

Reviews on Long COVID

A scope of the literature: update

July 2022

The NIHR Policy Research Programme Reviews Facility is a collaboration between the following:

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

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Introduction

This report is the second quarterly update of the rapid scope of published and ongoing systematic reviews related to Long COVID that was originally conducted for the Department of Health and Social Care in England in November 2021.¹ The first update covered the period November 2021 to the end of March 2022.² For the current update, we identified systematic reviews and review protocols focused on Long COVID that were published between the start of April and the end of June 2022. Long COVID was conceptualised broadly as any symptoms or effects that persist or develop after acute COVID-19 infection.

Identification of reviews

We amended the search strategy used for this update to increase sensitivity and precision. Most notably, we included several additional review-related terms - meta-synthesis, pooled analysis, and realist synthesis. To identify relevant research for previous reports, we searched the living systematic map of Long COVID-19 evidence maintained by staff at the London-York NIHR Policy Reviews Facility. We were unable to use the map for this update owing to a technical issue beyond our control. Instead, we searched the CINAHL database in addition to the other two sources used for previous reports. These were:

- The PROSPERO database. (An International prospective register of systematic reviews). We searched using the terms long COVID; post COVID; post-acute sequelae; PASC; post-acute COVID; long term COVID. Records tagged as Long COVID in the database were also screened.
- PubMed. We searched for records with COVID and review related terms in the title or abstract fields. The PubMed search strategy is provided in Appendix 1 (page 18). The terms used for the searches of PubMed and CINAHL were identical.

The inclusion criteria applied to reviews in this update were consistent with previous reports. To be included, reviews needed to have a primary focus on Long COVID (however conceptualised and defined) and be systematic in nature. A review was considered systematic if it reported some search terms and inclusion criteria and also reported the number of references retrieved and the number of studies included. Reviews could focus on adults and/or children and include primary studies of any design or other reviews (i.e. reviews of reviews). We did not apply criteria relating to the length of time 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. Titles and abstracts were screened by one reviewer; two reviewers screened the full text of papers.

Key findings

We screened 415 records and identified **28 reviews that had been published since the end of March and 59 new protocols for ongoing reviews**. The flow of studies through the review is shown in Appendix 2 (page 19). Table 1 (page 2) provides a summary of all reviews identified for this update by focus. The full reference and aim/research questions for the reviews are provided on pages 2-17.

¹ Raine G, Sutcliffe K, Sowden A (2021) Reviews on Long COVID: A scope of the literature. London: EPPI Centre, UCL Social Research Institute, UCL Institute of Education, University College London.

² Raine G, Sutcliffe K, Sowden A (2022) Reviews on Long COVID: A scope of the literature. Update April 2022. London: EPPI Centre, UCL Social Research Institute, UCL Institute of Education, University College London.

Table 1: Summary of reviews published between April-June 2022

Review status Main focus	Systematic review
Published reviews	
Treatment/rehabilitation	3
Symptoms/effects	22*
Risk factors; risk factors & prevalence	3
Ongoing reviews (protocols)	
Treatment/rehabilitation	12
Prevention	2
Health and social	1
Symptoms/effects	31
Risk factors; risk factors & prevalence	10
Pathobiology	3

* Includes 1 pre-print and 2 papers identified in previous reports as pre-prints.

We identified a smaller number of recently published reviews (n=28) and new protocols for ongoing reviews (n=59) compared to our previous report in April (n=54 & n=73), but that covered a slightly longer period between mid-November 2021 and the end of March 2022. We did not identify any reviews of reviews or living reviews from our latest search of the literature.

Over three quarters of published reviews focused on the frequency or risk of persistent symptoms and effects (n=22). The majority of new reviews that we identified through PROSPERO also focused on symptoms and effects (n=31); a fifth were related to treatment/rehabilitation (n=12). A similar proportion of protocols in our previous report were focused on treatment/rehabilitation (23%). Notably, three of the 12 ongoing reviews are examining the effectiveness of COVID-19 vaccination for treating or preventing long COVID symptoms (#9 Rahman et al., 2022; #12 Tandarto et al, 2022; and #13 Poethko-Mueller et al, 2022).

1) Reviews published between April and June 2022

Treatment & rehabilitation

1. Aryana et al. Appropriate Timing and Type of Physical Training in Patients with COVID-19 for Muscle Health and Quality of Life: A Systematic Review. *J Nutr Metab.* 2022;2022:6119593. <https://doi.org/10.1155/2022/6119593>

Aim: To investigate physical training on muscle health and quality of life in patients with COVID-19.

NB: Paper had a separate section on post-COVID patients.

2. Carson & Hemenway. A Scoping Review of Pharmacological Management of Postacute Sequelae of Severe Acute Respiratory Syndrome Coronavirus 2 Infection in 2021. *Am J Ther.* 2022;29(3):e305-e21. <http://doi.org/10.1097/MJT.0000000000001486>

Aim: To assess medical literature for any evidence supporting or refuting use of any medications to specifically treat Post-acute sequelae of SARS-CoV-2 infection (PASC).

