

Long COVID: State of the Art, Challenges, and Perspectives from the Field in Catalonia 2026

Multidisciplinary Collaborative Group for The Scientific Monitoring of Covid-19

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Long COVID: State of the Art, Challenges, and Perspectives from the Field in Catalonia 2026

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Please note that key concepts relevant to the management of Long COVID are evolving rapidly. This committee has established a mechanism to update its recommendations in light of new developments, and the most up-to-date information will be available on the website: <https://www.isglobal.org/ca/gcmsc>

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01 SUMMARY

Long COVID (LC) has emerged as a significant public health challenge following the COVID-19 pandemic. Data from the COVICAT cohort indicate that approximately 23% of individuals infected with SARS-CoV-2 during the early stages of the pandemic experienced symptoms lasting at least three months. Although the incidence of LC has declined substantially with widespread vaccination and the emergence of the Omicron variant, a considerable number of people continue to experience persistent health problems.

In Catalonia, based on available data, we estimate that **around 250,000 people** may have been affected by LC, although this figure is likely to fall short of the true burden of the condition. Despite this substantial impact, healthcare resources remain limited, with only one multidisciplinary LC unit currently available in the region. Furthermore, there is no coordinated national programme dedicated to LC, and most research activities depend on competitive funding mechanisms and European research calls.

Patients also face challenges beyond healthcare. Insufficient recognition and validation of LC within both healthcare and labour systems can delay diagnosis, limit access to appropriate care, and negatively affect quality of life and well-being, and contribute to anxiety, depression, social isolation and psychological distress. Continued efforts in research, clinical care, mental health support and policy development are needed to better understand, manage, and support people living with LC. Two Catalan cohorts, COVICAT and one led by Mateu *et al.*, are providing insight into the evolution of COVID-19.

This document analyses the **situation of LC in Catalonia** from three complementary perspectives: research, clinical practice, and the experiences of affected individuals. It identifies the main bottlenecks and priorities, providing recommendations to guide decision-making, improve care, and offer an adequate response to those affected. It is primarily addressed to public administrations and competent authorities, as well as to the professionals involved and the general public.

02 INTRODUCTION

An estimated 400 million people worldwide (about 6% of adults and 1% of children) had experienced LC by 2023. Although the prevalence has declined since the height of the pandemic, the burden of LC remains substantial (Al-Aly Z *et al.* 2024) . The economic toll is substantial, with global costs estimated at \$3.7 trillion in 2022 alone (OECD), and projected annual GDP losses of 0.1-0.2% (equivalent to around USD 135 billion per year) over the next decade, comparable to the entire annual health budget of Spain (OECD).

Despite this burden, policy responses have lagged; health systems are not providing the comprehensive care and support required by people with LC, and research funding remains insufficient. A recent study in the US found that, although the morbidity burden of LC is comparable to that of Alzheimer's disease and asthma, it receives only 14% of the research funding relative to the disability it causes (Bonuk *et al.* 2026)

LC encompasses a **wide range of symptoms** affecting multiple organ systems and can occur even after asymptomatic or mild SARS-CoV-2 infections or reinfections. According to the WHO definition, these symptoms appear within three months from infection, last for at least two months, and cannot be explained by an alternative diagnosis.

Clinically, LC is a complex condition that can affect the cardiovascular, nervous, immune, reproductive and/or gastrointestinal systems. This clinical heterogeneity makes it **difficult to define and diagnose**. Common manifestations include cognitive dysfunction (or brain fog), fatigue, dysautonomia (dysfunction of autonomic body processes such as heart rate and blood pressure), and post-exertional malaise. Several of these symptoms overlap with those of other infection-associated chronic conditions, collectively referred to as **post-acute infectious syndromes** (PAIS). Longitudinal studies, including one conducted in a Catalan cohort (Kogevinas *et al.*, 2025), suggest that more than half of affected individuals continue to experience symptoms two years after the initial infection. However, among severe LC cases, recovery can be even lower: less than 7% over two years for a cohort in a specialised LC unit (Mateu *et al.*, 2023; Xie *et al.*, 2024).

The **underlying causes** of LC are not yet fully understood, and different subtypes likely arise from different biological processes. Proposed mechanisms include viral persistence (infectious virus, viral RNA, or viral proteins), infection-triggered autoimmunity, reactivation of latent viruses, tissue damage driven by inflammation, and alterations in microbiota or energy metabolism.

