

Long Covid

Learning over the last year from those with lingering symptoms

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Introduction

The emergence of a novel Coronavirus from Wuhan China in late 2019, has had dramatic and unimaginable effects on health, economy, education and the way we interact. The rapid spread of this virus had led to the World Health Organisation declaring a pandemic in March 2020. The number of people affected thus far has been beyond comprehension with current estimates at 191 million reported cases globally. So far to date in the UK there have been 5.52 million known cases, of which 129,000 have died.

Acute Covid infection is now well recognised by both medical professionals and the wider population, yet beyond the official features of new or persistent cough, fever, and change in smell or taste, clinicians have been aware of asymptomatic sufferers and through the SPECTOR study a range of other less common symptoms such as diarrhoea, headaches and other vague and non-specific symptoms which may raise suspicion of acute infection.

Findings from the REACT-2 study estimate that over 2 million people however are suffering with prolonged symptoms beyond their acute illness. In the first and second waves, these were poorly defined, with patients seeking answers to their persisting, enduring and disabling symptoms which lingered for weeks after they had initially contracted Covid. Very little was known about the natural history of the disease now commonly referred to as Long covid. With upto 30% of positive cases still symptomatic after 3 weeks in the UK, this will undoubtedly place a tremendous strain on health and social care.

This essay aims to share awareness into definitions, patterns of illness, aetiologies, knowledge of red flags and clinical considerations, recovery and rehabilitation.

Personal Stories

Large numbers of health care workers have been adversely affected by COVID-19 infection, many acquiring it whilst working with limited awareness of infectivity, testing and PPE particularly in the first wave.

As case numbers started to rise, there was little awareness that sequelae may persist beyond the public health messages of self limiting illness. Social Media enabled a growing voice of unheard stories during the first wave. "Long haul" Support groups on facebook, #longcovid started to trend on twitter, and sufferers started to compare symptoms, seek answers and collaborate on Education. Both authors found the support particularly from the Long Covid Doctor's Facebook group to be an eye opener, and have since collaborated on numerous projects, publications, and engaged as patient participants with ongoing research into Long Covid. One of their key aims to to spread and educate colleagues across the world on the effects of Long Covid, and have worked in collaboration with various local and international organisations including Mount Sinai Hospital in New York.

A personal story

I acquired Covid 19 in the first wave of the pandemic in April, working as a GP. Little was known about the severity or spread at the time. Testing was hard to come by, if non existent, and in my health care setting we were screening only for people returning from South East Asia as being high risk. Government and public health policy on social distancing, masks and isolation were in early stages, and of course there were PPE shortages. But more importantly there was little foresight about the possible impact and effects of this virus on our health and world.

My initial symptoms of dry cough and myalgia, flu like symptoms were mild and un concerning. Similar to the transient viral infections that most Health professionals encounter during winter months, yet do not prevent them from working. However as time progressed fatigue and breathlessness started to develop. I noted a resting tachycardia, which was unusual as I was previously fit. Luckily around week 3, a handful of tests were offered to health care professionals in the local area. Following an initially inconclusive result (lost or inadequate sample) a retest at day 25 came back positive.

The guidance was that covid was a self limiting mild illness, which may affect those with pre-existing conditions, frail or immuno-suppressed, and may last for 2-3 weeks. However as the days passed by, I realised I was feeling worse rather than better.

Access to health care was changing, and face to face assessment by a clinician was hard to come by, and in the early days of primary care adopting telephone assessment, shared understanding and perception of the virus amongst clinicians was variable. After several un reassuring encounters with primary care, I presented to hospital acutely short of breath at week 6.

Some of the complications that were being reported including delayed thromboemboli, fibrosis and myocarditis were excluded.

Whilst this was reassuring, I was discharged without answers for my ongoing symptoms. I sought subsequent private opinions, albeit virtually, and after further reassuring tests including a HRCT scan I was informed this may just take time and rehabilitation. Over the last year, I have made significant improvements with enduring symptoms of fatigue, dysphonia, tachycardia, and shortness of breath; but the memories of traumatic and fearful experiences are still raw.

