Literature screening report

Long COVID: Evolving Definitions, Burden of Disease and Socio-Economic Consequences

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Abstract

Long-term health consequences of SARS-CoV-2 increasingly receive the attention of researchers, healthcare providers and policy makers. The understanding of this novel syndrome is emerging and countries worldwide have launched initiatives to respond to the needs of persons living with Long Covid. This review provides a summary of existing evidence on medical/clinical, social, economic, and broader healthcare system aspects of the novel syndrome. The specific research questions on definitions of Long COVID, burden of disease, symptoms, risk factors, social and economic impact of Long COVID and healthcare responses to Long COVID in Europe have been developed together with FOPH in order to serve their needs best. In this living review, we perform umbrella reviews or systematic reviews for each question depending on whether systematic reviews exist or not.

For this first version of the review, we included and analyzed 11 reviews. A universally accepted term and definition for post-acute and long-term SARS-CoV2 sequelae does not exist. We identified 10 terms with Long Covid being the most commonly used. Some defined Long Covid broadly "as not recovering for several weeks or months following the start of symptoms that were suggestive of COVID-19, irrespective of previous COVID-19 testing", i.e. including clinically confirmed and suspected cases.

Other definitions refer to the presence of at least one symptom, a symptom complex or not having recovered at a certain time after infection.

Estimates of prevalence are very heterogeneous due to large methodological variation of primary studies, recruitment methods (e.g. hospital, non-hospital, self-selection), follow-up periods and Long COVID definitions. For initially hospitalized patients prevalence estimates range from 51-89% up to three months after infection and between 47-76% beyond three months. Studies with initially treated outpatient or either out- or inpatient, being population based or not, prevalence estimates range from 13-36% up to three months after infection and between 3-53% beyond three months. These estimates need to be viewed with caution for several reasons. First, the prevalence of certain symptoms is rarely placed in relation to their prevalence in persons without SARS-CoV-2 infection before or during the pandemic. Second, reported estimates currently primarily rely on non-random, convenience samples and not on randomly selected, population-based samples. Third, certain population subgroups, including the elderly or children remain underrepresented. Finally, most estimates are based on samples recruited during the first half of 2020.

More than 50 symptoms have been reported across the studies included in the reviews. The most commonly mentioned symptoms include fatigue, followed by headaches, breathing difficulties, smell and taste disturbances, cognitive impairments, sleep and anxiety disorders. Some persons living with Long Covid exclusively experience fatigue or upper respiratory complaints, while others multiple and multi-system symptoms. Some studies also report about relapsing-remitting disease, with periods of improvements and flare-ups, also described as the "corona coaster". The evidence for pediatric Long COVID patients remains scarce, however, there are indications of multisystem inflammatory syndrome development, as well as a range of symptoms that are also common among adults. Most existing reviews did not classify disease and symptom severity based on indicators such as number of medical visits or inability to work.

The quality of current data does not provide solid grounds for confidently identifying risk factors yet. Some of the reviews suggest that sex (female), older age, comorbidities, severity of acute disease and obesity are associated with Long Covid. Beyond physical activity levels, none of the reviews reported on protective factors.

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In terms of social and economic impact the current but still limited evidence suggests that a substantial proportion of persons living with COVID reports functional restrictions that often require life-style changes, restricted social life, impact on family life and limited ability to care for others. Some studies suggest that Long COVID negatively affected work life and led to related financial difficulties. But estimates for the proportion of persons not being able to (fully) return to work or face financial challenges vary widely and require more context-specific research, also for Switzerland. The broader economic implications of Long COVID are yet unclear.

Finally, a number of countries responded to the medical and social needs persons with Long Covid. The UK appears to be most advanced with multidisciplinary Long Covid clinics, online platform for information and guidance for self-management and care pathways and remote follow-up of persons who are at risk or have Long Covid.

