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Definition of Post-COVID-19 Condition Among Published Research Studies

Ubonphan Chaichana, MSc; Kenneth K. C. Man, PhD; Anthony Chen, MSc; Ian C. K. Wong, PhD; Jacob George, PhD; Peter Wilson, MD; Li Wei, PhD

Introduction

As of February 2023, there have been approximately 759 million confirmed cases of COVID-19 infections globally¹ and some individuals have experienced persistent symptoms, such as fatigue and shortness of breath, after recovering from the initial illness from COVID-19. The UK National Institute for Health and Care Excellence (NICE),² the World Health Organization (WHO),³ and the US Centers for Disease Control and Prevention (CDC)⁴ have published their definitions of post-COVID-19 condition (PCC) between December 2020 and October 2021, with some discrepancies between them. Despite the growing volume of research on lasting symptoms of COVID-19, the definition has not been universally agreed on. This study aimed to describe how post-COVID-19 condition has been defined to date in studies on this topic.

+ Invited Commentary

+ Supplemental content

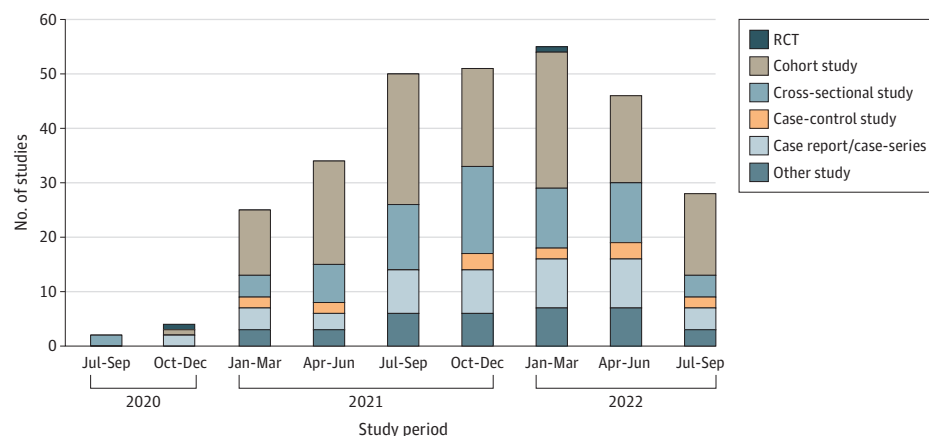
Author affiliations and article information are listed at the end of this article.

Methods

We conducted a descriptive study on PCC definition following the STROBE reporting guideline and performed the literature search using the PRISMA checklist in PubMed on October 26, 2022. A total of 7087 studies containing information on PCC were identified from February 1, 2020, to October 26, 2022. Definition of PCC (eAppendix in Supplement 1), study type, country where the study was conducted, and manuscript submission date were extracted from the publications and are presented chronologically (eAppendix in Supplement 1).

Two investigators (U.C. and A.C.) reviewed the studies and screened titles and abstracts independently and cross-checked a 10% sample of the data collected from the studies. When submission dates were not available, the publication dates were used to determine the study time. Exemption from ethical approval was indicated by the University College of London Ethics Committee. SPSS Statistics for Windows, version 28 (IBM Corp) was used for data analysis.

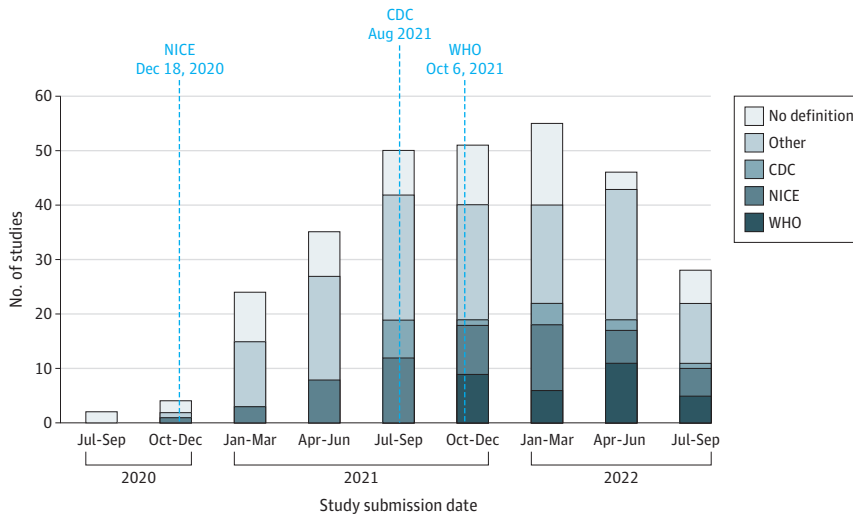
Figure 1. The Proportion of Post-COVID-19 Condition Study Designs Over Time



RCT indicates randomized clinical trial.

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Figure 2. Use of Post-COVID-19 Condition Definition by Organization and Submission Date



CDC indicates Centers for Disease Control and Prevention; NICE, UK National Institute for Health and Care Excellence; WHO, World Health Organization.

Results

Among 7087 studies, we excluded 6792 that were not relevant to PCC (eg, SARS-CoV-2 vaccines, commentary, systematic review, and full articles in languages other than English). The remaining 295 studies were included, consisting of 2 randomized clinical trials (0.7%), 134 cohort studies (45.4%), 66 cross-sectional studies (22.4%), 13 case-control studies (4.4%), 45 case reports or case series (15.3%), and 35 studies using other designs (11.9%) (Figure 1). Of these, 167 studies (56.6%) were conducted in European countries. We found that only 102 studies (34.6%) used 1 of the 3 organizational definitions for their studies (NICE: 56, WHO: 31, and CDC: 15). A total of 193 studies (65.4%) did not follow any of the 3 definitions for PCC and 6 studies were submitted for publication before NICE released their PCC definition (ie, before December 18, 2020) (Figure 2).

Of 193 studies that did not follow any of 3 definitions, 129 studies (66.8%) used their own definitions for PCC (eg, presence of chronic symptoms that last >5 months or after 2 weeks of SARS-CoV-2 infection), while 64 studies (33.2%) did not define PCC.

Discussion

We found substantial heterogeneity in defining PCC in the published studies, with almost two-thirds (65.4%) not complying with the definitions from the NICE, CDC, or WHO. This study highlights major issues in comparing interventions and outcomes between these reported studies in PCC due to differences in definition. The differences also result in considerable variation when translating findings into clinical management and cost-effectiveness assessments of interventions in patients with PCC. The clinical management of PCC must be evidence-based and include a personalized approach. A clearer definition of PCC is timely so that clinical trial evidence can reliably be applied to clinical management and the well-being of patients with PCC can be improved.

Our study has some limitations. We conducted the literature search only in PubMed. Furthermore, the NICE updated their PCC definition in November 2022 after we finished the study screening. However, the updated definition would not affect our study and would only apply to studies conducted after November 2022.

ARTICLE INFORMATION**Accepted for Publication:** February 8, 2023.**Published:** April 5, 2023. doi:10.1001/jamanetworkopen.2023.5856**Open Access:** This is an open access article distributed under the terms of the [CC-BY License](#). © 2023 Chaichana U et al. *JAMA Network Open*.**Corresponding Author:** Li Wei, PhD, UCL School of Pharmacy, 29-39 Brunswick Square, London WC1N 1AX, United Kingdom (l.wei@ucl.ac.uk).**Author Affiliations:** UCL School of Pharmacy, London, United Kingdom (Chaichana, Man, Chen, Wei); Laboratory of Data Discovery for Health (D24H), Hong Kong Science Park, Hong Kong Special Administrative Region, China (Man, Wong, Wei); Centre for Medicines Optimisation Research and Education, University College London Hospitals National Health Service (NHS) Foundation Trust, London, United Kingdom (Man, Wong, Wei); Centre for Safe Medication Practice and Research, Department of Pharmacology and Pharmacy, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong Special Administrative Region, China (Man, Wong); Ninewells Hospital, University of Dundee Medical School, Dundee, United Kingdom (George); University College London Hospitals NHS Foundation Trust, London, United Kingdom (Wilson).**Author Contributions:** Ms Chaichana and Dr Wei had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.*Concept and design:* Chaichana, Man, Wong, Wei.*Acquisition, analysis, or interpretation of data:* Chaichana, Man, Chen, George, Wilson, Wei.*Drafting of the manuscript:* Chaichana, Chen.*Critical revision of the manuscript for important intellectual content:* All authors.*Statistical analysis:* Chaichana, Chen.*Obtained funding:* Wong.*Administrative, technical, or material support:* Chen.*Supervision:* Man, Wilson, Wei.**Conflict of Interest Disclosures:** Ms Chaichana reported receiving a scholarship from the Royal Thai Government outside the submitted work. Dr Man reported receiving grants from the Hong Kong Research Grant Council during the conduct of the study; grants from CW Maplethorpe Fellowship, European Commission Horizon 2020, and the National Institute for Health and Care Research; and personal fees from IQVIA Ltd outside the submitted work. Dr Wong reported receiving grants from the Hong Kong Health and Medical Research Fund, Amgen, Bristol-Myers Squibb, Pfizer, Janssen, Bayer, GSK, Novartis, the Food and Health Bureau of the Government of the Hong Kong Special Administrative Region, the UK National Institute for Health and Care Research, the European Commission, and the National Health and Medical Research Council in Australia outside the submitted work; receiving consulting fees from IQVIA outside the submitted work; and serving as a paid nonexecutive director of Jacobson Medical in Hong Kong and a paid consultant to the World Health Organization. Dr Wilson reported receiving personal fees from the Pfizer Advisory Board and the Roche Drug Safety Monitoring Board outside the submitted work. Dr Wei reported receiving grants from the National Institute Health Research Health Technology Assessment, Hong Kong Innovation and Technology Commission, Diabetes UK, The Cure Parkinson's Trust, and BOPA-PRUK outside the submitted work. No other disclosures were reported.**Funding/Support:** This work was partially supported by grant C7154-20G from the Research Grants Council of Hong Kong under the Collaborative Research Fund Scheme.**Role of the Funder/Sponsor:** The funding organization had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.**Data Sharing Statement:** See [Supplement 2](#).**REFERENCES**

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SUPPLEMENT 1.

eAppendix. Search Strategy

SUPPLEMENT 2.

Data Sharing Statement