How are inequalities in health from Long COVID being exacerbated and what are the strategic implications for more equitable support for those with enduring clinical sequelae of infection?

ASPHER Statement

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1. *Introduction*

COVID-19 posed unparalleled challenges to healthcare systems and public health, and to societal functions as a whole. While the pandemic may appear to be less severe in 2022, nevertheless the burden of Long COVID has grown and draws attention to addressing its long-term consequences. The clinical impacts have been amplified and multiplied by social factors, the structural and organisational fragility of the response to acute infection and the underestimation of the longer-term consequences for individual and population health and wellbeing. That is the case with inequalities, since the association between ethnicity and health inequity in acute COVID-19 has been extensively explored, while the association of such inequalities with Long COVID has received less attention. However, it appears that Long COVID is also exacerbating ethnic, economic and health inequalities in affected patients, similar to what has already been found for acute COVID-19.

There is a variety of ways in research and health systems for capturing these impacts. We explore below the scope of Long COVID starting from various definitions used and addressing the link between epidemiology and inequalities from higher exposure and the greater adverse outcomes. We can view Long COVID-19 as a cluster of different complex syndromes. The epidemiology of Long COVID does not readily mirror severity of acute illness, and it can affect those infected independently of their age and sex. This review also focuses on childhood post-acute and persistent infection syndromes and provide specific consideration of children living through the pandemic as forms of adverse childhood experiences. ASPHER recommendations or call to actions are also presented.

An example of an underlying analytical public health framework is shown below (Figure 1), to acknowledge the sequelae and their relationship with wider determinants of health, including for COVID-19 infection and Long COVID. The intersectionality of different determinant and the mechanisms by which they act should alert us to the seriousness of Long COVID's threat to health equity in the next decade.

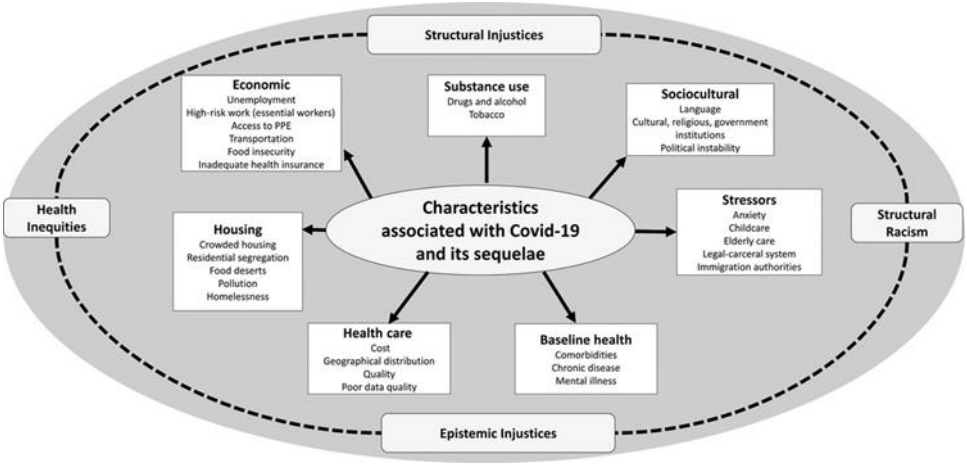

Figure 1. Relationship Between Structural Inequalities and COVID-19, from: Berger Z, Altiery DE Jesus V, Assoumou SA, Greenhalgh T. Long COVID and Health Inequities: The Role of Primary Care. *Milbank Q*. 2021;99(2):519-541. doi:10.1111/1468-0009.12505

2. *Definitions of Long COVID*

The term "Long COVID" appeared for the first time in March 2020, when some patients (including affected clinicians) started sharing experiences on social media, paying particular attention to the possible sequelae of COVID-19 disease. This new clinical terminology quickly moved from patients, through various media, to scientists and experts and to policy channels [1].

Attempts to epidemiologically outline the condition referred to as "Long COVID" estimate that up to 10-20% of all patients with COVID-19 may present with persistent symptomatology weeks or months after the acute infection [2]. Subsequently, scientific and medical societies began to provide definitions of the condition. The adoption of the term Post-Acute COVID syndrome (PACS) covering COVID sequelae has been also proposed [3]. Nevertheless, Long COVID and PACS are often used interchangeably.

