SYNTHESIS ARTICLE – ARTICLES DE SYNTHÈSE

MEDICAL SCIENCES

OPEN ACCESS

LONG COVID: CHALLENGES AND COMPLICATIONS – A SYSTEMATIC REVIEW

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https://doi.org/10.38045/ohrm.2025.3.01 CZU: 616.98:578.834.1-06

ABSTRACT

Introduction Long COVID, a condition that follows the acute phase of COVID-19, presents diverse clinical, psychological, and socioeconomic challenges, with complications such as fatigue, cognitive impairment, musculoskeletal issues, and mental health conditions. Despite its impact, the burden of long COVID symptoms on public health remains underexplored. This systematic review synthesizes current evidence on the complications and challenges of long COVID to inform healthcare providers and policymakers.

Material and methods A systematic literature search was conducted using PubMed and Scopus databases for studies published between January 2020 and August 2024. Articles were selected based on inclusion criteria, including both qualitative and quantitative studies. The review adhered to PRISMA guidelines, and the risk of bias was assessed using the NIHR risk-of-bias tool.

Results A total of 23 studies from 17 countries were included. Findings presented a multifaceted burden, with physical symptoms such as fatigue (5.5%–84.4%), brain fog (67%), headaches (5%–76.6%) and sleep disturbances (22%–60.9%). Psychological impacts were also prominent, with anxiety and depression frequently reported. Socioeconomic consequences were substantial, with up to 42.3% of individuals unable to return to work.

Conclusions Long COVID poses significant challenges to individuals and public health systems. Despite emerging insights, there are substantial gaps in understanding and managing long COVID, underscoring the need for further research and comprehensive healthcare strategies.

Keywords Long COVID, Post COVID-19 Syndrome, Post SARS-CoV2, COVID-19.

SINDROMUL POST-COVID: PROVOCĂRI ȘI COMPLICAȚII – O REVIZUIRE SISTEMATICĂ

Introducere Sindromul post-COVID, o afecțiune care survine după faza acută a COVID-19, presupune diverse provocări clinice, psihologice și socioeconomice, incluzând complicații precum oboseala, tulburările cognitive, problemele musculo-scheletale și afecțiunile de sănătate mintală. În pofida impactului său, manifestarea simptomelor asociate sindromului post-COVID asupra sănătății publice rămâne insuficient investigată. Această revizuire sistematică sintetizează dovezile actuale privind complicațiile și provocările sindromului post-COVID și a fost realizată cu scopul de a informa cadrele medicale și factorii de decizie.

Material și metode A fost realizată o cercetare sistematică a literaturii în bazele de date PubMed și Scopus pentru studii publicate între ianuarie 2020 și august 2024. Articolele au fost selectate pe baza unor criterii de includere, fiind luate în considerare atât studii calitative, cât și cantitative. Revizuirea a respectat ghidul PRISMA, iar riscul de biais a fost evaluat utilizând instrumentul de estimare a riscului de biais al NIHR.

Rezultate Cercetarea a inclus 23 de studii din 17 țări. Rezultatele au relevat un profil simptomatic complex: oboseală (5,5%–84,4%), disfuncții cognitive (67%), cefalee (5%–76,6%) și tulburările de somn (22%–60,9%). Impactul psihologic a fost de asemenea semnificativ, anxietatea și depresia fiind raportate frecvent. Consecințele socioeconomice au fost considerabile, până la 42,3% dintre persoane neputând să revină la muncă.

Concluzii Sindromul post-COVID reprezintă o provocare serioasă atât pentru un individ luat în parte, cât și pentru întreg sistemul de sănătate publică. În pofida progreselor înregistrate, ne confruntăm încă cu lacune semnificative în domeniul conștientizării și gestionării acestei afecțiuni. Acest fapt evedențiază necesitatea desfășurării unor cercetări suplimentare și a elaborării unor strategii de îngrijire complexe.

Cuvinte-cheie Long COVID, Sindrom post-COVID-19, Post SARS-CoV-2, COVID-19.