3. Fugazzaro et al. Rehabilitation Interventions for Post-Acute COVID-19 Syndrome: A Systematic Review. *Int J Environ Res Public Health.* 2022;19(9). <https://doi.org/10.3390/ijerph19095185>

Aim: To explore the effectiveness of rehabilitation interventions for adult patients with post-acute COVID-19 syndrome (PASC) by reporting the main changes in outcomes after the experimental interventions.

Symptoms and effects

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

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

NB: An earlier version of this review was included in a previous report.

5. Alahyari et al. Post-COVID-19 hematologic complications: a systematic review. *Expert Rev Hematol.* 2022;15(6):539-46. <https://doi.org/10.1080/17474086.2022.2080051>

Aim: To comprehensively assess all reported post-COVID hematologic complications.

6. Alkodaymi et al. Prevalence of post-acute COVID-19 syndrome symptoms at different follow-up periods: a systematic review and meta-analysis. *Clin Microbiol Infect.* 2022;28(5):657-66. <https://doi.org/10.1016/j.cmi.2022.01.014>

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

NB: An earlier version of this review was included in a previous report.

7. Almas et al. Post-acute COVID-19 syndrome and its prolonged effects: An updated systematic review. *Ann Med Surg (Lond).* 2022:103995. <https://doi.org/10.1016/j.amsu.2022.103995>

Aim: To estimate the prevalence of persisting COVID-19 signs and symptoms after recovery.

8. Alosaimi et al. Cardiovascular complications and outcomes among athletes with COVID-19 disease: a systematic review. *BMC Sports Sci Med Rehabil.* 2022;14(1):74. <https://doi.org/10.1016/j.amsu.2022.103995>

Aim: To measure the prevalence of cardiac complications suffered by COVID-19 athletic patients.

9. Banerjee et al. Risk of incident diabetes post-COVID-19: A systematic review and meta-analysis. *Prim Care Diabetes.* 2022. <https://doi.org/10.1016/j.pcd.2022.05.009>

Aim: To summarize the available literature and provide a pooled estimate of the risk of developing incident diabetes following hospital discharge or at least 28 days after the COVID-19 diagnosis compared to matched controls.

10. Chen et al. Global Prevalence of Post COVID-19 Condition or Long COVID: A Meta-Analysis and Systematic Review. *J Infect Dis.* 2022. <https://doi.org/10.1093/infdis/jiac136>

Aim: To examine the worldwide prevalence of post-coronavirus disease 2019 (COVID-19) condition, through a systematic review and meta-analysis.

11. Crivelli et al. Changes in cognitive functioning after COVID-19: A systematic review and meta-analysis. *Alzheimers Dement.* 2022;18(5):1047-66. <https://doi.org/10.1002/alz.12644>

Aim: To conduct a systematic review and meta-analysis of the cognitive effects of coronavirus disease 2019 (COVID-19) in adults with no prior history of cognitive impairment.

NB: An earlier version of this review was included in a previous report.

12. de Oliveira Almeida et al. A systematic review on physical function, activities of daily living and health-related quality of life in COVID-19 survivors. *Chronic Illn.* 2022;17423953221089309. <https://doi.org/10.1177/17423953221089309>

Aim: To analyse the published studies that investigated the physical function, activities of daily living and health-related quality of life in COVID-19 survivors.

13. Durstenfeld et al. Cardiopulmonary exercise testing to evaluate post-acute sequelae of COVID-19 (Long COVID): a systematic review and meta-analysis. *medRxiv.* 2022. <https://doi.org/10.1101/2022.06.15.22276458>

Aim: To estimate the effect of SARS-CoV-2 infection on exercise capacity including those with and without long COVID symptoms and to identify potential causal pathways for reduced exercise capacity after SARS-CoV-2 infection.

NB: This is a pre-print.

14. Fancello et al. Sensorineural Hearing Loss Post-COVID-19 Infection: An Update. *Audiol Res.* 2022;12(3):307-15. <https://doi.org/10.3390/audiolres12030032>

Aim: The aim of this paper is to evaluate the possible association between sensorineural hearing loss and COVID-19 infection.

15. 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 discuss the main findings regarding HRQoL in post-COVID-19 patients who required hospitalization.

NB: An earlier version of this review was included in a previous report.

16. Frosolini et al. Magnetic Resonance Imaging Confirmed Olfactory Bulb Reduction in Long COVID-19: Literature Review and Case Series. *Brain Sci.* 2022;12(4). <https://doi.org/10.3390/brainsci12040430>

Aim: To clarify radiological alterations of olfactory pathways in patients with long COVID-19 characterized by olfactory dysfunction.

17. Gupta et al. Long COVID in Children and Adolescents. *Prim Care Companion CNS Disord.* 2022;24(2). <https://doi.org/10.4088/PCC.21r03218>

Aim: The objective of this article is to review the literature on long COVID in children and adolescents post-SARS-CoV-2 infection to understand epidemiologic trends, preventive measures, and treatment options.

