 syndrome and associated health complications among hospitalised and non-hospitalised patients? 2) What is the prevalence of ongoing symptomatic COVID 19 and post COVID 19 syndrome and associated health complications among hospitalised and non-hospitalised patients when stratified by age, sex, ethnicity and deprivation?

32. Rycroft et al. A living systematic review of the impacts of COVID-19 on the health-related quality of life across Black, Asian and minority ethnic (BAME) groups. https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021238645

Review question(s): 1) What is the impact of COVID-19 on the health-related quality of life among BAME groups? 2) How does the impact of COVID-19 on health-related quality of life differ across BAME groups? 3) What is the relationship between the reported secondary diagnosis of COVID-19 and impact of the health-related quality of life among BAME groups?

NB: Population of interest is people of a BAME ethnicity with active COVID-19 or who had recovered; both primary research studies and systematic reviews will be included.

33. Welsh et al. Long term COVID-19 (Long COVID) in children and young people: a living systematic review.

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020226624

Review question(s): 1) What is the prevalence of Long COVID in children and young people? 2) What symptoms and symptom patterns are seen in Long COVID in children and young people? 3) What are the physical, psychological, and social consequences of Long COVID in children and young people? 4) What are the lived experiences of children and young people, and their families? 5) What are the prognostic factors associated with the development and adverse outcomes of Long COVID (in terms of duration, severity and impact)?

Standard systematic reviews

34. Alves et al. Sleep quality post-COVID-19: a systematic review.

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021279192

Review question(s): Can COVID-19 infection lead to changes in the quality of sleep of individuals after infection?

35. Austhof et al. Symptom profile, frequency, duration, and severity of post-acute and chronic sequelae of COVID-19: a rapid systematic review.

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021278166

Review question(s): To determine the prevalence, frequency, duration, and severity of post-acute and chronic sequelae after COVID-19 infection.

36. Ávila Cabral et al. Long-term impact of COVID-19 on executive functions: A systematic review and meta-analysis.

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021262961

Review question(s): 1) What is the prevalence of neurocognitive disorders and neurologic manifestations that affect executive functions in post-COVID-19 syndrome patients? 2) How does

neurologic manifestations during ongoing symptomatic COVID-19 correlates with executive functions impairment in post-COVID-19 syndrome?

NB: review now completed not yet published.

37. Awan et al. What is the lived experience of long COVID in ethnic minorities in the UK? A systematic review.

<u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021266236</u> Review question(s): What is the lived experience of long COVID in ethnic minorities in the UK?

38. *Ayuzo-del-Valle et al. Long-term effects of COVID-19 in Children : A systematic review and meta-analysis.

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021275408

Review question(s): 1) What is the prevalence of long-term effects of COVID-19 in Children? 2) What are the long-term effects of COVID-19 in children?

NB: Now published as Lopez-Leon et al. Long COVID in Children and Adolescents: A Systematic Review and Meta-analyses. medRxiv. 2022.03.10.22272237; https://doi.org/10.1101/2022.03.10.2227223

- 39. Baye et al. The global prevalence of pulmonary fibrosis among post-COVID-19 follow-up patients. <u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021275832</u> Review question(s): Is pulmonary fibrosis prevalent among post-COVID-19 follow-up patients?
 - 40. Bezerra da Silva Maciel et al. Prevalence of gastroenterological symptoms in survivors of coronavirus disease 2019 (COVID-19): a systematic review and meta-analysis. https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021269492

Review question(s): To determine the prevalence of persistent gastrointestinal symptoms after hospital admission for COVID-19.

41. Bikkannavar et al. Prevalence and characteristics of headache associated with SARS-CoV-2 infection: a systematic review, meta-analysis and discussion. https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021235146

Review question(s): 1) What is the prevalence of headache attributed to SARS-CoV-2 infection, including in Long COVID? 2) What are the characteristics/categories of these headaches? 3) What is the prevalence of different categories of headaches attributed to SARS-CoV-2 infection, including in Long COVID?

42. Cavalini et al. A systematic review and meta-analyses exploring the main symptoms and mental health of long-term COVID-19. https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021265259 Review question(s): 1) What are the main skeletal muscle, neurological, and/or physical disorders of long-term COVID-19? 2) What are the common symptoms amongst acute COVID-19 and long-term COVID-19? 3) What are the main mental health outcomes in long-term COVID-19? 4) What are the main pain symptoms in long-term COVID-19? 5) What is the current treatment that has been offered to these patients?

