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Long COVID science, research and policy

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Long COVID represents the constellation of post-acute and long-term health effects caused by SARS-CoV-2 infection; it is a complex, multisystem disorder that can affect nearly every organ system and can be severely disabling. The cumulative global incidence of long COVID is around 400 million individuals, which is estimated to have an annual economic impact of approximately $1 trillion—equivalent to about 1% of the global economy. Several mechanistic pathways are implicated in long COVID, including viral persistence, immune dysregulation, mitochondrial dysfunction, complement dysregulation, endothelial inflammation and microbiome dysbiosis. Long COVID can have devastating impacts on individual lives and, due to its complexity and prevalence, it also has major ramifications for health systems and economies, even threatening progress toward achieving the Sustainable Development Goals. Addressing the challenge of long COVID requires an ambitious and coordinated—but so far absent—global research and policy response strategy. In this interdisciplinary review, we provide a synthesis of the state of scientific evidence on long COVID, assess the impacts of long COVID on human health, health systems, the economy and global health metrics, and provide a forward-looking research and policy roadmap.

Long COVID is best defined as the constellation of post-acute and long-term health effects caused by SARS-CoV-2 infection[1–3]. Long COVID was initially reported by patients who coined the term and, through research and advocacy, drove much of the progress in understanding this condition over the past several years (Fig. 1).

Long COVID is a complex, multisystem disorder that affects nearly every organ system, including the cardiovascular system[4], the nervous system[5–8], the endocrine system[9–11], the immune system[12,13], the reproductive system[14] and the gastrointestinal system[15]. It affects people across the age spectrum (from children[16–18] to older adults[19,20]), people of different race and ethnicities, sex and gender, and baseline health status[21]. Cardinal manifestations include brain fog (or cognitive dysfunction)[7], fatigue, dysautonomia (which commonly manifests as postural orthostatic tachycardia syndrome (POTS))[22] and post-exertional malaise[23]. Many of the health effects seen in long COVID are shared across several infection-associated chronic conditions, also called post-acute infection syndromes[23–26].

The epidemiology of long COVID is influenced by various factors. The Omicron variant of SARS-CoV-2 is associated with less risk of long COVID than the Delta and pre-Delta variants[27]. Vaccines (before infection) and antivirals (during the acute phase of infection) may reduce the risk of long COVID. Reinfection, on the other hand, is a risk factor for long COVID[28,29]; even if individuals did not experience long COVID after a first SARS-CoV-2 infection, they remain at risk of developing it with subsequent infections[28–30]. Reinfection can trigger de novo long COVID or exacerbate the severity of existing long COVID[28,29]. Cumulatively, two infections yield a higher risk of long COVID than one infection and three infections yield a higher risk than two infections[28,29].

A unifying thread of evidence across most studies evaluating the risk of long COVID is the finding that the risk increases as the severity of acute infection increases[3]. People who had severe COVID-19 that necessitated hospitalization exhibit a higher risk of long COVID than those with mild COVID-19. However, because most people around the

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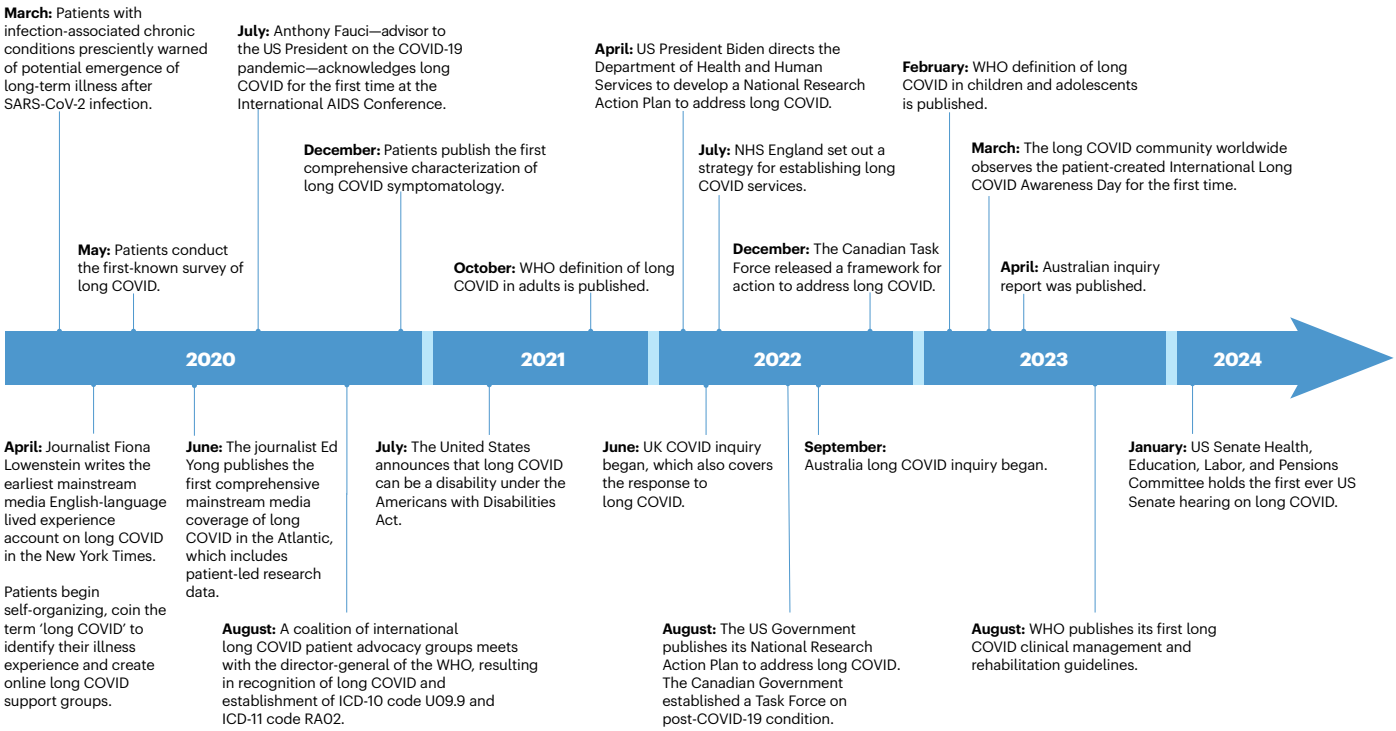

Fig. 1 | A brief timeline of key events and milestones in the history of long COVID. The history of long COVID has been defined largely by the patients themselves. In March 2020, as the COVID-19 pandemic began to unfold across the globe, patients with infection-associated chronic conditions presciently warned of the potential emergence of long-term illness after SARS-CoV-2 infection[293]. The first mainstream written personal account of non-recovery from acute COVID-19 was an op-ed by the American journalist Fiona Lowenstein in the *New York Times* in April 2020 (ref. 294). Around the same time, patients began self-organizing, coined the term long COVID[295] and conducted the first known survey—which was subsequently formally published—documenting the breadth of symptomatology experienced by people with long COVID[42]. Considerable activity then ensued, including mainstream media coverage (first by Ed Yong in *The Atlantic*)[296], recognition by national governments (of the United States[281], Canada[297], United Kingdom[298], European Union[299], Australia[300] and others) and the WHO. Patients continue to lead the way in advocacy and research, which led the US Senate to hold its first-ever hearing on long COVID[275,301]. This timeline was curated to provide a brief overview of the history of long COVID, with a focus on the role played by patients and advocates, and does not comprehensively include all events and milestones. ICD, International Classification of Diseases.

globe had mild COVID-19, they constitute more than 90% of people with long COVID, despite their lower relative risk compared with that of people with severe COVID-19 (ref. 31).