18. Healey et al. Symptoms and signs of long COVID: A rapid review and meta-analysis. *J Glob Health.* 2022;12:05014. <https://doi.org/10.7189/jogh.12.05014>

Aim: To identify the incidence of symptoms and signs of long COVID and to investigate if they differed in patients with ongoing symptomatic COVID-19 and post-COVID-19 syndrome.

19. Huntley et al. Pulmonary function test and computed tomography features during follow-up after SARS, MERS and COVID-19: a systematic review and meta-analysis. *ERJ Open Res.* 2022;8(2). <https://doi.org/10.1183/23120541.00056-2022>

Aim: To describe and compare the longitudinal pulmonary function and computed tomography (CT) features of patients recovering from SARS, MERS and COVID-19.

NB: Published online previously as a pre-print.

20. Lemes et al. Acute and post-acute COVID-19 presentations in athletes: a systematic review and meta-analysis. *Br J Sports Med.* 2022. <https://doi:10.1136/bjsports-2022-105583>

Aim: To report on acute and postacute COVID-19 presentations in athletes.

NB: Paper had a separate section on post-acute COVID presentations.

21. Lopez-Leon et al. Long-COVID in children and adolescents: a systematic review and meta-analyses. *Sci Rep.* 2022;12(1):9950. <https://doi.org/10.1038/s41598-022-13495-5>

Aim: To estimate the prevalence of long-COVID in children and adolescents and to present the full spectrum of symptoms present after acute COVID-19.

NB: Published online previously as a pre-print.

22. Ma et al. Long-Term Consequences of COVID-19 at 6 Months and Above: A Systematic Review and Meta-Analysis. *Int J Environ Res Public Health*. 2022;19(11).
<https://doi.org/10.3390/ijerph19116865>

Aim: To review the data available to evaluate the long-term consequences of coronavirus disease 2019 (COVID-19) at 6 months and above.

23. Mirmosayyeb et al. Post COVID-19 infection neuromyelitis optica spectrum disorder (NMOSD): A case report-based systematic review. *Mult Scler Relat Disord*. 2022;60:103697.
<https://doi.org/10.1016/j.msard.2022.103697>

Aim: To evaluate neuromyelitis optica spectrum disorder in patients following COVID-19 infection.

24. Wang et al. Retinal microvascular impairment in COVID-19 patients: A meta-analysis. *Immun Inflamm Dis*. 2022;10(6):e619. <https://doi.org/10.1002/iid3.619>

Aim: To assess the presence of retinal microvascular impairment in COVID-19 patients.

NB: All included studies comprised recovered COVID patients.

25. Zeng et al. A systematic review and meta-analysis of long term physical and mental sequelae of COVID-19 pandemic: call for research priority and action. *Mol Psychiatry*. 2022:1-11.
<https://doi.org/10.1038/s41380-022-01614-7>

Aim: To systematically review the current evidence of the long-term health consequences of COVID-19 infection.

Risk factors; Risk factors & prevalence

26. Hama et al. Post COVID-19 pulmonary fibrosis; a meta-analysis study. *Ann Med Surg (Lond)*. 2022;77:103590. <https://doi.org/10.1016/j.amsu.2022.103590>

Aim: To investigate the prevalence of post-COVID-19 pulmonary fibrosis and the potential risk factors.

27. Khoja et al. Clinical Characteristics and Mechanisms of Musculoskeletal Pain in Long COVID. *J Pain Res*. 2022;15:1729-48. <https://doi.org/10.2147/JPR.S365026>

Aim: To describe the prevalence, risk factors and the plausible mechanisms of musculoskeletal pain in Long COVID.

28. Sylvester et al. Sex differences in sequelae from COVID-19 infection and in long COVID syndrome: a review. *Curr Med Res Opin*. 2022:1-9.
<https://doi.org/10.1080/03007995.2022.2081454>

Aim: To uncover differential effects of sex on sequelae from coronavirus disease 2019 (COVID-19) and on long COVID syndrome.

Protocols of ongoing reviews related to Long COVID published between April 2022 and June 2022

Treatment & rehabilitation

1. Beqaj & Hadžiomerović. The effect of physiotherapy in the rehabilitation of patients after hospitalization due to COVID-19. PROSPERO 2022 CRD42022333448 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022333448

Review question(s): What is the effect of physiotherapeutic intervention in patients who were previously hospitalized due to COVID-19?

2. Carvajak et al. Effects of Neuromuscular Electrical Stimulation (NMES) on post-COVID-19 patients: a systematic review. PROSPERO 2022 CRD42022332036 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022332036

Review question(s): Is Neuromuscular Electrical Stimulation effective compared to placebo for increasing muscular mass, muscular strength and functional independence in patients with post-COVID-19 syndrome?

3. Chen et al. The effect of physical activity and exercise on long COVID: a systematic review and meta-analysis. PROSPERO 2022 CRD42022327778 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022327778

Review question(s): Can physical activity or exercise alleviate long COVID in COVID-19 survivors?