Current literature provides a still patchy picture and the evidence should therefore only be considered as provisional. Further knowledge gaps remain, especially on prevalence, risk factors, protective factors and Long COVID's socio-economic impact. But overall, the current evidence suggests that Long Covid is of substantial public health relevance and that generated knowledge should ideally be holistic, including the broader medical, public health and socio-economic dimensions of Long COVID, enabling and informing crucial healthcare and policy responses.

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Content

Preamble

A large number of scientific publications become available on a daily basis, reflecting the rapid development of knowledge and progress of science on COVID-19 related issues. Leading authorities should base decisions or policies on this knowledge; hence they need to master the actual state of this knowledge. Due to the large number of publications shared daily, decision makers heavily depend on accurate summaries of these publications, in the different public health domains. Therefore, the authors of this report were mandated by the Swiss School of Public Health plus (SSPH+), on request of the Federal Office of Public Health (FOPH), to inform the FOPH on recent findings from the literature.

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Background

Long-term health consequences of SARS-CoV-2 are increasingly being reported worldwide, gradually receiving the attention of researchers, healthcare providers and policy makers. A study from the University Hospital of Geneva found that 32% of 669 in- and outpatients included in a cohort reported at least one symptom after, on average 6 weeks with fatigue, dyspnea, and loss of taste or smell being the most common persistent symptoms[1] . The population-based Zurich Coronavirus Cohort study found that 26% of the first 431 patients enrolled from March to August 2020 have not recovered fully after 6 – 8 months, with around 10% still severely impaired[2] . Long COVID is novel syndrome that is broadly defined by the persistence of physical and/or mental symptoms following a SARS-CoV-2 infection for a longer than usual period of time. The definitions and terminology around that novel syndrome are emerging and incoherent. Equally emerging is our understanding on how to diagnose, treat and manage Long COVID, with evidence rapidly evolving, however, many questions remaining unanswered. Funding bodies around the world launched funding opportunities on the long-term consequences of COVID-19. Congress of the United States (US) approved funding of more than one billion US $ and the United Kingdom Research and Innovation (UKRI) issued a call for research into the longer-term effects of Covid19 in non-hospitalized individuals with funding of 18.5 English £[3] [4] . In the meantime, those affected describe an impairing, debilitating and complex disease, sometimes keeping them out of work and social life[5] . Generated knowledge should ideally be holistic, including the broader public health and socio-economic dimensions of Long COVID, enabling and informing crucial healthcare and policy responses. While many European countries have launched initiatives to establish care and support pathways for Long COVID patients, the need for stronger and more targeted action remains.

Aim

To provide a summary of existing evidence on the public health implications of Long COVID. This is to be achieved through a holistic focus, combining the medical/clinical, social, economic, and broader healthcare system aspects of the novel syndrome. The specific research questions have been developed together with FOPH in order to serve their needs best.

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Questions addressed

- What are the evolving definitions of Long COVID?
- What is the current Long COVID burden of disease?
- What are the reported Long COVID symptoms, as well risk and protective factors?
- What is the current social and economic impact of Long COVID?
- What healthcare and social system responses to Long COVID that in Europe?

Methodology

We conducted a systematic review of reviews (umbrella review) following PRISMA guidelines. We searched the following electronic databases: Medline (EBSCOhost), CINAHL (EBSCOhost), WHO COVID-19 (including Elsevier, MedRxiv) and Embase (excluding Medline). We developed a sensitive search strategy consisting of the following keywords: "COVID-19", "Covid", "SARS-CoV-2", "chronic-COVID", "long-COVID". "long COVID", "long-term COVID", "post-COVID", "long-term symptom". "long-term clinical features", "long-term sequela", "long-term complication", "long-term impact", "long-term implication", "long-term consequence", "long-term effect", "post-acute", "long-tail", "recurrent", "lingering", "persist", "post-discharge", "prolonged symptom", "post-chronic", "long-haul". Keywords were combined and refined using Boolean operators and truncations, adjusted to each of the databases. We additionally searched google scholar, screening the first five result pages. Finally, we manually screened the reference lists of all included reviews. All references were screened in duplicate, at title and abstract, as well as full-text level. The fifth research question (healthcare and social system responses) was addressed through the manual screening of key governmental and other relevant webpages.

