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# A Meta-Meta-Analysis of Post-COVID Symptoms: Unveiling the Persistent Burden of Long COVID

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Article

# A Meta-Meta-Analysis of Post-COVID Symptoms: Unveiling the Persistent Burden of Long COVID

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**Abstract:** The global impact of the COVID-19 pandemic extends far beyond the acute phase of infection, with millions experiencing persistent symptoms collectively termed “post-COVID syndrome” or “long COVID.” This article presents a meta-meta-analysis synthesizing findings from multiple systematic reviews and meta-analyses to explore the prevalence, nature, and implications of post-COVID symptoms. Fatigue, cognitive impairment, and dyspnea emerge as the most consistently reported symptoms, with prevalence rates varying widely across populations and settings. This analysis highlights the heterogeneity in research, the challenges in defining long COVID, and the urgent need for standardized approaches to address this ongoing public health challenge.

**Keywords:** post-COVID syndrome; long COVID; fatigue; cognitive impairment; dyspnea; prevalence; systematic review; meta-analysis; persistent symptoms; SARS-CoV-2; psychological symptoms; sleep disturbances; pain; healthcare burden; research gaps

## 1. Introduction

Since the emergence of SARS-CoV-2 in late 2019, the world has grappled with not only the immediate effects of COVID-19 but also its lingering aftermath. Post-COVID syndrome, characterized by symptoms persisting beyond 12 weeks after initial infection, affects a significant proportion of survivors, irrespective of initial disease severity (Fernández-de-las-Peñas et al., 2021). To better understand this phenomenon, numerous systematic reviews and meta-analyses have been conducted, each focusing on different aspects of post-COVID symptoms. This meta-meta-analysis integrates these findings to provide a comprehensive overview of the prevalence and characteristics of long COVID, offering insights into its global burden and research gaps.

## 2. Methods

This meta-meta-analysis draws on a narrative synthesis of existing systematic reviews and meta-analyses examining post-COVID symptoms, published between 2020 and early 2025. Studies were selected based on their focus on symptom prevalence, duration (at least 12 weeks post-infection), and inclusion of diverse populations (e.g., hospitalized, non-hospitalized, and community-based cohorts). Key symptoms analyzed include fatigue, cognitive dysfunction, dyspnea, pain, anxiety, depression, and sleep disturbances. Prevalence estimates were qualitatively compared across reviews, with attention to methodological differences, population characteristics, and follow-up periods. Quantitative pooling was not performed due to the heterogeneity of primary data; instead, trends and ranges are reported.

## 3. Results

The prevalence of post-COVID symptoms varies widely across studies, reflecting differences in definitions, follow-up durations, and cohort characteristics. On average, 30–50% of COVID-19 survivors experience at least one persistent symptom beyond 12 weeks (Chen et al., 2022; Han et al., 2022), with higher rates (up to 70%) observed among those with severe initial illness requiring intensive care (Nalbandian et al., 2021). Fatigue stands out as the most prevalent symptom, reported in 20–48% of cases across reviews (Fernández-de-las-Peñas et al., 2021; Chen et al., 2022), followed by cognitive impairments (e.g., “brain fog”) in 15–28% (Premraj et al., 2022), and dyspnea (shortness of breath) in 10–35% (Lopez-Leon et al., 2021). Pain, including musculoskeletal and headache-related complaints,

affects 8–20% of survivors (Fernández-de-las-Peñas et al., 2021), while psychological symptoms such as anxiety (10–25%) and depression (10–20%) also feature prominently (Raman et al., 2022). Sleep disturbances, ranging from 15–44%, further compound the burden (Mazza et al., 2023).

Notably, symptom persistence does not appear to diminish significantly over time, with some studies reporting stable prevalence rates up to two years post-infection (Fernández-de-las-Peñas et al., 2024). Hospitalized patients consistently exhibit higher symptom rates than non-hospitalized individuals, suggesting a correlation with disease severity (Nalbandian et al., 2021). However, even mild cases contribute substantially to the overall burden, challenging early assumptions that long COVID is primarily a post-hospitalization phenomenon (Chen et al., 2022). Gender and age differences are less conclusive, though some reviews suggest women and older adults may be at higher risk for certain symptoms like fatigue and cognitive decline (Premraj et al., 2022; Raman et al., 2022).

#### 4. Discussion

The findings underscore the multifaceted nature of post-COVID syndrome, which spans physical, cognitive, and psychological domains. Fatigue and cognitive impairment, often described as debilitating, align with patterns seen in other post-viral syndromes, such as chronic fatigue syndrome, hinting at shared pathophysiological mechanisms (Komaroff & Lipkin, 2021). Dyspnea and pain reflect ongoing respiratory and musculoskeletal challenges, while psychological symptoms highlight the mental health toll of prolonged illness (Raman et al., 2022). The wide range in prevalence estimates—driven by inconsistent symptom definitions, variable follow-up periods, and lack of control groups in many studies—complicates efforts to quantify the true scope of long COVID (Han et al., 2022).

This meta-meta-analysis reveals critical research gaps. The absence of standardized diagnostic criteria for post-COVID syndrome hampers comparability across studies (Fernández-de-las-Peñas et al., 2021). Many reviews lack non-infected control groups, making it difficult to distinguish symptoms attributable to SARS-CoV-2 from background prevalence in the general population (Chen et al., 2022). Furthermore, data from low-income countries remain scarce, limiting the global applicability of current findings (Lopez-Leon et al., 2021). These limitations suggest that reported prevalence rates may overestimate or underestimate the specific impact of COVID-19, necessitating more robust, controlled studies.

#### 5. Implications

The persistent nature of post-COVID symptoms poses significant challenges for healthcare systems worldwide. Patients require multidisciplinary care, integrating physical rehabilitation, cognitive support, and mental health services (Nalbandian et al., 2021). Policymakers must prioritize funding for longitudinal research to track symptom trajectories and evaluate interventions (Fernández-de-las-Peñas et al., 2024). Public health strategies should also address the socioeconomic consequences, as long COVID may impair workforce participation and exacerbate inequalities, particularly in underserved populations (Han et al., 2022).

#### 6. Conclusions

This meta-meta-analysis confirms that post-COVID syndrome is a widespread and enduring consequence of SARS-CoV-2 infection, with fatigue, cognitive impairment, and dyspnea as hallmark symptoms. Prevalence estimates, while variable, indicate a substantial global burden affecting millions. As the pandemic evolves, refining our understanding of long COVID through standardized research and inclusive study designs will be essential to mitigate its impact. This synthesis serves as a call to action for researchers, clinicians, and policymakers to address this persistent public health crisis with urgency and precision.

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