4. Dhivagaran & Butt. A systematic review and quality appraisal of clinical practice guidelines for the management of long COVID. PROSPERO 2022 CRD42022333254 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022333254

Review question(s): What is the quantity and quality (O) of management clinical practice guidelines (I) for adult patients with long COVID (P)? Which management recommendations are duplicated or inconsistent between guidelines (C)?

5. Dillen H, et al. Outpatient rehabilitation in patients with post-COVID-19 condition: a systematic review. PROSPERO 2022 CRD42022330205 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022330205

Review question(s): Which outpatient rehabilitation therapies in patients with post-COVID-19 condition improve symptoms (physically and mentally) and difficulties in carrying out activities (work, education and leisure)?

6. Hawke et al. Interventions for mental health, cognition, or psychological wellbeing among individuals with long COVID: a systematic review. PROSPERO 2022 CRD42022318678 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022318678

Review question(s): 1. What interventions have been tested for mental health, cognition, or psychological wellbeing among individuals with long COVID? 2. What is the design and quality of the trials? 3. What are the outcomes of the interventions?

7. Igwesi-Chidobe et al. Characterisation of long COVID and the effectiveness of non-pharmacological treatments: a systematic review. PROSPERO 2022 CRD42022321281 Available from:
https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022321281

Review question(s): What are the characterisations of long COVID from the available literature? What are the non-pharmacological treatments for long COVID? What is the effectiveness of the available non-pharmacological treatments for long COVID?

8. Jha et al. Effect of inspiratory muscle training on pulmonary parameters in post COVID patients: a systematic review. PROSPERO 2022 CRD42022325440 Available from:
https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD4202232544

Review question(s): To systematically review the effect of inspiratory muscle training on pulmonary parameters in post COVID patients (in the ICU and after hospital discharge) on the basis of available evidence.

9. Rahman et al. Effect of COVID-19 vaccines for the treatment of people with post-COVID-19 condition. PROSPERO 2022 CRD42022330821 Available from:
https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022330821

Review question(s): What are the effects of COVID-19 vaccines for the treatment of people with post-COVID-19 condition?

10. Saif et al. Effect of pharmacological interventions for the treatment of people with post-COVID-19 condition. PROSPERO 2022 CRD42022330873 Available from:
https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022330873

Review question(s): What are the effects of pharmacological interventions for the treatment of people with post-COVID-19 condition?

11. Smith et al. Interventions for improving long-COVID symptomatology: a systematic review and meta-analysis. PROSPERO 2022 CRD42022335907 Available from:
https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022335907

Review question(s): To investigate interventions for improving long-COVID symptomatology.

12. Tandarito et al. The effectiveness of COVID-19 vaccination on symptoms of long COVID: a systematic review. PROSPERO 2022 CRD42022321783 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022321783

Review question(s): To investigate the effectiveness of COVID-19 vaccination on symptoms of long COVID.

Prevention

13. Poethko-Mueller et al. Effectiveness of vaccination against Long COVID: A systematic evidence synthesis. PROSPERO 2022 CRD42022328481 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022328481

Review question(s): Are vaccinations against COVID-19, administered before SARS-CoV-2 infection, effective against Long COVID?

14. Liu et al. Effects of SARS-CoV-2 vaccine on reducing COVID-19 sequelae in the real-world study: a systematic review and meta-analysis. PROSPERO 2022 CRD42022340472 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022340472

Review question(s): What are the effects of SARS-CoV-2 vaccine on reducing COVID-19 sequelae?

Health and social

15. Greer et al. Evidence brief: employment, education, and continuing care outcomes among individuals following COVID-19. PROSPERO 2022 CRD42022337281 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022337281

Review question(s): What is the prevalence of adverse employment-related outcomes in adults with a history of COVID-19? Do employment-related outcomes differ in adults with a history of COVID-19 compared to those with no COVID-19? What is the prevalence of adverse post-secondary education-related outcomes in adults with a history of COVID-19? Do post-secondary education-related outcomes differ in adults with a history of COVID-19 compared to those with no COVID-19? What is the prevalence of need for residential long-term care services, rehabilitation services, in-home services, or family caregiver services in adults with a history of COVID-19? Does need for residential long-term care services, rehabilitation services, in-home services, or family caregiver services differ in adults with a history of COVID-19 compared to those with no COVID-19?

Symptoms and effects

16. de Oliveira Almeida et al. Determinants of cardiorespiratory fitness measured by cardiopulmonary exercise testing in COVID-19 survivors: A systematic review with meta-analysis and metaregression. PROSPERO 2022 CRD42022325991 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022325991

Review question(s): What exposures can impact VO₂ mean exercise intolerance in patients with Post COVID Syndrome?

17. Bocchino et al. Fibrosis or NOT fibrosis? Long-term chest computed tomography lung sequelae of COVID-19 pneumonia: a systematic review and meta-analysis. PROSPERO 2022 CRD42022341258 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022341258

Review question(s): Does COVID-19 pneumonia lead to pulmonary fibrosis in the long-term?