Studies evaluating recovery from long COVID are sparse and inconsistent[32]; this is largely due to use of various definitions, incomplete accounting for all the manifestations of long COVID and misclassification of remission as 'recovery'[33]. However, studies carefully evaluating individual manifestations show that recovery rates are generally low at 1 year[34], and several studies show only 7–10% fully recovered at 2 years[30,33,35,36]. Furthermore, some manifestations of long COVID, including heart disease, diabetes, myalgic encephalomyelitis and dysautonomia are chronic conditions that last a lifetime[31,37–39]. Adding to this are the concerns about the possible emergence of new latent sequelae—that have not yet been characterized—years after the acute infection[37,40,41].

The impact of long COVID is not limited to the health and well-being of individual patients and their communities. Owing to its prevalence and the breadth of its clinical manifestations[42–46], it represents a major public health crisis[47]; it strains health systems and national economies, and threatens progress on global health, including the Sustainable Development Goals (SDGs).

In this interdisciplinary review, we provide a brief synthesis of the current state of scientific evidence on long COVID, including knowns, unknowns and the key controversies. We provide an assessment of the impacts of long COVID on human health, health systems, the economy and global health metrics and, finally, we provide a forward-looking research and policy roadmap that we hope will stimulate global discussion on how to address the challenge of long COVID.

State of the science on long COVID

The global burden

Estimating the global burden of long COVID presents substantial challenges due to the variability in study designs and populations, follow-up times, choice of control groups (for example, whether studies evaluated people with negative SARS-CoV-2 tests or no known SARS-CoV-2 infection as controls), assessment of baseline health before the infection (to ascertain emergence of a true new health condition) and definitions of what constitutes 'long COVID'[48,49]. Variation in risk estimates also reflects the dynamic nature of the pandemic itself, which gave rise to many variants and subvariants, each yielding potentially different rates of long COVID; the effect of COVID-19 vaccines and use of antivirals in the acute phase, which may reduce the risk of long COVID; and the effect of SARS-CoV-2 reinfections, which contribute additional risk[28,29].

Few countries established surveillance systems to estimate the burden of long COVID at the population level. Data from the US Centers for Disease Control and Prevention (CDC)'s National Health Interview Survey show that in 2022, 6.9% of US adults[50] and 1.3% of children[51] ever had long COVID. Data from the Medical Expenditure Panel Survey—a nationally representative survey of US adults—found that 6.9% of adults had ever had long COVID as of early 2023 (ref. 52). Estimates from the CDC's Household Pulse Survey show that prevalence of current long COVID in US adults was around 6.7% in March 2024 (ref. 53). In the United Kingdom, point prevalence estimates from the Office of National Statistics show that 2.9% of the UK population (including children) were experiencing self-reported long COVID in March 2023 (ref. 54). Overall, estimates of the burden of long COVID in the general

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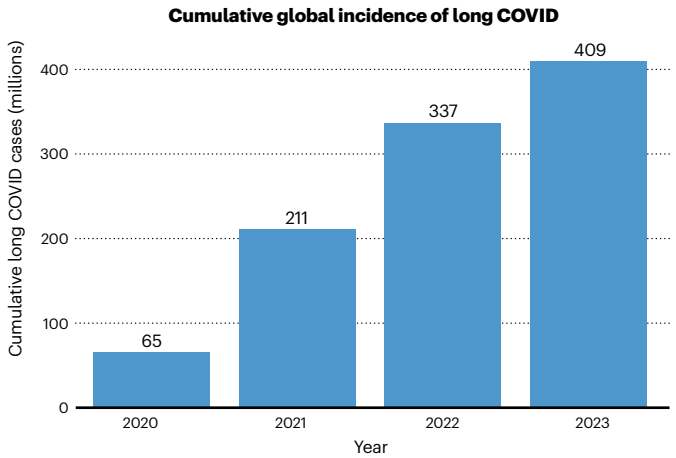

Fig. 2 | Estimated global cumulative incidence of long COVID. We estimated the global incidence of long COVID on the basis of meta-regression estimates that pool together all the available evidence. Considering the Institute for Health Metrics and Evaluation's annual estimates of SARS-CoV-2 infections[31,55–59] and assuming the lower risk estimate of 6.2% for long COVID at 3 months after infection[31], a proportion symptomatic cases among infections of 65% (ref. 31), and a reduction in the risk of long COVID for 2022 and 2023 (to account for the combination of the putative lower severity of the Omicron variant and the mildly protective effect of vaccination)[60], the estimated cumulative global incidence of long COVID was 65 million, 211 million, 337 million and 409 million in 2020, 2021, 2022 and 2023, respectively.

population converge around a point prevalence of 6% to 7% in adults and ~1% in children[50–54].

Also important are estimates of the incidence of long COVID, which can be informed by high-quality meta-analyses of large-scale cohort studies among people infected with SARS-CoV-2. For instance, one analysis pooled results from 54 studies in 22 countries and estimated that approximately 6.2% of symptomatic COVID-19 survivors experience at least one of three common symptom clusters at 3 months after acute infection, across all ages and accounting for different severity levels of the initial infection and pre-COVID health status[31]. This analysis only considers three major symptom clusters in long COVID (fatigue with bodily pain/mood swings, and cognitive and respiratory symptom clusters); however, it sets a conservative benchmark to estimate the global risk of long COVID[31].

We estimated the global incidence of long COVID on the basis of meta-regression studies that pool together all the available evidence[31] (Fig. 2). Incorporating a number of assumptions, including the Institute for Health Metrics and Evaluation's annual estimates of SARS-CoV-2 infections[31,55–59], a proportion symptomatic cases among infections of 65% (ref. 31), and a reduction in the risk of long COVID for 2022 and 2023 to account for the putative lower severity of the Omicron variant and the effect of vaccination[60], we estimated a cumulative global incidence of long COVID by the end of 2023 of approximately 400 million. It is crucial to emphasize that these estimates only represent cases arising from symptomatic infections and are likely to be conservative. The actual incidence of long COVID, including cases from asymptomatic infections[61] or those with a broader range of symptoms, is expected to be higher. Furthermore, the estimates do not account for the added burden of long COVID due to reinfection[29] and the possibility of latent risks (that is, risks that are not yet manifest and may emerge years or decades after infection)[3,37,41]. The emergence of new variants, changes in public health measures and changes in the effectiveness and uptake of vaccination may also substantially influence these estimates in the future.

While it is challenging to provide estimates of new cases with high precision, the current evidence makes it compellingly clear that long COVID represents a substantial and ongoing challenge to global health.

Mechanisms of long COVID

The pathophysiological mechanisms of long COVID are still being elucidated[2,62], and it is unlikely that a single mechanism can explain the broad and heterogeneous set of symptoms and diseases spanning various organ systems. Long COVID likely represents a disease with many subtypes; each may have their own risk factors, biological mechanisms and disease trajectory, and may respond differently to treatments[3]. Multiple pathological pathways may be engaged depending on various factors, including prior environmental exposures, genetic makeup, age, sex, prior health, microbiome health, viral characteristics (SARS-CoV-2 variant, viral load), the immune response (which may be influenced by prior infections, vaccines and use of immunosuppressive agents) and medical treatments (antivirals, steroids). All of these drivers likely shape the human host response during the acute phase of SARS-CoV-2 infection and may trigger pathophysiological mechanisms that ultimately produce phenotypes of long COVID.