LC can affect people of any age, sex, ethnicity, and health status. However, several **risk factors** have been identified, including female sex, age under 50, low socioeconomic status, severe acute SARS-Cov-2 infection, and pre-existing chronic conditions such as asthma, obesity and diabetes (Farre *et al.*, 2025). Environmental factors, such as exposure to air pollution, may also prolong duration of LC symptoms (Lammi *et al.*, 2025). Protective factors include vaccination prior to infection, infection during the Omicron period (probably linked to vaccination campaigns), regular physical activity, and adequate sleep (Chow *et al.*, 2024).

02 INTRODUCTION

LC and other PAIS remain under-recognised and poorly managed in most health systems, with limited diagnostic tools and treatment options.

Against this backdrop, this document presents the **situation of LC in Catalonia**, Spain, from **three complementary perspectives**: research, clinical practice, and patient experience, and identifies major bottlenecks and priorities for action.

LONG COVID BURDEN IN CATALONIA

The exact number of people currently living with LC in Catalonia is difficult to determine. By January 2021, before vaccines became available, 406,000 COVID-19 cases had been confirmed. Based on the 23% LC prevalence in the COVICAT cohort, we estimate that **at least 92,000 people** had developed LC during this period, of whom between 48,000 and 72,000 had moderate or severe symptoms. In contrast, only around **14,000 cases** are **currently recorded** in the healthcare system.

By July 2022, the cumulative number of confirmed COVID-19 cases had reached 2.76 million. Taking into account infections among vaccinated people, an estimated 84,000 additional cases of LC would have occurred, bringing the minimum estimate to **176,000 cases by July 2022**. However, this figure does not represent the current number of people affected: some of the initial cases have recovered, while new infections and reinfections have continued to occur, and the estimates do not include undiagnosed infections.

Assuming an estimated incidence of 5–6% following infection with Omicron variants and an observed partial recovery rate of 20–35%, it is reasonable to estimate that more than **250,000 people in Catalonia may currently have symptoms compatible with LC**. The uncertainty in the available data reinforces the need for specific surveillance and follow-up systems to better understand the prevalence, severity and evolution of the condition.

03 LONG COVID CHALLENGES

Research progress on LC remains constrained by several structural challenges, foremost among them the lack of sustained and proportional funding.

Funding challenges

In Spain, research on LC has largely relied on general competitive funding calls or European calls rather than a dedicated national initiative. As a result, many projects are relatively small and often dependent on short-term funding, limiting the development of large national cohorts, long-term follow-up studies, and clinical trials.

This gap is evident in the Acción Estratégica en Salud (AES) calls of the Instituto de Salud Carlos III. Between 2023 and 2025, only around six funded projects specifically addressed LC - a very small fraction of the hundreds of biomedical projects supported during the same period. This level of investment contrasts sharply with the estimated two million people in Spain (Pollan M *et al.*, 2020, Perez B *et al.*, 2021, Torres *et al.*, 2023) who may experience persistent symptoms after SARS-CoV-2 infection, highlighting a clear mismatch between the scale of the problem and research investment. Recently, Veijer *et al.* 2026, have shown a substantial increase in healthcare resource use and associated costs in healthcare and society as a whole.

In contrast, other countries have launched dedicated national programs to address LC. In the US the NIH RECOVER initiative has allocated more than \$1.7 billion to support large-scale cohort studies, biomarker discovery, and clinical trials. Germany plans to invest €500 million between 2026 and 2036 to support coordinated research and care networks. United Kingdom's NIHR has already invested around £50 million and is expanding funding for post-acute infection syndromes (PAIS), including LC and ME/CFS, with a focus on platform trials for treatments and management strategies.

Structural challenges

Beyond funding, the clinical and biological heterogeneity of LC presents a major scientific challenge. The condition likely encompasses multiple overlapping disease mechanisms and phenotypes, underscoring the need for well-characterized cohorts and harmonized datasets to identify reproducible biomarkers and clinically meaningful patient subgroups.

These challenges are compounded by differences in clinical definitions, diagnostic criteria and data collection methods across studies, limiting comparisons between cohorts and the generation of robust, generalisable evidence.

Such limitations are particularly evident in **Spain**, where the absence of coordinated national programs further constrains access to harmonized clinical data and longitudinal biological samples. In this context, the COVICAT cohort constitutes one of the main research efforts to understand LC in Catalonia, providing vital information on epidemiology, risk factors and underlying biological mechanisms.

