Long COVID: Integrating Evidence on Multisystem Manifestations, Mental Health Outcomes, and Quality-of-Life Impacts

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Abstract—Long COVID (post-acute sequelae of SARS-CoV-2 infection, PASC) is a complex health challenge marked by persistent, relapsing, multisystem symptoms beyond the acute phase. It affects physical, cognitive, and psychological domains across age groups and severities, straining healthcare systems. This review seeks to compile and critically evaluate available evidence on long COVID, with special emphasis on risk factors, clinical manifestations, diagnostic complexity, mental health outcomes, and management strategies. The aim is to provide an integrated perspective to guide clinicians, researchers, and policymakers in addressing the broad and evolving challenges posed by long COVID. Eligible studies included cohort analyses, cross-sectional surveys, qualitative interviews, systematic reviews, guidelines, and policy documents, selected for relevance to symptoms, mental health impact, diagnostic criteria, risk factors, and management. Long COVID presents highly heterogeneous, often relapsing symptoms across multiple organ systems, including fatigue, respiratory and cardiovascular issues, gastrointestinal disturbances, musculoskeletal pain, and dermatologic changes. Mental health impacts—such as anxiety, depression, PTSD-like symptoms, sleep disturbances—are major drivers of reduced quality of life. Diagnostic challenges arise from symptom overlap and inconsistent definitions, while risk factors include age, sex, comorbidities, socioeconomic status, and acute illness severity. Long COVID imposes a sustained, multidimensional burden. Addressing it requires clearer diagnostic criteria, consistent definitions, integrated care models including mental health and social support, and prevention strategies like vaccination. Coordinated research is essential to identify mechanisms, modifiable risk factors, and effective, equitable management to reduce long-term impacts and health inequities.

Keywords— Post-Acute COVID-19 Syndrome, COVID-19, Quality of Life, Mental Health, Cognitive Dysfunction

1. INTRODUCTION

The COVID-19 pandemic has had an unprecedented impact on global health, society, and economies, with acute infections leading to millions of hospitalizations and deaths worldwide. As the immediate crisis phase subsides in many regions, attention is shifting to the enduring consequences of infection that extend well beyond viral clearance [1, 2, 3]. Among these, long COVID has emerged as a significant and complex clinical entity characterized by the symptoms continuing or newly developing for several weeks or months after acute illness [4, 5, 6].

Long COVID represents not merely a biomedical problem but a multifaceted public health challenge [2, 3]. A growing body of evidence indicates that its symptoms can affect multiple organ systems and often fluctuate over time, making diagnosis and management difficult [7, 8]. Commonly reported features include profound fatigue, dyspnea, cognitive dysfunction, and mental health disturbances such as anxiety, depression, and sleep disruption [5, 6, 9, 10, 11, 12]. Importantly, long COVID affects people across the full spectrum of initial disease severity, including those who experienced mild or asymptomatic acute infections, complicating assumptions about who is at risk [4, 13].

The implications of long COVID extend beyond individual health to broader societal and economic domains. Patients often report reduced ability to work, participate in daily activities, or maintain social roles, leading to substantial impacts on health-related quality of life and increasing demand for healthcare resources [4, 6, 14]. Health systems, already strained by pandemic response, face the additional challenge of providing multidisciplinary care that can address the complex and overlapping physical, cognitive, and psychological dimensions of this condition [1].

Despite growing recognition, long COVID remains poorly defined in many respects [4, 14, 15, 16, 17]. The absence of standardized diagnostic tests or biomarkers, along with variable clinical criteria, complicates efforts to determine the true prevalence and burden of the condition [1]. Research into its underlying mechanisms continues to evolve, with hypotheses ranging from persistent inflammation and immune dysregulation to autonomic nervous system disturbances and neuroinflammation [7, 9, 18, 19]. These uncertainties pose barriers not only to accurate diagnosis but also to the development of effective interventions and policy responses.

Given its wide-ranging impact on individuals, communities, and health systems, long COVID demands careful study and sustained attention. This review aims to synthesise current knowledge on long COVID with a particular focus on its mental health consequences and effects on quality of life. By examining definitions, epidemiology, pathophysiology, symptom patterns, diagnostic challenges, and management strategies, the goal is to provide a comprehensive resource to guide clinicians, researchers, and policymakers in responding to this evolving public health concern.