Like many others with persisting symptoms, I have lived with the uncertainty of not knowing when this will get better, the disappointment of having to fight for investigation, reassurance, and exploration of symptoms, and struggled to get rehabilitation to assist with recovery due to restrictions in services. I found help through various long covid groups online. In particular a Doctor's group with over 1200 members of the medical profession, from this we have shared personal anecdotes and gained an understanding of the condition and how it presents differently and also to support colleagues who have received

little understanding from colleagues in the same profession. Another real positive to come out of the groups is that patient stories are extremely powerful, and have stimulated questions about aetiologies and treatments for sequelae, which have prompted independent research and collaboration.

Definitions

In the initial waves of the pandemic, a lack of accessibility, reliability and availability of mass testing had meant that many patients with Acute Covid infection did not have a documented test. **Therefore reported symptoms consistent with previous Acute Covid infection and associated ongoing symptoms is enough to consider a diagnosis of long covid once other conditions have been excluded, even in the absence of a positive PCR test.**

Finally in January 2021, NICE established definitions of syndromes after acute COVID infection. Long covid is defined as “Signs and symptoms that continue or develop after acute COVID and persisting for 12 weeks or more.”

This definition was vital, because it is now estimated that 10-30% of people having acquired Acute Covid continue with persisting symptoms. Using the correct codes in clinical symptoms will prompt appropriate referral, follow up and care navigation for patients.

Acute COVID	Signs and symptoms of COVID-19 for <4w. <i>SNOWMED CT code: Acute COVID-19 infection</i>	Most symptoms Resolving in the first 12w after infection	Life- threatening complications may develop at any time: if suspected, investigate urgently.
Long COVID	Ongoing symptomatic COVID-19: signs and symptoms of COVID-19 from 4–12w. <i>SNOWMED CT code: Ongoing symptomatic COVID-19</i>		
	Post-COVID-19 syndrome: signs and symptoms that developed during/ after an infection consistent with COVID-19 that persist for >12w and are not explained by an alternative diagnosis: <ul style="list-style-type: none">● Presents with clusters of symptoms that can affect any system in the body. Symptoms can fluctuate and change with time.● Can be considered before 12w while investigating for an alternative cause for symptoms. <i>SNOWMED CT code: Post COVID-19 syndrome</i>	A minority of patients will have symptoms that persist >12w.	

It can be argued that it be more appropriate to use the terminology Post Acute Covid Syndrome or PACS, to recognise that the disease as a continuum following initial infection and that symptoms are enduring, whilst we do not fully recognise the condition. This terminology has certainly been adopted by several long covid services.

Epidemiology

Whilst numbers reported remain uncertain, due to variations in coding, linging, reporting and recording of symptoms, current estimates are in excess of 2 million. Prior to data from NHS coded records, much early data regarding Long Covid was derived from patient self reporting apps such as The Covid Symptom Study app. Whilst there was some differences in age and gender make up compared to the standard UK population, it was initially extrapolated that 1 in 7 people would be unwell for at least 4 weeks, 1 in 20 for 8 weeks, and one in 45 for 12 weeks or more. As the virus has mutated different populations seem to be affected, data from the ongoing

REACT study of over 500,000 positive patients has shown that 6% of patient at least 1 ongoing troublesome symptom past 12 weeks, and 2% have 3 or more symptoms.

Whilst it is recognised that hospitalisation, particularly with intensive care input lends itself to developing longer term physical, psychological symptoms and impact on function. Long covid seems to be prevalent in large numbers of non-hospitalised patients too, and further research is needed to understand this.

The pandemic has highlighted many health inequalities that exist within our society and Long Covid too is reflective of this. Preliminary data from Imperial college which feeds into the ONS, and is due to be published soon shows that the prevalence of persistent symptoms are 1.5 times more prevalent in women than men, and that the risk of persistent symptoms increase with each decade or life. Other indicators which are associated with probability of persistent symptoms were obesity, smoking, and deprivation. This study interestingly reports Asian ethnicity being associated with a lower probability.