04 THE RESEARCH PERSPECTIVE

4.1. Research coordination and cohort structure

Research on LC within the **COVICAT cohort** is mainly coordinated by two teams in Catalonia . Epidemiological analyses are led by ISGlobal (Manolis Kogevinas) with immunological contributions from the group led by Carlota Dobaño. Genomic and biobank components are coordinated by the IGTP through the GCAT (Genomes for Life) project (Rafael de Cid), which provides the cohort infrastructure, biological samples, and genetic and molecular data.

COVICAT is a population-based longitudinal cohort in Catalonia built on pre-pandemic cohorts, particularly GCAT, with extensive baseline health, lifestyle, and electronic health record data. Around 10,000 adults were followed through repeated surveys and biological sampling (2020, 2021 and 2023). Among them, 2,764 individuals with confirmed SARS-CoV-2 infection completed all three surveys and form the core population for LC analyses. The cohort integrates socio-demographic, clinical, behavioural, occupational, serological and vaccination data, including linkage to electronic health records, although under-registration of LC symptoms is likely.

4.2. Key findings: burden, trajectories and risk factors

COVICAT provides one of the clearest estimates of LC burden and evolution in the general Catalan population (Kogevinas *et al*, 2025). Among infected participants, approximately **23% developed symptoms** lasting at least three months, indicating that roughly one in four infected adults experienced prolonged health effects. LC often follows a long course: among those affected in 2021, **56% still reported symptoms** two years later. Three main clinical subtypes were identified: a mild respiratory form, a mild neuromuscular form, and a severe multi-organ subtype. The latter was more strongly associated with persistent symptoms, suggesting **distinct clinical trajectories** requiring different management approaches.

Beyond physical symptoms, LC is also associated with a substantial burden of anxiety, depression, sleep disturbances and reduced quality of life, highlighting the need for integrated physical and mental health care.

Risk factors included female sex (particularly under 50), lower socioeconomic status, obesity, pre-existing chronic conditions (especially respiratory and mental health), and severity of the acute infection.

Occupational factors contribute not only to the risk of SARS-CoV-2 infection but also to the development of LC. Among workers with documented SARS-CoV-2 infection 24% developed LC, with higher risks among occupations involving frequent contact with the public or close interaction with colleagues, including healthcare, education, retail and transport workers.

04 THE RESEARCH PERSPECTIVE

Night shift work and sleep disruption were additional risk factors for LC. Furthermore, LC can impair work ability, prolong sickness absence and hinder return to work. (de Matteis *et al.*, 2026; Papantoniou K *et al.* 2026, Delano *et al.*, 2026).

Protective factors included vaccination prior to infection, infection during later variant waves (e.g. Omicron) compared to earlier variants (e.g. Delta), higher levels of physical activity, and adequate sleep (6-8 hrs). Vaccination shortly after infection was also associated with a lower risk of persistent symptoms.

4.3. Emerging biological insights

The COVICAT cohort includes detailed serological and immune biomarker data, enabling investigation of underlying mechanisms. Higher antibody levels following infection (before vaccination) were associated with increased risk of LC, suggesting a role for immune response patterns.

Sex differences were also observed, with women showing a higher prevalence and persistence of symptoms. These differences were not explained by stronger antibody responses pointing to other biological mechanisms that remain under investigation.

Plans for future research

COVICAT represents **one of the few population-based longitudinal resources** in Europe capable of addressing the long-term health consequences of COVID-19 and informing public health responses.

Future work within COVICAT cohort will focus on:

- continued follow-up, including a new timepoint in 2026.
- improved surveys to estimate symptom prevalence across the whole cohort.
- identification of biological markers and immune mechanisms
- analysis of occupational, environmental and social determinants
- effect of vaccination, reinfections, and viral variants
- integration of clinical, epidemiological, clinical and biomarker data to inform prevention and care

05 THE HEALTHCARE PERSPECTIVE: INSIGHTS FROM THE UNITAT MULTIDISCIPLINAR DE COVID PERSISTENT AL HOSPITAL GERMANS TRIAS I PUJOL ON HEALTHCARE PATHWAYS FOR LC

At present, access to specialised care for LC in Catalonia is highly limited. Only **one multidisciplinary unit** is currently available, at Hospital Germans Trias i Pujol in Badalona.

