

SYNOPSIS

Review of “Short-term and Long-term Rates of Postacute Sequelae of SARS-CoV-2 Infection A Systematic Review”

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One-minute summary

- The authors performed a systematic review of persistent symptoms in Coronavirus Disease 2019 (COVID-19) survivors. The systematic review included 57 studies examining the short and long-term persistent postacute sequelae (PASC) of Coronavirus Disease 2019 (COVID-19). The sample size of eligible COVID-19 survivors was 250,351 with a mean age of 54.4 years (standard deviation [SD]: 8.9), 56.0% were male and 79.0% were hospitalized during acute infection.
- The median proportion of COVID-19 survivors experiencing at least 1 PASC at varying times since diagnosis or hospital discharge:
 - **1 month (short-term):** 54.0% (interquartile range [IQR]: 45.0–69.0)
 - **2–5 months (intermediate-term):** 55.0% (IQR: 34.8–65.5)
 - **≥6 months (long-term):** 54.0% (IQR: 31.0–67.0)
- The median frequency of PASC between low- and middle-income countries (56.0%; IQR: 43.5–67.0) and high-income countries (54.6%; IQR: 33.0–68.3) were similar, respectively. Out of the 57 studies, 45 (78.9%) were from high-income countries defined as median gross national income greater than \$12,536.
- The most commonly reported symptoms, by symptom group were (only those with a median proportion >20% included here):
 - **Neurological:** difficulty concentrating (23.8%; IQR: 20.4–25.9)
 - **Mental health:** generalized anxiety disorders (29.6%; IQR: 14.0–44.0), sleep disorders (27.0%; IQR: 19.2–30.3) and depression (20.4%; IQR: 19.2–21.5)
 - **Respiratory:** increased oxygen requirement (65.0%; IQR: 39.3–76.1), chest imaging abnormalities (62.2%; IQR: 45.8–76.5), pulmonary diffusion abnormalities (30.3%; IQR:

22.1–38.5), dyspnea (29.7%; IQR: 14.2–37.0) and ground glass opacification (23.1%; IQR: 19.7–43.0)

- **Functional mobility impairment:** general impairment (44.0%; IQR: 23.4–62.6) and mobility decline (20.2%; IQR: 14.9–30.6)
- **General and constitutional:** fatigue or muscle weakness (37.5%; IQR: 25.4–54.5) and general pain (32.4%; IQR: 22.3–38.4)
- **Dermatological:** hair loss (20.8%; IQR: 17.4–23.4)
- The authors concluded that greater than 50% of COVID-19 survivors experienced PASC 6 months after recovery, and that PASC patients could overwhelm health care resources, especially in low- and middle-income countries.

Additional information

- Studies were included if they had adults and/or children with a previous COVID-19 diagnosis and reported PASC frequencies. PASC was defined as the presence of at least 1 abnormality diagnosed by (1) laboratory investigation, (2) radiologic pathology, or (3) clinical signs and symptoms that were present at least 1 month after COVID-19 diagnosis or after discharge from the hospital.
- **Limitations noted by authors:**
 - The authors did not conduct a meta-analysis due to high heterogeneity in the data and reported only medians with interquartile ranges.
 - The authors acknowledge that there is no consensus on the definition of PASC, which led to considerable heterogeneity in the data and made it difficult to compare percentages between studies.
 - Authors were unable to stratify the risk of PASC by severity of initial illness (e.g., community-based vs. hospitalized vs. required care in an intensive care unit vs. required invasive life-sustaining measures) or by pre-existing comorbidities, patient age, or other factors that may affect an individual patient's risk of PASC.
 - There was also a lack of standard reporting making it difficult to analyze PASC sequelae and not all symptoms were reported at specific time points, which limited analysis of long-term effects.
 - In addition, many of the studies were found through manually searching references, which suggests better database indexing is needed for PASC studies in order to conduct subsequent studies.

PHO reviewer's comments

- As the authors indicated, the lack of a standardized definition of PASC, and using different baseline time point are major limitations. The World Health Organization (WHO) has recently

published a case definition of post COVID-19 condition which will allow a better estimate of the burden of the condition.¹

- In this review, 79% of the studies participants were hospitalized; therefore this can't be generalized to the overall individuals infected with SARS-CoV2, but rather can be more appropriately reflective of hospitalized patients. In Ontario, as of October 28 2021, only 5% of all COVID-19 infections resulted in hospitalizations.²
- Vaccination might impact (i.e., improve or change) the incidence, the duration or the severity of the post-COVID-19 condition in vaccinated individuals who might get infected in comparison to those who are unvaccinated. Including vaccination status is essential to help interpreting any trends related to this condition.
- The authors do not mention the limitations and caveats associated with systematic reviews. For example, since the authors did not perform a grey literature search, their results might be biased towards a positive result due to publication bias.
- The Ontario Science Table has estimated that between 57,000 to 78,000 Ontarians had or might be presently affected by the post-COVID 19 condition.³
- A group of investigators from five Provinces including Ontario are partnering to conduct the Canadian COVID-19 Prospective Cohort Study (CAN COV) with the objectives to better understand impact and predict both short and long-term outcomes (early to 1-year) in COVID-19 patients (2000 in total: 1000 non-hospitalized and 1000 hospitalized) and their caregivers.
 - Results from this initiative will be helpful for the planning and management of needed health system resources including developing supportive policies to alleviate the burden of this condition.⁴

References

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