18. Celis et al. Short, mid, and long-term complications after multisystem inflammatory syndrome in children (MIS-C): systematic review. PROSPERO 2022 CRD42022336784

Available from:

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022336784

Review question(s): What are the short, mid and long-term complications after multisystem inflammatory syndrome in children (MIS-C)?

19. Cha et al. The psychosocial impact of Long-COVID: a systematic review. PROSPERO 2022 CRD42022341094 Available from:

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022341094

Review question(s): 1. What are the psychosocial consequences experienced by individuals with Long-COVID? 2. What is the quality of previous studies on the psychosocial consequences of Long-COVID?

20. Chen et al. Characterizing exercise outcomes in long COVID: a systematic review and meta-analysis. PROSPERO 2022 CRD42022331179 Available from:

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022331179

Review question(s): Does COVID-19 have a long-term adverse effect on exercise outcomes in adults?

21. Crawley et al. A rapid systematic review and meta-analysis of the prevalence of anxiety and depression symptoms in children with Long COVID. PROSPERO 2022 CRD42022319573

Available from:

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022319573

Review question(s): What is the prevalence of anxiety and depression in children who have had COVID-19 compared to children who have not had COVID-19?

22. Daodu et al. The impact of long COVID-19 on health outcomes among adults with pre-existing cardiovascular disease: a systematic review. PROSPERO 2022 CRD42022331549

Available from:

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022331549

Review question(s): What is the impact of long COVID-19 on the health of adults with pre-existing cardiovascular disease?

23. Dickinson & Mai. Study protocol for a systematic review of human and animal studies of neuropathological changes and imaging features in central and peripheral nervous systems

after COVID-19 infection. PROSPERO 2022 CRD42022336434 Available from:
https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022336434

Review question(s): What are the neuropathological changes and imaging features in the central and peripheral nervous system caused by COVID-19 infection in human and animal models?

24. Hawkings et al. A systematic review of the prevalence of gastrointestinal symptoms and illness after acute COVID-19 infection. PROSPERO 2022 CRD42022315792 Available from:
https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022315792

Review question(s): The objective is to provide a review of the prevalence of gastrointestinal symptoms and illness following COVID-19 infection once patients have recovered from the acute infection.

25. Foo et al. The phenomenon of functional gastrointestinal disorders (FGID) post-COVID-19 infection: a systematic review and meta-analysis. PROSPERO 2022 CRD42022325555 Available from:
https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022325555

Review question(s): Are functional gastrointestinal disorders possible sequelae of post-COVID-19-infection? What is the prevalence of post-COVID-19 infection functional gastrointestinal disorders?

26. Giussani et al. Neurology and post-COVID manifestations: present findings, critical appraisal, and future directions. PROSPERO 2022 CRD42022325505 Available from:
https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022325505

Review question(s): The aim of our review is to answer the following clinical questions: 1. What is the prevalence of (persistent, worsening or new) neurological manifestations in patients affected by COVID-19 surviving the acute phase (at 3-6-12-18-24 months of follow-up)? 2. In patients affected by COVID-19 surviving the acute phase and with pre-existing neurological manifestations, what is the risk of experiencing (persistent, worsening) or developing new neurological manifestations compared to those without pre-existing neurological manifestations? 3. In patients affected by COVID-19 surviving the acute phase and with severe disease, what is the risk of experiencing (persistent, worsening) or developing new neurological manifestations compared to those with mild-moderate disease? 4. In patients affected by COVID-19 surviving the acute phase and hospitalized, what is the risk of experiencing (persistent, worsening) or developing new neurological manifestations compared to those not hospitalized?

27. Hassan et al. Prevalence of mental health problems in children and adolescents with long COVID and effective interventions: a systematic review and meta-analysis. PROSPERO 2022 CRD42022335716 Available from:
https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022335716

Review question(s): What are the prevalence of mental health problems (depression, anxiety, sleep problems etc.) among children and adolescents with long COVID from primary studies? What are the effective interventions for anxiety and depression among children and adolescents with long COVID?

28. Joli et al. Post-COVID-19 fatigue. PROSPERO 2022 CRD42022320676 Available from:
https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022320676

Review question(s): What are the signs, symptoms, risk factors, pathophysiology and therapy approaches of post-COVID fatigue?

29. Kilinc et al. The psychosocial aspects of the lived experience of long-COVID: a systematic review and meta-ethnography. PROSPERO 2022 CRD42022343091 Available from:
https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022343091

Review question(s): The psychosocial impact of living with long-COVID has received limited attention (Maxwell, 2020) and should not be overlooked in favour of purely medical and rehabilitation approaches to symptoms (Lyons et al., 2020). This review aims to synthesise current evidence to identify and explore key themes which illustrate the psychosocial aspects of the lived experience of long-COVID; looking beyond the impact of long-COVID symptoms and experiences of healthcare, to the broader psychosocial impact of living with long-COVID.