Several mechanistic pathways have been proposed for long COVID, including viral persistence, immune dysregulation, mitochondrial dysfunction, complement dysregulation, prothrombotic inflammation and microbiome dysbiosis[3,7,12,63–69] (Fig. 3). Viral persistence (either replicating virus or viral RNA or protein fragments)—which may be common[70]—in immune-privileged sites may trigger chronic low-grade inflammation and tissue injury[63,71–73], and may correlate with long COVID symptomatology[72].

Studies have demonstrated persistence of the virus in extrapulmonary sites, including the brain and coronary arteries, of individuals with severe COVID-19 (refs. 68,74). Studies in human and mouse brain organoids showed that SARS-CoV-2 infection induces fusion between neurons and between neurons and glial cells, which may progressively lead to formation of multicellular syncytia compromising neuronal activity[75]. Neuroimaging studies performed in humans 10 months after they 'recovered' from mild-to-moderate SARS-CoV-2 infection showed significant alterations (commensurate with 7 'years of healthy aging') of cerebral white matter, including widespread increases of extracellular free water and mean diffusivity (indicative of inflammation) encompassing all brain lobes[76]. Pre- and post-SARS-CoV-2 infection imaging studies showed structural abnormalities and accelerated aging in the brains of people with mild-to-moderate SARS-CoV-2 infection[74,77,78]. Even in the absence of direct infection in the brain, a transient respiratory infection with SARS-CoV-2 induces prolonged neuroinflammatory responses, activation of microglial cells and impaired neurogenesis[64,77]. In addition to neuroinflammation, people with brain fog due to long COVID were shown to have disrupted blood–brain barriers[79].

Abnormalities in the immune system have been documented in people with long COVID, including increased humoral responses directed against SARS-CoV-2; higher antibody responses against Epstein–Barr virus (EBV)[66], varicella zoster virus (VZV)[66] and cytomegalovirus[67] (suggesting possible reactivation of herpesviruses[80]); exhausted T cell responses[12,66]; and uncoordinated cross-talk between the cellular and humoral adaptive immunity[12,13]. Autoimmune responses triggered by SARS-CoV-2 infection may underlie long COVID symptoms[81,82]. Passive transfer of IgG antibodies from patients with long COVID to healthy mice recapitulated heightened pain sensation and locomotion deficits[82,83].

In the heart, SARS-CoV-2 infects coronary vessels, preferentially targeting coronary artery plaque macrophages and inducing plaque inflammation[68]. Vascular disease in long COVID is likely triggered by complement activation, red blood cell lysis, platelet activation and thromboinflammation—leading to altered coagulation and tissue injury[67,84]. Dysfunctional hypothalamic–pituitary–adrenal response with inappropriately low levels of cortisol may mediate some of the symptomatology observed in long COVID (including fatigue, sleep abnormalities and metabolic derangements)[66], and has been seen in those with persistent respiratory symptoms of long COVID[80]. SARS-CoV-2 infection may lead to reduced intestinal absorption of

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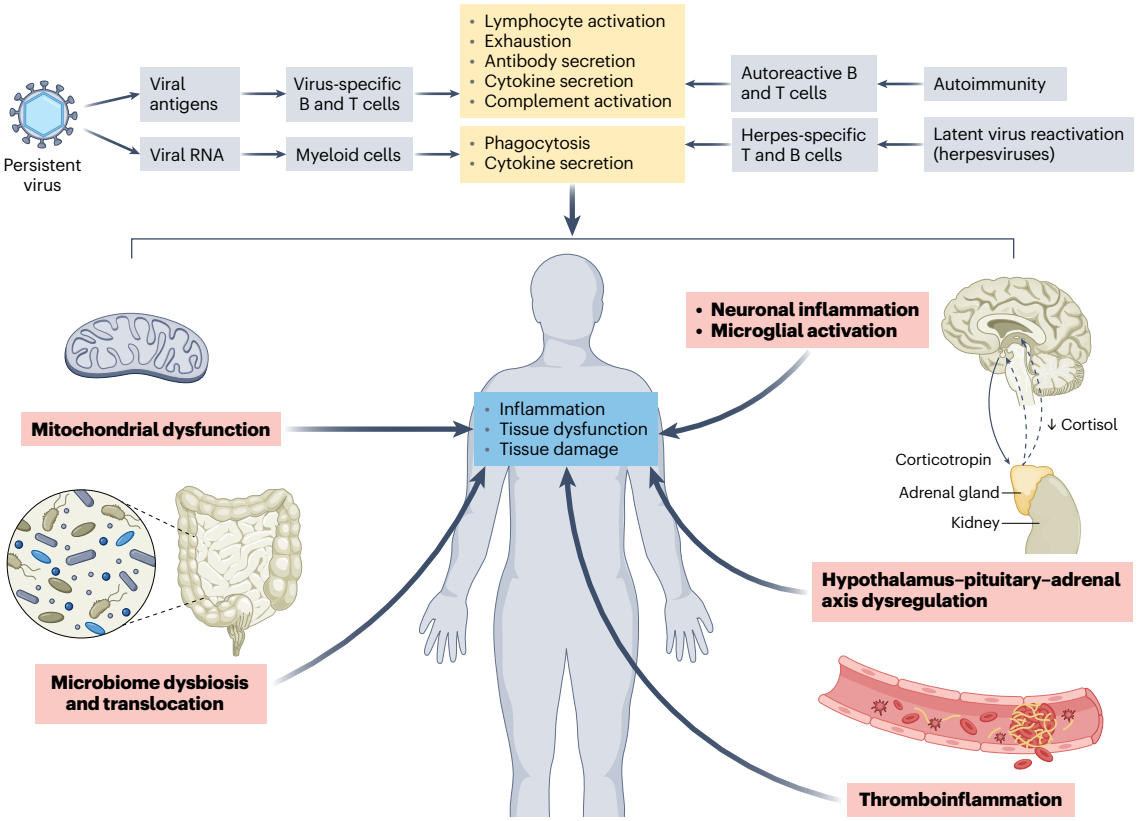

Fig. 3 | Mechanisms of long COVID. Initial triggers (gray boxes) include viral persistence in tissue reservoirs (or immune-privileged sites) and possible replication of SARS-CoV-2 leading to the generation of viral antigens and RNA, which stimulates adaptive and innate immune cells, respectively. This can lead to immune cell activation, cytokine secretion, T cell exhaustion, antibody secretion against SARS-CoV-2 antigens and complement activation (top yellow box). Innate recognition of viral RNA by myeloid cells can lead to enhanced phagocytosis and cytokine secretion and inflammasome activation (bottom yellow box). These events can trigger autoimmunity (bystander activation or molecular mimicry) and reactivation of dormant herpesviruses (EBV, VZV) and uncoordinated cross-talk between cellular and adaptive immunity. Immune activation can cause downstream pathologies (pink boxes), including mitochondrial dysfunction and impaired energy metabolism; microbiome dysbiosis and translocation and gut nervous system dysregulation; neuronal inflammation, activation of microglia and immune cells with reduced neurogenesis and loss of oligodendrocytes and myelinated axons, possible fusion between neurons and neurons and glial cells and formation of multicellular syncytia, which compromises neuronal activity; dysfunctional hypothalamic–pituitary–adrenal response leading to inappropriately low levels of cortisol; complement activation, endothelial inflammation, platelet activation and red blood cell lysis leading to thromboinflammation and tissue injury. These mechanisms are non-exclusive and may cause inflammation, tissue dysfunction and tissue damage (blue box) leading to clinical manifestations of long COVID.

tryptophan (a serotonin precursor) and subsequently reduced levels of circulating serotonin, which may impair cognition via reduced vagal signaling[85]. SARS-CoV-2 infection may also lead to mitochondrial dysfunction, systemic metabolic abnormalities and abnormal skeletal muscle response to exercise—including exercise-induced myopathy and tissue infiltration of amyloid-containing deposits and leukocytes[65].