According to the NICE (UK) recent rapid guidelines (March 2022), if symptoms continue or develop after acute COVID-19 infection and cannot be explained by an alternative diagnosis, two scenarios occur: ongoing symptomatic COVID, if the symptomatology reaches 12 weeks after the onset of acute symptomatology (estimated at 1 in 5 patients), or 'post COVID-19 syndrome' if the time of 12 weeks is exceeded (estimated at 1 in 10 patients) [4]. Moreover, the National Institutes of Health and the US Centers for Disease Control and Prevention (CDC) define Long COVID as sequelae that extend beyond 4 weeks after the initial infection [5].

However, laboratory data for SARS-CoV-2 should not be the only basis for diagnosis, because of issues with laboratory test availability, accessibility, feasibility, and accuracy, particularly in the early phase of the pandemic, but also now as testing capacity has been reduced in many countries. Also, many infected people were not hospitalized and had "mild" symptoms, with the chance of later health concerns not adequately addressed [6]. In October 2021, the WHO provided a definition by a Delphi consensus, stating that: "*Post COVID-19 condition occurs in individuals with a history of probable or confirmed SARS-CoV-2 infection, usually 3 months from the onset of COVID-19 with symptoms that last for at least 2 months and cannot be explained by an alternative diagnosis*" [7].

Long COVID spans from manageable symptoms with little impact on functional ability to severely debilitating disease with objective organ damage, but sometimes the distinction between recovery from post–intensive care unit syndrome and ongoing COVID-19 pathology is not clearly defined or reported in studies [8]. In the confusion of different and overlapping definitions, ASPHER should seek to promote greater clarity to that debate so that all the involved stakeholders (patients, clinicians, public health professionals, researchers, policymakers and politicians) can move forwards through shared language.

From a clinical perspective, Long COVID includes persistent symptoms, early complications, and long-term complications [9] and poorer quality of life [10]. The reported symptoms and other clinical features by frequency are fatigue, decline in quality of life, muscular weakness, joint pain, dyspnoea, cough, persistent oxygen requirement, anxiety/depression, sleep disturbances, PTSD, cognitive disturbances (brain fog), headaches, palpitations, chest pain, thromboembolism, chronic kidney disease, and hair loss [11]. Comparing symptom prevalence after symptomatic COVID-19 the most commonly present symptoms are fatigue, dyspnoea, and joint and muscle pain [12].

A meta-analysis reported that 80% of patients with COVID-19 developed one or more long-term symptoms [13]. This study estimated much higher than previously reported prevalence, suggesting that the true extent of long-term COVID-19 is still to be further explored. The majority of the effects reported were clinical symptoms. In this case, the five most common symptoms were fatigue (58%), headache (44%), attention disorder (27%), hair loss (25%), and dyspnoea (24%). Pathologies such as stroke and diabetes mellitus are also reported [13]. Despite differences between studies, a higher prevalence of neurological and respiratory symptoms emerges [14–16]. More serious long-term complications seem to be reported especially in patients who were hospitalised with severe COVID-19. Here, cardiovascular, respiratory, dermatological, neurological, and mental health symptoms were reported [17].

History of severe acute infection, requiring ICU care, defines the particular condition of post-ICU syndromes (PICS) and can be viewed as one of the first recognised forms of Long COVID, which could therefore be interpreted as a cluster of different complex syndromes. PICS has been specifically defined as “new or worsening impairments in physical, cognitive, or mental health status arising after critical illness and persisting beyond acute care hospitalization” [18]. The rehabilitation is often lengthy as clinical sequelae can last months or even years [19].

Long COVID symptoms exacerbate and prolong the consequences of the infection over time, interacting with the patient's comorbidities, problems related to individual susceptibilities, treatment types, and non-specific consequences related to hospitalisation [20]. When estimating the burden of Long COVID, the synergistic effect of new COVID-related symptoms on the person’s baseline health and wellbeing (frailty, lifestyle and genetic, previous conditions) may go unnoticed, worsening the quality of life more than COVID itself.

There are many questions on how well the patient care pathway or journey happens. For instance, can we clarify how social determinants in healthcare access for severe illness combine with co-morbidity, and also take into account iatrogenic illness/ complications of treatment/variable access to rehabilitation /continuity of social welfare support/patient deconditioning/ or loss of carer support?

As data about Long COVID have emerged, studies that explore the risk of persistent and new clinical sequelae of acute COVID-19 infection have accumulated with symptoms including respiratory problems (difficulty breathing or shortness of breath), fatigue, hypertension, memory and concentration difficulties, kidney injury, mental health diagnosis, hypercoagulability, cardiac rhythm disorders being reported [21].

In a large cohort study, Xie and colleagues explored the cardiovascular sequelae of COVID-19, and their findings were expanded in a Swedish cohort study, where the rate ratios were highest in patients with critical COVID-19 [22]. They found that beyond the first 30 days of infection, there was an increased 1-year risk of cerebrovascular disorders, dysrhythmias, inflammatory heart disease, ischaemic heart disease, heart failure, and thromboembolic disease. These risks are significant both in the group of cases with pre-existence of cardiovascular disease or comorbidities and also in the group of people were hospitalised for acute COVID-19 infection. In addition, incidence rate ratios were significantly increased 70 days after Covid-19 for deep vein thrombosis, 110 days for pulmonary embolism, and 60 days for bleeding [23]. Research will be needed into

roles of underlying pathophysiological dysfunctions, such as in immune and in reticuloendothelial systems.

The mental health consequences of COVID-19 are of particular concern given existing knowledge of the adverse consequences on quality of life when multimorbidity affects physical and mental health [24]. Substantial morbidity in the 6 months after COVID-19 infection was reported. Risks were greatest in, but not limited to, patients who had severe COVID-19 [25].

Summarizing, from the definitions of Long COVID and the reported clinical (or subclinical) manifestations, a multifaceted framework has emerged. Long COVID currently appears like an umbrella term for different and often not clearly defined syndromes. However, it is crucial to differentiate Long COVID that is affecting specific organs, from PICS, a known problem that is woefully underfunded and for which services are scarce, or from persistent COVID infection, where the virus hides in the body waiting to be reactivated. The recognition of underlying etiologic pathways could help further classify clusters of symptoms and diagnose and how to treat them accordingly. For example, it is debatable whether Post-Covid Neurological Syndrome should be addressed as a distinct entity or as a part of Long COVID spectrum. Moreover, there is an overlap in clinical and biological features with other infections. As an example, post-infectious fatigue syndrome, affecting up to one third of patients at 16-20 weeks post symptom onset, is also reported following several different viral, bacterial, or protozoal pathogens, including Epstein-Barr virus, dengue virus, chikungunya virus, Ebola virus, Coxiella burnetii, and Giardia lamblia [26,27]. All such phenomena can call for extended, tailored rehabilitation systems and practical support in managing loss of activities of daily living and income support, plus support to sustain employment and education. The in-common and the unique presentations could help discern between non-specific host immunological response and symptoms related to viral persistence or direct damage. To be more specific, in the latter case, COVID-19 related symptoms may depend on viral persistence or be immune-mediated new conditions comprising of neurological/neuropsychiatric or mental health problems, with new organ damage or new multi-morbidity. It is not yet clear enough whether "Long-COVID" represents a new, post-viral syndrome that may have longer term complications, particularly where previous definitions were largely based on symptoms and are not related to pathophysiological indicators of active viral infection [28].

The World Health Organization has also created a global COVID-19 clinical platform case report form for clinicians and patients to collect and report more consistent information, to pursue better understanding of the spectrum of post-COVID-19 conditions and recovery [29]. While the impact of acute infection on quality of life and wellbeing has been investigated, fewer studies have investigated the multi-faceted problems related to Long COVID, which is surpassing the acute infection as a public health concern, because its burden and consequences on the population, especially people who are already vulnerable, is not fully known. This assumption of additional unmet need links to the vast scope of COVID-19 inequalities, and the requirement to address them among the multiple enduring shadows casted by the pandemic [30]. In fact, in addition to the problem of Long COVID in generic terms, from the perspective of equity that prevails in a Public Health vision, we are particularly concerned about those people who are at greater risk of this condition or the availability of the aftercare necessary to address these issues, identifying possible inequalities at the outset to try to ensure that we try not to leave anyone unprotected. There is a need for a more comprehensive debate about health inequalities from acute COVID-19 infection

that will lead to strong and equitable patient rehabilitation and recovery systems. This is in addition to the health implications of acute and post-acute infection, while exploring Long COVID and looking at the problem from a broader perspective. Otherwise, the vast array of related inequalities may be marginalised or missed in the necessary focussed processes of defining pathology/condition. Patients' health care, social care, employment, financial benefits or penalties, how they are perceived in society, and how they perceive themselves depend on these definitions. Thus, public health strategies should also be based on the daily realities of those living with the conditions being defined [31].

3. Long COVID in children and young people

A special focus should be placed on children's and adolescents' health. Consideration of Long COVID in children and young people requires that the impact of persistent and post-acute symptoms and organ damage can be distinguished from onset of a new chronic condition. As with adults, the difference between symptoms related to the viral persistence, or not to the virus with the emergence of a new condition causing post-viral disability should be separated from post-COVID-19 organ damage and specific patterning of physical and mental health problems. This separation is necessary to ensure that assessment, treatment and rehabilitation pathways are tailored to meet their distinct needs and that both are funded adequately.

All age groups are affected by Long COVID, including children. More specifically, only 4% of affected children/adolescent had critical symptoms [32] and the median Infection Fatality Rate was the lowest in 7 years old persons (0.0023% (0.0054% at 1 years versus 0.0118% at 19 years)) [33]. However, evidence of long COVID in children and adolescents is limited, and scientific studies to date do not reach significant and conclusive evidence on the topic, also failing to discriminate between symptoms attributable to Long COVID from non-infective pandemic-driven hazards, including exposures associated social restrictions. Symptom clusters are similar to those experienced by adults. However, the prevalence of COVID-19 in children and adolescents is on the rise [34,35]. According to the report from the UK Office for National Statistics (June 2022), the prevalence of ongoing symptoms following COVID-19 infection in children of 2 years and older was 0.41% for age 2-11 and 1.47% for age 12-16. [36]. Given the large number of children and adolescents infected with SARS-CoV-2, the impact of even a low prevalence of persistent symptoms would be considerable [37–40].

Looking at the topic from the acute infection perspective, Molteni and colleagues' results highlighted that acute COVID-19 in children usually lasts around a week even if some children (4.4% in this sample) experience prolonged illness duration. Symptoms recover usually within two months (symptom duration >56 days in 1.8% children) [41]. Some children who tested negative for SARS-CoV-2 also had persistent and burdensome illness. However, to date, few studies explore the epidemiology, assessment and treatment of long COVID in children and young people. It should be also noted that baseline levels of health, wellbeing and disability in young people vary between countries and this aspect is intertwined with the specific national policies issued for COVID-19 in younger people.

In addition, there may be emerging or hitherto unrecognised syndromes or disorders where COVID-19 infection plays a role. Current international interest in Hepatitis of Unknown Origin in

young children is an example detailed analysis of whole blood markers for SARS CoV-2 is required [42], and either confirmed or ruled out as a risk factor or co-factor eventually by international consensus. A possible role for SARS-CoV-19 in generating some hepatic damage in children has also been recently flagged up [43]. COVID-19 infection has also led to clusters of new diseases, like in the "Multisystem Inflammatory Syndrome in children" or the haematological, neurological and cardiovascular complications. It would be sensible also to undertake population-based cohort studies on COVID-19 exacerbations of chronic and disabling severe health problems in children, such as neurological, respiratory and cardiac, to assess their needs and formulate care plans.

In several countries children and young people reporting increasing symptoms pre and during COVID (related for example to variable and discontinued access to practical, youth and mental health support). In fact, the further dimension of the impact of COVID in children and young people is the reality of the pandemic as an adverse childhood experience. A recent systematic review on the impact of COVID-19 on children and adolescents shows that there are several potential mental and emotional consequences of epidemics such as COVID-19, H1N1, AIDS and Ebola [44]. The disorders highlighted on the parent-child dyad are: anxiety or severe depression among parents and acute stress disorder, post-traumatic stress, anxiety disorders and depression among children.

Adverse experiences in young people, (including poverty, violence, abuse, parental death or serious illness, poor living conditions, bullying, minoritisation, stigmatisation, social exclusion) increase the risk of developmental delays and health problems in adulthood, such as cognitive impairment, problematic drug and alcohol use depression and noncommunicable diseases [44]. The risk of experiencing COVID-19, of having a family member experience severe COVID-19 or of being bereaved, are all more common among children and young people who have already lived through adverse childhood experiences. This adds to the neurological/psychological impacts of Long COVID, considering that the most common post-COVID-19 symptoms in children/adolescents are fatigue, lack of concentration, and muscle pain [45]. While addressing the direct consequences of Long COVID in young people, attention should be posed on the indirect ones as well. The Long COVID experienced by parents, as well as the burden of inequalities and social determinants of health, have repercussions for the well-being of young people.

4. Managing Long COVID and other enduring sequelae of infection

European countries have responded differently to this new challenge, focusing on supplying healthcare services rather than defining long term plans and investing in Long COVID research. Specialist Long COVID clinics are reported to be operating in Belgium, France, Germany, UK, and Spain, and guidance for healthcare professionals has been provided in Italy, Norway, Estonia, and Sweden. However, additional resources need to be allocated to research, treatment development and the identification of services for the assessment, treatment, rehabilitation and practical support to address the burden of disease from long COVID and related conditions[46]. The UK has four countries with differences in their healthcare systems that can highlight emerging models of care, as for instance in Scotland [47,48]. Pre-covid models for post-ICU care should also be re-examined to ensure that they can be scaled up to address PICS for COVID (and in preparation for

future pandemics). A continuous program of research, service evaluation and quality improvement should be put in place [49].

The United States Department of Health and Human Services and the Department of Justice released a guidance statement on "long COVID" as a disability under the Americans with Disabilities Act, the Rehabilitation Act of 1973, and the Patient Protection and Affordable Care Act 2010. These Acts provide protections for individuals with disabilities to allow for full and equal access to civic and commercial life. This statement classifies "long COVID" as a disability if it substantially limits, either physically or mentally, one or more major life activities. An individualized assessment is needed to determine whether a person's symptoms fit these criteria [50].

5. Strengthening the focus on inequalities

According to Berger and colleagues, to improve the care of vulnerable populations with Long COVID, it is necessary to understand, acknowledge, and engage with the densely intertwined patterns of disadvantage and inequity operating at global, national, community, and individual scales [51].

Disadvantaged populations are at higher risk of exposure to and infection by COVID, due to their life and work conditions, and are more likely to experience negative outcomes [51–54]. Therefore, the consequences of Long COVID should be considered in light of the impact that fragile population groups would experience, amplifying the burden of infection and inequity in healthcare assessment leading to socio-economic, ethnic and geographical inequities in case ascertainment that also need to be addressed [51].

For example, post-COVID symptoms, in particular fatigue, have forced many affected people to take days or even weeks off from work, causing a negative impact on their economic conditions [51]. In a large study conducted in 56 countries, among 3072 subjects with confirmed or suspected COVID-19 and duration of illness over 28 days, almost half (45%) reported reduced working hours due to ongoing symptoms; 22% stopped working 6 months after the onset of the disease [55]. The vulnerable in society have less job security, less flexibility in their roles, and less entitlement to sick pay and occupational health services. However, they are disproportionately represented among essential workers [56]. In addition to being at a greater risk of acute COVID-19, essential workers also face an increasing burden of Long COVID [51]. Furthermore, the economic considerations are amplified especially in those countries where health care is not free at the point of use for all the population. For many patients, the direct costs would be a deterrent from seeking medical care. Even though the government had allocated funds for COVID-19 testing and vaccination, the long-term post-COVID follow-up treatments are usually not covered in many countries [57,58]. In addition, the accessibility of care should be considered. People living in medically underserved areas, who include predominantly Black and minority ethnic groups, may have inadequate access to primary care. Yet vulnerable groups also have more comorbidities and hence a greater need for care [51].

The need for population health approaches has emerged and is increasingly obvious [59]. Without tackling inequalities, neither COVID-19 itself nor its long-term effects can begin to be addressed.

Longitudinal studies are needed to highlight the interaction of different morbidities and vulnerabilities on disabilities, quality of life and social inclusion [60,61].

In addition to the need to define and measure all sequelae better, we need to prevent COVID by addressing all of the inequities in the model below. This includes addressing inequity in access to specific COIVID related prevention, treatment and care, evaluating services, undertaking longitudinal research into the life course and quality of life impacts and developing teaching materials required to ensure that healthcare professionals, employers and public can recognize and respond appropriately - all in partnership with the communities at increased risk as well as people experiencing Long COVID and those who have living experience of other chronic multisystem disorders. Current systems for rehabilitation and support, such as in cardiac and pulmonary rehabilitation, will need to be reassessed, strengthened and adapted [62–64].

6. Mitigating risk of Long Covid

Dedicated policies should be put in place to mitigate the impact of Long COVID, providing tools to facilitate rehabilitation and long-term management of symptoms, for example, sickness absence from work or tailored educational programmes in schools. The UK NHS introduced long term COVID-19 related sickness absence and support programme for its directly-employed workforce [65]. In the American scenario, Long COVID can be a disability under the ADA, Section 504, and Section 1557 if it substantially limits one or more major life activities [66]. This kind of recognition helps the patient feel entitled to seek treatments and rehabilitation. Public health professionals and policymakers should promote the recognition of long COVID, as a proper diagnosis, and therefore promote dedicated healthcare services. As a chronic condition, Long COVID (and the patients) would benefit from a systematic approach and simplified process for recognising disability arising from new diagnoses as a protected characteristic under equalities and rights legislation.

The fragmented perspectives to addressing long COVID weaken the ability to manage all the different dimensions of the problem. While sustaining the efforts on strategies for the primary prevention of infection, because preventing SARS-CoV-2 infection appears to be the most effective way to prevent long COVID and its innumerable complications, mitigation measures are complex [22]. It is plausible that the fragmentary nature of the available data and the novelty of the subject are among the factors leading to the differences and difficulties in dealing with Long COVID in a harmonious and systematic manner. A greater emphasis on pan WHO European Region access to data could facilitate and promote the execution of large cohort and registry studies and understand the dimension of risk of negative health outcomes in the years after COVID-19 infection. To optimise case ascertainment, rapid access to diagnostic testing, clinical assessment and treatment for COVID and post COVID symptoms.

Another relevant aspect that should be considered is related to COVID-19 vaccination strategies, since vaccination has the potential to reduce the frequency and severity of Long COVID.

Vaccination appears to reduce levels of Long COVID but the impact across the diverse range of clinical features is not clear, particularly with the continuing emergence of new variants. Some studies suggest that vaccination might halve the risk of long COVID or have no effect at all [67].

Antonelli and colleagues found that the odds of having symptoms for 28 days or more of post-vaccination infection were approximately halved by having two vaccine doses [68]. This result suggests that the risk of Long COVID is reduced in individuals who have received double vaccination, when additionally considering the already documented reduced risk of infection overall [68]. Similarly, an Israeli cross-sectional study on more than three thousand patients showed that vaccination reduces the risk of Long COVID [69]. In addition, the UK Health Security Agency's review highlighted that fully vaccinated people were about half as likely as partially vaccinated or unvaccinated people to develop Long COVID symptoms lasting more than 28 days and that the vaccines' effectiveness against Long COVID symptoms was highest in people aged 60 years and over [70].

On the contrary, in another work, Taquet, Dercon and Harrison said that vaccination doesn't affect several features of Long COVID, while evaluating composite Long COVID outcome in the 6 months after infection. However, fully vaccinated participants were less likely to be diagnosed with anosmia, fatigue, hair loss, interstitial lung disease, myalgia, and other pain, than unvaccinated participants [71]. There is a need to clarify any such residual uncertainties, such as whether and which clusters of symptoms or pathological mechanisms are reduced by vaccination.

The literature is not conclusive on the topic, and more studies are needed to clarify the incidence of Long COVID in partially and fully vaccinated people and additionally whether vaccination protects people from Omicron-induced Long COVID. We also need to know about any impact of repeated infections in generating Long-COVID as more people experience recurrent episodes of Omicron on top of previous variants, and it emerged that Omicron-induced Long COVID cases are adding up [36]. Recent evidence in June 2022, suggests that the Omicron variant generates a smaller percentage of Long COVID cases than the Delta variant, and that vaccination is overall protective. However, we should remember that relative risk is only part of the public health analysis and that absolute risk to populations can be very high while there are minimal or absent prevention strategies in 2022 and beyond [72].

Some surveys have been conducted to explore the impact of vaccination on symptoms in Long COVID patients. In Strain and colleagues' work, 57.9% of participants reported improvements in symptoms following vaccination [73]. In addition, in Tran and colleagues' work, COVID-19 vaccination lowers the severity and life impact of Long COVID at 120 days among patients with persistent symptoms [74].

It could be considered that Long COVID affects a significant proportion of people with acute COVID disease, therefore, reducing the denominator (which is the number of people with acute disease) of the equation, through vaccination, will reduce the population at risk of Long COVID.