30. Kuniduzi & Abudula. To better identify the frequent symptoms and diagnoses experienced by kidney transplantation recipients with post COVID-19 conditions (PCC): a systematic review and metaanalysis. PROSPERO 2022 CRD42022331594 Available from:
https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022331594

Review question(s): What are the common symptoms and diagnoses that lead to disability in kidney transplantation recipients with post-COVID-19 conditions (PCC)?

31. Kustanti et al. Post-COVID-19 memory impairment: A meta-analysis. PROSPERO 2022 CRD42022321370 Available from:
https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022321370

Review question(s): What is the global prevalence estimate of post-COVID-19 memory impairment?

32. Lampsas et al. Flow-mediated dilation impairment in convalescent COVID-19 patients: a systematic review and meta-analysis. PROSPERO 2022 CRD42022342040 Available from:
https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022342040

Review question(s): What is the standardized endothelial impairment, assessed by flow-mediated dilation (FMD) of the brachial artery, in individuals recovering from COVID-19 compared to non-COVID-19 controls?

33. Lee et al. Long COVID and its cardiac complications. PROSPERO 2022 CRD42022338488 Available from:
https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022338488

Review question(s): Incidence and description of cardiac sequelae of long COVID syndrome.

34. Liu J, et al. Comparison of long-term consequences of COVID-19 among different variants of concern: a systematic review and meta-analysis. PROSPERO 2022 CRD42022339964 Available from:
https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022339964

Review question(s): What is the difference of long-term consequences of COVID-19 between different variants of concern?

35. Loaiza-Fernandez et al. Characterization of post-acute COVID-19 manifestations in adults: long COVID symptoms? An overview of systematic reviews and meta-analysis. PROSPERO 2022 CRD42022335552 Available from:
https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022335552

Review question(s): What symptoms and manifestations have been described in COVID-19 adult survivors following acute illness, as probable symptoms of long COVID?

36. Marjenberg et al. A systematic review of the burden of post-COVID-19 syndrome. PROSPERO 2022 CRD42022331682 Available from:
https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022331682

Review question(s): What is the burden of post COVID-19 syndrome (4 or more weeks from the onset of COVID-19), including the risk of long-term sequelae (fatigue, shortness of breath, cognitive dysfunction and back pain), the impact on health-related quality of life, and the impact on direct and indirect costs compared to non-COVID-19 controls?

37. Matar & Mahmoud. Incidence of Guillain-Barre syndrome post COVID-19: a systematic review. PROSPERO 2022 CRD42022318681 Available from:
https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022318681

Review question(s): In COVID-19 associated GBS patients, what are the current epidemiological, clinical and pathophysiological characteristics?

38. Mundra et al. Hepatic sequelae of post-acute COVID-19 syndrome - a systematic review. PROSPERO 2022 CRD42022321890 Available from:
https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022321890

Review question(s): Does long COVID damage the liver in adults with post-acute COVID-19 syndrome?

39. Muthuka & Wambura. Post-acute COVID-19 sequelae: Prevalence and Relative Risk in Persons Living with HIV. PROSPERO 2022 CRD42022328509 Available from:
https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022328509

Review question(s): 1. What is the prevalence of Post-acute COVID-19 sequelae in persons living with HIV? 2. Is there a Post-acute COVID-19 sequelae risk difference between persons with and without HIV? 3. Are there possible moderators of Post-acute COVID-19 sequelae in persons living with HIV?

40. Qamar et al. New-onset Parkinsonism as a COVID-19 infection sequela: a systematic review and meta-analysis. PROSPERO 2022 CRD42022325061 Available from:
https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022325061

Review question(s): Does the current COVID-19 pandemic trigger Parkinsonism symptoms in infected individuals as a post COVID neurological complication?

41. Sanchez-Ramirez et al. Long post COVID-19 cardiorespiratory involvement and fatigue in children and teens: a systematic review and meta-analysis. PROSPERO 2022 CRD42022327478 Available from:
https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022327478

Review question(s): What is the prevalence of chest CT abnormalities, cardiorespiratory involvement and fatigue in children and teenagers 12 weeks post-COVID-19 infection?

42. Tan et al. The narrative experiences of patients with long COVID: a qualitative evidence synthesis. PROSPERO 2022 CRD42022323400 Available from:
https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022323400

Review question(s): What are the experiences of patients suffering from long COVID?

43. Tran & Nguyen. Exploring prevalences and types of sleep disturbances in post-acute COVID-19 syndrome over time: systematic review and meta-analysis. PROSPERO 2022 CRD42022340136 Available from:
https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022340136

Review questions: What are the prevalences and types of sleep disturbances in post-acute COVID-19 patients over time? Are there specific factors or subgroups of patients associated with sleep problems persistent beyond 4 weeks from the onset of acute COVID infection?

44. Thirunavukkarasu et al. Incidence and risk of new-onset diabetes after recovery from COVID-19: a systematic review and meta-analysis. PROSPERO 2022 CRD42022207274 Available from:
https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022207274

Review question(s) What is the incidence and the risk (compared with no COVID-19 group/those with other respiratory viral illness) of new-onset diabetes after recovery from COVID-19?