The proposed mechanisms of long COVID share similarities with those of other post-acute infection syndromes, which are beyond the scope of this article and are discussed in detail elsewhere[24].

Prevention, treatment and care models

Non-pharmaceutical interventions (for example, masking, improved indoor air quality) can reduce the risk of SARS-CoV-2 infection and consequently reduce the risk of long COVID. COVID-19 vaccines may partially reduce the risk of long COVID in adults by 15–70% (mean, ~40%)[86–89]; they may also partially reduce the risk of long COVID in children[90,91]. In nonhospitalized individuals (mild-to-moderate COVID-19) who have at least one risk factor for the development of severe COVID-19, use of the SARS-CoV-2 antivirals (ritonavir-boosted nirmatrelvir and molnupiravir) in the acute phase may reduce the risk of long COVID[92–97]. However, the effectiveness of these antivirals in reducing risk of long COVID in low-risk groups, including younger individuals with no comorbidities[98], has not been evaluated. Simnotrelvir—a new SARS-CoV-2 antiviral available in China[99]—resulted in earlier reduction in viral load and faster resolution of acute symptoms (than placebo)[100], but its effectiveness against long COVID has not yet been evaluated. Exploratory analyses showed that another new SARS-CoV-2 antiviral, ensitrelvir (currently available in Japan), reduced the risk of long COVID when initiated in the acute phase of COVID-19 (refs. 101,102). Furthermore, metformin (initiated within 7 days of SARS-CoV-2 infection) has been shown to reduce the risk of long COVID in a randomized controlled trial[103].

Evidence for long COVID treatments is beginning to emerge, but it is still limited. A randomized, double-blind, placebo-controlled trial showed that treatment with a synbiotic preparation (a gut microbiome modulator) alleviated multiple symptoms of long COVID—highlighting the need to further explore microbiome modulators as potential therapeutics in this setting[104]. Another randomized, controlled trial showed that a 15-day course of ritonavir-boosted nirmatrelvir did not reduce the burden of long COVID symptoms in comparison to ritonavir with placebo[105].

Due to near-total absence of evidence from randomized clinical trials to guide treatment decisions, approaches for the assessment and treatment of respiratory sequelae[106], cardiovascular complications[107], fatigue[108], cognitive symptoms[109], autonomic dysfunction (including POTS)[110–114] and neuropsychiatric impairment[115,116] in adults and

Table 1 | Estimated impact of long COVID on national economies in 2024[a,b]

	Brazil	France	Japan	Saudi Arabia	Spain	Taiwan	United Kingdom	United States
Hours lost for those that exit the workforce (in millions)	508.8	182.8	1,100	442.4	106	230.4	158.9	953.6
Hours lost for those that reduce work hours (in millions)	196.6	72.5	442.4	163.3	41.1	86	61.7	366.3
Hours lost for those that continue working after acute infection (in millions)	97.9	40	222	65	20.7	36.3	31.3	177.5
Total work hours lost (in millions)	803.3	295.1	1,800	670.7	167.8	352.7	251.8	1,500
GDP loss due to long COVID (in billions of US dollars)	11	21	72.2	24.4	7.8	12.2	15.5	152.6
Percentage GDP loss due to long COVID	−0.50%	−0.60%	−1.60%	−2.30%	−0.50%	−1.5%	−0.50%	−0.50%

[a]Data from ref. 170. [b]The eight countries were selected on the basis of data availability.

children[117] are based on evidence of treating similar symptomatology from other conditions—including myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) and Gulf War illness[26,118–120].

Care for people with long COVID varies widely across settings and practitioners[118,119,121–123]. It is often challenged by lack of widespread recognition and understanding of long COVID among medical professionals, constrained resources and competing demands on healthcare systems still recovering from the shock of the pandemic, lack of standardized care pathways, lack of definitive diagnostic and treatment tools, and a general pervasive pandemic fatigue with an urge to 'move on'[124,125]. Much of the global burden of long COVID remains undiagnosed, particularly in low-resource settings, and in many instances are erroneously attributed to psychosomatic causes[126].

Overall, care models for long COVID are evolving, with substantial variability across health systems[127]. While there is still no empirical evidence evaluating comparative effectiveness of long COVID care models[121], optimal models should be context dependent—based on available resources, expertise and the population being served[121,128].

Impacts of long COVID

In addition to its impact on patients' daily lives and health outcomes, long COVID has a devastating impact on communities and can have wide-reaching ramifications for health systems, national economies and global health metrics.

Impact on individuals and communities

Long COVID drastically affects patients' well-being and sense of self, as well as their ability to work, socialize, care for others, manage chores and engage in community activities—which also affects patients' families, caregivers and their communities[129]. Over three quarters of people with long COVID report a moderate or severe impact on general well-being[130]. The high rates of cognitive and physical symptoms also affect individuals' identity and sense of self. One in four people with long COVID limit activities outside work in order to continue working[131]. Many patients with long COVID experience social exclusion, isolation and stigma, often from medical providers[43,132–134]. These challenges are exacerbated by societal barriers to the inclusion of people with disabilities and chronic illnesses.

Impact on health systems

Because of the large burden of long COVID and its multisystemic effects[135], it has profound impacts on health systems[136,137]. Patients with long COVID frequently require ongoing medical care and multiple specialist consultations to manage their complex symptoms. This increased demand exacerbates existing pressures on health systems, leading to longer wait times, potential delays in essential care and increased costs. In the United States, people with long COVID are more likely to report unmet healthcare needs in the past year because of costs and difficulties finding a clinician and getting an appointment when needed[138]. These issues are exacerbated in low- and middle-income countries[126,139]. Furthermore, the lack of standardized diagnostic criteria, treatment protocols and models of care for long COVID adds to the complexity and places additional burdens on healthcare providers[137,140,141].

Perhaps the most enduring challenge to health systems lies in the rise in the burden of non-communicable diseases (NCDs; for example, cardiovascular disease and diabetes) as a consequence of SARS-CoV-2 infection[4,5,9,10,15,136,142–152]. NCDs are chronic conditions that require lifelong care, impact health system utilization (competing for access and quality of care) and raise healthcare costs[137].

Impact on economies

Long COVID strains individual financial health[153] and has wide and deep ramifications on national economies[154–159]. In addition to the substantial direct healthcare costs[160], there is also financial strain on support services and disability benefits. In addition, long COVID affects labor participation, employment and productivity of impacted individuals and their caregivers[129,156,161–163]—resulting in depleted savings, food and housing insecurity[131,164] and negative impact on labor supply, thereby fueling labor shortages[156]. Studies indicate a significant percentage of individuals with long COVID experience a reduced ability to work or may be unable to work at all[165]. A report by the US Brookings Institute estimated that between 2 and 4 million US adults were out of work because of long COVID in 2022 (ref. 165). A US Federal Reserve Bank report found that people with long COVID had 10% less likelihood of being employed and worked 25% to 50% fewer hours when employed than uninfected individuals[166]. Survey data from the UK's Trades Union Congress show that 20% of people with long COVID were not working and that an additional 16% were working reduced hours[167]. An analysis by the European Commission suggested that long COVID had a negative impact on the European labor supply of 0.2–0.3% in 2021 and 0.3–0.5% in 2022 (ref. 168).

Quantitative estimates of the total economic impact of long COVID remain preliminary. A study in 2022 estimated the economic cost of three key parameters in the United States, including lost quality of life ($2,195 billion), cost of lost earning ($997 billion) and spending on healthcare ($528 billion), for up to a total cost of $3.7 trillion[154,155]—this amounts to $11,000 per capita or 17% of the 2019 gross domestic product (GDP). These economic losses are on par with the global 2008 Great Recession. Assumptions included in these estimates are that burden of disability from long COVID is on par with that of ME/CFS and that long COVID lasts on average for 5 years[155].

Among OECD (Organization for Economic Co-operation and Development) countries, a preliminary conservative estimate suggested that excluding the direct costs of healthcare, long COVID is likely costing OECD countries as much as $864 billion to $1.04 trillion per year due to reductions in quality of life and labor force participation[169]. A recent analysis by the Economist Impact (a think tank of The Economist) suggested that the economic cost of long COVID in 2024 is expected to be around 0.5% to 2.3% of the GDP of several large economies[170] (Table 1). On the basis of all the available data, a conservative

estimate of the annual global economic toll of long COVID could be around $1 trillion amounting to 1% of the 2024 global GDP[154,155,169,170].

Impact on the SDGs

The profound immediate health, social and economic shocks triggered by the COVID-19 pandemic have undermined the ability of many countries to achieve the SDGs by 2030 (ref. 171). In addition to the immediate effect of the pandemic, its long tail—in the form of long COVID—presents a more profound and enduring challenge to SDGs than the direct initial disruptions[171].

Long COVID's multifaceted impact jeopardizes progress across many SDGs, particularly those aimed at promoting health and economic well-being, and reducing inequalities[172–179]. Long COVID can limit access to and quality of healthcare[136,137], reduce labor participation, worsen poverty and hinder economic productivity[169], and exacerbate existing inequalities[180–183]. Table 2 lists the impacts of long COVID on several of the SDGs and identifies which collaborative, multi-sectoral partnerships and actions are needed to address these impacts.

The full extent to which long COVID will undermine the SDGs is still evolving and is difficult to fully quantify[174,175]; a deeper understanding of the full scope and scale of this impact is needed.

Research and policy roadmaps

Substantial work lies ahead to address the broad and multifaceted challenges posed by long COVID—including preventing further increase in the number of people with long COVID and addressing the care needs of people already impacted[184]. Responding to these challenges will require coordinated, long-term policy response and visionary research strategies, guided by the principles of health equity and patient centeredness[185–187]. We developed the following research and policy roadmaps on the basis of our assessment of the evidence and policy gaps, as well as our own clinical, research and policy experience and in partnership with patients.

Research roadmap

Biological mechanisms. Leading mechanistic hypotheses (discussed above) should be examined carefully, particularly for their interactions and potential to guide disease management, trials to test existing drugs and the development of new drugs[3]. Continued investigation (via animal models[188,189] or other approaches) of neuroinflammation, immune dysregulation, sex differences[190], tissue damage and susceptibility features, including genomic[191], epigenomic[192–194] and other '-omics', is warranted. In evaluating the mechanisms of long COVID, detailed assessment of specific manifestations, for example, understanding the pathophysiology of post-exertional malaise, may yield mechanistic insights that guide clinical management[65,195,196].

That SARS-CoV-2 leads to long COVID is unlikely to be a unique property; many other viral agents (including influenza, SARS, Middle East respiratory syndrome, EBV, Dengue, Ebola, Polio, Chikungunya, West Nile virus, Ross River virus, Coxsackie B and VZV) and nonviral agents (*Coxiella burnetii*, *Borrelia*, *Giardia lamblia*) also lead to post-acute and long-term health effects[24,197]. A deeper understanding of the similarities and distinctions in the biological mechanisms of long COVID and other infection-associated chronic conditions is needed[2,3,24–26,198–214].

Diagnostics. A research agenda is needed to foster the development, testing and validation of more advanced imaging, new blood tests, molecular probes, '-omics' and novel approaches to tissue investigation and analyses—toward better diagnosis of long COVID. Traditional imaging techniques may not reveal abnormalities in long COVID that may be evident in more advanced imaging. For example, new imaging technologies, including magnetic resonance imaging (MRI) with xenon-129 (^{129}XE-MRI)[215] for lungs, diffusion MRI to map glial activity[216], imaging for glymphatic functioning[217] and arterial spin labeling MRI[218] for cerebral blood flow, have identified abnormalities in long COVID where conventional imaging has not. In a preliminary study, imaging flow cytometry was shown to detect fibrin microclots, which may be more abundant in people with long COVID than controls[219]. Whole-body positron emission tomography imaging using a highly selective radiotracer ([^{18}F]F-AraG) that allows anatomical quantification of activated T lymphocytes, showed increased radiotracer uptake indicative of T cell activation in various anatomic sites (for example, spinal cord, lungs) that were associated with long COVID[220]. These imaging modalities—along with other approaches—should be further investigated for their potential to establish diagnosis of long COVID, to guide trial designs, and for targeted disease management.

Biomarkers are helpful, not only as diagnostics, but also to aid in risk stratification (to guide trials and choice of treatment), determine potential subtypes of disease, and assess severity, prognosis and response to treatment. Candidate biomarkers include immune cell phenotypes, cytokines/chemokines, immunoglobulins, complement and coagulation proteins, acute phase proteins, endocrine markers and markers of neurologic or vascular injury[66,67,73,221,222]. Integrated '-omics' analyses[223,224], including genomic, epigenomic, transcriptomic[225], proteomic[226–228], metabolomic[229], lipidomic[230], and microbiome[231] profiling, may help identify fingerprints for various types of long COVID. However, because of the complexity of long COVID and its diverse manifestations, which likely represent distinct mechanistic pathways, a single or even a panel of laboratory tests may not achieve high-enough performance. Sequela-specific approaches for biomarker discovery may also be productive[221].

In addition to imaging modalities and biomarkers, harnessing health data from wearable biosensors and other sources may also be useful for diagnosis and to identify triggers and track disease activity.

Epidemiology and clinical course. Studies to understand the incidence, prevalence, severity and trajectory of long COVID over time are critical[35,36,232,233]. Comprehensive understanding of risk factors, including social determinants of health, genetic, environmental, dietary, health behavior (for example, smoking) and other risks of long COVID, is also important.

Research to identify the putative subtypes (or clusters of sequelae) of long COVID has yielded variable results thus far[234–237]; greater clarity is needed on putative subtypes and how might they differ in terms of epidemiological features (for example, risk factors), clinical course and potential response to treatment.

Real-world evidence using high-quality data and advanced causal inference approaches (for example, target trial emulation) to evaluate effectiveness of therapeutic interventions will complement evidence generated by randomized trials[238,239]. This is particularly relevant in the evaluation of the long-term effects of therapeutic interventions and risks of rare adverse events; trials may have a relatively short follow-up, limiting assessment of long-term outcomes. Moreover, trials may not be adequately powered to detect rare adverse events.

Because long COVID is a new entity (it has been in existence for less than 5 years), longitudinal studies to characterize the long-term health trajectories of people with long COVID—up to 10 years, 20 years and 30 years—are needed, to understand rates and predictors of recovery and relapse of the various manifestations. These long-term studies will also help identify any latent consequences of the disease (that is, impacts that have not yet been realized) and secondary consequences (for example, the downstream health effects that emanate from long COVID). For example, understanding whether people with cognitive dysfunction (or brain fog) are at a higher risk of developing neurodegenerative diseases later in life is critical.

Comparative analyses to understand the post-acute and long-term health consequences of SARS-CoV-2 infection (and reinfection) versus other infections (for example, seasonal and pandemic influenza, respiratory syncytial virus infections and others) is important to enhance

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Table 2 | Impacts of long COVID on SDGs and cross-sector partnerships to address them

SDG	Impacts of long COVID	Cross-sector partnerships and institutional actions needed to address these impacts
1: No poverty	**Lost income**: long COVID can impact people's ability to work and can push individuals into poverty due to lost wages and reduced earning potential. **Increased healthcare costs**: Medical expenses, even with insurance coverage, can lead to financial hardship, exacerbating poverty. **Strained social safety nets**: Increased reliance on disability benefits and other social programs can strain budgets meant to eliminate poverty.	**Partnerships**: Government agencies, insurance providers, employers, financial institutions and social service organizations. **Actions**: Governments should expand social safety nets, financial assistance programs, insurance coverage, and disability services and support systems to mitigate financial impacts of long COVID on individuals. Employers should offer flexible work arrangements and paid sick leave. Social services organizations should develop support systems to help address unmet needs of people impacted by long COVID.
2: Zero hunger	**Increased food insecurity**: People with long COVID may experience greater rates of food insecurity.	**Partnerships**: Government agencies and social service organizations **Actions**: Governments should add and expand food assistance programs while also making it easy to apply and removing recertification requirements to cut down on cognitive exertion. These programs can be in partnership with social service organizations.
3: Good health and well-being	**Increased burden of chronic disease**: Many of the components of long COVID are chronic conditions that last a lifetime (for example, new-onset heart disease). **Reduced quality of life**: long COVID health symptoms diminish quality of life and well-being. **Limited access to care**: Individuals with long COVID may face barriers to accessing healthcare providers, treatments and rehabilitation services, especially in areas with limited healthcare resources. **Strained health systems**: These may lead to reduced access to and quality of care.	**Partnerships**: Governments, employers, research institutions, healthcare systems, health profession societies, health providers, community health workers, public health institutions, patient advocacy groups, academic institutions, accrediting bodies and health licensing authorities. **Actions**: Governments should commit to long-term sustained investment in research to prevent and treat long COVID, improve quality of life and ease the burden of disability and disease associated with long COVID. Governments should mandate improved indoor air quality (to reduce risk of COVID infections and reinfections). Employers should promote healthy work environments, including improving indoor air quality, sick leave policies and support systems for employees. Governments should work with healthcare systems, health professions societies, providers, community health workers, public health institutions and advocacy groups to ensure education and training of health providers, expand access to affordable and equitable high-quality healthcare and ensure public awareness and understanding of long COVID. Academic institutions, accrediting bodies and health licensing authorities should ensure that health providers are trained in the recognition and management of long COVID.
4: Quality education	**Challenges to education**: Students and educators with long COVID may face disruptions to learning and teaching.	**Partnerships**: Educational institutions, healthcare providers and government agencies. **Actions**: Educational institutions should provide accommodations for students and educators with long COVID. Educational institutions should invest in improving indoor air quality. Governments should invest in research to understand the impacts of long COVID on educational attainment and how to best mitigate it.
5: Gender equality	**Threat to gender equality**: Women, who are more likely to experience some forms of long COVID, could face skepticism of their symptoms (hindering access to care), and may experience greater setbacks in career advancement and economic security.	**Partnerships**: Government agencies, health professions societies, healthcare providers, employers, research institutions, researchers and advocacy groups. **Actions**: Governments should fund research on sex differences in long COVID and develop targeted policies to address inequalities. Healthcare providers should be trained to recognize and address sex differences in the manifestations (and potentially treatment response) of long COVID. Advocacy organizations ought to champion gender equality and actively redress any gender-based disparities.
8: Decent work and economic growth	**Labor force disruption**: Reduced work hours or withdrawal from labor participation due to long COVID contribute to productivity losses and hinder economic growth. **Business impact**: Workforce shortages and absenteeism strain businesses, potentially impacting their ability to thrive. **Hindered innovation**: The impact of some symptoms of long COVID, including brain fog and other cognitive difficulties may affect people's ability to innovate and create.	**Partnerships**: Governmental agencies, employers, labor unions and advocacy organizations. **Actions**: Addressing long COVID should be viewed as an economic imperative. Governments should quantify and track the impact of long COVID on their economies. Governmental budgetary planning and resource allocation (for healthcare, research, services and support systems) should take into consideration the impact of long COVID on the economy, ensuring that resources are proportionately distributed to mitigate these effects. Employers should offer flexible work arrangements and support for employees with long COVID. Labor unions and advocacy organizations should promote employee protections and benefits.
10: Reduced inequalities	**Disproportionate impact on marginalized communities**: People who are socioeconomically marginalized, such as low-income individuals, minoritized racial and ethnic groups, transgender people and those with preexisting health conditions, may be disproportionately affected by long COVID, which may exacerbate or deepen existing inequalities. **Limited access to services and support systems**: People in under-resourced communities may struggle to access necessary care and support for managing long COVID and its downstream consequences, widening disparities.	**Partnerships**: Governments, health professions societies, health systems and healthcare providers, community-based organizations and advocacy groups. **Actions**: Governments should invest in targeted outreach and support programs for marginalized communities. Health professions societies, health systems and healthcare providers should expand access to care in underserved areas. Governments and health systems should partner with community-based organizations and advocacy groups to understand needs and provide culturally relevant education and support services. Community-based organizations and advocacy groups should advocate for equity in the allocation and distribution of resources.
11: Sustainable cities and communities	**Strained infrastructure**: long COVID can strain healthcare infrastructure and support services in urban areas; limited resources in rural communities are further strained leading to increased urban–rural inequalities.	**Partnerships**: Governments, healthcare systems and advocacy organizations. **Actions**: Governments and healthcare systems should invest in healthcare infrastructure and support services to ensure adequate capacity and quality of care in both urban and rural areas (for example, by ensuring equitable availability of broadband connectivity and availability and access to telehealth services). Advocacy organizations should advocate for the needs of people with long COVID in both urban and rural areas.
17: Partnerships for the goals	**Need for a collaborative multi-sectoral approach**: The complexity and interconnectedness of the impacts of long COVID on SDGs necessitate a collaborative multi-sectoral approach.	**Partnerships**: Governments, international intergovernmental and nongovernmental organizations, research institutions, economic and multi-sectoral coalitions (for example, OECD and Asia-Pacific Economic Cooperation), health professions societies and advocacy organizations. **Actions**: Strengthen global cooperation and coordination to address the challenge of long COVID. Facilitate global multi-sectoral collaboration, sharing of expert knowledge and best practices, and sharing of resources across sectors and borders.

our understanding of similarities and differences in their epidemiology and clinical course[197,240–242].

Quantifying the burden of NCDs attributable to long COVID would bring greater clarity to the extent to which billions of SARS-CoV-2 infections around the world may have impacted the global epidemiology of NCDs. The effects of long COVID on global health metrics, including SDGs, should also be periodically evaluated.