2. MATERIALS AND METHODS

This review is based on systematic literature searches in PubMed, Scopus, and Embase, covering studies published between 2020 and 2025. Search terms included "long COVID," "post-acute sequelae of COVID-19," "quality of life," "mental health," "diagnosis," and "management", "cognitive dysfunction." Eligible articles included quantitative and qualitative research, systematic reviews, expert guidelines, and policy documents. Studies were screened for relevance to symptomatology, mental health impact, diagnostic criteria, risk factors, and therapeutic approaches, with disagreements resolved by consensus among reviewers.

3. RESULTS

A. Definitions and Conceptual Framework

Long COVID, also called post-acute sequelae of SARS-CoV-2 infection (PASC), describes a range of symptoms that persist or arise after acute infection, often extending 12 weeks or more [6, 19]. Terminology is not consistent across studies or clinical guidelines, leading to varied definitions and thresholds for duration [15]. WHO, NICE, and other authorities propose criteria based on persistent symptoms unexplained by other diagnoses, but these frameworks differ in detail [1, 4]. This inconsistency complicates surveillance and research comparisons. Diagnostic criteria often emphasise clinical assessment, patient history, and exclusion of alternative causes [1]. Conceptual models help make sense of this heterogeneity.The biopsychosocial model examines the interplay of biological factors such as immune alterations, psychological elements such as anxiety, and social conditions including stigma and healthcare access [15, 19]. Syndromic approaches group overlapping symptoms, recognising long COVID as a complex, multifactorial condition that requires integrated understanding and management [6, 19].

B. Epidemiology and Global Burden

Estimates of long COVID prevalence vary significantly across studies due to differences in definitions, duration thresholds, and population samples [16, 19]. Reported rates range from small proportions of mild cases to large percentages among previously hospitalised patients [17, 20]. Geographically, prevalence patterns reflect testing availability, health system capacity, and demographic differences [21]. Age, sex, and pre-existing health conditions contribute to risk variations [8, 21, 22]. Long COVID exerts a heavy burden on healthcare systems, increasing demand for consultations, specialist referrals, and ongoing care [15, 21, 22]. Beyond health services, it also imposes societal costs through work absenteeism, disability

claims, and reduced productivity [6]. Addressing these challenges is complicated by inconsistent surveillance systems, limited longitudinal data, and variability in diagnostic coding, making it difficult to achieve accurate, comparable global burden estimates.

C. Pathophysiology and Mechanisms

Current understanding of long COVID pathophysiology indicates a complex, multifactorial process involving several interacting mechanisms. Immune dysregulation has been highlighted as a core feature, with ongoing low-level inflammation, autoimmunity, and altered immune responses that may fail to resolve after acute infection [13, 19]. These immune abnormalities can include persistent viraemia, weak or absent antibody responses, and chronic inflammatory reactions that contribute to prolonged symptoms [15].

Hypotheses of occult viral persistence suggest that fragments of viral RNA or proteins may remain in certain tissues, sustaining immune activation and inflammatory pathways over time. Such persistent immune stimulation could explain the relapsing and remitting nature of symptoms reported by many patients [19, 23]. Endothelial dysfunction and coagulation activation are also proposed mechanisms, as SARS-CoV-2 infection can lead to vascular inflammation and microthrombosis, impairing oxygen delivery and contributing to fatigue and organ-specific symptoms. This vascular component may help explain the widespread systemic manifestations and exercise intolerance seen in long COVID populations [19, 24].

Autonomic nervous system involvement has been described, with patients reporting symptoms such as palpitations, dizziness, and temperature dysregulation that suggest autonomic imbalance. Such dysfunction may arise from immune-mediated injury or persistent inflammation affecting autonomic pathways, further complicating symptom management [19, 24]. Neuroinflammatory processes are suspected drivers of cognitive dysfunction, often referred to as "brain fog," as well as psychiatric symptoms like anxiety and depression [9, 18]. Studies have described the neuropsychiatric burden of long COVID, including depression, anxiety, sleep disturbances, and concentration difficulties that persist for months after acute infection [2, 6, 9, 12]. Psychosocial and psychoneuroimmunological factors are also important, as mental health stressors - including post-traumatic stress, uncertainty, and social isolation - can interact with biological processes to exacerbate or sustain symptoms [15, 17, 22]. The biopsychosocial impact of long COVID has been emphasised, with reports of long-term disability, functional impairment, and reduced quality of life affecting patients' ability to work and participate fully in society [22, 25].

