

Post-COVID or long-COVID? That is the question

Giuseppe Lippi, Fabian Sanchis-Gomar, Brandon M. Henry

Authors' reply We thank Chirumbolo et al.¹ for appreciating our narrative review on long-COVID previously published in this journal,² as well as for their additional considerations, which allow us to emphasize some important concepts of this intricate and still enigmatic syndrome.

To this end, we would like to underline a series of aspects and apparent inaccuracies reported in the letter of Chirumbolo et al.² First, the authors incorrectly referenced the World Health Organization (WHO) and Centers for Disease Control and Prevention, citing our article and referring to long-COVID as a condition “with symptoms lasting for 6 months or longer.” This definition is not reported in our article, since we used the one currently endorsed by the WHO, that is, “continuation or development of new symptoms 3 months after the initial SARS-CoV-2 infection, which persist for at least 2 months.”³

The following part of the letter is then devoted to a somewhat “metaphysical” debate about the type and duration of symptoms in patients who recover from SARS-CoV-2 infection, which has questionable clinical significance in daily clinical practice. Specifically, the authors argue that the definition of long-COVID shall be reserved for those cases when symptoms persist for several months after the pandemic's end. This statement is conceptually misleading. Even though nobody can predict when (or even if ever) this pandemic will cease, the WHO has just recently reiterated the concept that COVID-19 is a global health threat.⁴ Thus, how long should we wait before we can identify and treat long-COVID patients? Many years or decades (potentially never, if COVID-19 turns into an endemic disease) are likely to pass before such a terminus is reached. The lack of a clear-cut demarcation between COVID-19 and post-COVID (or long-COVID) symptoms is another drawback in the message delivered by Chirumbolo et al.¹ Unlike what the authors state, there is no real difference between a post-COVID syndrome and a permanent COVID-19 inflamed status, since persisting inflammation after recovering from SARS-CoV-2 infection is one of the leading underlying biological

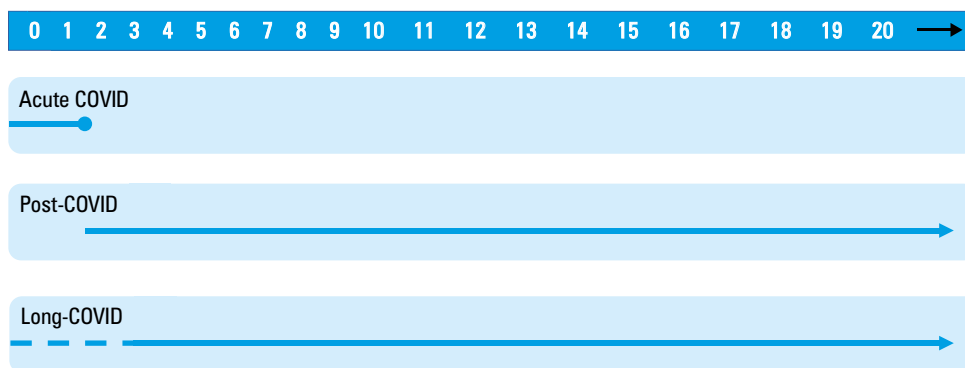
mechanisms of long-COVID, as recently proven by Gomes and colleagues.⁵ When symptoms persist for a long time, we could use many diagnostic tools to identify their underlying nature. For example, respiratory impairment deriving from a cardiopulmonary cause can be easily distinguished from that caused by an infective pulmonary disease using simple, relatively cheap, and noninvasive testing, such as cardiac echography and / or measuring natriuretic peptide levels.⁶

Another inaccuracy reported by Chirumbolo et al.¹ which may denote insufficient familiarity with the immunologic response developing in patients with SARS-CoV-2 infection, refers to the use of a “periodic immunological follow-up” based on measuring serum-specific immunoglobulin M / immunoglobulin G to identify new SARS-CoV-2 infections. Irrespective of the cost and impracticability associated with such a practice (clinical laboratories would be swamped with otherwise unjustified SARS-CoV-2 serology), the humoral response after breakthrough infections is unreliable, since the assessment of the early anti-SARS-CoV-2 antibodies titer is dramatically biased by COVID-19 vaccination and previous infections, thus becoming uninterpretable.⁷

In conclusion, we are less optimistic than Chirumbolo et al.¹ and not confident in providing a definitive answer to the question “Post-COVID or long-COVID?” At the same time, these 2 definitions have a potentially large overlap,⁸ as also summarized in [FIGURE 1](#). Since everything coming after something else is inherently “post,” categorizing the persistence of symptoms, and even laboratory / radiologic abnormalities after recovering as post-COVID is conceptually correct, irrespective of their duration (short or long). In effect, the concept of a post-viral syndrome is not new or exclusive to COVID-19; it was described decades ago and can occur after other common viral infections, such as Epstein-Barr virus, Coxsackie viruses, Ross River virus, human herpesvirus 6, cytomegalovirus, and seasonal flu, among others. Likewise, reserving the definition of long-COVID to those cases without

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FIGURE 1 Persistent symptoms after diagnosis (months) of SARS-CoV-2 infection



otherwise explainable symptoms or functional derangements still present up to 3 months after a documented SARS-CoV-2 infection and persisting for months thereafter seems reasonable.⁸ Therefore, giving an answer to the question “Post-COVID or long-COVID?” becomes a conjectural effort with meaningless implications on managed care.

ARTICLE INFORMATION

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CONFLICT OF INTEREST None declared.

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