In contrast, services previously established in other public hospitals (e.g. Hospital Clínic, Hospital de Sant Pau) have been discontinued, and successful local models, such as the North Metropolitan approach implemented at CAP Bufalà (Badalona), have not been scaled up. Planned care pathways have also not been fully implemented.

These gaps contribute to **significant territorial inequities**. In some areas, LC remains poorly recognised within primary care, and patients have limited or no options to seek alternative providers, particularly in low-resource municipalities with only one general practitioner.

In addition, **underdiagnosis** remains a major challenge (del Cura 2022), and there is a lack of robust, territorial-level data on the number and characteristics of affected patients. This limits the ability to design effective long-term strategies, both in terms of healthcare planning and socio-labour impact.

The expectations of LC patients do not differ from those with other chronic conditions: they seek consistent clinical follow-up, access to appropriate diagnostic tests, and care delivered within their local healthcare networks.

All together, LC generates additional demand on the healthcare system and an increase in care costs, which could be reduced through a more efficient and better coordinated organisation of services (Veijer *et al.*, 2026)

06 THE LIVED EXPERIENCE PERSPECTIVE: INSIGHTS FROM INTERVIEWS WITH LONG COVID CATALUNYA ASSOCIATION AND OTHER PATIENT ORGANISATIONS

LC affects not only physical health but also social, economic, and psychological well-being (Busquets-Garcia *et al.* 2025). Patients in Catalonia report multiple, interrelated barriers across key areas:

6.1 Barriers in access to care

- Limited recognition of the condition among healthcare professionals, reflecting insufficient training and awareness.
- Geographical inequalities in access to specialised care. The existence of a single specialised unit (Badalona) requires many patients to travel long distances.
- Financial barriers, despite universal healthcare. Out-of-pocket costs (transport, medication, physiotherapy, private mental health care) create inequalities in quality of care and recovery.

6.2. Workplace barriers

- Insufficient workplace adaptations (e.g. flexible hours, remote work, adjusted tasks), often without adequate legal or economic protection.
- Job loss or resignation due to inability to meet work demands
- Difficulties re-entering the labour market, as many available jobs are incompatible with patients' functional limitations
- Lack of structured, individualized return-to-work programmes involving healthcare professionals, employers and occupational health services.

6.3. Social barriers

- Social isolation, driven by poor physical and mental health combined with lack of social recognition of the condition.

6.4. Administrative barriers

- Lack of prioritisation and resources for LC within the health system, limiting adequate follow-up and care
- Underdiagnosis and inconsistent recognition across professionals and care levels
- Challenges in sick leave management, including with reports of medical discharge decisions without adequate consultation and incentives to reduce sick leaves related to mental health and musculoskeletal conditions
- Limited institutional engagement, with patient organisations reporting insufficient dialogue with healthcare authorities to improve care pathways.
- Occupational insurance providers and the management of non-work-related chronic conditions
- Difficulties obtaining recognition of permanent disability, despite marked reductions in functional capacity in some patients.

06 THE LIVED EXPERIENCE PERSPECTIVE: INSIGHTS FROM INTERVIEWS WITH LONG COVID CATALUNYA ASSOCIATION AND OTHER PATIENT ORGANISATIONS

6.5 Psychological and social impact

The psychological impact of LC arises both from the disease itself and from the prolonged uncertainty, functional limitations, loss of employment, financial insecurity and repeated experiences of disbelief within healthcare and social systems. Delayed recognition, only formally defined by WHO in 2021, and ongoing scepticism among some healthcare professionals have left many patients without a clear diagnosis, contributing to distress and uncertainty.

Patients frequently report repeated and often inconclusive medical consultations across primary and specialist care, leading to frustration and a sense of abandonment. These challenges are exacerbated by an overstretched healthcare system, which is difficult to navigate for individuals experiencing fatigue and cognitive impairment.

Affected individuals often report the need to repeatedly justify their symptoms, sometimes without the tools or support to do so. Cultural, socioeconomic, and educational factors also influence how symptoms are perceived, communicated, and managed.

The lack of recognition and validation within healthcare settings has been described as a form of symbolic violence (Camacho *et al.* 2025), whereby patients' experiences are often treated with disbelief. Stigma is further reinforced by the absence of specific biomarkers and the predominance of subjective, often fluctuating symptoms.

