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Prevalence of long COVID-19 among healthcare workers: a systematic review and meta-analysis protocol

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ABSTRACT

Introduction A proportion of those who survive the acute phase of COVID-19 experience prolonged symptoms, commonly known as long COVID-19. Given that healthcare workers (HCWs) face an elevated risk of acute COVID-19 compared with the general population, the global burden of long COVID-19 in HCWs is likely to be large; however, there is limited understanding of the prevalence of long COVID-19 in HCWs, or its symptoms and their clustering. This review will aim to estimate the pooled prevalence and the symptoms of long COVID-19 among HCWs infected with SARS-CoV-2 globally, and investigate differences by country, age, sex, ethnicity, vaccination status and occupation.

Methods and analysis A systematic review and meta-analysis will be conducted. Medline (via Ovid), CINAHL (via EBSCO), Embase (via Ovid), PsycINFO (via EBSCO), *OpenGrey* (grey literature) and *medRxiv* (preprint server) will be searched from the 31 December 2019 onward. All research studies and preprint articles reporting any primary data on the prevalence and/or the symptoms of long COVID-19 among adult HCWs will be included. Methodological quality will be assessed using the Joanna Briggs Institute Critical Appraisal Checklist for Studies Reporting Prevalence Data. Outcomes are anticipated to be the prevalence of long COVID-19 among HCWs around the world and trajectory of symptoms. Data synthesis will include random-effect meta-analysis for studies reporting prevalence data of long COVID-19 following SARS-CoV-2 infection among HCWs. The results will be presented with a 95% CI as an estimated effect across studies. Heterogeneity will be assessed using I² statistic. Where meta-analysis is inappropriate, a narrative synthesis of the evidence will be conducted.

Ethics and dissemination Ethical approval is not needed as data will be obtained from published articles. We will publish our findings in a peer-reviewed journal and disseminate the results of our review at conferences.

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STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Our protocol outlines a novel systematic review and meta-analysis on the prevalence of long COVID-19 among healthcare workers globally.
⇒ Use of robust methods and the inclusion of grey literature (eg, preprints).
⇒ Results will inform urgently needed public health policies on long COVID-19.
⇒ Lack of consistency of terms related to ethnicity may be a barrier to stratification.
⇒ Definitions of long COVID-19 may vary as the topic is still evolving.

INTRODUCTION

COVID-19 has spread across the world causing over six million deaths and significant morbidity globally.[1] Evidence has emerged that some patients with COVID-19 experience long-term symptoms and complications that extend beyond the acute phase of infection. This is now widely known as long COVID-19.[2] Symptoms of long COVID-19 include, but are not limited to: muscle weakness; loss of smell and taste; fatigue; 'brain fog'; breathlessness; anxiety and depression.[3–5] However, many of these more persistent symptom profiles are less well understood and researched than those experienced during the acute phase.[6] The aetiology underlying the symptoms observed is also unclear.[7] Many healthcare professionals have avoided making a single diagnosis, opting instead for multiple diagnoses including permanent damage to vital organs, postintensive care syndrome, postviral fatigue syndrome and continued COVID-19 syndrome.[8] Healthcare workers (HCWs), particularly those from ethnic minorities, are at increased risk of COVID-19 infection and adverse outcomes. Finally, it is unclear whether or how ethnicity is related to long COVID-19.[9 10]

The WHO defines long COVID as 'occurring three months from the onset of COVID, with symptoms that last at least two months that cannot be explained by any alternative diagnosis'.[11] The National Institute for Health and Care Excellence (NICE) differ

in their definition and state long COVID to be 'signs and symptoms that develop during or after the COVID infection persisting for 4–12 weeks or more, that cannot be explained by any other diagnosis'.[2] This definition produces two classifications: 'ongoing symptomatic COVID' from 4 to 12 weeks and 'post-COVID syndrome' from after 12 weeks.[2] Both definitions function as 'exclusion criteria' which could potentially lead to missed diagnoses of long COVID. Therefore, NICE recently proposed a more inclusive definition such as 'signs and symptoms that continue or develop after acute COVID' which include both ongoing symptomatic COVID and post-COVID-19 syndrome.[12]

Many ongoing research studies seek to understand the long-term impacts of SARS-CoV-2 infection better.[13–15] However, available data so far have been heterogenous and vulnerable to biases, preventing a precise definition or population risk stratification.[16] Early data from the Office for National Statistics in the UK suggest a higher risk of long COVID-19 in females.[17 18] Other risk factors include increasing age and body mass index.[19] Individuals from ethnic minority groups are at higher risk of morbidity and mortality from acute COVID-19 compared with white groups.[20 21] The Scientific Advisory Group for Emergencies in the UK attribute these differences to ethnic differences in SARS-CoV-2 exposure rates, susceptibility and vulnerability to disease, social factors, and consequences of pandemic control measures (eg, the impact of lockdowns on jobs).[22] However, the prevalence and impact of long COVID-19 in people from ethnic minority groups remains unknown. Furthermore, the prevalence of long COVID-19 in HCWs has not been studied.[23 24] This is of urgent public health importance, since HCWs will have much higher exposure to COVID-19 than the general population, and therefore have a higher risk of infection compared with those form the general population. Furthermore, there may be a higher degree of stress due to working throughout a pandemic which may exacerbate risk factors following acute infection for the development of long COVID-19.[25–27] Finally, ethnic minority groups are also over-represented in healthcare institutions such as the National Health Service (NHS), UK and many HCWs emigrate to the UK from countries such as the Philippines, India, Jamaica and South Africa.[28] The prevalence and direct effects of long COVID-19 on the diverse NHS workforce, and indirect effects, such as impact on patient care, warrant further study.