However, anecdotally, as there is a disproportionate percentage of healthcare workers of Ethnic minority background compared to the population at a large, there are many colleagues from minority groups affected by disabling symptoms of COVID. As with other health indicators, I suspect that there is a large degree of under-reporting of long covid symptoms in ethnic minority communities. There is currently a research study being planned to consider the experiences of patients from these groups, and that they may be under reporting due to a variety of factors including stigma, discrimination, access to alternative care for symptoms, and variation in understanding of the disease.

Furthermore, whilst the vaccination programme is making tremendous progress in the UK, and despite mutations currently we are seeing both an encouraging decline in cases and deaths, there remains the question about whether vaccination will protect against the future development of long covid.

Symptoms

The complexity of the Covid pandemic, has meant that patients present to healthcare at different stages of their illnesses. It has been noted, that whilst some symptoms may develop shortly after acute illness, many have reported relapses of variable intensity of symptoms occurring sporadically several weeks or months later.

The aetiology is unknown, but likely to be multifactorial. There are theories regarding persistent viral load, reinfection or reactivation of dormant virus, effects on mitochondria leading to deconditioning, or whether there are immune mediated or ongoing inflammatory reactions. Infact patients who have been infected by other coronaviruses, such as during the SARS and MERS pandemics previously have also reported persistent respiratory, pain, and neuropsychiatric symptoms.

Whilst we do not fully understand the condition, it is imperative to consider the possibility of pathologies, distinct and unrelated to Covid-19 infection that may coincidentally develop in individuals including vascular events, autoimmune phenomena, and malignancies. Therefore it is vital that clinicians are not biased either positively or negatively by a history of acute Covid infection, and maintain curiosity

in their patient's stories and evaluate symptoms based on merit. Especially as the natural incidence of other diseases will only increase in coming months due to delayed presentations resulting from lockdown.

Although COVID-19 was primarily introduced as a respiratory tract infection. It has been found to damage the vascular endothelium of multiple other organs, notably the heart, brain, and kidneys, resulting in a multisystem disorder.

Look out for red flag symptoms, such as those found in transient ischaemic attack, stroke, pulmonary embolism, ischaemia, tachyarrhythmia, and myocarditis; cases of all of these have been seen post-COVID. Patients who sound or look very sick may need immediate medical help.

Assess the patient as you normally would, and consider referral to the usual acute specialties if suspicion is raised.

Red Flags
Severe or Worsening Shortness of Breath
New low pulse oximetry saturations <94% at rest or desaturation on exercise
Unexplained Chest pain
Severe dizziness or syncope
Palpitations or tachycardia at rest or minimal exertion
New neurological symptoms such as confusion, dysphasia, weakness
Severe psychiatric symptoms / suicidal ideation
Multisystem inflammatory syndrome in Children

Primary care follow up is important, and several appointments may be required to understand and investigate multiple symptoms. The patient perspective is vital here and it is important for clinicians to keep an open mind and think about possibilities of illness. This is still a new disease and until we understand the effects the virus has on multiple organs, and develop a sustainable evidence base it is important not to dismiss symptoms.

Lingering enduring symptoms deserve evaluation in the same manner that would be done pre-pandemic, with known empirical symptomatic

treatment potentially helpful, investigation and speciality referral as appropriate. Many patients may have delayed presentation due to lack of awareness of long covid, fear of health care settings, changes to access, and fear of dismissal. Although this was initially anecdotal, there is now a growing evidence base of possibility of significant pathology in patients with long covid.

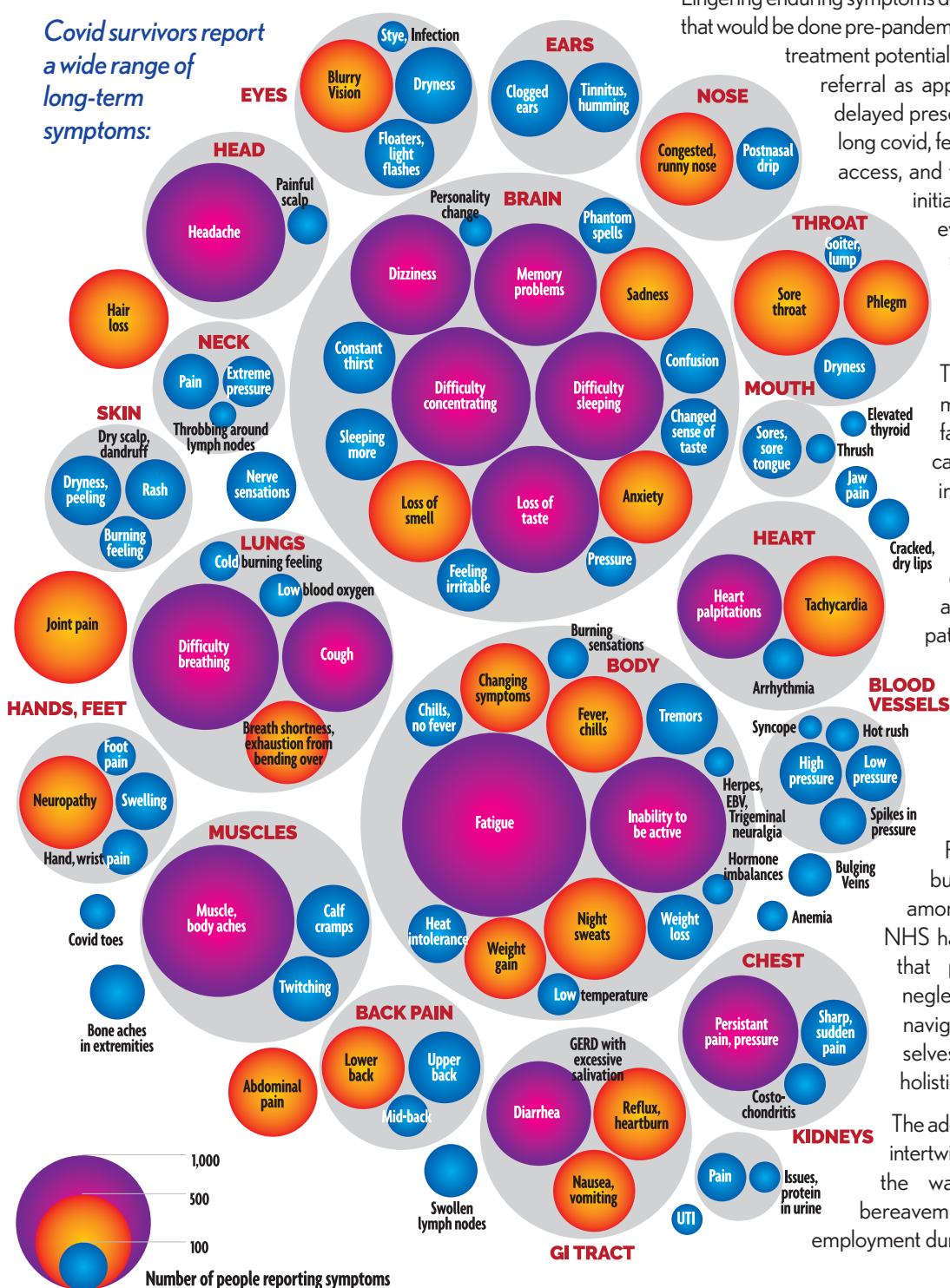
Psychological effects.

There is an unfortunate paradigm in medicine that we as clinicians can all fall into. "If the test is negative, and we can not explain the symptoms, it must be in the patient's head?" It is well recognised that new chronic illness, lack of continuity of care, and clinician confidence can all lead to uncertainty and affect psychological well being of patients, leading to stress and anxiety. Many long covid sufferers have not had access to the reassurances they deserve due to changes in access, resources and limited knowledge base surrounding their condition thus far.

Further factors such as Stress, burnout, and awareness of long covid amongst clinicians when demand on the NHS has been unprecedented has meant that patients have felt unheard and neglected this far, and many have had to navigate access to care pathways themselves, even exploring alternative and holistic therapies, or private opinions.

The added complexity of physical symptoms intertwined with traumatic experiences along the way related to access to care, bereavement and loss of loved ones or employment during the pandemic. Social challenges

Covid survivors report a wide range of long-term symptoms:



imposed by national lockdown, isolation, and reduced contact with support networks and hence coping mechanisms, have also created an entangled web of stories compounding the symptoms in many long covid patients. It is therefore natural and expected there will be a spectrum of psychological stresses that co-exist in patients suffering longer term unexplained illnesses, varying from stress, anxiety, depression and PTSD. It is therefore vital that patients have access to and are signposted to support services, yet pertinantly physical symptoms must not be dismissed until adequately explored as patients have been extremely vulnerable over the last year, and telling their stories requires a lot of courage.

Long-Covid clinics

The emergence of 69 long covid clinics being set up nationally is welcome news. The complexity of long covid means that primary care will struggle to manage problems in limited time frames available in each GP consultation, and although follow up is always an option. Secondary care clinics are often organ specific, and due to the multi-symptom presentations of long covid patients requires a holistic view. So the concept of a one stop clinic to investigate, treat and rehabilitate patients is much needed. However many patients and even clinicians do not know of their existence or roles in their localities, and there is

high levels of regional variation in what each clinic provides. Funding streams are also very tight, so the ideal service in an already stretched NHS dealing with repeated waves of acute infections is limited in what it can offer.

Many operate on a tiered structure with self care resources available to all. Referrals are made from primary care initially, and are triaged, and initial appointments may vary from being remote or face to face. Tools such as the Yorkshire Assessment Tool have been developed and used to screen for problems. Clinics may be GP led, yet have advice and guidance pathways with access to diagnostics and specialists, but models locally vary. There is often also Multi-Disciplinary Team involvement with IAPT psychologists, physiotherapists, Occupational Therapists, Speech and Language therapists, and often respiratory and chronic fatigue team involvement to help rehabilitate.

Prior to referral basic blood tests including FBC, U&E, LFT, CRP, TFT, hba1c and vitamin D level are often required. A BNP to screen for heart failure, and a chest x-ray by 12 weeks should also be performed. Although a negative D-Dimer and Troponin are useful to exclude the presence of acute cardio-respiratory illnesses, if they are being considered the patient should really be assessed in hospital and not primary care, and admission indicated. Oxygen saturations, pulse and a baseline ECG are often helpful, and if possible a 1 minute sit to stand test to check for desaturations on exertion may help to inform acute referral rather than long covid clinic referral.

Symptom Clusters / Conditions to consider	
Fatigue and Post Exertional Malaise	<p>This is very common, fatigue should be considered a symptom of an underlying problem. Consider screening for the usual culprits of fatigue including thyroid function, vitamin deficiencies, adrenal insufficiency, anaemia, insomnia and mental health problems. Ensure other systemic red flags are considered including weight loss, sweats, lymphadenopathy. It may also occur as part of myocarditis or MCAS. So keep an open mind and exclude other pathologies first.</p> <p>Post exertional malaise is commonly reported and poorly understood, and may be immediate or delayed. Recommending Activity Pacing rather than Graded Exercise Therapy is now thought to be a key part of long covid management.</p>
Neuro-cognitive	<p>A range of psychiatric symptoms are reported. Insomnia is common, multifactorial and can be incredibly disabling. Behaviour modification is key. CBT is evidence based and effective, and available on the NHS through Sleepstation. Additionally disruption of normal routines due to the pandemic can impact on circadian rhythm, suggesting a role for melatonin if pharmacotherapy is being considered.</p> <p>Brain-fog, confusion, and forgetfulness have all been commonly documented amongst sufferers. Heightened sensitivity towards auditory, olfactory and visual stimuli have also been distressing. Whilst neurocognitive assessment maybe hard to come by, online programmes and apps which have been used with other traumatic and degenerative brain conditions, are in development to provide opportunities for neurocognitive rehabilitation for patients to use at home and will hopefully be available through long covid clinics.</p>
Cardio-respiratory and Thrombo-embolic	<p>There is growing evidence of endothelial involvement post Acute Covid, and there have been numerous cases of venous thromboemboli post Acute covid, so consider this in patients presenting with pleuritic pain, acute shortness of breath, swollen legs, or acute neurological symptoms suggestive of embolic stroke. Investigate or refer acutely as appropriate.</p> <p>Cardiac manifestations such as myo/pericarditis can have viral based aetiologies and there have been cases post covid too. Persistent tachycardia is common and although may be due to deconditioning, it should be investigated in normal ways to exclude abnormalities.</p> <p>Consider the possibility of delayed pulmonary emboli or fibrosis in those with persistent breathlessness. Although asthma and dysfunctional breathing and hyperventilation, have been reported.</p>
Auto-immune / Endocrine	<p>Endocrine organs have ACE receptors, consider pituitary, thyroid, pancreas, adrenals. Diabetes mellitus and thyroiditis have been reported, so consider screening as appropriate.</p>
Mast Cell Activation Syndrome (MCAS)	<p>Patients will typically present with a constellation of recurrent seemingly unrelated symptoms. These may be:</p> <ol style="list-style-type: none"> cutaneous and systemic (urticaria, angioedema, flushing, tachycardia, dyspnoea. gastrointestinal - abdominal cramps, diarrhoea, nausea and vomiting oculonasal - congestion, nasal discharge, itchy and watery eyes, polyuria, cognitive dysfunction and anaphylaxis have also been seen. <p>Consider antihistamines / H2 receptor antagonists / montelukast, and referral to an immunologist</p>
Dysautonomia	<p>The two most common presentations are Postural Orthostatic Tachycardia Syndrome (POTS), symptoms include palpitations, syncope, chest pain, tremor and sweating on standing up; and Inappropriate Sinus Tachycardia. It is important to exclude red flag emergencies first, and then consider an active stand test, ECG, 24 hour BP and heart rate monitoring and an echo. Management strategies currently include increase salt and water intake, avoidance of caffeine and alcohol, compression garments, and referral to cardiology. Cardio-selective betablockers or ivabradine may be considered and have been shown to be effective.</p>