Altogether, these interlinked mechanisms underscore the heterogeneity and complexity of long COVID, which manifests as a multisystem condition with overlapping, variable, and often relapsing symptoms [13, 19]. Recognising this complexity is essential for developing effective, holistic management approaches and guiding further research into tailored treatment strategies.

D. Symptomatology: A Multisystem Condition

Long COVID manifests as a complex, multisystemic condition with a highly diverse clinical presentation that can change over time [13, 19, 24]. Generalized symptoms such as profound fatigue, malaise, and post-exertional symptom exacerbation are among the most frequently reported and often persist for months, severely limiting patients' daily activities and quality of life [6, 26, 27]. Fatigue in particular is consistently cited as the most prevalent symptom in cohort studies, affecting more than half of patients even at 3-6 months after infection [6, 27].

Respiratory manifestations are common and include persistent dyspnea, chest tightness, and chronic cough [6, 26, 28]. These symptoms may be related to residual airway inflammation, parenchymal lung changes, microvascular injury, or altered breathing patterns [26, 28, 29]. Studies have described prolonged pulmonary symptoms and exercise intolerance even in patients who had mild initial infections, with mechanisms including endothelial dysfunction, microclot formation, and persistent inflammation of lung tissue [5, 6, 28, 29].

Cardiovascular involvement is also a significant feature of long COVID. Patients report palpitations, chest discomfort, exercise intolerance, and symptoms of orthostatic intolerance or postural orthostatic tachycardia syndrome (POTS) [5, 6, 26, 30]. These issues are thought to reflect autonomic dysregulation, persistent endothelial injury, and a prothrombotic state. Biomarker studies have documented elevated D-

dimer levels and evidence of microclots long after the acute phase, suggesting ongoing thrombotic risk [26, 30].

Gastrointestinal symptoms such as abdominal pain, nausea, diarrhea, constipation, and appetite loss have been frequently documented [5, 26]. Mechanistic hypotheses include persistent viral particles in the gut, dysbiosis of the intestinal microbiome, mucosal inflammation, and immune-mediated damage [26]. The relationship between gastrointestinal and mental health symptoms in long COVID may be complex, as persistent GI symptoms can contribute to psychological distress, while anxiety and low mood may exacerbate symptom perception [6, 31].

Musculoskeletal complaints, including myalgia, arthralgia, generalized muscle weakness, and joint pain, are widespread and may persist for many months [26, 32]. These symptoms are often relapsing and remitting, resembling conditions such as chronic fatigue syndrome or fibromyalgia [6, 32]. Underlying mechanisms are thought to involve chronic low-grade inflammation, immune dysregulation, and altered pain processing [26, 32].

Dermatologic findings, although less common, have been reported and include rashes, urticaria, livedo reticularis, and hair loss (telogen effluvium). These may reflect microvascular changes, immune-mediated processes, and emotional stress [33].

Oral cavity involvement has also been observed in some patients, with persistent dry mouth, taste alterations, and mucosal lesions, potentially linked to local viral persistence, altered saliva composition, and immune responses [34].

Importantly, these diverse symptoms often occur together in complex patterns, and their severity can vary widely among patients [6, 19]. While neurological and psychiatric manifestations - such as cognitive dysfunction, anxiety, and depression - are also key features of long COVID, these will be discussed in detail in subsequent sections. This broad constellation of symptoms underscores the importance of a comprehensive, multidisciplinary approach to diagnosis, monitoring, and management.

E. *Impact on Mental Health*

Mental health outcomes are increasingly recognized as a core dimension of long COVID, significantly shaping overall disease burden, recovery trajectories, and health-related quality of life [35]. Psychological symptoms frequently reported among long COVID patients include anxiety, depression, post-traumatic stress-like reactions, emotional dysregulation, and sleep disturbances [9, 12, 35]. Prevalence estimates vary across studies, reflecting differences in populations, disease severity, measurement tools, and follow-up duration [12, 36]. Nonetheless, systematic reviews and cohort data consistently indicate elevated rates of anxiety and depressive symptoms compared to the general population, persisting for months after the acute phase [37].

Anxiety and stress-related symptoms in long COVID may present as feeling jumpy at unexpected events, heightened awareness of potential dangers, difficulty concentrating, irritability, difficulty falling or staying asleep, bodily reactions, and being upset by reminders [35]. PTSD-like phenomena have also been observed, including intrusive memories of hospitalization or intensive care, avoidance behaviors, hyperarousal, and emotional numbing - particularly among those who experienced severe acute illness or traumatic medical interventions [38].

Sleep disruption represents another prominent concern, encompassing difficulty initiating or maintaining sleep, non-restorative sleep, and circadian rhythm disturbances. These sleep problems may intensify fatigue, cognitive dysfunction, and emotional reactivity, creating self-perpetuating cycles of distress and impairment [35, 36]. Emotional dysregulation is also frequently reported, with patients describing irritability and anger outbursts [35, 38].

Beyond traditional psychiatric symptoms, long COVID has been linked to increased rates of suicidal ideation and reductions in overall life satisfaction, highlighting a broader impact on psychological well-being. Daily functional impairments - such as difficulties with self-care, work, and social roles - have been identified as key mediators in the relationship between persistent physical symptoms and mental health outcomes. Structural equation modeling suggests that functional challenges can exacerbate common mental disorders, which in turn may amplify PTSD symptoms and suicidal thoughts, underscoring the interconnected pathways linking physical illness and psychological distress [37].

Biological mechanisms are thought to contribute to these psychological symptoms. Chronic low-grade inflammation, persistent immune activation, and neuroinflammatory pathways may directly affect brain function, influencing mood, cognition, and stress responsivity [9, 18, 36]. Dysregulation of the hypothalamic-pituitary-adrenal axis, autonomic imbalance, and alterations in neurotransmitter signaling have also been proposed as contributors to psychiatric sequelae in long COVID [39, 40]. These pathophysiological factors likely interact with psychosocial stressors - such as financial insecurity, role loss, and uncertainty about recovery - to sustain or amplify mental health difficulties over time [36].

Given the multifaceted origins of mental health problems in long COVID, integrating psychological care into multidisciplinary management is critical. Routine screening should include assessment of anxiety, depression, PTSD-like symptoms, suicidal ideation, sleep disturbances, and functional impairments [9, 12, 35]. Given the complex and varied neuropsychiatric symptoms in long COVID, multidisciplinary approaches are recommended, and further research is needed to develop evidence-based treatment strategies that address patients' needs and support recovery [36].

F. Cognitive Dysfunction and Neurological Sequelae

Cognitive impairment, often referred to as "brain fog," is one of the most persistent and disabling features of long COVID, affecting a substantial proportion of patients well beyond the acute phase of infection [11, 40, 41, 42]. Studies consistently report difficulties with memory, attention, executive functioning, information processing speed, and verbal fluency, even among those with mild initial illness or no hospitalization history [4, 41]. Symptoms may fluctuate over time, with many patients describing relapsing or worsening episodes triggered by physical or mental exertion and stress [6].

Neuropsychological testing has documented measurable deficits in domains such as working memory, psychomotor coordination, and executive control, with a significant proportion of survivors performing below normative expectations even months after recovery [11, 43]. Some cohorts report that over 60% of patients demonstrate at least mild cognitive impairment on structured assessments [6, 11]. These cognitive challenges often contribute to broader functional limitations, reducing patients' ability to work, manage daily responsibilities, and maintain social roles [6].

Advanced neuroimaging studies provide evidence of subtle but meaningful brain changes in long COVID populations. Observed findings include reduced gray matter volume, signs of neuroinflammation, altered white matter integrity, and disrupted functional connectivity in regions associated with memory, attention, and emotional regulation. Mechanistic hypotheses point to persistent neuroinflammatory processes, endothelial dysfunction leading to hypoperfusion, blood-brain barrier disruption, and possible residual viral reservoirs sustaining chronic immune activation [42, 43].