INTRODUCTION

The world faced an unprecedented challenge due to the emergence of the COVID-19 pandemic, which led to increased morbidity and mortality. The COVID-19 disease was caused by the novel severe acute respiratory syndrome (SARS) coronavirus-2 (SARS-Cov-2) (1). COVID-19 presented with a wide array of manifestations, with most cases being a mild infection (80%). However, 20% of infected patients could develop severe disease, and 5% may become critically ill and develop pneumonia or acute respiratory distress syndrome, thus necessitating mechanical ventilation and intensive care unit hospitalization (2). COVID-19 patients with accompanying comorbid ailments (hypertension, diabetes mellitus, cardiac/renal disorders, etc.) were most vulnerable to developing life-threatening complications (septic shock, acute respiratory distress syndrome, etc.), finally resulting in the patient's death (3). Long COVID posed a new problem as the globe struggled to deal with the fallout from this unprecedented public health emergency. It was in the Spring of 2020 that the term Long COVID was described by patients who were not recovering from the acute COVID-19 infection (4). After the initial acute infection, like many other viral disorders, a multitude of long-lasting symptoms had been described. A provisional definition would be persistent symptoms and potential sequelae beyond four weeks from onset, of which the main features are breathlessness, cognitive impairment, fatigue, anxiety and depression (5). The often mentioned "brain fog" is characterized by difficulties with concentration, memory and executive function (6). Post-viral syndrome is more common in depressed patients but can occur after a number of viral infections, for example EBV, HSV and HTLV (7). Globally, these manifestations have had a substantial influence on people's everyday functioning and quality of life. The World Health Organization has defined long COVID as the emergence or persistence of new symptoms three months following the original SARS-Cov-2 infection, and these symptoms must last for at least two months with the absence of an alternate diagnosis (8). As per existing research, the total anticipated cost in the United States alone by autumn of 2021 from direct economic losses combined with COVID-19-related mortality, morbidity, and relative mental health effects was $16 trillion (9).
Within two years of the pandemic's onset, extensive information was gathered on the effects of long COVID, its treatment, and prevention strategies (10). However, the exact nature and its burden of long COVID symptoms on public health is not investigated widely. With the increasing number of patients across the world witnessing prolonged symptoms and complications due to Coronavirus disease, we conducted this systematic review to provide a thorough overview of the disease by synthesizing the available data on the challenges and complications associated with long-COVID. This review aims to identify the most common clinical complications and challenges associated with long COVID across global populations.

MATERIAL AND METHODS

SEARCH STRATEGY

The systematic review of literature was conducted using the 2020 Preferred Reporting Items for Systematic Literature Reviews and Meta-Analyses (PRISMA) guidelines and was registered with the Prospective Register of Systematic Reviews (PROSPERO). The registration ID of this review is CRD42024578106, and it can be accessed at https://www.crd.york.ac.uk/prospero/#myprospero. The PRISMA guidelines includes a 27-item checklist which attests to transparency, iteration and complete reporting for systematic reviews. The literature search was conducted on PubMed and Scopus databases. We used the following Medical Subject Headings (Mesh) terms for

our literature search – "challenges" OR "complications" (Subheading) AND "Post-Acute COVID-19 Syndrome"(Mesh). We also assessed the references of the selected articles to ensure that no study is missed while doing the initial searches.

ELIGIBILITY CRITERIA:

This systematic review considered as inclusion and exclusion criteria the following items:

Inclusion Criteria

- Studies published in English language;
- Studies discussing the challenges and complications of long COVID/post COVID-19 syndrome;
- Qualitative and Quantitative studies;
- Studies published since January 2020 to August 2024.

Exclusion Criteria

- Studies focusing on acute COVID-19;
- Studies published in languages other than English;
- Review articles, Systematic reviews, Case series/reports, commentaries not reporting primary findings were excluded;
- Studies discussing only about a particular challenge or complication of long-COVID with a disease condition;
- Studies that hypothesize post-COVID-19 sequelae.

STUDY SELECTION

Two independent researchers conducted the literature search in August 2024 using specified inclusion and exclusion criteria. In the initial stage, literature studies were screened on the basis of title and abstracts. Further, an in-depth review of the selected studies was performed to assess their eligibility for this review based on the inclusion criteria. The studies which had discussed about challenges and complications of long COVID were included in this review and independently analyzed by two researchers. Any disagreements among the researchers were settled by careful deliberation; if agreement could not be reached, the principal investigator, a third researcher, was consulted to make the final decision.

DATA EXTRACTION

The findings from each of the selected studies were compiled into Microsoft Excel. We assessed the findings under the following sub-headings: title of the study, authors, year in which study was conducted, sample size, country, type of study, result, and outcomes (challenges and complications of long COVID) to present a summary of our findings.