Trials to test therapeutics for long COVID. When it comes to clinical trials for long COVID therapeutics, innovation, urgency and scale are all needed[243,244]. Long COVID is a complex disease with many manifestations that are likely driven by several different biological mechanisms, and may need different therapeutic approaches. Approaches that reimagine trial design to incorporate the complexities of the disorder and meaningfully incorporate patient input—from trial inception to completion—are needed[244,245]. This may include large-scale platform trials with adaptive designs that would test a large battery of potential drug candidates to quickly identify treatments for the various forms of long COVID.

There is a large array of existing drugs that could be readily repurposed and clinically evaluated to address existing hypotheses from viral persistence to immune system dysfunction to vascular damage. Some of these drugs include SARS-CoV-2 antivirals, neutralizing monoclonal antibodies against SARS-CoV-2, non-SARS-CoV-2 antivirals (targeting reactivated EBV and VZV), immunomodulators (for example, JAK–STAT inhibitors, checkpoint inhibitors), anticoagulants, histamine 1 and 2 antagonists, metformin, GLP-1 receptor agonists, SGLT2 inhibitors, microbiome modulators, anti-inflammatory agents, and drugs that improve glymphatic functioning[2,62,246]. Research agendas must also include development of new antivirals and other new targeted drugs to prepare for the possibility that repurposed drugs may not be sufficiently effective[247–249]. Testing and evaluation of combinations of treatments should also be undertaken when evidence suggests complementary or synergistic mechanisms of action.

Innovation in developing and validating entry criteria and clinical endpoints for long COVID trials is also needed, along with cultivating support for these parameters from stakeholders, including regulators such as the US Food and Drug Administration and European Medicines Agency[250]. Endpoints must include newly developed or improved patient-reported outcomes specific to long COVID and should reflect the often cyclical or relapsing–remitting dynamic of many manifestations of long COVID—with particular focus on tracking post-exertional malaise, a pathophysiological state that impacts all collected data.

Care delivery and health systems research. Research—including comparative analyses—to evaluate the cost and effectiveness of various care pathways in improving quality of care and outcomes in people with long COVID is needed[121,127,251]. Research to identify and address health inequities and barriers to effective care, especially in low- and middle-income countries, in low-resource settings and in underserved communities, is essential[252].

Economic impacts. The effect of long COVID on human capital[253], labor participation, productivity losses (workforce absenteeism, presenteeism and disability) and other economic indicators (including job retention, career advancement and income instability) should be thoroughly evaluated. Research should explore potential disparities in the economic impact of long COVID across various demographic groups, including racial and ethnic minorities, urban and rural communities, socioeconomically marginalized populations, and individuals with preexisting health conditions.

In addition, studies are needed to quantify the direct healthcare costs associated with long COVID. The costs of disability and support systems required to address the needs of people with long COVID should be quantified. The strain that these costs pose on payors (insurance providers and governments) should also be evaluated.

Understanding the economic barriers to healthcare access and affordability for people with long COVID is also important. This includes evaluating out-of-pocket expenses, insurance coverage gaps, and disparities in access to care, rehabilitation services and support services.

Societal impacts. Long COVID affects individual lives and impacts societal well-being. Understanding the effects of long COVID on societies is important, along with understanding the social responses, the perceptions and the genesis and propagation of stigma. Improved knowledge of the social consequences of being affected by long COVID—for example, lost friendships, strained marriages and reduced ability to network—along with the interplay between them and health outcomes, will help to inform supportive interventions. It will also be important to evaluate the burden on caregivers, families and social groups.

Research to develop a deeper understanding of the causes and consequences of misinformation, disinformation and anti-science rhetoric (for example, long COVID denialism) and how to effectively combat them is also needed[254]. Identifying ways to improve science communication, scientific literacy and public trust in science and to bridge the science–policy gap would all help to improve public understanding, as well as the scientific and policy responses to long COVID[254].

Medical anthropology should also contextualize the response of the science and medicine profession to long COVID within the broader history of medicine. This should include comparative analyses to evaluate and juxtapose the response to long COVID against the responses to the aftereffects of the 1889–1892 flu pandemic and the 1918 flu pandemic and other health crises, including the AIDS crisis in the 1980s[198,199,201,255–257]. Careful anthropologic analysis of how the medical profession approached long COVID as a new disease that emerged in the context of the COVID-19 pandemic is important. It will not only provide historic insights and greater context for our collective response, but also offer insights into how we can optimize responsiveness to emergence of new infection-associated diseases in the future.

Policy roadmap

Given the wide-ranging impact of long COVID on society and the inadequate response thus far, priorities for policy changes are vast. Policies are necessarily dependent on context, resources and various other considerations. The recommendations outlined below are general guidelines that may be adapted to fit the needs of various locales.

Prevention of long COVID. The best way to prevent long COVID is, plainly, to prevent SARS-CoV-2 infection or reinfection in the first place. Masking, especially in high-risk places[258] (for example, healthcare settings), is important—along with isolation guidelines and sick leave policies that permit people with infection to recuperate at home, thereby diminishing the probability of transmission and reducing the risk of long COVID[45].

Although vaccines may reduce the risk of long COVID, vaccine policies in much of the world restrict vaccine availability to high-risk groups. These policies consider risks of death and hospitalization in the acute phase (which are manifest primarily in older adults and those with comorbidities) and ignore the risk of long COVID. Adding to these policy challenges are the low rates of vaccine uptake in 2023–2024 among eligible populations[259]. Vaccine policies must consider the risk of long COVID, as well as the risk of hospitalization and death during the acute phase of SARS-CoV-2 infection; and strategies to improve vaccine uptake (for example, pairing the COVID-19 vaccine with the annual influenza vaccine and other approaches) should be utilized to achieve wider vaccine coverage and greater protection to populations.

Because SARS-CoV-2 is likely to remain for decades to come, it is important to develop long-term, sustainable prevention solutions. Airborne transmission risk assessment tools, such as the one developed by the World Health Organization (WHO), help inform risk reduction strategies[260]. Ventilation and air filtration systems can play a major role in reducing the risk of infection with airborne pathogens[261]. Calls have been made for mandatory improved air quality standards for public spaces and policies that would support design and equipment of homes to meet these standards[261]. Investment in infrastructure supporting improved indoor air quality will help reduce the risk of SARS-CoV-2 transmission and other airborne pathogens and will ensure greater resilience against future threats from airborne pathogens[262]. Amelioration of indoor air quality also has the added benefit of reducing risk of health effects due to indoor air pollutants[263–265], thereby improving human health, well-being, productivity and learning[261,262,266]. Investment in vaccine technologies to develop more durable, variant-proof vaccines that are not rendered ineffective by ongoing mutations of the SARS-CoV-2 virus are important. Vaccine technologies that induce strong mucosal immunity to block SARS-CoV-2 infection and transmission are also needed[267].

Supporting people with long COVID. Because of the considerable impacts of long COVID on people's ability to work and care for themselves, it is imperative that an adequate response to the long COVID crisis involves ensuring people have the financial, physical and emotional support[132]. Streamlining of disability benefit processes, as well as increased access to home and community-based services and food and cash assistance is critical. Workplace policies that support individuals with long COVID could include flexible working hours, increased breaks to allow for pacing, the option for remote work, and sick leave policies. Funding should be provided to support patient groups and community-based organizations, which can provide and connect people to critical supports and services.

