

## Correspondence

Check for updates

# Reply: How Can Chronic COVID (Long-COVID Syndrome) Be Diagnosed and Treated?

#### Jun-Won Seo 💿 1 and Joon Young Song 💿 2

<sup>1</sup>Division of Infectious Diseases, Department of Internal Medicine, Chosun University College of Medicine, Gwangju, Korea

<sup>2</sup>Division of Infectious Diseases, Department of Internal Medicine, Korea University College of Medicine, Seoul, Korea

 See the letter "How Can Chronic COVID (Long-COVID Syndrome) Be Diagnosed and Treated?" in volume 56 on page 559.

#### Dear Editor:

We appreciate Josef Finsterer's insightful comments on our article and would like to address the points raised [1, 2]. Current research demonstrates that coronavirus disease 2019 (COVID-19) vaccines can help prevent or reduce the risk of long COVID, a condition characterized by prolonged symptoms following a severe acute respiratory syndrome coronavirus 2 infection. In addition to the evidence presented in the guideline, several studies suggest that COVID-19 vaccines may be effective in preventing long COVID, possibly by decreasing the initial severity of the infection and promoting faster viral clearance [3-6]. Additional studies reported that vaccinated individuals had a reduced risk of developing long COVID-related symptoms compared to unvaccinated individuals, even when vaccines were administered after an initial infection [7-9]. One large-scale study conducted by the Veterans Affairs healthcare system demonstrated that the rate of new long COVID cases decreased significantly with each subsequent COVID-19

Received: Nov 25, 2024 Accepted: Nov 27, 2024 Published online: Dec 12, 2024

**Corresponding Author:** Joon Young Song, MD, PhD Division of Infectious Diseases, Department of Internal Medicine, Korea University Guro hospital, Korea University College of Medicine, 148 Gurodong-ro, Guro-gu, Seoul 08308, Korea. Tel: +82-2-2626-3052, Fax: +82-2-2626-1105 Email: infection@korea.ac.kr

### **Open Access**

variant, especially among vaccinated individuals [10]. Approximately 70% of this reduction was directly attributed to vaccination, while changes in the virus itself accounted for the rest.

These findings suggest that vaccines not only help prevent severe illness but also play a key role in mitigating long-term impacts. Altogether, these studies reinforce the value of COVID-19 vaccination in both minimizing immediate risks and potentially reducing the long-term burden of long COVID. Our guidelines do not advocate that everyone, including those who previously experienced adverse events from the COVID-19 vaccine, should be recommended to receive the COVID-19 vaccine specifically for Long COVID prevention. Additionally, as mentioned in the guidelines, results on the effectiveness of the vaccine in alleviating symptoms are mixed, with both positive and negative findings, making it difficult to draw definitive conclusions. We believe further quantitative research is necessary.

© 2024 by The Korean Society of Infectious Diseases, Korean Society for Antimicrobial Therapy, The Korean Society for AIDS, and Korean Society of Pediatric Infectious Diseases

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (https:// creativecommons.org/licenses/by-nc/4.0/) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

# IC Infection & Chemotherapy

The diagnostic criteria for long COVID are still unclear. and there are currently no biomarkers that can reliably diagnose long COVID to the extent that they could be included in the diagnostic criteria. As a result, various respected academic organizations and journals have proposed different terminology and diagnostic criteria [11-15]. Recently, Thaweethai et al. proposed a datadriven diagnostic framework that integrates 12 key symptoms while acknowledging their interconnection with other health issues, enabling a symptom-based scoring system to identify long COVID cases [15]. This framework addresses the complexity and heterogeneity of symptoms associated with long COVID. By offering a structured methodology for diagnosing long COVID, the definition has the potential to aid in identifying affected populations, supporting research into its mechanisms, and guiding interventions for prevention and treatment. Although evidence of specific pathophysiological changes occurring at the three-month mark after COVID-19 onset is insufficient, in this guideline, we define chronic COVID-19 syndrome as the persistence of one or more symptoms or signs that began during the acute phase or afterward, cannot be explained by another condition, and continue beyond three months following a COVID-19 diagnosis. This definition aligns with the one used by the World Health Organization.

