


Inequity and disparities mar existing global research evidence on Long COVID

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Abstract: Since the pandemic began in December 2019, SARS-Cov2 has accentuated the wide gap and disparities in socioeconomic and healthcare access at individual, community, country, and regional levels. More than two years into the current pandemic, up to three-fourths of the patients are reporting continued signs and symptoms beyond the acute phase of COVID-19, and Long COVID portends to be a major challenge in the future ahead. With a comprehensive overview of the literature, we found that most studies concerning long COVID came from high and upper-middle income countries, and people of low-income and lower-and-middle income regions and vulnerable groups with comorbid conditions have been neglected. Apart from the level of income, there is a significant geographical heterogeneity in investigating the Post-Acute Sequelae of COVID-19 (PASC) or what we call now, long COVID. We believe that these recognizing health disparities is crucial from equity perspective and is the first step toward global health promotion.

Keywords: COVID-19, Long COVID, Long haulers, Post COVID syndrome, SARS-Cov2, PASC, Post-Acute Sequela of COVID-19, chronic COVID syndrome

Growing concerns about the long-lasting consequences of the COVID-19 infection currently dominate the global discourse. More than two years into the current pandemic, up to 10–20% of the

patients are reporting continued signs and symptoms beyond the acute phase of the disease (1). Despite its recognition and a widespread acknowledgement of this prolonged illness period, there was no explicit

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and widely accepted definition or nomenclature for this emerging syndrome. It has been variously referred to as: 'acute post-infection COVID', 'Long COVID', 'Long haulers', 'Lingering COVID-19', 'chronic COVID syndrome', and 'PASC (Post-Acute Sequelae of COVID-19)' (2). Recently, the World Health Organization named this entity the 'Post COVID-19 Condition' and proposed its definition as 'the illness that occurs in people who have a history of probable or confirmed SARS-CoV-2 infection; usually within three months from the onset of COVID-19, with symptoms and effects that last for at least two months. The symptoms and effects of the post-COVID-19 condition cannot be explained by an alternative diagnosis' (1). Given this backdrop, this paper elaborates on the underlying disparities in the current literature concerning the populations and countries that have been studied to fully understand the long-lasting COVID-19 research on medical and socioeconomic impacts.

Since the pandemic began in December 2019, SARS-Cov2 has accentuated the already existing wide treatment gap, disparities in socioeconomic status, and access to healthcare between 'the haves and the have nots'. Apart from the global hardship and devastation that this pandemic has caused, those living in low- and middle-income countries (LMICs), who were already struggling with poor access to healthcare services, have been hit the hardest (3) directly due to the spread of the virus or as a consequence of the pandemic. Meager resources are allocated to research in these regions, and little is known about the effects this syndrome has had in these regions.

An exemplar here is the Global Research Collaboration for Infectious Disease Preparedness and the UK Collaborative on Development Research that have created a COVID-19 Research Coordination and Learning Initiative (COVID CIRCLE initiative) in recognition of this gap (4). While regions in LMICs have a lot of experience and expertise in managing disease outbreaks at a massive scale, with epidemics such as Ebola and HIV, most COVID-19 research globally comes from high-income countries prioritizing their population and system needs, and there is a need to leverage the experience of these lesser-known geographies to create new solutions. The COVID CIRCLE priority setting meeting reached an unanimous decision on

the need to facilitate collective efforts to strengthen COVID-19 research in LMICs as an immediate research funding priority.

Given this backdrop, we are offering a secondary analysis and an extension to a systematic scoping review published at the earliest stages of Long COVID emergence (2) earlier. We carried out a comprehensive literature search on 30 January 2021 to evaluate the potential disparities in research and reporting regarding Long COVID. Using relevant search words, that is, 'long COVID' or 'long haulers' or 'post-acute COVID' or 'chronic COVID syndrome,' we searched without language restriction via Cochrane Library, PsycINFO, PubMed, Embase, Scopus, and Web of Science. With a rigorous selection strategy, and after removing duplicates, screening the titles/abstracts and full texts, searching the reference lists and citations of the included papers for eligibility by two independent authors, a total of 67 publications in English with original data were retrieved.