43. Chaurasia et al. Oral manifestations in COVID-19 infection: a systematic review and meta-analysis. <u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021273982</u>
Review question(s): 1) What are the oral signs and symptoms reported in COVID-19 disease? 2)
What are the most common oral signs and symptoms in COVID-19 disease? 3) Does age, sex and severity of COVID-19 disease affect the oral manifestations? 4) How frequently have oral signs and symptoms been reported in symptomatic COVID-19 patients having mild to severe forms of the disease? 5) Are oral signs and symptoms reported in post-COVID-19 patients?

44. *Crivelli et al. Cognitive consequences of COVID-19: a systematic review. https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021243026

Review question(s): To evaluate cognitive impairment after SARS-CoV-2 infection in persons with or without pre-pandemic cognitive impairment.

45. Cruickshank et al. What is the impact of long term COVID-19 on workers in healthcare settings? A rapid review of current evidence.

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021288181

Review question(s): The objective of this systematic rapid review is to assess the effects of long COVID among healthcare workers and its impact on their self-reported health status, professional working lives, personal circumstances and use of health services.

46. Cuba-Fuentes et al. A systematic review of the frequency of long-term patient-reported constitutional and respiratory symptoms related to COVID-19: a new long COVID syndrome? <u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020208154</u>

Review question(s): What is the frequency of long-term constitutional and respiratory symptoms related to COVID-19 infection?

47. Dassanayakege et al. Post COVID-19 outcomes of older people: a systematic review and meta-analysis.

<u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021287503</u> Review question(s): 1) What are the prevalence of acute post COVID-19 outcomes of older people? 2). What are the prevalence of chronic post COVID-19 outcomes of older people?

48. Delanerolle et al. A systematic review exploring the prevalence of autonomic dysfunction amongst COVID-19 patients <u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021235351</u> Research question: 1) What is the prevalence of autonomic dysfunction amongst COVID-19 patients? 2) What is the prevalence of autonomic dysfunction amongst SARS and MERS patients? 3)What are the common autonomic dysfunction denominators across MERS vs. SARS vs. COVID-19? 4) What is the prevalence of neuropsychiatric outcomes amongst COVID-19 vs MERS vs SARS patients? 5) What are the autonomic parameters affected? 6) What are the current treatments offered to these patients?

49. Deng et al. The prevalence of long-term effects of COVID-19: a systematic review and prevalence meta-analysis.

<u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021266569</u> Review question(s): For patients with long-term complications from COVID-19, what is the prevalence of each type of complication.

50. Di Matteo et al. COVID syndrome: symptoms and stratified follow up. A systematic review. https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021283689

Review question(s): How many studies have considered post COVID 19 follow-up and what symptoms and timing have they investigated?

NB: Review now completed not published.

51. Divakaruni et al. Prevalence of gastrointestinal manifestations in COVID-19 cases - a systematic review.

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021278999

Review question(s): 1) What is the prevalence of Gastrointestinal manifestations in COVID19 cases? 2) Is there any difference of prevalence of GI manifestations of COVID19 according to age, health status, vaccination status, country? 3) Is there any relation between severity of GI symptoms and carrier status, prolonged COVID19 symptoms, multi system inflammatory disorder, ICU admissions, severity of COVID19, the spread of COVID19?

52. Firdaus et al. Respiratory and neuropsychiatry sequelae in post COVID-19 condition: a systematic review.

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021274568

Review question(s): 1) What are the clinical manifestation and profile (laboratory, radiological and functional) of Post COVID-19 condition associated with sequelae in the respiratory and neuropsychiatry system among adults? 2) What are the predisposing condition or risk factors of Post COVID-19 condition associated with sequelae in the respiratory and neuropsychiatry system among adults?

53. Gesser et al. Functioning, fatigue and quality of life in survivors of critical COVID-19 cases after hospital discharge: a systematic review. https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021258356

Review question(s): What are the short and long-term impairments to functioning, fatigue and quality of life in survivors of critical COVID-19 cases after hospital discharge?

54. Htet et al. Long term clinical outcomes among survivors of ICU admitted COVID-19 patients 3 months and beyond: A systematic review and meta-analysis. https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021277961

Review question(s): 1) What are the clinical outcomes among survivors of critically ill COVID-19 patients, 3 months and beyond? 2) What are the factors associated with the outcomes among survivors of critically ill COVID-19 patients, 3 months and beyond? 3) Is there a correlation between the severity of illness with clinical outcome 3 months and beyond among survivors of critically ill COVID-19 patients?