As mentioned in the correspondence by Finsterer [2], when evaluating fatigue, one of the primary symptoms of long COVID, it is necessary to differentiate it not only from conditions like myasthenia gravis, but also from various other musculoskeletal disorders. For this purpose, we have comprehensively outlined the need for detailed medical history taking, physical examinations, various blood tests, imaging for musculoskeletal assessment, and electromyography.

This guideline also recommends comprehensive assessments for long COVID patients experiencing cognitive impairment or brain fog symptoms, including various tests such as brain magnetic resonance imaging to rule out other underlying causes. Additionally, it advises consulting with specialists in neurology and psychiatry for further evaluation.

Lastly, the literature we reviewed was up to June 2023, and it took approximately eight months to complete the publication for guideline development and revision. This is an unavoidable delay that can also occur with other guideline publications. To address this, we plan to update the guidelines, and indeed, we aim to revise this guideline next year to include any literature that was missed.

#### **ORCID** iDs

Jun-Won Seo https://orcid.org/0000-0002-2806-1863 Joon Young Song https://orcid.org/0000-0002-0148-7194

#### Funding

This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the National Institute of Infectious Diseases, National Institute of Health, Korea (grant number: HD22C2045).

#### **Conflict of Interest**

JYS is editorial board of *Infect Chemother*; however, he did not involve in the peer reviewer selection, evaluation, and decision process of this article. Otherwise, no potential conflicts of interest relevant to this article was reported.

#### **Author Contributions**

Conceptualization: JWS, JYS. Investigation: JWS, JYS. Resources: JWS. Software: JWS. Supervision: JYS. Validation: JYS. Writing - original draft: JWS. Writing - review & editing: JWS, JYS.

### REFERENCES

- Seo JW, Kim SE, Kim Y, Kim EJ, Kim T, Kim T, Lee SH, Lee E, Lee J, Seo YB, Jeong YH, Jung YH, Choi YJ, Song JY. Updated clinical practice guidelines for the diagnosis and management of long COVID. Infect Chemother 2024;56:122-57. PUBMED | CROSSREF
- Finsterer J. How can chronic COVID (long-COVID syndrome) be diagnosed and treated? Infect Chemother 2024;56:559-60.
  CROSSREF
- Ceban F, Kulzhabayeva D, Rodrigues NB, Di Vincenzo JD, Gill H, Subramaniapillai M, Lui LMW, Cao B, Mansur RB, Ho RC, Burke MJ, Rhee TG, Rosenblat JD, McIntyre RS. COVID-19 vaccination for the prevention and treatment of long COVID: a systematic review and meta-analysis. Brain Behav Immun 2023;111:211-29. PUBMED | CROSSREF
- Watanabe A, Iwagami M, Yasuhara J, Takagi H, Kuno T. Protective effect of COVID-19 vaccination against long COVID syndrome: a systematic review and meta-analysis. Vaccine 2023;41:1783-90. PUBMED | CROSSREF
- Choi S, Lee H, Eum SH, Min JW, Yoon HE, Yang CW, Chung BH. Severity of COVID-19 pneumonia in kidney transplant recipients according to SARS-CoV-2 vaccination. Infect Chemother 2023;55:505-9. PUBMED | CROSSREF
- 6. Choi WS. Adult immunization policy in Korea. Infect Chemother 2023;55:317-21. PUBMED | CROSSREF
- 7. Tran VT, Perrodeau E, Saldanha J, Pane I, Ravaud P. Efficacy of first dose of covid-19 vaccine versus no vaccination on

# IC Infection & Chemotherapy

symptoms of patients with long covid: target trial emulation based on ComPaRe e-cohort. BMJ Med 2023;2:e000229. PUBMED | CROSSREF