45. Williams & Zis. COVID-19 related neuropathic pain. PROSPERO 2022 CRD42022330381 Available from:
https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022330381

Review question(s): To investigate COVID-19 related neuropathic pain.

46. Zhang et al. Risk for newly diagnosed diabetes after SARS-CoV-2 infection: A systematic review and meta-analysis. PROSPERO 2022 CRD42022330723 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022330723

Review question(s): Although there is evidence that diabetes is associated with poor prognosis for COVID-19, little is known about the risk of diabetes after COVID-19.

Risk factors; Risk factors & prevalence

47. Agarwal et al. Long Haul COVID 19 and its associate risk factors: A Systematic review of follow up studies on SARS COV 2 infection. PROSPERO 2022 CRD42022340175 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022340175

Review question(s): 1) What are the long haul COVID-19 sequelae? 2) What are the risk factors of long haul COVID-19 sequelae?

48. Cafe et al. Association between food consumption, emotional eating and spirituality with a post COVID-19 conditions: systematic review. PROSPERO 2022 CRD42022329433 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022329433

Review question(s): Is there an association between food consumption, emotional eating and spirituality with a better recovery from COVID-19?

49. Harding et al. Diabetes as both a risk factor and an outcome for long-COVID-19: a systematic review. PROSPERO 2022 CRD42022326929 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022326929

Review question(s): 1: Are people with vs. without diabetes more likely to develop long COVID-19, also known as the post-acute sequelae of COVID-19 (PASC)? 2: Are people with vs. without COVID-19 more likely to develop incident diabetes?

50. Ismail et al. Clinical manifestations and predictors of post-acute COVID-19 syndrome in paediatric patients: a systematic review and metaanalysis. PROSPERO 2022 CRD42022332158 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022332158

Review question(s): What are the prevalence, clinical manifestations and predictors of post-acute COVID-19 syndrome in the paediatric population?

51. Lai et al. Risk of newly diagnosed diabetes after COVID-19 infection: a systematic review and meta-analysis. PROSPERO 2022 CRD42022337841 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022337841

Review question(s): To analyse and combine all the available evidence focused on risk of newly diagnosed diabetes following a previous diagnosis of COVID-19 and to increase understanding surrounding factors that affect diabetes risk in COVID-19 patients.

52. Li et al. Factors associated with long COVID syndrome (4 weeks or more): a comprehensive meta-analysis. PROSPERO 2022 CRD42022320807 Available from:

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022320807

Review question(s): In this review, we attempt to explore a wide variety of risk factors, such as sex, age, and other demographic/social-economical characteristics, associated with differing types of long COVID syndrome.

53. Reyes-Long et al. Could microRNAs shed light on risk factors of developing chronic pain-like symptoms in post COVID-19?. PROSPERO 2022 CRD42022318992 Available from:

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022318992

Review question(s): Could microRNAs be employed as diagnostic molecules for patients with the possibility of developing chronic pain-like symptoms after COVID-19?

54. Santa Maria et al. Factors associated with the development of cardiac sequelae, in post-acute COVID-19 syndrome, and potential prognostic factors in patients with this condition: a systematic review. PROSPERO 2022 CRD42022336460 Available from:

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022336460

Review question(s): Which factors are associated with the development of cardiac sequelae in post-acute COVID-19 syndrome? What is the incidence of the main outcomes related to patients with cardiac sequelae in post-acute COVID-19 syndrome and what are the potential prognostic factors for patients with this condition?

55. Salisu-Olatunji et al. COVID-19 outcomes and their sociodemographic determinants among people living with multiple long-term conditions (MLTCs): a systematic review and meta-analysis. PROSPERO 2022 CRD42022322567 Available from:

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022322567

Review question(s): What are the direct and indirect impacts of COVID-19 infection on health outcomes and mortality among people living with multiple long-term conditions (MLTCs)?

NB: An outcome of interest is a long COVID diagnosis

56. Zhang et al. Pattern and risk factors of cognitive impairment in the disease course of COVID-19: a meta-analysis and systematic review. PROSPERO 2022 CRD42022334200 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022334200

Review question(s): To quantitatively estimate the prevalence of diverse domains and the related risk factors of cognitive impairment in COVID-19 patients and survivors among the disease courses development.

NB: Population of interest is both COVID-19 patients and post COVID-19 individuals.

Pathobiology

57. Li et al. A meta-analysis of post-acute Covid syndrome (PASC) and serum cytokines. PROSPERO 2022 CRD42022342262 Available from:
https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022342262

Review question(s): How does post-acute Covid syndrome correlate with different serum cytokine levels?

58. Pollak et al. Association between inflammatory markers and Long COVID: a systematic review and meta-analysis. PROSPERO 2022 CRD42022333437 Available from:
https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022333437

Review question(s): In patients with post-acute sequelae of COVID-19 (PASC, or long COVID), this review aims to explore the association between inflammatory biomarkers and PASC (long COVID); investigate if there is evidence of differential inflammatory biomarker levels between a) PASC (long COVID) patients versus patients who have recovered from acute COVID-19 who do not have persistent symptoms ("Recovery group"), b) PASC versus healthy controls, or c) PASC versus other disease control group.