Eligibility criteria

- report a systematic methodology (systematic review, meta-analyses, scoping reviews)
- thematically focus (entirely or partially) on Long COVID (in abstract and main body)

Risk of bias (quality) assessment

- Risk of bias of included reviews and primary studies was assessed at this stage of the review yet. A quality assessment will be conducted in the future and for the final scientific publication.
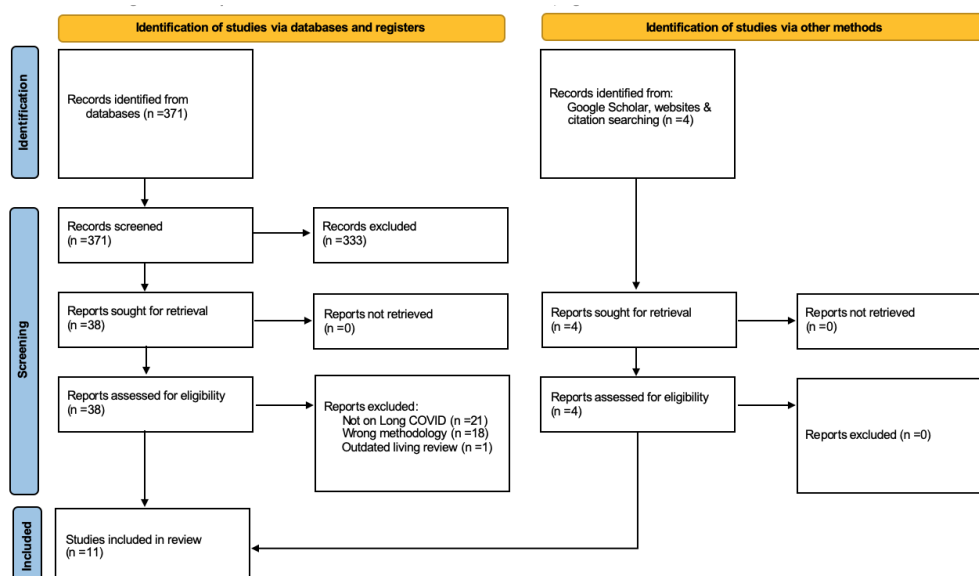
Data extraction, analysis and synthesis

Data was extracted with a pre-defined data extraction sheet including methodological characteristics (type of review, number of included studies, socio-demographic focus, geographic distribution of primary studies) and four different sections, each corresponding to one of the research sections. Information was synthesized narratively and guided by the five research questions.

Results and Findings

Our database searches yielded 374 references. 335 of those were excluded at title and abstract screening and 39 manuscripts were screened full-text. That led to the exclusion of 32 further studies, either for not addressing Long COVID (n=19), not being systematic reviews (n=11), or being older versions of already included living systematic reviews (n=2). Database searches led to the final inclusion of 7 reviews. Google Scholar and reference list searches yielded additional 4 studies. Thus, we included and analyzed a total of 11 reviews. Figure 1 provides the PRISMA flowchart of our searches.

Figure 1: PRISMA Flowchart

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One the included studies was published in 2020, 7 in 2021 and 3 are currently published as preprints. Most studies were traditional systematic reviews (n=3), followed by rapid reviews (n=2), rapid living systematic reviews (n=2), pragmatic reviews (n=2) and a systematic review with a meta-analysis (n=1). Only one addressed pediatric patient, one middle aged and young adults and the remaining (n=9) did not report a specific socio-demographic focus. Those that specifically addressed the geographic distribution of their primary studies, emphasized that most of them are from Europe and the USA, with almost none conducted in low-income settings.