A GP colleague who works in a long covid clinic reflected on her experience so far and is finding the service is being pushed to the limits, "We do not have the exact data yet, but the majority of patients that have had covid in the community require a medical review. The most common symptoms I see are shortness of breath, chest pain and tachycardia, fatigue, headaches, ongoing smell, taste, voice disorders and brain fog. Many patients are quite significantly sob with chest pain and I always have to try and assess if they are desaturating. If very unwell I either send them to ED or ambulatory care or fast track them to the respiratory Covid recovery clinic in hospital. They are reviewed face to face, have lung function tests and a CTPA. I can also request an urgent CTPA.

We are in the process of trying to set up a secondary care MDT and possible one stop clinic.

All of the patients who are breathless are referred to pulmonary rehab which they find very helpful.

I also refer many to the chronic fatigue team but we can only do this once medical problems have been ruled out."

The pandemic has upset the balance of the usual waiting times for essential investigations and even impacted on urgent clinic reviews. The inadequacies of care coordination between agencies, the risks assumed by existing pathways and limits to NHS resources have been exposed, with patients are waiting unacceptable periods of time for simple investigations such as 24 hour tapes and Echocardiograms. Even urgent referrals to specialities face unacceptable delays, and this will no doubt impact significantly on outcomes for patients with potential for delayed and missed diagnosis and poorer health outcomes, not to mention delayed return to function impacting on both employment and functionality.

Summary

Consider that the sequelae after acute covid infection can be multi-system, fluctuate and last for prolonged periods. The medical profession is only just beginning to describe cases, so evidence for any interventions are still limited and usually based on expert consensus or anecdote. It is therefore vital that we focus on the possibility of illness rather than probability in initial stages, and symptoms are screened for and diagnostic nets cast wide in patients who remain symptomatic. Long covid will leave an impact on the NHS for years to come, and there is an opportunity to support your patients through the unknown with compassion and courage so they may have access to appropriate health care.

Other Resources

www.yourcovidrecovery.nhs.uk

Adult Cardiorespiratory Enhanced and Responsive Service, Homerton University Hospital NHS Foundation Trust. Post COVID-19 patient information pack

Hertfordshire Community NHS Trust. Information pack for patients who have had COVID-19 or COVID-19 symptoms

Royal College of Occupational Therapists. How to conserve your energy— practical advice for people during and after having COVID-19

Chartered Society of Physiotherapy. COVID-19: the road to recovery activity planner

Mental Health Foundation. How to look after your mental health during the coronavirus outbreak

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