Importantly, these neurological sequelae rarely occur in isolation. They are frequently accompanied by the previously mentioned psychiatric symptoms, such as anxiety, depression, sleep disturbances, and PTSD-like reactions, with bidirectional relationships that can exacerbate overall disease burden and complicate recovery [9, 12, 35, 43]. The overlap of cognitive and emotional symptoms underscores the need for comprehensive, multidisciplinary approaches to assessment and care [42, 43].

Recovery trajectories remain highly variable. While some patients show gradual improvement over six to twelve months, others report persistent or even worsening symptoms over time [6, 43]. Rehabilitation challenges include the lack of standardized protocols for cognitive recovery in this population and the need to adapt strategies used in other neurological conditions, such as acquired brain injury, to address long COVID's unique and multifaceted nature [42]. Recommended approaches often emphasize individualized pacing, cognitive rehabilitation techniques, and integrated mental health support to address the complex interplay between neurocognitive and psychological factors in long COVID [44, 45].

G. Impact on Health-Related Quality of Life (HRQoL)

Health-related quality of life (HRQoL) in individuals with long COVID is profoundly and persistently compromised, reflecting the multidimensional burden of this condition well beyond its acute phase [46, 47]. As previously described, long COVID involves a constellation of lingering symptoms spanning physical, cognitive, and psychological domains that collectively erode functional capacity and well-being [46, 48]. Research demonstrates that quality of life impacts associated with long COVID can persist for at least two years, with recovered and symptomatic individuals alike reporting greater difficulties across

domains such as fatigue, pain, mental health, daily functioning, and cognitive performance compared to those without long COVID [46].

Patient-reported outcome measures, including the PROMIS-29, EQ-5D-5L, SF-36, and Satisfaction with Life Scale (SWLS), consistently reveal significantly lower scores in long COVID populations relative to healthy controls or pre-COVID baselines [46, 47, 48, 49]. These deficits are not limited to somatic health: they extend to mental health dimensions such as anxiety, depressive symptoms, sleep quality, and emotional regulation, underscoring the interplay between physical symptoms and psychological distress [48, 49, 50]. Functional impairments often disrupt employment, daily self-care, and social participation, contributing to loss of independence and diminished life satisfaction [25, 47, 49].

Moreover, disparities in HRQoL outcomes have been observed across demographic and socioeconomic groups. Age, sex, pre-existing comorbidities, and social determinants of health - including employment status, ethnicity, and access to care - emerge as significant predictors of poorer HRQoL, suggesting that long COVID may exacerbate existing health inequities [47, 49, 50]. For instance, older adults may be more likely to report reduced mobility and pain, illustrating age-related differences in physical health impacts. Studies have also highlighted that female patients are at higher risk for persistent symptoms and reduced HRQoL, with proposed explanations including biological vulnerability related to sex-specific immune differences [50, 51].

Importantly, even in populations with initially mild or asymptomatic acute infections, substantial HRQoL reductions have been documented long after viral clearance [46]. This finding challenges assumptions about risk profiles and underscores the need for broad-based screening and support. Furthermore, the complexity of HRQoL impacts often includes bidirectional interactions among physical disability, mental health problems, and social consequences such as stigma and reduced income security [25, 31, 47]. As patients navigate healthcare systems, they frequently report feelings of being dismissed or inadequately supported, compounding psychological stress and eroding trust in care pathways [31].
Overall, the evidence underscores that long COVID imposes not just an individual clinical burden but a public health challenge that strains health systems and deepens societal inequities. Addressing these persistent and unequal HRQoL impacts requires integrated, multidisciplinary approaches to care that encompass physical rehabilitation, mental health services, social support, and targeted policy interventions to ensure equitable access and mitigate the broader consequences of this evolving condition [39, 44].

H. Risk and Protective Factors

As previously discussed, long COVID is a heterogeneous condition whose risk is shaped by multiple, interacting factors rather than a single determinant [7, 8]. Age emerges as a consistent predictor, with older adults generally more vulnerable to persistent symptoms and reductions in health-related quality of life, likely reflecting both immunosenescence and a greater burden of pre-existing conditions [52]. Female sex has also been repeatedly associated with elevated long COVID risk, a pattern observed across diverse cohorts and hypothesized to involve differences in immune responses and health-seeking behaviours [51, 52, 53]. Race and ethnicity have also been identified as potential risk modifiers, with evidence suggesting that minoritized populations may face higher risk due to overlapping social determinants and healthcare inequities [54]. Acute illness severity plays a critical role: individuals who experienced severe or hospitalised COVID-19 tend to report higher rates of lingering symptoms, although cases following mild or asymptomatic infection remain well documented, challenging simplistic risk models [4, 53, 54]. Comorbidities such as obesity, hypertension, and respiratory diseases increase susceptibility, both through direct physiological vulnerability and by complicating recovery trajectories [8, 52]. Socioeconomic and psychosocial dimensions also warrant attention; limited access to healthcare, financial insecurity, and social marginalisation can exacerbate long COVID risk by delaying diagnosis, limiting treatment options, and intensifying stress [54]. Conversely, protective factors may include vaccination - which appears to reduce the likelihood or severity of long COVID in some studies - as well as robust social support networks and psychological resilience that may buffer stress and aid coping [3, 55, 56]. These complexities underscore the need for nuanced risk assessment that considers biological, clinical, and social dimensions to inform screening, prevention, and tailored care strategies.

I. *Diagnostic Challenges*

As already noted, defining long COVID remains problematic given its varied presentations and lack of a single, universally endorsed framework [1, 4, 14]. Diagnostic uncertainty is compounded by the broad and evolving spectrum of complaints that can involve multiple organ systems and vary over time, requiring clinicians to carefully differentiate them from other conditions [7, 8]. Instead of standardized protocols, current practice often depends on symptom-led evaluation and ruling out alternative explanations, leaving significant room for inconsistency in approach [1, 4]. In many primary care settings, symptoms may be under-recognized or recorded in unstructured ways, limiting effective follow-up and complicating surveillance efforts [57]. Children and adolescents pose particular challenges, with few tailored diagnostic guidelines and a risk of under-detection due to atypical or less clearly defined symptom patterns [1, 58]. Additionally, patients frequently report feeling dismissed or encountering stigma when seeking help, while clinicians face constraints of time, training, and resources that can hamper comprehensive assessment [59]. Addressing these barriers calls for more consistent diagnostic pathways, better integration of multidisciplinary input, improved training for healthcare providers, and equitable access to care across diverse populations [59, 60].

J. *Prevention*

While much of the clinical response to long COVID focuses on managing established symptoms, prevention remains a critical strategy for reducing disease burden. Vaccination against SARS-CoV-2 has consistently been associated with a lower risk of developing long COVID or experiencing severe, persistent symptoms. Studies suggest that prior immunization can attenuate the likelihood of long-term sequelae even in breakthrough infections, underscoring its role as a key preventive measure [3, 56]. Beyond vaccination, preventive public health approaches incorporate measures such as improving ventilation and encouraging masking to lower the risk of acute COVID-19 infections, thereby helping to reduce cases of Long COVID. Public health institutions have an essential role in advancing evidence-informed prevention, increasing community awareness, supporting surveillance activities, and ensuring people can access appropriate services [61]. These approaches aim not only to limit acute COVID-19 morbidity and mortality but also to reduce the long-term individual and societal impacts of post-acute sequelae.

K. *Management and Treatment Strategies*

Given its diverse, multisystemic, and often relapsing nature, long COVID requires an integrated, patient-centred management approach that addresses physical, psychological, and social dimensions of care. Current best practices emphasize multidisciplinary teams involving primary care providers, specialists, rehabilitation professionals, and mental health services to deliver coordinated assessment and treatment plans [1, 55].

Management typically begins with comprehensive clinical evaluation aimed at ruling out alternative diagnoses and identifying symptom patterns to guide individualized care [1]. Symptom-targeted pharmacotherapy may be considered for specific complaints - such as pain management, antihistamines for mast cell activation symptoms, or low-dose naltrexone - though robust evidence remains limited and emerging [62].