What are the evolving definitions of Long COVID?

Terminology

A universally accepted definition for post-acute and long-term SARS-CoV2 sequalae does not exist. While this review has adopted the term Long COVID, being the currently most widespread and broad description of long-term SARS-CoV-2-related complications [6] and the term most accepted by persons living with Long Covid, the literature provides a very diverse set of terminology, descriptions and definitions. Some of the commonly used terms include "Long Haulers," "Post-acute COVID-19", "Persistent COVID-19 Symptoms", "Post COVID-19 manifestations", "Post COVID-19 syndrome", "chronic COVID-19 syndrome", "post-infectious COVID-19", "post-acute sequelae of SARS-CoV-2 infection" (PASC) and "post COVID-19 recovery syndrome" [6] -[12] . Inevitably, the reason for the abundant terminology but yet missing commonly agreed upon and precise definition is the emerging nature of Long COVID itself, as well as of evidence around it, which still lacks consensus on the range, prevalence, and duration of symptoms[13] .

Definitions

Michelen et al. [13] attempted to broadly and pragmatically define long COVID as not recovering for several weeks or months following the start of symptoms that were suggestive of COVID-19, irrespective of previous COVID-19 testing [13]. That definition includes clinically confirmed and suspected cases and considers that many patients do not have the access to adequate testing[12] [13] . Beyond symptoms, others also include abnormal, but potentially asymptomatic clinical parameters persisting as part of Long COVID[7] . Several reviews referred to the recently published National Institute for Health and Care Excellence (NICE) guidelines, which classify Long COVID in two categories: (1) "ongoing symptomatic COVID-19" for symptoms lasting from 4 to 12 weeks and (2) "Post-COVID-19 syndrome" for persisting symptoms beyond 12 weeks after disease onset; both

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categories only hold if symptoms cannot be explained by alternative diagnoses[6] [11] [13] . Others disagree with that "by exclusion" approach, as it might fail to capture the very broad spectrum of post-acute complications[12] , including SARS-CoV-2-triggered new health conditions and worsening of pre-existing health conditions[6] . The dynamic review of the National Institute for Health Research (NIHR) expanded that notion by emphasizing that Long COVID might not be a single condition, but multiple syndromes, such as the post intensive care syndrome, post viral fatigue syndrome and long-term COVID syndrome[6] . More specific approaches proposed specific Long COVID subtypes, depending on whether disease manifestation is due to (1) left-over symptoms from acute infection, (2) infection-triggered organ dysfunctions or (3) infection-triggered new syndromes [6] [14] . Terminology also varies between studies conducted in Switzerland, with the population-based Zurich Coronavirus Cohort study using the term "Post-COVID-19 Syndrome" [2] and the Geneva-based cohort study "Long COVID"[1] .

In the absence of a commonly agreed definition, many of the included reviews simply referred to "long-term effects of COVID-19" or "late onset complications of COVID-19", setting the cut off for symptom duration or absence of full recovery at a minimum of 3 weeks after onset of symptoms, diagnosis, hospital admission or discharge [7] [13] [15] .

What is the current Long COVID burden of disease?

Long COVID's novel and emerging nature does not allow for confident prevalence estimates yet. Those systematic reviews that reported prevalence, did so with caution and emphasized their large heterogeneity and non-comparability of individual estimates. This is due to large methodological variation of primary studies, including their sample recruitment methods (e.g. hospital, non-hospital, self-selection), as well as follow-up periods and Long COVID definitions (e.g. symptomatic only)[6] . Therefore, whenever possible, all prevalence estimates provided below are provided with additional information on the sample sizes, follow-up periods and whether the sample includes hospitalized patients or non-hospitalized patients. Follow-up periods are provided in mean or median (as reported by reviews) number of weeks. Reviews reporting number of days were roughly transformed by in weeks to improve the section's readability. Table 1 provides the currently lowest and highest prevalence estimates, as reported in the 11 included reviews and divided by sample source