RISK OF BIAS ASSESSMENT

The risk of publication bias was performed using the R package and Shiny web app for visualizing risk-of-bias assessments which has been introduced by the National Institute of Health Research (NIHR) (11). The 2020 version of the software was used for the analysis. A total of 23 studies met the inclusion criteria and were included in our systematic review. The tool assessed the studies under the following domains 1. Bias arising from the randomization process 2. Bias due to deviations from intended interventions 3. Bias due to missing outcome data 4. Bias in measurement of the outcome 5. Bias in selection of the reported result and 6. Overall Bias.

RESULTS

A total of 23 articles meeting the inclusion criteria were selected in this review. Our initial search revealed 5083 articles, and after exclusion of articles based on title, abstract, study design, and duplicate records, we included 23 studies in our review. The selection process adheres to the guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA); (fig. 1) depicts the selection process.

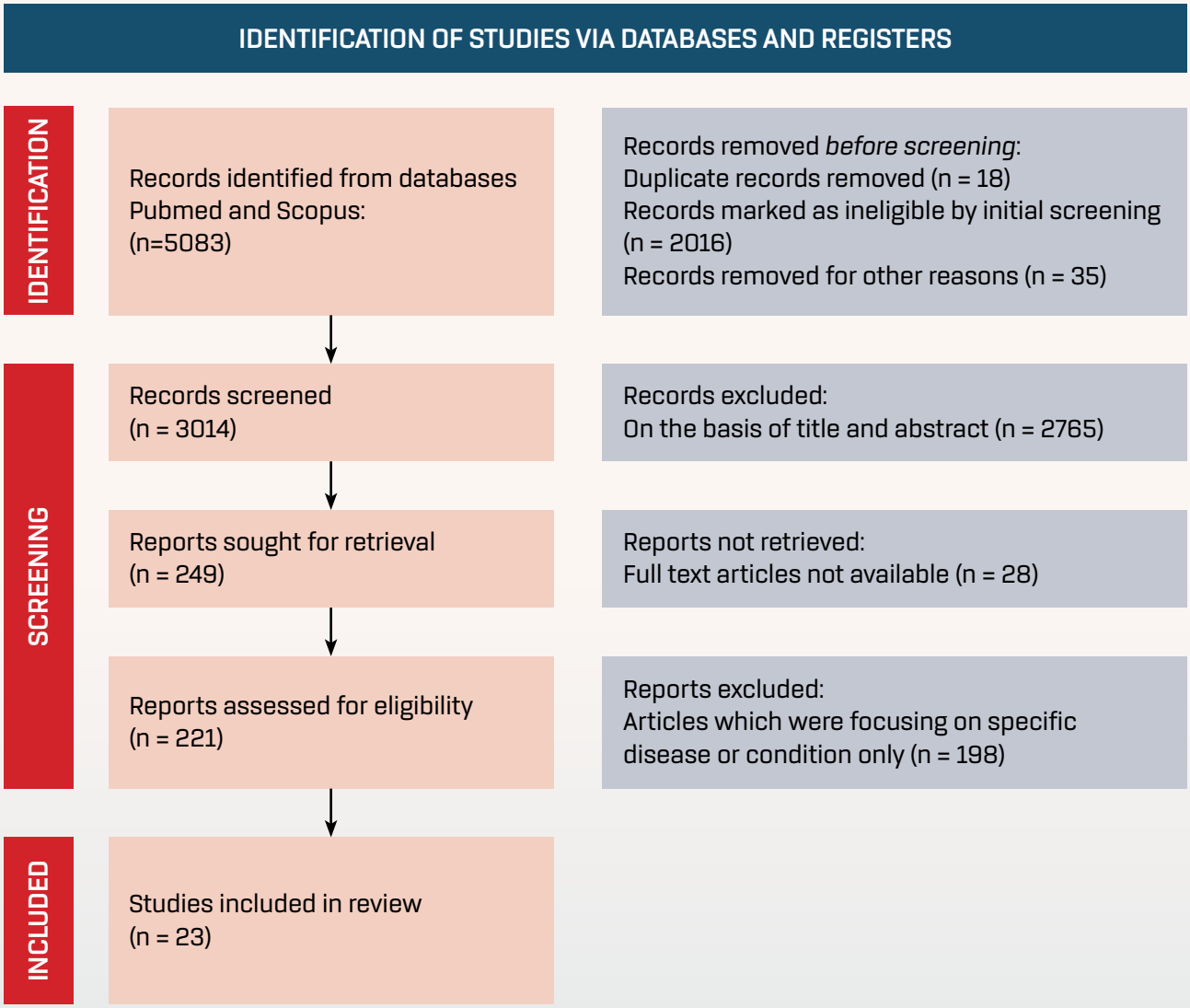

Figure 1. Prisma flowchart.

STUDY CHARACTERISTICS

The selected studies included were cross-sectional studies, cohort studies, and observational studies published from January 2020 to August 2024. A detailed representation of the included studies is depicted in (tab. 1).

Table 1. Table of study characteristics.

Author	Year	Sample Size	Country	Study Type	Findings
Tabacof et al. (12)	2022	156	US	Cross-sectional study	Fatigue – 82%, brain Fog – 67%, headache – 60%, sleep disturbances – 59%, reduction in patients in full – time work (pre – COVID: 76%, post – COVID: 41%), anxiety disorder – 19%, major depressive disorder – 28%
Twomey et al. (13)	2022	213	UK US Canada	Cross-sectional	Persistent symptoms for more than 6 months – 72.3%, lacking healthcare support – 33%, not able to work – 42.3%, reduced working hours – 41.8%, Chronic fatigue – 71.4%, breathing discomfort – 55.2%
Naik et al. (14)	2021	1234	India	Observational study	Persistent symptoms – 40.11%, long COVID symptoms reported beyond 12 weeks – 9.9%, myalgia – 10.9%, Fatigue – 5.5%.
Gerard et al. (15)	2021	549	France	Prospective Cohort Study	6 months follow – up – reduced muscle strength – 14.3%, malnutrition and weakness – 91%, impairment – 18.5%, Asthenia – 16%, Mood disorder & anxiety – 10%, Dyspnea – 7.6%
Walker et al. (16)	2023	3754	UK	Cross-sectional study	Pain/Discomfort – 96.2%, Anxiety/Depression – 95%, Lost ≥1 day from work in the previous 4 weeks – 51%, Unable to work at all – 20%, Functional impairment (moderate to severe) – 53%
Mutiawati et al. (17)	2022	215	Indonesia	Cross-sectional study	Persistent Fatigue – 17.7%, prolonged headache – 72%, poor quality of life – 21.4%
Imoto et al. (18)	2022	285	Japan	Cross-sectional study	In 50% patients: persistent fatigue, alopecia, concentration & memory problems, sleeplessness, joint pain, and headache – >50%
Gutierre Canales et al. (19)	2022	206	Mexico	Observational study	Persistence of 1 or more symptoms – 73.3%, fatigue – 36.9%, anxiety – 26.2%, headache – 24.8%, alopecia – 22.8%, inability to walk – 5.8%
Badinlou et al. (20)	2022	507	Sweden	Cross-sectional study	Depression – 55%, anxiety – 20.5%, insomnia – 60.9%, post-COVID impairments and severe fatigue linked to poor mental health outcomes
Tsuzuki et al. (21)	2022	457	Japan	Cross-sectional	Persistence of at least 1 symptom longer than 4 weeks after COVID-19 symptom onset – 44%, persistent Fatigue – 12.7%, Alopecia – 12%
Titzede - Almeida et al. (22)	2022	236	Brazil	Cohort study	Persistent fatigue – 21.2%, headache – 19.1%, myalgia – 16.1%, memory complaints – 39.8%, anxiety >33%, depression – 45%, declined sleep quality – 45.8%, sleepiness – 41.5%
Kim et al. (23)	2022	678	Korea	Prospective study	Concentration Difficulty – 22.4%, cognitive dysfunction – 21.2%, amnesia – 19.9%, depression – 17.8%, fatigue and anxiety – 16.2%, mobility problems – 7.9%, problems with daily activities – 15.4%, pain/discomfort – 22%, anxiety/depression – 40.7%
MacEwan et al. (24)	2022	21	US	Qualitative study	Patients faced care barriers from providers' disbelief, struggled to communicate symptoms, felt helpless, and worried about long-term health impacts.

Author	Year	Sample Size	Country	Study Type	Findings
Balderas et al. (25)	2023	215	Mexico	Prospective study	Children with Persistent Symptoms at 2 Months – 32.6%, patients with comorbidities – 67.4%, long-term sequelae – anxiety, alopecia
Reuschke et al. (26)	2022	1.4 M	UK	Observational study	Left employment – 11.4%, employment exits in elementary occupations – 43%
Sykes et al. (27)	2021	134	England	Observational study	Breathlessness (compared to pre – COVID-19 state) 60%, myalgia – 51.5%, anxiety – 47.8%, extreme fatigue – 39.6%, low mood – 37.3%, sleep disturbance – 35.1%
Delbressine et al. (28)	2021	239	Belgium, Netherlands	Longitudinal study	Participants unable to be physically active or perform sports at 6 months – 12%, weekly walking time at 6 months follow up:90 (30-150) min./week (lower than pre – COVID-19;)
Asadi-Pooya et al. (29)	2021	58	Iran	Observational study	Fatigue – 21%, shortness of breath – 12%, exercise intolerance – 12%, walking intolerance – 9%, sleep difficulty – 5%, muscle pain – 5%, joint pain – 5%, headache – 5%
Karaarslan et al. (30)	2021	118	Turkey	cohort study	Rheumatic and musculoskeletal symptom at 6 months – 43.2%, fatigue 31.6%, joint pain – 18.6%, myalgia – 15.1%, dyspnea – 25.3%, hair loss – 20.0%
Rass et al. (31)	2022	76	Austria	Observational cohort study	New and persistent neurological disorders – 12%, fatigue – 38%, concentration difficulties – 25%, forgetfulness – 25%, sleep disturbances – 22%, myalgia – 17%, limb weakness – 17%, headache – 16%, impaired sensation – 16%, hyposmia – 15%, cognitive deficits – 18%, depression – 6%, anxiety – 29%, post – traumatic stress disorder – 10%
Shah et al. (32)	2022	300	Nepal	Prospective study	Fatigue – 28.3%, shortness of breath – 6.7%, alopecia – 18.3%, anosmia – 4.3%, ageusia – 4.3%
Degaldo-Alonso et al. (33)	2022	77	Spain	Cross sectional study	Patients reported symptoms influencing work capacity – 97.4%, cognitive issues – 92.2%, fatigue – 84.4%, headache – 76.6%, sleep disorders – 70.1%, weakness – 66.2%, anxiety/depression – 5%, dizziness – 55.8%, dyspnea – 59.7%, cognitive complaints – 46.8%
Bungenberg et al. (34)	2022	49	Germany	Longitudinal observational study	Fatigue – 74%, cognitive complaints – 70%, difficulties in attention and concentration – 56%, memory complaints – 38%, smell and/or taste disturbances – 52%, sleep problems – 44%, headache – 22%

Our selected studies were conducted in multiple geographic locations, which included 17 countries. The majority of the selected studies were conducted amongst adults aged 18 years or more, while 2 (25, 29) studies were conducted in children. The minimum sample size in 1 of the studies was 21 (24), which was a qualitative study conducted in the US, while the largest sample size was 3754 (16) in a cross-sectional study design conducted in the UK.

As per the findings from the included studies of our review, we have divided the results into the following categories of physical and neurological symptoms, psychological and social impact, challenges in healthcare delivery services, employment-related issues and impairment of health-related quality of life.

Physical and Neurological Symptoms

Fatigue was the most commonly reported long COVID symptom, with prevalence ranging from 5.5% to 84.4% across studies (12–23, 27, 29–34). This was followed by brain fog or cognitive impairment, reported in up to 67% of cases (12), and headaches, with a prevalence ranging from 5% to 76.6% (12, 17, 18, 19, 22, 29, 31, 33, 34). Sleep disturbances were observed in 22% to 60.9% of participants (12, 18, 20, 22, 27, 31, 34), while myalgia or reduced muscle strength ranged from 10.9% to 51.5% across studies (14, 22, 27, 30, 31). Studies conducted in Austria and Germany further highlighted the persistence of neurological symptoms, including concentration difficulties, cognitive impairment, and memory complaints in individuals with long COVID (31, 34).

Psychological and Social Impact

Long COVID is associated with significant psychological and social repercussions, particularly anxiety and depression, with reported prevalence ranging from 5% to 95% across studies (12, 15–16, 19–20, 22–23, 25, 27, 31, 33). Mental health has also been significantly impacted by the social isolation and loss of habits caused by long COVID.

Challenges in Healthcare Delivery Services

Patients also faced challenges in healthcare delivery services during Long COVID. In a qualitative study conducted in the US, patients reported concerns regarding the lack of comprehension of the healthcare professionals and the lack of addressing long-term COVID symptoms (24). In another study across the UK, US, and Canada, 1/3rd of the long-COVID patients reported not receiving assistance from their medical healthcare team for their chronic symptoms (13).

Employment-Related Concerns

Long-term COVID has significantly impacted employment. In a study in the US, there was a significant decline in the proportion of patients working full-time from 76% pre-COVID to 41% post-COVID (12). In a study in the UK, the authors reported 20% of post-COVID patients were unable to work at all, and 51% missed at least 1 workday in the past 4 weeks due to long COVID symptoms (16). In another study in the UK, 11.4% of patients with long COVID had left their jobs (26), and 31.6% of patients reduced their working hours post-COVID in a study conducted in Spain (33).

Health-Related Quality of Life with Physical Inactivity

Physical inactivity and reduced functional ability are common consequences of long COVID. In a study in the US, patients were likely to exercise for 150 minutes less per week after contracting COVID-19 (12). As per a study in Belgium, 44% of patients were unable to do physical activities at 3 months post-infection. Even though this improved to 12% at 6 months, the walking time continued to be less than pre-COVID levels even after 6 months (28).

ASSESSMENT OF RISK OF BIAS

Risk of bias was assessed using the R-based ROBVIS software package. Of the 23 included studies, 16 (69.6%) were rated as having a low risk of bias, 5 studies (21.7%) had some concerns, and 2 studies (8.7%) showed a high risk of bias (Figures 2 and 3). Each study was evaluated across five key domains: randomization process, deviations from intended interventions, missing outcome data, measurement of outcomes, and selection of the reported results.

		RISK OF BIAS DOMAINS				
		D1	D2	D3	D4	D5
STUDY	Study 1	+	+	−	−	+
	Study 2	+	+	−	−	−
	Study 3	+	+	×	−	−
	Study 4	+	+	−	+	+
	Study 5	+	+	−	−	−
	Study 6	+	+	−	−	+
	Study 7	+	+	−	−	−
	Study 8	+	+	−	−	−
	Study 9	+	+	−	−	−
	Study 10	+	+	−	−	−
	Study 11	+	+	−	−	+
	Study 12	+	+	−	−	+
	Study 13	+	+	×	×	+
	Study 14	+	+	−	−	+
	Study 15	+	+	×	−	+
	Study 16	+	+	−	−	+
	Study 17	+	+	−	−	+
	Study 18	+	+	×	−	+
	Study 19	+	+	−	−	+
	Study 20	+	+	×	−	+
	Study 21	+	+	−	−	+
	Study 22	+	+	−	−	+
	Study 23	+	+	×	−	+

Domains:

D1: Bias arising from the randomization process.

D2: Bias due to deviations from intended intervention.

D3: Bias due to missing outcome data.

D4: Bias in measurement of the outcome.

D5: Bias in selection of the reported result.

Judgement

× High

− Some concerns

+ Low

Figure 2. Illustration of the Risk-of-Bias Domains.

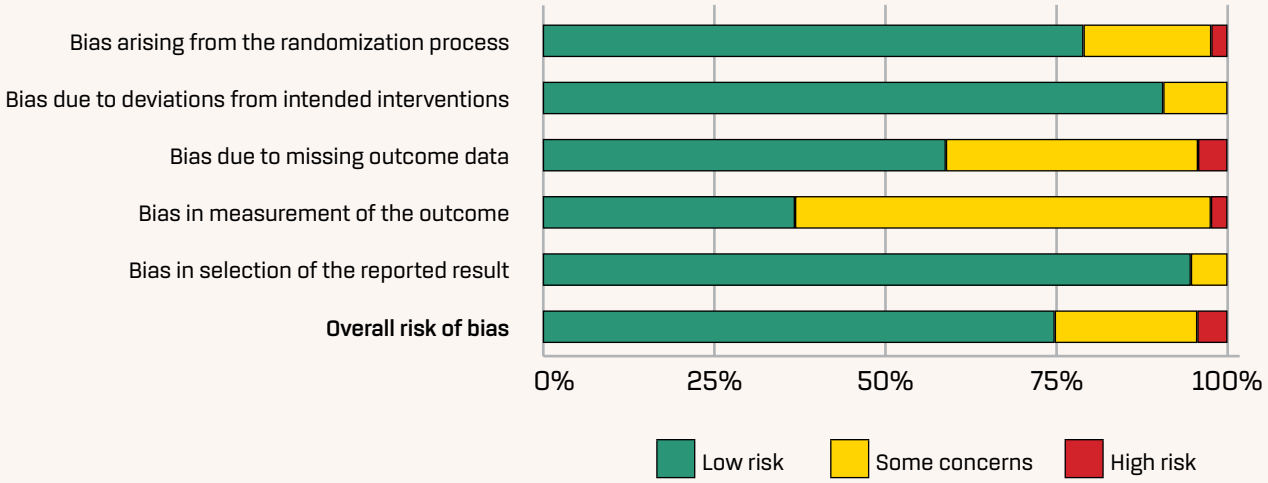

Figure 3. Depiction of the Overall Risk of Bias.

DISCUSSIONS

Long COVID refers to persistent or newly developed symptoms occurring after the acute phase of SARS-CoV-2 infection, often lasting weeks to many months. In some individuals, new symptoms may emerge after an asymptomatic period following recovery from the acute infection (35). This systematic review highlights the complex and far-reaching impacts of Long COVID on individuals' physical, neurological, and psychological health, as well as on the healthcare system and overall quality of life.

FATIGUE AND MUSCULOSKELETAL SEQUELAE

Musculoskeletal complications are among the most common and significant outcomes experienced by long COVID survivors, with predominant symptoms including persistent fatigue, muscle pain (myalgia), muscle weakness, joint pain (arthralgia), and skeletal muscle damage (36). The most common symptom that has affected individuals was found to be fatigue, as reported in many studies (37, 38). We observed heterogeneity in the prevalence rates of fatigue, ranging from 5.5% (14) to 84.4% (33) across the included studies. This variation could be attributed to differences in study designs (e.g., cross-sectional vs. cohort vs. qualitative), sample sizes (ranging from 21 to over 1.4 million participants), and timing of post-COVID symptom assessments. Physiological mechanisms underlying these complications may include direct viral infection, systemic inflammation, and lifestyle disruptions. Studies have identified ACE2 receptors and TMPRSS2 proteins in musculoskeletal tissues, suggesting that SARS-CoV-2 may directly infect these areas. (39). Additional pathological findings such as muscle fiber atrophy, necrosis, immune cell infiltration, and neuronal demyelination further contribute to the biological basis of fatigue and weakness (40, 41, 42). Lifestyle changes during the pandemic (e.g., reduced activity, poor sleep) may have compounded these outcomes (43).

COGNITIVE AND NEUROLOGICAL IMPAIRMENTS

Cognitive dysfunction, including memory loss, impaired concentration, brain fog, and sleep disturbances, was frequently reported (31, 34). A meta-analysis reported significant cognitive impairments in Long COVID patients, including deficits in executive function, memory, attention, and processing speed (44). Another review found persistent neurological symptoms – such as encephalitis, seizures, mood swings, and brain fog – lasting up to 2–3 months post-infection (45). Studies reported significant cognitive and neurological

impairments in Long COVID patients, including deficits in executive function, memory, attention, processing speed, as well as symptoms like encephalitis, seizures, mood swings, and brain fog lasting up to 2–3 months post-infection (44, 45). Additionally, our study reported similar findings, including fatigue, forgetfulness, sleep disturbances, limb weakness, cognitive deficits, and post-traumatic stress disorder even a year after infection (31). Neuropsychiatric symptoms in COVID-19 survivors are linked to the virus entering brain cells via ACE2 receptors and TMPRSS2, while severe cases may trigger cytokine storms causing thrombotic issues like DIC (46, 47).