Lessons can be learned from other vaccine programmes such as with Measles [75,76] and Ebola [77], and how to reduce the health and other vaccine inequality burdens on populations [78,79].

Areas where there is less vaccination coverage, provide the substrate for the emergence and spread of variants. Therefore, the most vulnerable sections of the population are more exposed to disease and adverse outcomes, creating a vicious cycle, including repeated infections. In addition to vaccination, personal protection (non-pharmacological measures), ventilation and air filtration are pivotal in reducing the risk of infection. In this context, the recent policy of lifting the

facial masks requirement could have a negative impact on the most highly vulnerable people in our European populations, particularly in higher risk indoor settings [80].

The reopening of schools was crucial, but several questions remain unanswered, such as on educational ability. For example, children with Long COVID syndromes may perform worse at school, and the requirement to minimise new disability-related inequalities by providing help during tests and examinations such as for children with attention-deficit should be carefully considered. Beyond that, there are many related broad social policy issues of equitable access to education and work that can be explicitly addressed in legislation and guidance for human rights and systems supporting social wellbeing and inclusion.

7. *Conclusions*

Long COVID is likely a cluster of multisystem syndromes whose manifestations, while partially overlapping with the acute presentation, vary widely among patients and are exacerbated by pre-existing comorbidities and vulnerabilities. As a new cause of multi-organ pathology, it is likely to show similar inequities to many other illnesses, in risks of exposure, in illness severity and outcomes, as well as in access to prevention and treatment. As a new disease model its management should benefit from the wider knowledge base on the epidemiology of multi-system disorders and how to improve health for people with multi-morbidity and learn lessons from other previous rehabilitation services. The emergency dictated by COVID and the pandemic, has highlighted systemic criticalities in the structure for the management of people with complex needs, vulnerabilities, chronic conditions and multi-morbidities. Healthcare systems (and especially primary care) has emerged as fragmented and unable to support the additional burden posed by COVID. Therefore, the system should be reviewed by supporting standardisation and implementation policies, especially considering the significant proportion of people who suffer, or will suffer, from long-term effects of acute infection. Looking at this from a workforce's standpoint, a balance between protecting the health of workers and the interests of employers should be achieved. Because of Long COVID, it is possible that many workers wouldn't be able to resume their work due to health, and occupational medicine should facilitate this process and mitigate the pandemic fatigue.

Long COVID should be classified as a preventable condition, and we should set down a marker for the requirement for internationally agreed diagnostic coding of disease, treatments and inclusion in amenable mortality lists. There is a need for standardized diagnostic and evaluation criteria for different clusters, while remaining open to differences in etiology. Data is crucial. Interlinking of data and open access could be used effectively to track post-infection development and course, use of services, effectiveness of interventions. This is compounded by the increasing demand for national health surveys and cohort studies.

Because of the complexity of COVID-19 infection and Long COVID, efforts must be focused on engaging a broader and renewed collaboration among public health stakeholders. These should take a broad, multidisciplinary approach identifying particularly vulnerable groups. Health services must be improved in proportion to the rapidly growing need, including new specialized training programs, care pathways for citizens and patients, and training for physicians. Better use of resources is also needed to ensure equitable access and distribution of health care, at the global,

national, community, and individual levels, to address health inequities. In conclusion, cooperation, on a global scale, is essential to ensure equity at all levels, providing not only more care and assistance to people with Long COVID-related syndromes, but also to the inequalities that influence and amplify the effect of the disease, enhancing access to vaccination, variants control, and population health strategies. A coordinated long-term global response strategy to properly address the challenges of Long COVID would be the best option for Public Health interests [81].

The wide range of enduring syndromes, complications, sequelae and resultant conditions that occur after COVID-19 infections will impact more on those already disadvantaged, marginalised and with most pre-existing health conditions that have a socio-economic gradient. Rehabilitation and recovery resources will need to be deployed extensively and equitably to reach those most in need across this spectrum of morbidity and disability.

8. Key recommendations

1) Surveillance and tracking of all Long COVID cases, including data on their pre-existing health inequalities and clinical vulnerabilities should be promoted, with regular reporting through from local government to national levels and with sharing across countries.

2) Research into Long COVID should look at comparative incidence and prevalence across those already experiencing health inequalities and in various vulnerable groups or settings.