- Byambasuren O, Stehlik P, Clark J, Alcorn K, Glasziou P. Effect of covid-19 vaccination on long covid: systematic review. BMJ Med 2023;2:e000385. PUBMED | CROSSREF
- 9. Edwards F, Hamilton FW. Impact of covid-19 vaccination on long covid. BMJ Med 2023;2:e000470. PUBMED | CROSSREF
- Xie Y, Choi T, Al-Aly Z. Postacute sequelae of SARS-CoV-2 infection in the pre-delta, delta, and omicron eras. N Engl J Med 2024;391:515-25. PUBMED | CROSSREF
- Soriano JB, Murthy S, Marshall JC, Relan P, Diaz JV; WHO Clinical Case Definition Working Group on Post-COVID-19 Condition. A clinical case definition of post-COVID-19 condition by a Delphi consensus. Lancet Infect Dis 2022;22:e102-7.
  PUBMED | CROSSREF
- National Institute for Health and Care Excellence (NICE). COVID-19 rapid guideline: managing the long-term effects of COVID-19. London: NICE; 2024.
- Yelin D, Moschopoulos CD, Margalit I, Gkrania-Klotsas E, Landi F, Stahl JP, Yahav D. ESCMID rapid guidelines for assessment and management of long COVID. Clin Microbiol Infect 2022;28:955-72.
  PUBMED | CROSSREF
- 14. National institutes of Health (NIH). COVID-19 topics. Long COVID. Available at: https://covid19.nih.gov/covid-19-information#whatis-long%20covid?-1. Accessed 24 November 2024.
- Thaweethai T, Jolley SE, Karlson EW, Levitan EB, Levy B, McComsey GA, McCorkell L, Nadkarni GN, Parthasarathy S, Singh U, Walker TA, Selvaggi CA, Shinnick DJ, Schulte CCM, Atchley-Challenner R, Alba GA, Alicic R, Altman N, Anglin K,

Argueta U, Ashktorab H, Baslet G, Bassett IV, Bateman L, Bedi B. Bhattacharvva S. Bind MA, Blomkalns AL, Bonilla H, Brim H, Bush PA, Castro M, Chan J, Charney AW, Chen P, Chibnik LB, Chu HY, Clifton RG, Costantine MM, Cribbs SK, Davila Nieves SI, Deeks SG, Duven A, Emery IF, Erdmann N, Erlandson KM, Ernst KC, Farah-Abraham R, Farner CE, Feuerriegel EM, Fleurimont J, Fonseca V. Franko N. Gainer V. Gander JC. Gardner EM. Geng LN, Gibson KS, Go M, Goldman JD, Grebe H, Greenway FL, Habli M, Hafner J, Han JE, Hanson KA, Heath J, Hernandez C, Hess R, Hodder SL, Hoffman MK, Hoover SE, Huang B, Hughes BL, Jagannathan P. John J. Jordan MR. Katz SD. Kaufman ES. Kelly JD, Kelly SW, Kemp MM, Kirwan JP, Klein JD, Knox KS, Krishnan JA, Kumar A, Laiyemo AO, Lambert AA, Lanca M, Lee-lannotti JK, Logarbo BP, Longo MT, Luciano CA, Lutrick K, Maley JH, Mallett G, Marathe JG, Marconi V, Marshall GD, Martin CF, Matusov Y, Mehari A, Mendez-Figueroa H, Mermelstein R, Metz TD, Morse R, Mosier J, Mouchati C, Mullington J, Murphy SN, Neuman RB, Nikolich JZ, Ofotokun I, Ojemakinde E, Palatnik A, Palomares K, Parimon T, Parry S, Patterson JE, Patterson TF. Patzer RE. Peluso MJ. Pemu P. Pettker CM. Plunkett BA. Pogreba-Brown K, Poppas A, Quigley JG, Reddy U, Reece R, Reeder H, Reeves WB, Reiman EM, Rischard F, Rosand J, Rouse DJ, Ruff A, Saade G, Sandoval GJ, Santana JL, Schlater SM, Sciurba FC, Shepherd F, Sherif ZA, Simhan H, Singer NG, Skupski DW, Sowles A, Sparks JA, Sukhera FI, Taylor BS, Teunis L, Thomas RJ, Thorp JM, Thuluvath P, Ticotsky A, Tita AT, Tuttle KR, Urdaneta AE, Valdivieso D, VanWagoner TM, Vasey A, Verduzco-Gutierrez M, Wallace ZS, Ward HD, Warren DE, Weiner SJ, Welch S, Whiteheart SW, Wiley Z, Wisnivesky JP, Yee LM, Zisis S, Horwitz LI, Foulkes AS; RECOVER Consortium. Development of a definition of postacute sequelae of SARS-CoV-2 infection. JAMA 2023;329:1934-46. PUBMED | CROSSREF