59. Seyedmirzaei et al. Blood interleukin 6 levels in post-COVID depression and stroke: a systematic review and meta-analysis. PROSPERO 2022 CRD42022332978 Available from:
https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022332978

Review question(s): In people with post-COVID-19 stroke or post-COVID-19 depression, how are the peripheral blood interleukin-6 (IL-6) levels changed?

Appendix 1: PubMed search strategy

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

#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] OR long haul* [tiab] OR post acute sequelae [tiab]

#3 COVID [tiab] OR COVID-19 [tiab] OR SARS-CoV-2 [tiab] OR coronavirus [tiab]

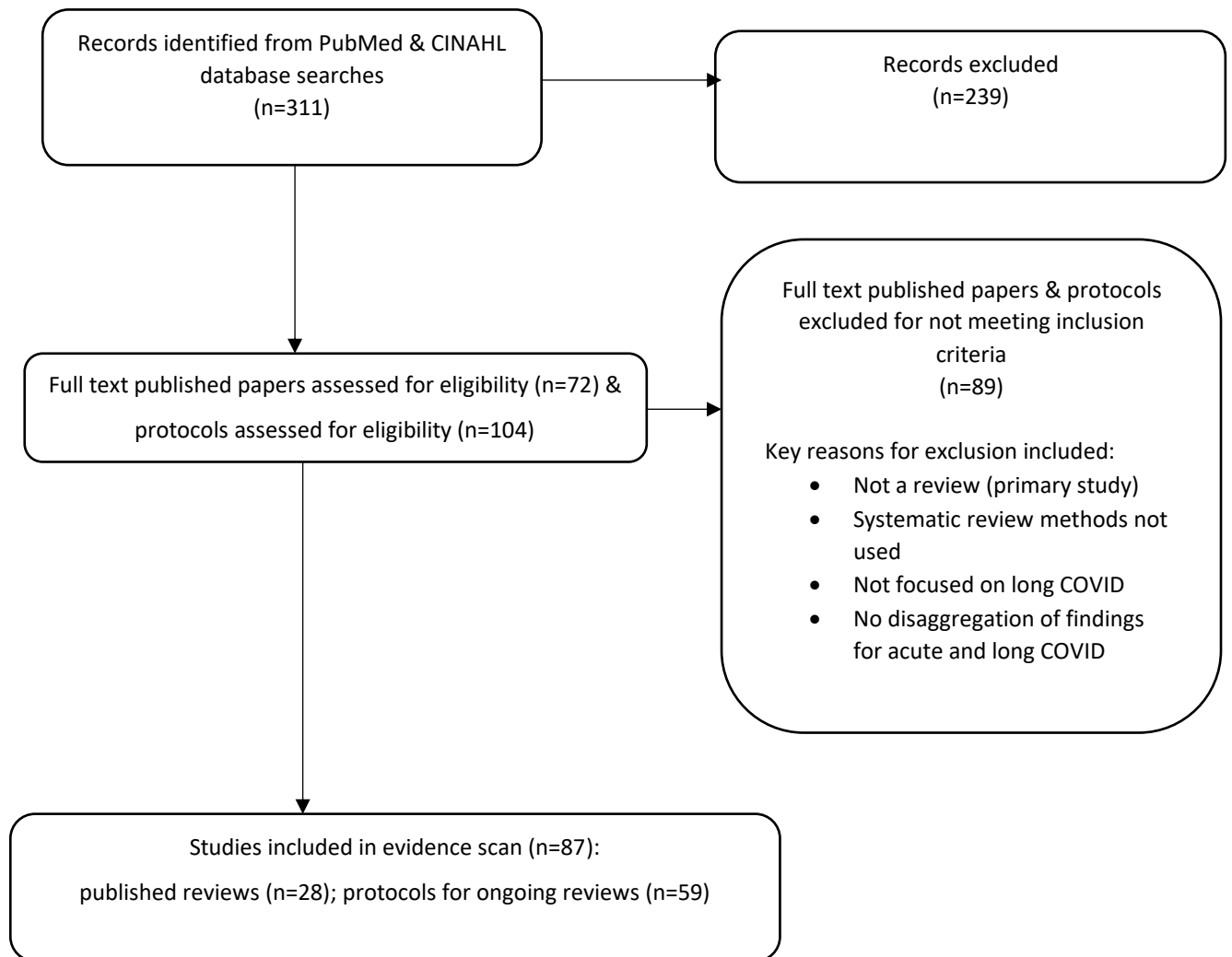
#4 #2 AND #3

#5 #1 OR #4

#6 review [tiab] OR meta-analysis [tiab] OR meta-synthesis [tiab] OR pooled analysis [tiab] OR realist synthesis [tiab]

#7 #5 AND #6

Appendix 2: Flow of studies through the review



The NIHR Policy Research Programme Reviews Facility aims to put the evidence into development and implementation of health policy through:

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

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