In this systematic review and meta-analysis, we aim to estimate the pooled prevalence and identify the symptoms of long COVID-19 among HCWs infected with SARS-CoV-2 virus, globally. We will then stratify our results by country, age, sex, ethnicity, SARS-CoV-2 vaccination status and occupation.

Objectives

1. Estimate the pooled prevalence of long COVID-19 among HCWs with a history of SARS-CoV-2 infection globally.

2. Estimate the prevalence of long COVID-19 among HCWs infected with a history of SARS-CoV-2 infection globally.

3. Identify the symptoms (and their clustering) among HCWs with long-COVID-19.

METHODS
Protocol design and registration
The development and design of this study protocol was in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses Protocol (PRISMA-P)[29] as shown in online supplemental appendix I. This study protocol is registered with the International Registration of Systematic reviews (PROSPERO), a platform for the international registration of prospective systematic reviews (CRD42022312781).

Eligibility criteria
All peer-reviewed and preprint articles reporting any primary data on the prevalence and/or the symptoms of long COVID-19 following confirmed, probable or suspected SARS-CoV-2 infection among adult (≥ 16 years old) HCWs (clinical and non-clinical staff), worldwide such as mixed-method studies, observational studies (including cross-sectional studies, retrospective and prospective cohort studies), case-control studies, and randomised and non-randomised controlled trials will be included.

Following the NICE definition of post-COVID-19 syndrome, we define long-COVID in this review as persistent/prolonged (constant, fluctuating or relapsing) symptoms and/or functional disability following SARS-CoV-2 infection for equal to or more than 4 weeks from onset of symptoms or from time of diagnosis, in people where the infection is self-reported, clinically diagnosed, and/or diagnosed through a laboratory test. As definitions have varied and changed overtime, we will also include any study that defines/reports the condition as 'long COVID-19' or persistent symptoms following SARS-CoV-2 infection in addition to studies reporting symptoms that align with our definition (even if studies have not defined it as 'long COVID-19').

Qualitative study designs not reporting prevalence data, and secondary analysis (ie, systematic reviews), will be excluded. Correspondence pieces and articles about predictive modelling, basic science or using animal data will be excluded.

Information sources
The following databases will be searched for articles, from the 31 of December 2019 onward Medline (via Ovid), CINAHL (via EBSCO), Embase (via Ovid), PsycINFO (via EBSCO) and *medRxiv* (preprint server).

The reference lists of eligible articles will also be searched manually to identify additional relevant studies, not identified in the original database search.

Search strategy

The PRISMA-Search Reporting Extension (PRISMA-S)[30] and the Peer Review of Electronic Search Strategies Evidence-Based Checklist[31] will be used to ensure the search strategy covers the review questions appropriately. A Boolean search strategy will be used with a combination of Medical Subject Headings and relevant text words to search systematically for relevant studies. The asterisk will be used for abridged terminology. Search terms have been created in consultation with the research team and a librarian to ensure that all relevant search terms are included, to develop a successful search strategy for each source of information and, therefore, to enhance the transparency and comprehensiveness of the review.[32] Search terms were developed from reviewing relevant research, systematic reviews and reports. The search terms will be piloted several times to refine their sensitivity and specificity before the searches are conducted.

A detailed search terms and strategy table was developed for the four databases. Online supplemental appendix II details the database-specific search strategy for Medline. An alert will be set in for the databases to allow the reviewer (AA) to remain up to date with the medical literature currently being published.

Selection process

All studies identified using our search strategy will be independently assessed for eligibility through title and abstract screening, followed by a full-text screening, carried out by a minimum of two researchers and according to the PRISMA checklist.

Data items

For each eligible study, we will extract the following data using a structured piloted data extraction form in Microsoft Office Excel with the fields: title, author name(s), author contact details, year of publication, journal name, study design, country setting/context, data collection years (start date and end date), inclusion criteria, exclusion criteria, sample size (N), participant characteristics/demographics (eg, age, sex, ethnicity, occupational role, existing comorbidities, hospital (re)admission), symptoms of long COVID-19, cases of long COVID-19 (n), the prevalence of long COVID-19, and prevalence of long COVID-19 by age, sex, country, ethnicity and vaccination status.

Data collection process

Two researchers will undertake data extraction independently, and discrepancies will be identified and resolved through discussion with the whole research team, and a third reviewer will be involved if required. Missing data in selected studies will be requested from study authors, where possible.

Outcomes and prioritisation

Our primary outcome is the prevalence of long COVID-19 among HCWs around the world. We will be looking at differences in prevalence by age, sex, country, ethnicity and vaccination status. Additional outcomes include (1) the nature and severity of long COVID-19 symptoms and their clustering and (2) the trajectory of the symptoms of long COVID-19.

Quality assessment

While extracting the data, the risk of bias will be assessed in relation to the review questions. The Joanna Briggs Institute critical appraisal checklist for prevalence studies will be used for each study which will enable us to distinguish between reliable studies, and studies with a strong possibility of bias, in the data synthesis stage. A discussion between the researchers will be conducted for any disagreements that occur during this process, and consensus will be achieved. Quality scores for the results of the assessment will be reported in a table. Studies will not be excluded on the basis of quality. However, sensitivity analyses will be carried out to examine the impact of study quality on the outcomes.

Data synthesis

A meta-analysis of the data will be carried out using Stata V.16.1 to calculate pooled estimates for the prevalence of long COVID-19 following SARS-CoV-2 infection among HCWs infected, globally. The results will be presented with a 95% CI as an estimated effect across studies. Heterogeneity will be assessed through the use of I^2 statistic.

Where appropriate, subgroup analysis will be carried out for the pooled prevalence of long-COVID in relation to country and ethnicity.

Patient and public involvement

No patients involved.

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