Access, quality and equity of care. Governments must work to build and expand access to long COVID care, in particular for marginalized communities (for example, rural and indigenous communities). Improving access to care may take various forms in different countries, depending on the structure of the healthcare system and the involvement of national and local governments in financially supporting healthcare services. Adequate coverage of long COVID treatments and rehabilitation services by insurance providers is requisite. Development of quality-of-care metrics for long COVID and policies to monitor and incentivize quality of care should be pursued[121]. As diagnostics and treatments are developed, governments must also ensure equitable access. Shining historical examples include the Brazilian National AIDS Program, which was established in 1996 in response to the HIV/AIDS crisis to ensure free and universal provision of antiretroviral drugs[268,269], and the Ryan White HIV/AIDS Program (based in the United States), which provides outpatient HIV care, treatment and support services to those without health insurance and fills gaps in coverage and cost for those with insurance limitations[270–272].

Professional education and training. Currently, very few medical schools and health professional training programs include in their curricula any meaningful training about identification and clinical management of infection-associated chronic conditions, including long COVID. A survey of physicians in the United States showed that 78% agree that long COVID is a problem but only about one-quarter feel prepared to address it[273]. Training of healthcare professionals to recognize and manage long COVID effectively must be prioritized. This includes embedding up-to-date information on long COVID and infection-associated chronic conditions into training curricula for health professions, as well as providing regular high-quality continuing education to qualified health providers.

Public health communication. Existing public health education on long COVID has been minimal. A survey in the United States showed that one-third of American adults still had not heard of long COVID as of August 2023 (ref. 274), and there remains very low awareness of long COVID in low- and middle-income countries. Through public education campaigns, governments must raise awareness about long COVID and the risk of chronic conditions after infection; combat social stigma across adults and children; and use a harm reduction framework to promote awareness of prevention measures (including vaccination, masking and improved indoor air quality)[258,260,261].

Supporting coordinated interdisciplinary research. To achieve the research priorities listed above, governments must substantially increase the amount of funding toward research. In the United States, existing calls for the establishment of a center for infection-associated chronic conditions at the US National Institutes of Health—with a funding request of at least $1 billion per year toward long COVID research and with additional substantial funding for other infection-associated chronic conditions—should be vigorously supported[275]. This proposal would create a coordinating entity to lead a long-term, large-scale interdisciplinary research portfolio to address long COVID research priorities. Other governments should also explore similar proposals.

Policies supporting research should explicitly mandate meaningful patient engagement in research from inception to implementation, and should leverage existing expertise (including scientific, clinical and lived experience) in infection-associated chronic conditions. Furthermore, meaningful efforts must be made to expand the pool of researchers working on infection-associated chronic conditions, by encouraging early career scientists and clinician–researchers to focus on these conditions and providing resources to current experts to lead training and research.

Given the complexity of long COVID and its similarities to other infection-associated chronic conditions, a coordinated approach that integrates research, policy and regulatory efforts across these conditions would reduce duplication of efforts and allow a more comprehensive understanding of the common underlying mechanisms, trial designs and potential treatment strategies.

Policies from funders are needed to mandate meaningful data sharing, which will maximize the utility and pooled insights that can be generated from existing health information. Current open data protocols are insufficient, laden with bureaucratic hurdles and do not allow access to primary data, and consequently do not enable meaningful analyses. Funders must establish data banks (a pioneering exemplar of this is the UK Biobank) for the collection, storage, analysis, retrieval and dissemination of data to make long COVID research more accessible in near real time, all while upholding data privacy and data security standards[276,277].

Building consensus on definitions and clinical endpoints for long COVID. Various interim definitions of long COVID exist[39,278–283], but there is not yet a universal consensus on the most optimal definition—which must be sufficiently nuanced to capture the complexity of the condition and its various manifestations. It is unlikely that a single definition will fit all needs. Consensus definitions that are optimized and empirically tested for various applications, including clinical care, epidemiological surveillance, and research, should be developed. Definitions must necessarily evolve to incorporate new understanding as the evidence base for long COVID grows.

Similarly, developing consensus on clinical endpoints for trials of long COVID is needed. Drug regulatory agencies in consultation with stakeholders, including patients and scientists, should lead in this arena and provide regulatory guidance on clinical endpoints for trials. These endpoints will also have to necessarily evolve as our understanding of long COVID expands.

Building consensus on definitions and clinical endpoints would catalyze progress in this field, remove barriers to entry for the pharmaceutical industry into long COVID trials and facilitate comparative analyses across studies.

Global coordination. The global nature of long COVID necessitates international cooperation in both research and policy. International bodies (for example, the WHO) should facilitate partnership and collaboration among countries across the globe. This collaboration is pivotal to coordinate and synergize efforts across the globe and accelerate progress on the different challenges posed by long COVID.

Professional societies for long COVID. Professional societies (national and global) should be established for long COVID. Because of the multisystemic nature of long COVID (and the other infection-associated chronic conditions), it does not fit neatly under any of the traditional organ-based organizational structures of medical care and research[284], hence the need for professional home(s) for long COVID and associated conditions. Dedicated professional societies could provide strategic leadership and guidance in the clinical management of long COVID and associated conditions[284]. They could serve as hubs to coordinate education, research and advocacy efforts[284]. These professional societies could play a major role in organizing and hosting national and international conferences, spearheading efforts to provide periodic synthesis of evidence that distills existing research into actionable insights guiding care of people with long COVID. The newly established Clinical Post COVID Society in the United Kingdom may be a promising example of this[284].

Preparedness for the next pandemic. We must reflect on our collective experience with COVID-19 to enhance resilience and preparedness for future pandemics[285–287]. A major lesson learned from long COVID is that pandemics leave in their wake a long tail of disease and disability[198]. This is not unique to the COVID-19 pandemic[198]; historical accounts show similar phenomena following previous pandemics[198,199,255]. Due to climate change, deforestation, human encroachment on animal habitat, increased frequency of travel, a growing livestock industry and other anthropogenic factors, the risk of zoonotic spillover and novel viral sharing among species is likely higher in the twenty-first century than it was in the twentieth century[286,288–292]. Many of the geographic areas that are most prone to these changes are also projected to have high population density—creating ripe conditions for pandemics[289,291]. Future pandemics are likely to also produce long-term disability and disease[198]. Investment in systems to measure the population-level incidence and prevalence of post-acute and chronic disease caused by infectious agents, including SARS-CoV-2, will aid in the characterization of the epidemiology of long COVID and will position us to be better prepared to deal with post-acute and chronic illnesses that will emerge in future pandemics. Incorporating the potential emergence of long-term health effects into initiatives for pandemic preparedness and resilience (for example, the WHO Preparedness and Resilience for Emerging Threats Initiative) is essential to optimize response to the long-term consequences of future pandemics.

Conclusions

Considerable progress has been made in the past several years in characterizing the epidemiology, clinical course and biology of long COVID. But much remains to be done. The scale of long COVID and its far-reaching impacts necessitate a robust and coordinated research and policy response strategy. Addressing the research and care needs of people impacted by long COVID will have broad benefits, potentially unlocking a better understanding of infection-associated chronic illnesses (an ignored area for decades) and optimizing our preparedness for the next pandemic.

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Competing interests

Z.A.-A. reports receiving consultation fees from Pfizer. L.M. reports consulting fees from Evidera. L.S. has received honoraria from consulting for Evidera. A.I. co-founded RIGImmune, Xanadu Bio and PanV and is a member of the board of directors of Roche Holding and Genentech.

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