55. Jamal et al. Prolonged post COVID-19 symptoms: A systematic review and dental considerations in COVID-19 recovered patients with prolonged symptoms. <u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021235714</u> Review question(s) What are the prolonged symptoms of COVID-19?

NB: Protocol indicates that both primary research studies and systematic reviews will be included.

- 56. Karki et al. Long term complication associated with SARS-CoV-2 infections: A systematic review. <u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021262334</u> Review question(s): What are the long-term health complications associated with SARS-CoV-2 infection?
 - 57. Kuodi et al. Characterisation of the long-term physical, mental and social health impacts of SARS-COV-2 infection: a systematic review and meta-analysis. https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021265890

Review question(s): What are the long-term physical and psychosocial health impacts of SARS-COV-2 infection?

58. Livingstone et al. Long-COVID: pulmonary sequelae. https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021272625

Review question(s): Broadly we are investigating long-COVID and the pulmonary effects that come with this. In particular, the area of pulmonary effects will be broken down into 3 sub-categories of 1 - symptoms (dyspnoea, shortness of breath etc), 2 - pulmonary imagining and their findings and 3 - measurements of respiratory function (i.e. spirometry, 6 minute walk test). We hope to explore these categories to provide a better understanding of pulmonary sequelae in long-COVID patients

59. Lui et al. The impact of post-COVID-19 syndrome on function and quality of life: a systematic review and meta-analysis.

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021274305

Review question(s): Which cluster symptom of post-COVID-19 syndrome has the greatest effect on function, and quality of life?

60. Mendes da Silva et al. Prevalence of symptoms in post-COVID-19 syndrome in adults after six months of infection: a systematic review.

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021262759

Review question(s): What is the prevalence of persistent symptoms in individuals with post-COVID-19 syndrome after six months of infection?

61. *Middleton et al. Patient-reported respiratory outcome measures in the recovery of adults hospitalised with COVID-19: a systematic review and meta-analysis. https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021242134

Review question(s): What is the respiratory symptomatic and functional recovery of patients with COVID-19 more than 8 weeks after hospitalisation?

62. Nersesjan et al. Delayed post-hypoxic leukoencephalopathy in COVID-19: a systematic review. <u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021232753</u>
Review question(s): In COVID-19 patients with an evident hypoxic event, followed by an intermittent recovery period and subsequent neurological and/or psychiatric deterioration with brain-MRI showing symmetric subcortical T2-hyperintensive lesions (P) is the overall disease course (I) compatible with previous described cases of delayed post-hypoxic leukoencephalopathy (DPHL) (C) or does the disease course in COVID-19 patients differ significantly?

NB: Review now discontinued.

63. Noormahomed et al. Post-COVID-19 complications and sequelae in HIV infected and uninfected patients: a systematic review and meta-analysis. https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021260056

Review question(s): Are the complications and sequelae after COVID-19 infection more prevalent and severe in HIV infected patients than in HIV uninfected patients?

64. Nursanti et al. Global prevalence of persistence prolonged complication among COVID-19 survivors: a meta-analysis.

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021251900

Review question(s): What is the pooled estimated prevalence of prolonged complication among COVID-19 survivors, including dizziness, chest pain, sleep difficulty, palpitation, weight loss, and hair loss, fatigue, hallucination?

65. Organ et al. The prevalence of long COVID-19 symptoms among people with neurodevelopmental disorders (NDD) and/or mental illnesses. https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021231279

Review question(s): The aims of this search are to summarise: 1) The prevalence of long COVID-19 symptoms among people with Neurodevelopmental disorders (NDD) such as Intellectual disability, autism etc. and/or mental illnesses following infection with COVID-19. 2) Sub analysis of the prevalence of neuropsychiatric symptoms experienced by people with NDD and/or mental illnesses and disorders following COVID-19 infection.

NB: Protocol indicates that both primary research studies and meta-analyses will be included.

66. Pan et al. The relationship between ethnicity and long-COVID-19: a systematic review and meta-analysis.

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020220981

Review question(s): To investigate the relationship between ethnicity and long-COVID-19.

67. Plentz et al. Pulmonary function, quality of life and functional capacity post COVID-19. https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021278807

Review question(s): 1) What is the impact on pulmonary function in post-COVID-19 patients? 2) What is the level of functional capacity of post-COVID-19 patients? 3) What is the status of the quality of life of post-COVID-19 patients?