Psychological support is an important component of care, helping patients manage anxiety, depression, PTSD-like symptoms, and adjustment challenges associated with persistent illness [1, 35]. Given the high prevalence of sleep disturbances and emotional symptoms, individualized strategies that include sleep hygiene measures, stress management approaches, and regular follow-up are recommended [63].
Rehabilitation plays a central role in restoring functional capacity and quality of life. Graded exercise programs, pacing strategies to manage post-exertional symptom exacerbation, respiratory physiotherapy, and cognitive rehabilitation may all be included depending on individual needs and tolerance [45, 53, 64]. Importantly, emerging guidelines highlight the need to monitor for adverse responses to exercise, such as orthostatic intolerance or symptom flare-ups, and adjust plans accordingly [64]. Telerehabilitation offers additional opportunities for accessible, patient-tailored interventions, especially in resource-constrained settings [44, 64].

Integrated care pathways aim to improve continuity and coordination of services by supporting effective information sharing and collaborative working across the healthcare system. This includes timely exchange of clinical records, care and rehabilitation plans between services, and the use of multidisciplinary meetings - whether virtual or in person - to ensure joined-up care. Providing patients with copies of their care plans, discharge summaries, and prescriptions empowers them to participate actively in their treatment. Sharing key baseline measures and ongoing assessments, such as oxygen saturation, heart rate, or functional status, helps maintain consistent care as patients transition between settings [1]. Despite increasing experience in managing long COVID, there remain significant knowledge gaps, highlighting the need for further research to develop effective interventions, improve rehabilitation approaches, and establish evidence-based guidelines that ensure equitable, high-quality care for all populations [65, 66].

4. DISCUSSION

This review highlights that long COVID is not a single, uniform condition but a complex and multifactorial syndrome involving a broad range of physical, cognitive, and psychological manifestations. The evidence synthesised in the results section demonstrates the persistence and heterogeneity of symptoms across organ systems, reflecting both biological and psychosocial influences. Such diversity underlines the need to view long COVID through an integrated, biopsychosocial lens rather than a narrow biomedical framework.

The reviewed studies emphasize that persistent immune dysregulation, chronic inflammation, endothelial dysfunction, and autonomic imbalance may interact with psychological and social stressors to sustain symptoms and delay recovery. This interplay between biological and psychosocial mechanisms helps explain the strong association observed between physical complaints and mental health outcomes. Fatigue, dyspnea, cognitive impairment, anxiety, and depression frequently coexist and appear to reinforce one another, contributing to cycles of functional limitation and distress.

Mental health outcomes are among the most consequential aspects of long COVID. Elevated rates of anxiety, depression, PTSD-like reactions, and sleep disturbances substantially shape patients' quality of life and recovery trajectories. These psychological burdens are intensified by social consequences such as reduced employability, loss of independence, and experiences of stigma or dismissal within healthcare systems. Such findings illustrate that effective management must address both physical and emotional health within the same framework.

Quality-of-life impairments reported across studies reflect not only symptom persistence but also systemic inequities in healthcare access, socioeconomic vulnerability, and gender-related differences in risk. Female patients and those with pre-existing comorbidities or limited social support are disproportionately affected. These observations point to the need for equitable care pathways and social policies that mitigate the long-term effects of the pandemic on marginalized groups.

Diagnostic uncertainty continues to present a major barrier to consistent recognition and treatment. The lack of standardized definitions, biomarkers, and clinical criteria limits data comparability and contributes to underdiagnosis in both primary and specialist care. In this context, integrated and multidisciplinary care models—combining physical rehabilitation, psychological support, and coordinated information sharing—are essential for improving outcomes and continuity of care.

Finally, prevention through vaccination and public health measures remains a critical strategy. Evidence suggests that vaccination reduces the risk and severity of long COVID, underscoring the value of preventive approaches alongside clinical management. Continued research and policy coordination are needed to refine diagnostic criteria, identify modifiable risk factors, and develop evidence-based interventions that address the condition's multidimensional burden.

5. CONCLUSIONS

Long COVID represents a sustained, multifaceted public health challenge characterized by persistent, relapsing symptoms that affect multiple organ systems and significantly reduce health-related quality of life. Its complexity arises from the interplay of biological mechanisms and psychosocial factors that extend well beyond the acute infection phase.

Effective responses require clearer diagnostic frameworks, integrated multidisciplinary care, and equitable access to rehabilitation and mental health services. Prevention through vaccination and coordinated research efforts will be central to reducing the long-term individual and societal impacts of this condition.

By integrating physical, psychological, and social dimensions of care, health systems can better support recovery and mitigate the enduring burden of long COVID.

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