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(previously hospitalized; non-hospitalized/mixed groups) and follow-up duration (below 12 weeks; 12 weeks and beyond)

Table 1: Lowest and highest prevalence estimates, by sample source and follow-up duration

Sample and follow-up duration	Prevalence estimates [1]	Sample sizes
hospitalized, symptoms <12 weeks		
lowest reported prevalence	50.9%[16]	(n=277)
highest reported prevalence	89% [17]	(n=119)
hospitalized, symptoms ≥12 weeks		
lowest reported prevalence	47% [18]	(n=2649)
highest reported prevalence	76% [19]	(n=1733)
non-hospitalized or mixed [2], symptoms <12 weeks		
lowest reported prevalence	13% [20]	(n=4182)
highest reported prevalence	36% [21]	(n=357)
non-hospitalized or mixed [2], symptoms ≥12 weeks		
lowest reported prevalence	2.3% [20]	(n=4182)
highest reported prevalence	53%[22]	(n=180)

[1] only those reported in at least one the included reviews.

[2] mixed non-hospitalized and hospitalized may or may not be a population-based

Only one review provided pooled prevalence estimates of 7 primary studies reporting at least one symptom at or beyond three weeks after disease onset, reporting an estimate of 80% (95% CI 65-92) [R4]. While such pooled estimates are grounded in quite heterogeneous primary studies and have to be viewed with caution, all other reviews narratively reported prevalence estimates of selected primary studies (n=7) or did not report any prevalence at all (n=3). A pragmatic review by Zapatero

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and colleagues from the Belgian Healthcare Knowledge Centre reported Long COVID prevalence estimates from 5.2% (n=496, >6-week follow-up) to 50.9% (n=277, 11-week follow-up). Studies that included hospitalized or emergency ward admitted patients, with overall higher severity of acute infection tended to report estimates at the higher end, while those that also included non-hospitalized patients reported a maximum prevalence of about 36% (n=357, <12-week follow-up) [11] .

Akbarialiabad et al. reported a similarly heterogenous picture with prevalence estimates ranging from 13% to 76%. Again, studies that exclusively focused on previously hospitalized patients reported overall higher estimates ranging from 49,6% (n=538, median 14-week follow-up) to 76% (n=1733, median 26-week follow-up) [12] . Studies that included non-hospitalized patients reported estimates from 13% (n=4182, 4 to 8-week follow-up) to 53% (n=180, mean 18-week follow-up) [12] . The comprehensive NIHR review suggests that at least 10% of all infected experience one persisting symptoms at and beyond 12 weeks, with estimates ranging from as low as 2.3% to as high as 89% [6] . For those previously hospitalized, prevalence estimates range from 47% (n=2649, median 31-week follow-up) to 89% (n=119, 4 to 6-week follow-up). For those who were never hospitalized, prevalence estimates range from 2.3% (n=4182, >= 12-week follow-up), to 15% (n=21359, >= 12-week follow-up) and 36% (n=357, <12-week follow-up). NHIR also emphasized the growing evidence of Long COVID in children with one study reporting a 54% prevalence of at least one symptom at about 4 months after diagnosis (n=129, mean 23-week follow-up)[6] [16] . Recent surveys conducted by the UK Office for National Statistics estimated that about 13% of children in the age group 2 to 11 and 14.5% in the age group 12 to 16 living in the UK had at least one persisting symptom 5 weeks after diagnosis[6] .

These estimates need to be viewed with caution for several reasons. First, the prevalence of certain symptoms is rarely placed in relation to their prevalence in persons without SARS-CoV-2 infection before or during the pandemic, which potentially leads to overestimations. Second, reported estimates currently primarily rely on non-random, often self-selected samples. A very small fraction of existing studies reports prevalence estimates based on randomly selected, population-based

samples. Third, certain population subgroups, including the elderly, care home residents, people with learning disabilities, as well as children remain underrepresented [6] . Finally, most the provided estimates are based on samples recruited during the early phase of the pandemic, where testing was not as widespread and captured cases were likely more severe.