68. Posso et al. The upcoming wave: clinical outcomes and sequelae in COVID-19 survivors: a systematic review and meta-analyses. https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021262688

Review question(s): What are the long-term clinical outcomes or sequelae in adults (>18 years) following COVID-19 recovery?

69. Ramos et al. Long-term outcomes and resource utilization after intensive care unit discharge for survivors of epidemic viral pneumonias: a systematic review. https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021190296

Review question(s): What are the long-term outcomes and resource utilization of survivors from critical illness due to epidemic viral pneumonias (SARS, MERS, H1N1 and COVID-19)?

70. Rodrigues et al. Adult prevalence and characteristics of muscle pain and joint pain associated with SARS-CoV-2: a systematic review, meta-analysis, and critical appraisal. https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021244419

Review question(s): 1) What is the prevalence of muscle pain and joint pain on COVID-19 cases globally? 2) Is there a difference in frequency and severity of muscle pain and joint pain between genders affected by COVID-19? 3) Is there a difference in the age of COVID-19 patients who report muscle and joint pain? 4) Did the patients use any medication to treat muscle and joint pain? 5) Whether muscle pain and joint pain are symptoms that remain after COVID-19 infection?

71. Sliwka et al. Post-COVID-19 symptoms in adults with asthma.

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021242960

Review question(s): 1) What are the long term (lasting \geq 12 weeks) symptoms caused by SARS-CoV-2 infection amongst patients with asthma? 2) Are the long term (lasting \geq 12 weeks) symptoms caused by SARS-CoV-2 in patients diagnosed with asthma different than in patients without asthma? 3) What does the evidence tell us about long-term consequences for the pulmonary function, asthma symptoms, intensity of pharmacological treatment, physical fitness and depressive symptoms of adults with asthma after SARS-CoV-2 infection? 4) Does the asthma control before SARS-CoV-2

infection influence the disease severity, pulmonary function and severity of long-term symptoms after infection? 5) Does the severity of acute SARS-CoV-2 infection influence the pulmonary function and long term symptoms?

72. Tabar et al. Long-term moderate to severe complications of COVID-19 infection since 2019 to date; a protocol for systematic review and/or meta-analysis. https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021240027

Review question(s): To study the long-term moderate to severe complications of COVID-19 infection since 2019 to date in patients of all ages who developed COVID-19.

73. Tan et al. Prognosis of smell and taste recovery in COVID-19 patients: a systematic review and one-stage meta-analysis of individual patient time-to-event data. https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021283922

Review question(s): 1) What is the percentage of COVID-19 patients with olfactory/gustatory dysfunction who recover their sense of smell/taste? 2) What percentage of patients develop persistent olfactory/gustatory dysfunction? 3) What is the time-to-recovery of smell/taste? 4) What are the prognostic factors in association with time-to-recovery or extent of recovery of smell/taste?

NB: Review now completed, not published.

74. Uribe et al. Psychiatric and neuropsychiatric signs and symptoms in patients with SARS-CoV-2 (COVID-19) infection, in the resolution phase: a systematic review and meta-analysis. https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021247057

Review question(s) What symptoms and signs of psychiatric and neuropsychiatric disorders may appear after the resolution of infection by SARS-CoV-2/COVID-19?

75. Velichkovsky et al. Cognitive deficits and impairments after COVID-19: systematic review and meta-analysis.

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021288003

Review question(s): What are cognitive impairments in people reconvalescent from COVID-19 in comparison to healthy controls?

- 76. Woodrow et al. The prevalence of long COVID: a systematic review. <u>https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020218351</u> Review question(s): What is the prevalence of prolonged symptoms and/or functional disability and/or new pathology following SARS-CoV2 infection among all people infected?
 - 77. Xu et al. Post-COVID-19 pain burden and quality of life in COVID-19 patients: a meta-analysis and systematic review. https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021272800

Review question(s) This pooled analysis aims to investigate the prevalence of pain related symptoms in patients after acute phase of COVID-19. Impact of COVID-19 on the quality of life and pain symptom among these populations in post-acute phase will also be evaluated.

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Evidence for Policy and Practice Information Centre (EPPI Centre) Social Science Research Unit, UCL Social Research Institute UCL Institute of Education, University College London 18 Woburn Square London WC1H 0NR

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Email: ioe.ssru@ucl.ac.uk Telephone: +44 (0)20 7331 5263