Out of 67 papers with original information, 43 were published as original articles, nine were case reports/series, and 15 were short articles. The World Bank (5) classification of countries in the 2021 fiscal year was set for categorization of the countries where the studies came from. Results are shown in global heat-maps in Figure 1.

Our analysis focused on the country and region where the original investigation was carried out. Italy, United Kingdom (UK), China, and the USA comprised most of the populations who were evaluated and reported for Long COVID. Of the 67 publications, 42 (62.6%) were from Europe and Central Asia populations, nine were from East Asia and Pacific, nine were from North America, two from the Middle East and North Africa, two from sub-Saharan, and one from South Asia, and three studies were cross-country analyses. The majority of studies (91%) came from high- and upper-middle-income countries. Moreover, all of the cohort, case-control, cross-sectional, longitudinal observational, and qualitative studies were from high- and upper-middle-income countries. Articles from low- and lower-middle-income countries were largely in the form of case reports.

To 9 March 2021, COVID-19 had affected 219 countries and territories (6). In our study, we found significant geographic heterogeneity regarding the populations studied. Of the nine original studies from North America, eight were from the USA and

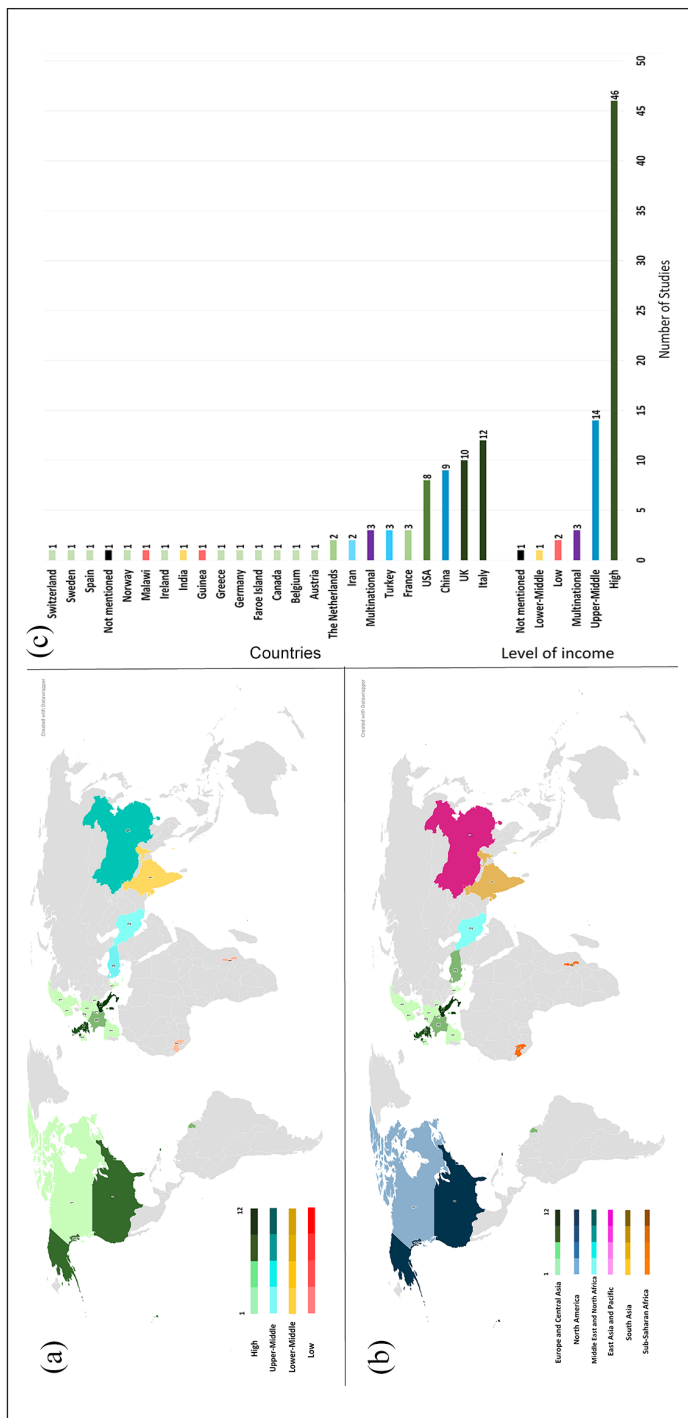


Figure 1. Global distribution of studies with original data (N=67), (a) based on level of income, (b) based on geographical region. Classifications are rooted in the World Bank classification for the 2020–2021 fiscal year. (c) Number of studies based on countries according to the level of income on the bar chart. Maps were created by Datawrapper ©.

one from Canada. In East Asia and the Pacific region, all original studies were from China. Out of 42 studies from Europe and Central Asia, Italy and the UK were the most common populations studied and reported 12 and 10 studies, respectively. The disparities were not limited to geographical regions; three countries (Italy, the UK, and the USA) accounted for 30 (65%) out of 46 original articles from the high-income countries.

In terms of Long COVID phenomena from the field of pediatrics, we only found two articles. One focused on the multi-system inflammatory syndrome in children affected by the virus, and another one was a case series of five children with COVID-19. The scarcity of investigations on pediatrics is compelling. Another clear gap was Long COVID in particular groups encompassing those with organ transplantation, hemodialysis patients, and patients on immunosuppressive therapy, highlighting the need for more research.

Unfortunately, there is a significant gap in the literature regarding Long COVID globally, reflecting the need for multi-country studies and diverse population analyses. This would allow for extensive subgroup analyses involving a wide range of ages, gender, race and ethnicities, occupations, and socioeconomic backgrounds. Also, the low number of studies reported from the low and middle-income countries (LMICs) by no means reflects fewer patients suffering from COVID-19 infection and complications.

Recognition of health disparities is crucial from an equity perspective and also is the first step towards improving global health research to achieve a healthy and just world. We believe that funding should prioritize and enable institutions from LMICs to carry out vital research on long COVID. The scarcity of publications from LMICs and regions such as Sub-Saharan Africa and South Asia may reflect a lack of resources and under-recognition of the condition of the long-term impact in those areas. We suggest providing funding, resources, and continued medical education for primary healthcare workers globally and especially in LMICs. Funding should also be directed toward studies focusing on children and those with specific medical conditions at higher risk of adverse health outcomes. Due to ongoing mitigation measures such as social distancing, travel and border restrictions, the current pandemic has made communities more isolated, impacted their

socialization and deactivated platforms for exchange. Such unintended measures have made societies more disconnected and distant. We believe that global health discussions have to address these issues and create bonding and synergies within research platforms to counteract possible disparities that some regions, researchers and institutions might continue to experience. In this regard, it is imperative for the decision- and policy-makers to view these challenges through the lens of equity.

On a final note, it is worth stating that the literature has exploded after conducting this research with papers published on this subject. Although this is a comprehensive analysis up to January 2021, future research is highly recommended to map the studies on this issue along the lines of global partnership and equity focusing on long COVID research on socioeconomic and health impacts.

Author contributions

All the authors have made a substantial contribution to the conception, design, analysis, and interpretation of data; they have also contributed to the article drafting and revising it critically for intellectual content

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Supplemental material

Supplemental material for this article is available online.

References

1. WHO. Coronavirus disease (COVID-19): post COVID-19 condition [Internet]. 2021 [cited 2021 December 16]. Available from: <https://www.who.int/news-room/questions-and-answers/item/coronavirus-disease-covid-19>
2. Akbarialiabad H, Taghrir MH, Abdollahi A, Ghahramani N, Kumar M, Paydar S, et al. Long COVID, a comprehensive systematic scoping review. *Infection*. 2021; 49: 1163–1186.
3. Murthy S, Leligdowicz A, Adhikari NK. Intensive care unit capacity in low-income countries: a systematic review. *PLoS One*. 2015; 10: e0116949.

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4. Norton AJ, Wiysonge CS, Habarugira J-MV, White NJ, Bayona MT, Hagen H-E, et al. Priorities for COVID-19 research response and preparedness in low-resource settings. *Lancet*. 2021; 397: 1866–1868.
 5. The World Bank. World Bank country classifications by income level: 2020–2021 [Internet]. 2020. Available from: <https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups>
 6. Worldometer. Reported cases and deaths by country or territory [Internet]. 2021 [cited 2021 March 9]. Available from: <https://www.worldometers.info/coronavirus/>