Prevalence estimates in Switzerland

Two Swiss cohort studies, one conducted in Zurich and one in Geneva reported that 26% (n=385, 24 to 32-week follow-up) and 32% (n=669, 4 to 6-week follow-up) of patients experience no full recovery yet or at least one persistent symptom [1] [2] , respectively. Both studies included hospitalized and as well as non-hospitalized patients. While the Zurich ZSAC cohort sampled from all cases reported to the health directorate of Zurich between March and early August the Geneva cohort was recruited from the services of the Geneva University Hospital. The population-based Zurich cohort additionally reported that about 10% of initially hospitalized patients were re-hospitalized [2] . This cohort recruited another randomly selected 1100 persons with SARS-CoV-2 since August and will provide more prevalence estimates from different follow up times after infection in due course.

What are the reported Long COVID symptoms, as well risk and protective factors?

Symptoms:

Symptoms are the primary focus of most identified reviews. The most commonly mentioned symptoms include fatigue, which also seems to be the most prevalent one (also amongst those with mild initial disease) [8] , followed by headaches, breathing difficulties, smell and taste disturbances, cognitive impairments, sleep and anxiety disorders. These were also the most commonly reported symptoms among patients in Switzerland [1] [2] .

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A group of patients exclusively experiences fatigue or upper respiratory complaints, while others

multiple and multi-system symptoms [6] . While many continuously experience one or multiple

symptoms, reviews report that some persons living with Long COVID experience relapsing-remitting

disease, with periods of improvements and flare-ups, also described as the "corona coaster" [6] [11]

. Symptoms are often reported as debilitating, having a strong negative impact on mental health and

quality of life [12] . The evidence for pediatric Long COVID patients remains limited, however, there

are indications of multisystem inflammatory syndrome development, as well as a range of symptoms

that are also common among adults, including fatigue, breathing difficulties, heart palpitations,

headaches, attention difficulties and cognitive deficits, muscle weakness and pain, dizziness, sore

throat, abdominal pain, depression and skin rashes [15] . Most existing reviews did not classify

disease and symptom severity based on indicators such as number of medical visits or inability to

work. These are important indicators, which, if combined with lived experience of symptoms, their

duration, as well as their interference with social life can provide a holistic picture of disease burden.

Table 2 provides a list of all reported potential Long COVID symptoms and the reviews they were

reported in.

Table 2: Reported Long COVID Symptoms

GENERAL	References
Fatigue	[6]–[9], [11]–[13], [15], [24], [25]
Headache	6], [7], [9], [11], [12], [15], [24]
Fever	[6] [9] [11] [12] [15]
RESPIRATORY	
Dyspnea / Breathlessness	6]–[9], [11]–[13], [15], [24], [25]
Chest pain	[9] [11] [15]
Cough	6], [9], [11], [12], [15], [24]
Pulmonary fibrosis	[8] [9] [25]
Lung hypoperfusion	[25]
Impaired lung function	[9] [11] [25]
Thromboembolism	[11] [13]
Sore throat	[6] [13] [15] [17]
Nasal congestion	[13]