PSYCHOLOGICAL AND SOCIAL IMPACT

Long COVID has significant social and psychological impacts. In included studies, it was observed individuals had high rates of anxiety (16.2%–55%), depression (up to 20.5%), and insomnia (up to 60.9%) among post-COVID patients (12, 20). These mental health issues are often linked to job loss, social isolation, poor physical health, and disrupted daily functioning. Patients also expressed concerns about long-term effects on life expectancy and aging, highlighting the ongoing psychological burden of the condition (24). A study reported that nearly half of the patients remained emotionally affected after 8 weeks, with 28 requiring further mental health care (50).

CHALLENGES IN HEALTHCARE

Long COVID has posed striking challenges for healthcare systems around the world. Patients have reported significant obstacles with regards to access to care, managing long-term symptoms, and receiving an adequate diagnosis. In a qualitative study conducted in the US, many patients felt their symptoms were disregarded or not adequately assessed by health professionals, and they often felt misunderstood by them. The study also reported patients being confused on how to effectively communicate their symptoms and concerns regarding the absence of well-defined treatment guidelines (24). The frustration and concern of patients battling with the long-term impacts of COVID-19 infection may have left them worried about the management of their prolonged symptoms in the future. A study reported that patients living with long COVID shared that they suffered with a range of symptoms and felt ‘abandoned’ and ‘dismissed’ by healthcare providers and got conflicting or limited advice (48). One third of patients in another study reported being ill or in a worse clinical condition than at the onset of infection, even at eight weeks (49).

IMPACT ON EMPLOYMENT AND DAILY FUNCTIONING

Beyond physical and neurological impacts, long COVID has significantly affected employment levels among patients who have reported a reduced working capacity or being unable to work at all, as reported in our included studies. (12, 13, 16, 26). The main reasons for reduced working hours and capacity to work were found to be fatigue, cognitive problems, and psychosocial variables, as reported in our studies. In another study, the authors reported that amongst 195 patients who were employed prior to hospitalization, 40% of them could not return to work within 8 weeks of discharge due to persistent symptoms or loss of job and of the ones who could resume work in this study, a quarter had to reduce their working hours or alter their responsibilities due to health issues (50) About 70% of previously admitted patients for COVID-19 also could not return to work at 3 months after admission, as reported in another study (51).

Health-related quality of life has also been known to be impacted by long COVID, especially with respect to physical inactivity. In a study in Belgium, 12% of participants post-COVID-19 were unable to be physically active and

perform sports at 6 months (28). In a study in Indonesia, 21.4% of patients reported poor quality of life due to headaches caused by post-COVID infection (17). 5.8% of patients in a study conducted in Mexico reported inability to walk as a frequent complication of long-term COVID (19) and 7.9% of patients had mobility problems, and 15.4% reported challenges with their daily activities in a study in Korea (23). Studies have attributed these impacts to marked deficits in mental health and a lack of social engagement (17, 23). An all-encompassing management of both physical and psychological disturbances can help reduce the impact of post-COVID symptoms on the daily lives of individuals.

Our findings highlight that long COVID follows a prolonged and multifaceted course, with symptoms like fatigue, brain fog, sleep disturbances, and myalgia persisting for months after infection. Studies reported physical, neurological, and psychological complications, with impacts on employment and access to healthcare. The persistence and overlap of these symptoms suggest that long COVID does not follow a uniform trajectory but varies based on individual, clinical, and contextual factors, necessitating long-term multidisciplinary care.

CONCLUSIONS

1. This systematic review comprehensively evaluates the challenges and complications faced by patients with long COVID. The insights derived from this review can help identify key specific areas for intervention, particularly in addressing clinical, psychological, and socioeconomic complications. Understanding these issues will enable the development of targeted strategies to mitigate the long-term effects of long COVID and improve patient outcomes.
2. The findings of this review are critical for healthcare policymakers and providers as they work to develop protocols that address the gaps in care for long COVID patients. The COVID-19 pandemic has underscored the need for upgraded healthcare systems, particularly in low- and middle-income countries, to adapt to new challenges, with long COVID complications as emerging public health challenge.
3. Our review emphasizes the urgent need for multidisciplinary post-COVID care pathways that seamlessly integrate physical, psychological, and social health services into routine healthcare. Such comprehensive approaches can strengthen clinical guidelines and support evidence-based policymaking, helping health systems become more resilient in managing long COVID and future public health challenges.

CONFLICT OF INTEREST

The authors have no conflicts of interest associated with the material presented in this paper.

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Date of receipt of the manuscript: 11.02.2025

Date of acceptance for publication: 24.07.2025