3) Cross-cutting policies to address the deeper issues related to inequalities should be implemented. This will need to include attention to occupational, housing, social care, educational and financial impacts on cases, those close to them and their disadvantaged communities.

4) Educational and support programs should be created for affected Long COVID patients, their carers and their wider communities, ensuring the sustainability of funding, effective interventions and evaluation over time.

5. We should work to increase the awareness of inequality, vulnerability and need for transparent equity in all interventional approaches, aimed at public health professionals, physicians and rehabilitation professionals, while also linking awareness-raising with those who live with and offer lay care for Long COVID patients.

6. Any uncertainty about role of vaccines in offering protection against Long COVID should be a major international research priority, particularly given that vaccine hesitancy and inequitable access to vaccines is evident in excluded groups.

7. There needs to be a special interest in child health regarding any Long COVID syndromes and other pandemic sequelae. This should be an area of epidemiological aetiological and interventional research, and also ensure evaluation of optimal outcomes for already disadvantaged and with anticipated associated poorer prospects for long term health status.

8. There are uncertainties about the eventual range of post COVID conditions, and an open and flexible model should be promoted that allows care and support to all who will need it, in whatever ways appropriate to the condition.

9. The primary prevention of Long COVID is an underlying pre-requisite by reducing exposure of populations, especially those unvaccinated, and if newer variants have worse sequelae. Those who assess the pandemic severity largely on the basis of severity of acute infections will underestimate the pandemic's severity and the appropriate intensity of any upcoming countermeasures. As we face a winter with fewer non-vaccine protections against respiratory viruses, we should consider those already disadvantaged and most vulnerable to Long COVID in setting strategic goals and plans.

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Appendix – table of Long Covid definitions

Nomenclature	Authoritative Sources	Diagnostic Features	Who is affected?	Key questions	Key References
Post covid-19 condition (Long covid)	WHO definition NIHR	>3 months, probable or confirmed infection, for 60 days	Add a comment on age distribution and gender	How different is this from other post-viral syndromes such as Chronic Fatigue Syndrome or ME?	**NIHR. A dynamic review of the evidence around ongoing Covid19 (often called Long Covid). 16.03.21 https://evidence.nihr.ac.uk/themed-review/living-with-covid19-second-review/**
Post-Intensive Care Syndrome (PICS)		PICS is defined as new or worsening impairment in physical (ICU-acquired neuromuscular weakness), cognitive (thinking and judgment), or mental health status arising after critical illness and persisting beyond	ICU patients	Is this specific to COVID-19 or how far related to generic issues from lengthy periods in ICU or other critical care and respiratory support?	https://doi.org/10.1164/rccm.202010-3823LE

		discharge from the acute care setting			
Multisystem inflammatory syndrome in children (MIS-C) associated with COVID-19		It shares clinical features with Kawasaki disease (KD), KD shock, and toxic shock syndrome. Clinical features include persistent fever, severe illness with involvement of multiple organ systems, and elevated inflammatory markers	Seen up to age – what is the range??	Can we define new features not seen with other infections?	
Post-Covid-19 neurological syndrome (PCNS)	?	Loss of taste and smell, cephalgia, dizziness, neuropsychiatric disorders, ischaemic stroke, encephalitis	Age and gender distribution comment		
Long Covid	GCMSC definition	Persistence of symptoms (present or not at the onset of the			

		infection) after 1 month of infection			
COVID-19 Sequelae	GCMSC definition	Irreversible tissue damage continuing after 12 weeks that could trigger different degrees of permanent dysfunction and associated symptomatology.			
Post-Acute COVID syndrome (PACS)	GCMSC definition	Long covid + sequelae		Distinguishing between PACS symptoms e.g. (cardiac symptoms) and PACS (cardiac) conditions?	
Persistent post-covid		>24 weeks			
Post COVID exacerbations of particular chronic		COPD and lung volume deterioration after acute	Patients with COPD before COVID-19 infection	What forms of pulmonary and wider rehabilitation	https://doi.org/10.1016/j.eclinm.2021.100789 https://doi.org/10.1016/j.arrct.2022.100185

conditions (examples)		infection recovery		or support are needed?	
		Heart Failure deterioration after acute infection recovery	Patients with heart failure before COVID-19 infection	What forms of cardiac and wider rehabilitation or support are needed?	https://www.internationaljournalofcardiology.com/article/S0167-5273(21)02045-3/fulltext#relatedArticles