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Sputum	[7] [12]
CARDIOVASCULAR	
Palpitations, arrhythmias	[7], [9], [15], [24]
Peri-, myoperi- and myocarditis	[13], [25]
Tachycardia	[8]
Cardiac stroke	[10]
Venous/arterial thrombosis	[10]
Myocardial inflammation	[12] [13]
Limb edema	[7] [12]
NEUROLOGICAL & MUSCOLOSCELETAL	
Hyperesthesia	[15]
Loss or altered smell	[6], [8], [9], [11]–[13], [15], [24], [25]
Loss or altered taste	[8], [9], [11]–[13], [15], [24] [25]
Numbness	[15]
Muscle weakness	[8], [12], [15], [24], [25]
Cognitive fatigue	[8]
Apathy	[8]
Stroke	[8] [10]
Neuropathy	[8] [11]
Myopathy	[8]
Myalgia	[9], [11]–[13], [15], [24]
Joint pain (arthralgia)	[8] [9] [11] [12] [15]
Intracerebral hematoma	[8]
Cerebral venous thrombosis	[8]
Bladder incontinence	[9] [13]
Swallowing difficulties	[9]
Encephalopathy	[10]
Dizziness / vertigo	[12], [13], [15], [24]
Tinnitus	[11]
Earache	[11]
Visual disorders / eye redness	[7] [11]
Excessive sweating	[12]
Chills	[12]
GASTROINESTINAL	
General gastrointestinal complaints	[6] [7] [9] [15]
Diarrhea	9], [11], [12], [15], [24]
Vomiting	15], [24]
Loss of appetite	[11] [15]
Nausea	[8] [11] [13]
Abdominal pain	[9] [15]

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Bowel incontinence	[9]
Acid reflux	[11]
MENTAL / COGNITIVE	
Brain fog and memory loss	[6], [9]–[13], [15], [24]
Depression	[11] [13] [15] [25]
Sleep disorders	[6], [9], [12], [13], [15], [24]
Attention disorders	[7], [9]–[11], [13], [15], [24]
Anxiety	[6] [8] [10] [13]
Posttraumatic symptoms	[6] [11] [13]
Executive functioning difficulties	[8] [11]
CUTANEOUS	
Skin rashes	[12], [13], [15], [24]
Alopecia	[7], [13], [24]
OTHER	
Multisystem inflammatory syndrome (MIS) (primarily in children)	[12] [15]
Abnormal chest X-Ray /CT	[7] [9] [11] [13] [25]
Abnormal brain MRI	[25]
Liver damage	[10]
Kidney damage	[10]
Elevated D-dimer	[7]
Elevated NT- proBNP	[7]
Elevated C-reactive protein	[7]
Elevated serum ferritin	[7]
Elevated procalcitonin	[7]
Elevated IL-6	[7]
Altered immune cell counts	[25]
Hypoproteinemia	[10]

Risk and protective factors

The novel and emerging nature of Long COVID, as well as the quality of current data does not provide

solid grounds for confidently identifying risk factors yet[7] [13] . Some of the reviews suggest that the

following factors might increase the risk for Long COVID development: (a) sex (female), (b), older age

(c) comorbidities (mental and physical), (d) severity of acute disease (e.g. hospitalization, higher

imaging scores, duration of oxygen supplementation, pneumonia), and (e) obesity[6] [8] [11] [13] [15] .

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For some of these factors, evidence seems to be mixed or symptom-depended. For example, smell and taste disturbances do not seem to be associated with most of these risk factors, and if so, are more common in younger age groups [12] [13] . Similarly, the NIHR review emphasizes that Long COVID seems to be more common in young adults (and children) than expected[6] . Two reviews reported that experiencing more than five symptoms during acute disease, including fatigue, headache, dyspnea, chest pain, sensitive skin, hoarse voice and myalgia had a higher risk progressing to Long COVID development, which might be stronger when taking age and sex into account [11] [12] . Mental symptoms, especially posttraumatic ones seem to be affecting younger people, women, and those with responsibilities for others[12] . Beyond physical activity levels[8] , none of the reviews reported on protective factors.

What is the current social and economic impact of Long COVID?

Understanding its full impact of Long COVID requires the careful consideration of its socio-economic implications. We focused on (a) family and social functioning, (b) work-related implications, (c) and broader economic consequences. Many Long COVID patients report functional restrictions that often require life-style changes, changes in physical activity levels and restricted social life [25] . They also report that Long COVID affects their family life and often limits their ability to care for others [6] . Neurological, cognitive and mental symptoms, such as anxiety or memory loss strongly impact daily living and quality of life, while routine activities, such as driving and cooking can become very difficult or even impossible [8] [11] [12] . For some patients, even those that were completely independent before, these limitations are often severe enough that require daily assistance [6] [11] . An important proportion of these previously independent patients experience Long COVID impairments that deem them full care dependent[6] . Inevitably, Long COVID is also expected to have a considerable impact

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on the workforce[6] . The NIHR review reports UK-based survey results with about 80% of all young patients (25 to 55 years) reporting that Long COVID has negative affected their work life, with about half of them additionally reporting related financial difficulties [6] . Other surveys report that about 45% of Long COVID patients were forced to reduce their workload at three months and beyond, while about 20% of them were not able to work half a year later [6] [11] . Studies that followed-up previously hospitalized patients report that 15-30% of those facing long-term symptoms remained out of work 6 to 10 weeks after hospital discharge[6] [25] . While there is no evidence on the broader economic implications of Long COVID yet, there is enough evidence that if affects a significant proportion of the formerly healthy working population, which will likely lead to long-term economic as well as healthcare system strains [6] [25] .

What healthcare and social system responses to Long COVID that in Europe?

Results:

Table 3 provides a list of current European health and social care responses.

Country	Responses [5]
United Kingdom	• NHS established care pathways for patients with symptoms 6 weeks after disease onset • NICE published Long COVID guidelines • Establishment of 40 NHS post-COVID clinics

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	• Launch of NHS "Your COVID Recovery" digital initiative, providing self-care and self-management support • Hospitalized COVID-19 patients followed-up at week 6 remotely
Germany	• Large hospitals offering Long COVID consultations and post-COVID outpatient services (focus on interdisciplinary care)
Italy	• Launch of post-COVID wards in some hospitals • Launch on multidisciplinary Post-COVID-19 Day-Hospital in Rome • Provision of post-COVID rehabilitation services by AbilityAmo (non-profit), including telemonitoring, home care, interdisciplinary and psychological support
Czech Republic	• Launch of post-COVID Care Centre for patients with symptoms 3 months after infection

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	• Increase collaboration of GPs with pulmonary specialists for long-term care of patients
Spain	• Guidelines for treating Long COVID patients, by Spanish Society of GPs • Rehabilitation guidance services provided by hospitals and primary care facilities, targeting Long COVID patients
Belgium	• Hospitals providing multidisciplinary services for post-ICU patients, at home or in specialized centers • Development of post-discharge care pathways

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Discussion / Conclusions

Long COVID is a rapidly emerging public health problem. Equally emerging is the need to fully understand its etiology, burden and broader implications. The multifaceted nature of its symptoms and the uncertainty around their progression and duration have far reaching consequences, primarily on individual lives, but ultimately on our socio-economic infrastructures. This living systematic review aimed to assess the current status of scientific evidence around Long COVID, focusing on its definitions, burden, determining factors and socio-economic implications. In order to establish a first knowledge landscape, the first version of this review is limited to systematic reviews.

Current literature provides a still patchy picture. In the absence of a universally agreed definition, terminology, definitions and classifications vary. A similarly large variation is seen in reported prevalence estimates, attributable to large measurement heterogeneity and bias. Very few prevalence estimates were retrieved from population-based, representative samples. Provided estimates should therefore only be considered as provisional. Further knowledge gaps remain, especially on risk factors, protective factors and Long COVID's socio-economic impact. It is key to accumulate more evidence on disease determinants since the number of people living with Long COVID will likely grow[12] . To accumulate targeted evidence that will capture the needs of those affected, we are planning a citizen science project, co-created with those living with and affected by Long COVID. The project aims to identify key needs and corresponding research priorities.

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Next Update

The next review update will:

- Synthesize new reviews (if any)
- Synthesize primary studies included in systematic reviews, screened for socio-economic impact
- Synthesize additional primary studies identified through update searches

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