6.6. Role of patient organisations in research and advocacy

The **collective of people affected by LC in Catalonia**, established in May 2020, has played a key role in advancing research and recognition of the condition at a time when it remained poorly recognised. Beyond advocacy, patient organisations have contributed to defining research priorities, recruiting participants for studies, disseminating scientific findings, supporting newly affected individuals, engaging with healthcare professionals and policymakers, and promoting recognition of LC within the Catalan Parliament and the health system. Their experience illustrates the value of meaningful patient involvement in research, healthcare planning and public policy.

07 FUTURE PRIORITIES

The three perspectives presented in this report—research, healthcare, and patient experience—converge on a common conclusion: LC represents a complex, chronic condition that remains **insufficiently recognised, inadequately managed, and underfunded**.

Addressing this gap requires coordinated action across research, healthcare systems, and social and labour policies.

Research priorities

Future LC research in Catalonia should prioritise these key areas:

- Large longitudinal cohorts with deep phenotyping and sample biobanking to define clinical phenotypes, their underlying biological endotypes, and their long-term trajectories.
- Multi-omic approaches to identify and validate biomarkers that can support diagnosis, prognosis, and patient stratification.
- Research integrating immune, metabolic, autonomic and neurocognitive dimensions, particularly for the most disabling phenotypes.
- Participation in multicentre intervention trials to move beyond descriptive research towards effective treatments.
- Stronger coordination between research platforms, biobanks, primary care and clinical units to translate discoveries into improved care.
- Use of primary care electronic health records and practice-based research networks as a unique opportunity to generate real-world evidence on LC, including incidence, trajectories, multimorbidity, healthcare utilisation, and long-term outcomes
- Adequate funding to achieve all these objectives.

Health system priorities

- Primary care should constitute the cornerstone of LC management. Strengthen primary care capacity to ensure early recognition, exclude alternative diagnoses, coordinate referrals when needed, and provide ongoing support throughout the often fluctuating course of the condition.
- Recognition of LC within existing clinical frameworks, for example by classifying patients as Complex Chronic Patients, to facilitate coordinated care.
- Systematic implementation of protocols to ensure consistent diagnosis, registration and follow-up across all regions in Catalonia.
- Strengthen primary care capacity by developing clear clinical guidelines and specific referral pathways for LC patients to ensure timely and appropriate care.

07 FUTURE PRIORITIES

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- Promote multidisciplinary case discussions involving primary care professionals.
 - Incorporate patient reported outcome measures (PROM) into routine follow-up.
 - Improve coordination between regional and national authorities to support a coherent and equitable response to LC.
 - Greater financial investment to achieve the aforementioned objectives, including training of healthcare professionals.

Social and patient-centered priorities

While some institutional steps have been taken, such as recognition by the Parliament of Catalonia and the Spanish Ministry of Health, these have not yet translated into comprehensive policy or care responses.

Disability assessment and social protection

- Reduction of waiting times for disability assessments.
- Increased awareness of LC among professionals responsible for disability evaluation.
- Revision of disability criteria to better reflect the functional limitations associated with the condition, particularly among younger patients with caregiving responsibilities.

Workplace adaptation and social protection

- Maintenance of temporary work incapacity while clinically indicated, recognising the fluctuating course of LC.
- Recognition of LC as a potentially disabling condition, in line with approaches such as the “Americans with Disabilities Act” in the United States.
- Adaptation of workplaces through flexible arrangements, including remote work, reduced hours, gradual return-to-work schemes, and job reassignment where necessary.
- Improved coordination between healthcare providers, occupational health services, employers, and disability assessment bodies.

Addressing these priorities will be essential to ensure scientific advances that translate into equitable care, adequate social protection, and improved quality of life for people living with LC.

08 CONCLUSION

- Approximately 23% of people infected with SARS-CoV-2 early in the pandemic developed symptoms lasting at least three months (COVICAT cohort).
- The incidence of LC has decreased considerably with Omicron and vaccination, but a considerable number of patients remain affected.
- Only one multidisciplinary LC unit is currently functioning in Catalonia.
- There is no coordinated national programme for LC; research relies largely on general competitive funding and European calls.
- Insufficient LC recognition and validation within the healthcare and labour systems negatively affect diagnosis, care and patient well-being.

In conclusion, although the incidence of LC has declined since the early pandemic, it remains an **important public health issue** in Catalonia, affecting tens of thousands of people with persistent health, social, and economic consequences.

Strengthening research, expanding multidisciplinary care, and improving recognition of the condition within healthcare and labour systems are essential to provide effective support for affected individuals and to inform future public health policies.

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In collaboration with:

