

# COVID-19

## Long COVID

Final Version, Sept 2021

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### CDI Clinical Practice Guidance Document Cover Sheet

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\* Refer to [HSE National Framework for developing Policies, Procedures, Protocols and Guidelines \(PPPGs\)](#)

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# 1. What is long COVID?

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the pathogen responsible for the COVID-19 pandemic which has caused unprecedented global morbidity and mortality. To date there have been over 160 million recorded cases worldwide and 3.3 million recorded deaths. It is generally cited that most people recover from 'mild' infections within 2 weeks and more serious disease within three weeks.

It is now recognised that persistent and prolonged symptoms can occur after acute COVID-19 infection. This is not unexpected as long term respiratory, musculoskeletal, and neuropsychiatric sequelae have been described for other coronaviruses (SARS and MERS).

While there have been many case reports of the most severe forms of COVID-19, the majority of the population does not develop symptoms severe enough to require hospitalisation. It is known that there is a spectrum of initial response to infection, ranging from asymptomatic individuals and those with only a few minor symptoms who stay home, to those who are hospitalised and those that die from illness. For many people throughout this spectrum, the symptoms linger, and new symptoms may arise well after the initial onset.

Scientific and clinical evidence is evolving on the subacute and long-term effects of COVID-19. An increasing number of reports and studies are now being published on the topic, however, at present there is no agreement on the definition or the terminology. The [NICE guideline scope](#) published on 30 October 2020 defines post-COVID syndrome as signs and symptoms that develop during or following an infection consistent with COVID-19 which continue for more than 12 weeks and are not explained by an alternative diagnosis. The definition says the condition usually presents with clusters of symptoms, often overlapping, which may change over time and can affect any system within the body.

## Timeline of Post-Acute vs Long-COVID

Persistent and prolonged symptoms after acute infection are referred to as Long COVID, post-acute COVID, ongoing symptomatic COVID-19, post COVID-19 syndrome, Long Haul COVID, ongoing COVID, chronic COVID or living with COVID.

For the purpose of this proposal, we defined post-acute COVID-19 as having ongoing symptoms that persist from 4 to 12 weeks after acute infection and Long COVID as symptoms beyond 12 weeks and not attributable to alternative diagnosis.

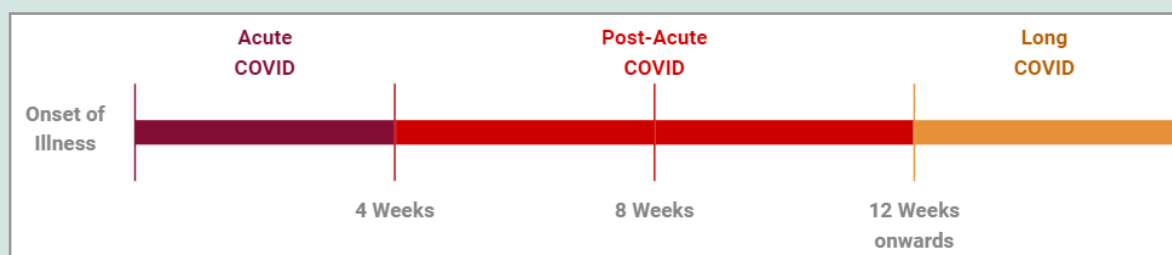


Figure 1. Timeline from onset of COVID-19 illness.

As a novel condition, the COVID-19 pandemic has presented the health service with a unique challenge in regard to the appropriate follow-up of affected patients. Among the anticipated complications of COVID-19 infection include long-term respiratory impairment and post-ICU complications such as neuromuscular dysfunction, psychological dysfunction, and cognitive impairment. In addition, there are patients which did not require hospitalisation that may go on to develop Long COVID symptoms and require intervention and management.

### Symptoms of Long COVID

People with long COVID report experiencing different combinations of the following symptoms. These effects can overlap with multiorgan complications, or with effects of treatment or hospitalization:

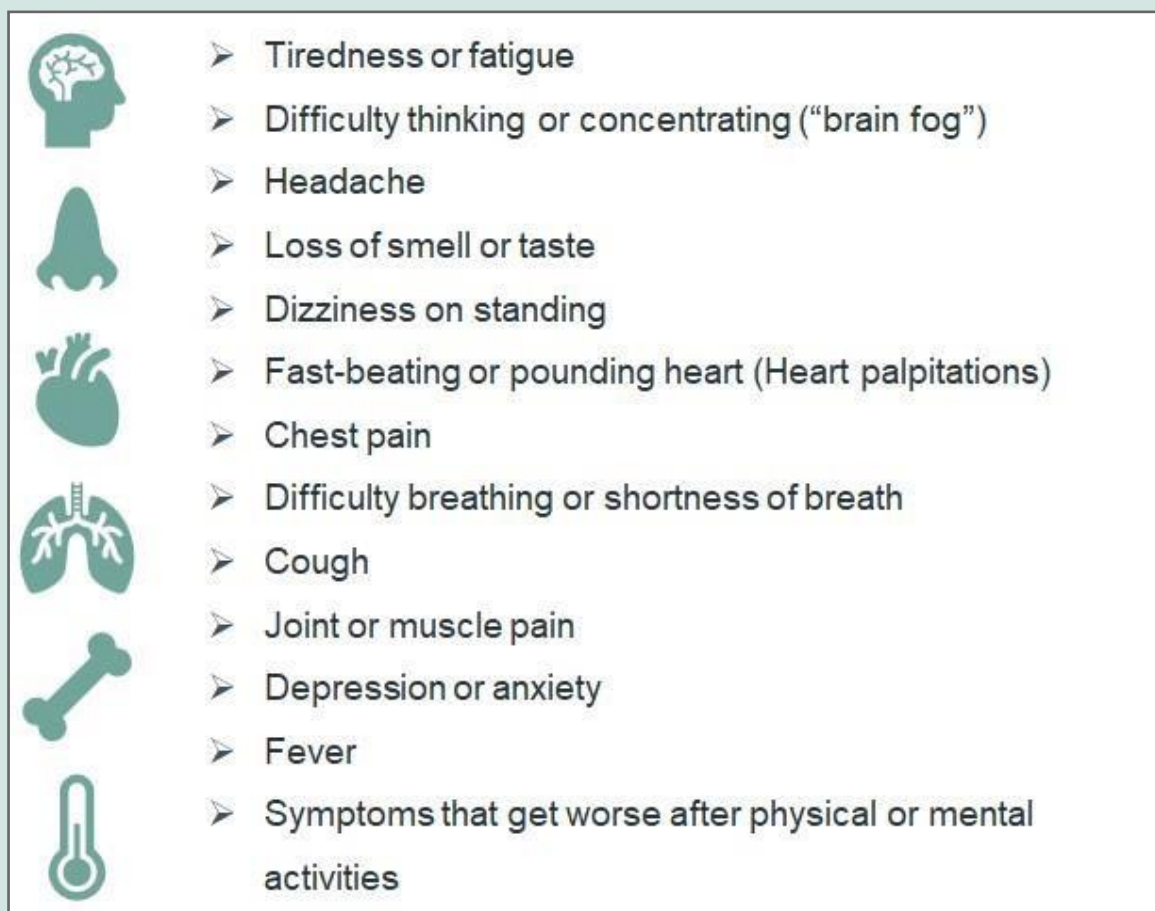


Figure 2. Wide range of long COVID symptoms. Non-exhaustive list.

Risk factors for Long COVID include:

- Older people (UK study found that long COVID affects around 10% of 18-49 year olds who get COVID-19, increasing to 22% of people >70)
- Women
- Presence of organ comorbidities (pre-existing respiratory disease, obesity, DM, HTN, chronic cardiovascular disease, CKD, post-organ transplant or active cancer)
- Those who had five or more symptoms in the first week of becoming ill
- Severe illness during acute COVID-19 and/or requirement for care in an ICU

## 2. Summary of studies to date

### Large variance for results of various Long COVID studies

There is currently a paucity of published research studies on Long COVID. Estimates of the prevalence of Long COVID vary widely (range 10% to 87.5%). The majority of studies have looked at the prevalence in patients discharged from hospital and the sample sizes in most studies are small. Comparison between studies is difficult due to different follow up periods, variation in the range of symptoms that are considered to be due to Long COVID and different measurement criteria. This lack of consistency around the definition and measurement of Long COVID makes it difficult to synthesise all the different emerging results.

- The WHO estimate that 10% of people who contract the virus develop Long COVID
- The UK Office of National Statistics estimate that 20% of people will still have symptoms 5 weeks post infection
- The UK COVID symptom study app found that around one in 20 had symptoms at 8 weeks and one in fifty had symptoms persisting for longer than 12 weeks.

(For a detailed summary of the various studies please refer to the appendix)

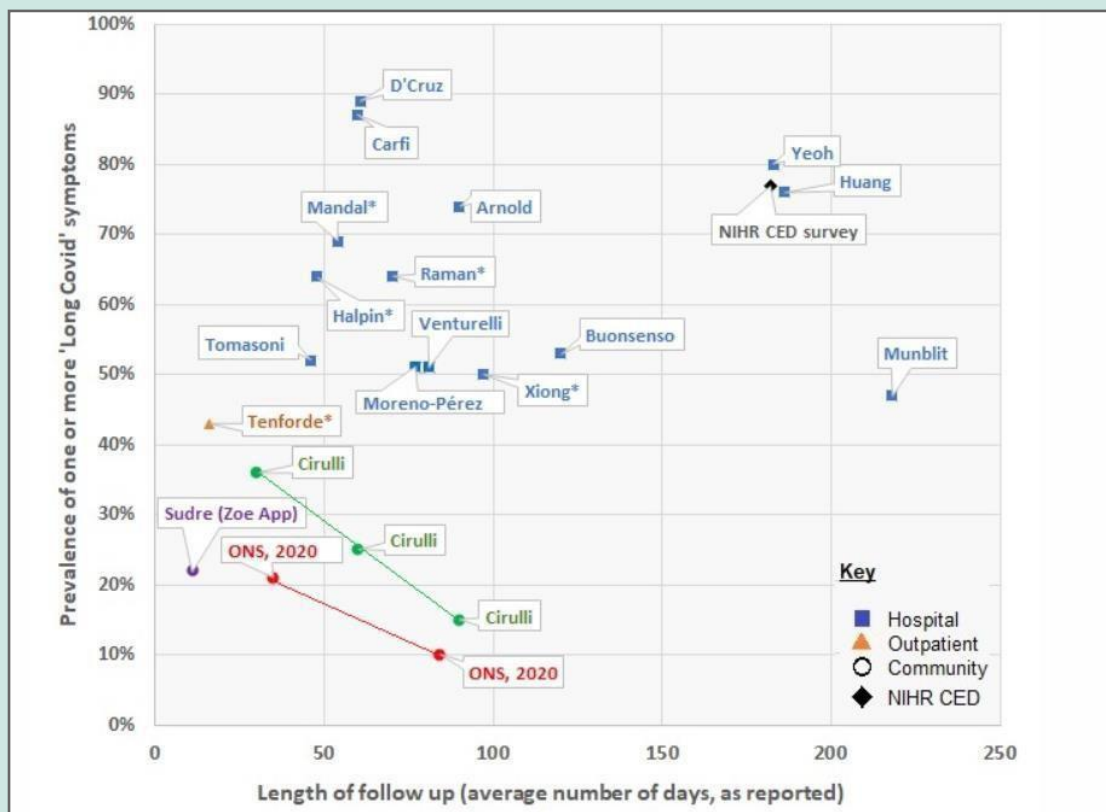


Figure 3. Prevalence of symptoms vs length of follow up for the various studies.

### 3. The 7 Principles for establishment of a Long COVID service

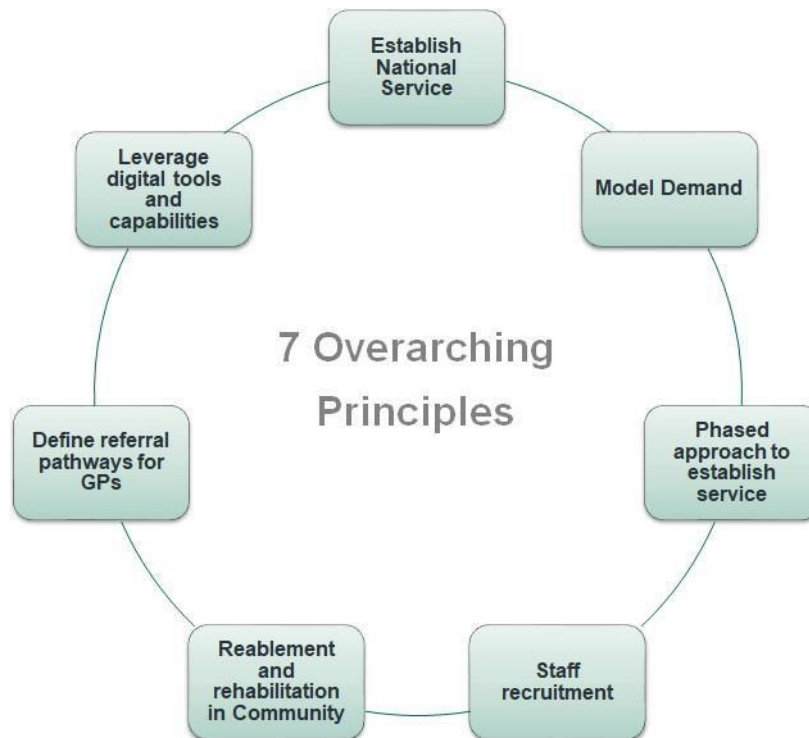


Figure 4. 7 Overarching principles for Long-COVID service

1. We **need to rapidly establish a national service** for those that require specialist follow up post COVID (<12 weeks) and patients that develop Long COVID (>12 weeks)
2. **Estimating the population need is challenging** however in order to direct resources to meet demand we need to model demand based on current best available knowledge, case incidence of COVID-19 and geographic need. This will have to be a dynamic process which adapts as we learn more from national and international research and practice
3. A **phased approach is needed in order to establish service** in the short term we need to leverage existing and additional capacity which is currently being recruited through the Winter and Pandemic plan, there needs to be an ongoing review of needs
4. Recruiting new staff will be required however this can be challenging and **will take a considerable amount of time**
5. In line with Slaintecare, we need to **ensure that as much reablement and rehabilitation care as possible is delivered in the community** as close to people's homes as possible and ensure that only cases requiring specialist input are referred to the hospital and those cases where possible are transferred back to the community as soon as it is feasible
6. **Referral pathways for GPs** need to be clearly defined
7. We **need to leverage digital tools and capabilities** in order to educate and empower as many patients as possible to lead and manage their own self care recovery and

rehabilitation plan.

## 4. Estimates of need (Description of methodology)

### 4.1 Estimates of need at a national level

To determine the estimated need for long COVID services a projection model was developed based on historical cases by setting and deaths to date.

The following limitations to the model need to be noted:

- The long term course of COVID-19 is unknown.
- The estimated prevalence is based on the current best available evidence and will need to be updated as our knowledge and understanding of the disease advances.
- In addition, there may be additional patients who, because of testing capacity and criteria, may have had COVID-19 illness but not had a positive PCR test.

#### Steps taken for Model

The following steps and assumptions were made in the process of creating this model:

**Step 1:** Calculate the number of cases by setting (ICU, Ward and Community) by month

**Step 2:** Subtract the number of deaths from the cases by setting by month

**Step 3:** Determine drop in symptomatic cases each month based on current studies. (E.g from a recent UK study it was estimated that 13.7% of community cases of COVID are still experiencing symptoms 12 weeks after onset of illness, see appendix for breakdown of %)

**Step 4:** Apply drops in symptomatic cases across each month of confirmed cases

	Onset	Month 1	Month 2	Month 3	Month 4	Month 5	Month 6	Month 7	Month 8	Month 9	Month 10	Month 11	Month 12
ICU	0%	100.00%	80.00%	60.00%	41.67%	23.33%	5.00%	4.17%	3.34%	2.51%	1.67%	0.84%	0.01%
Ward	0%	70.00%	47.50%	25.00%	17.50%	10.00%	2.50%	2.09%	1.67%	1.26%	0.84%	0.43%	0.01%
Community	0%	25.00%	19.35%	13.70%	9.47%	5.23%	1.00%	0.84%	0.67%	0.51%	0.34%	0.18%	0.01%

Figure 5. Breakdown of drop in people experiencing symptoms after infection

- Note:
1. Percentages in blue represent figures from various studies
  2. Figures in between blue columns were calculated by applying a constant drop between study figures
  3. Assumed that there will be very few people with symptoms 1 year after onset of illness
  4. We exclude people who are experiencing acute symptoms (<4 weeks from onset)

	ICU	Ward	Community
Post-acute symptoms	108	728	6,016
Long-COVID symptoms	207	1,297	13,428

Figure 6. Summary Table of projection model: Estimated figures for month of May 2021

The following graphs shows a historical breakdown of people experiencing Post-acute and Long-COVID symptoms

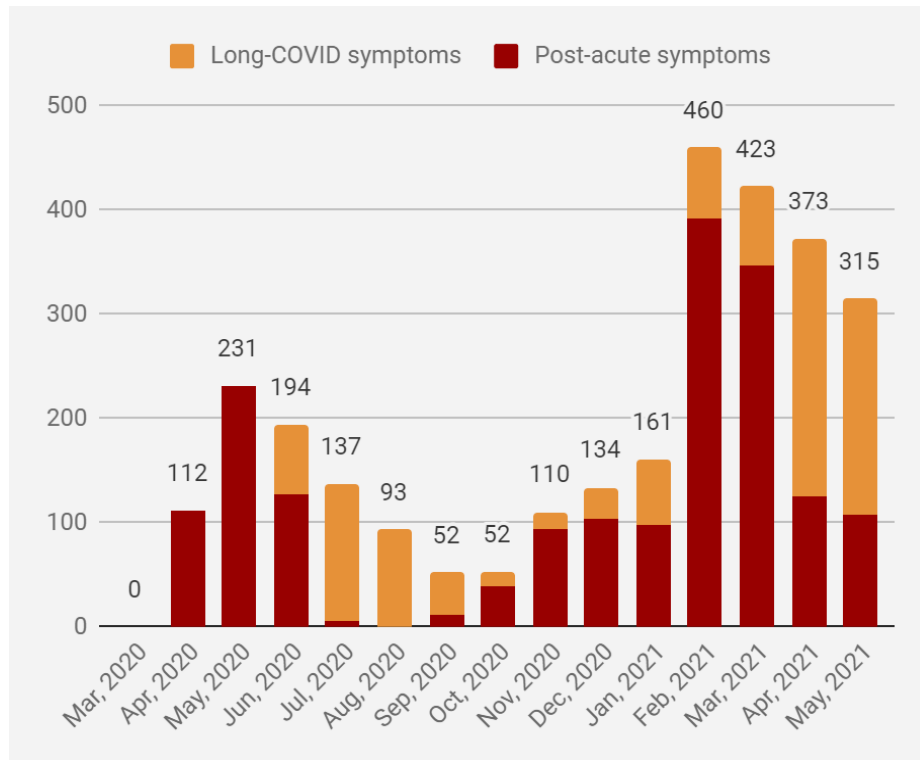


Figure 7. ICU Patients with post-acute and long-COVID

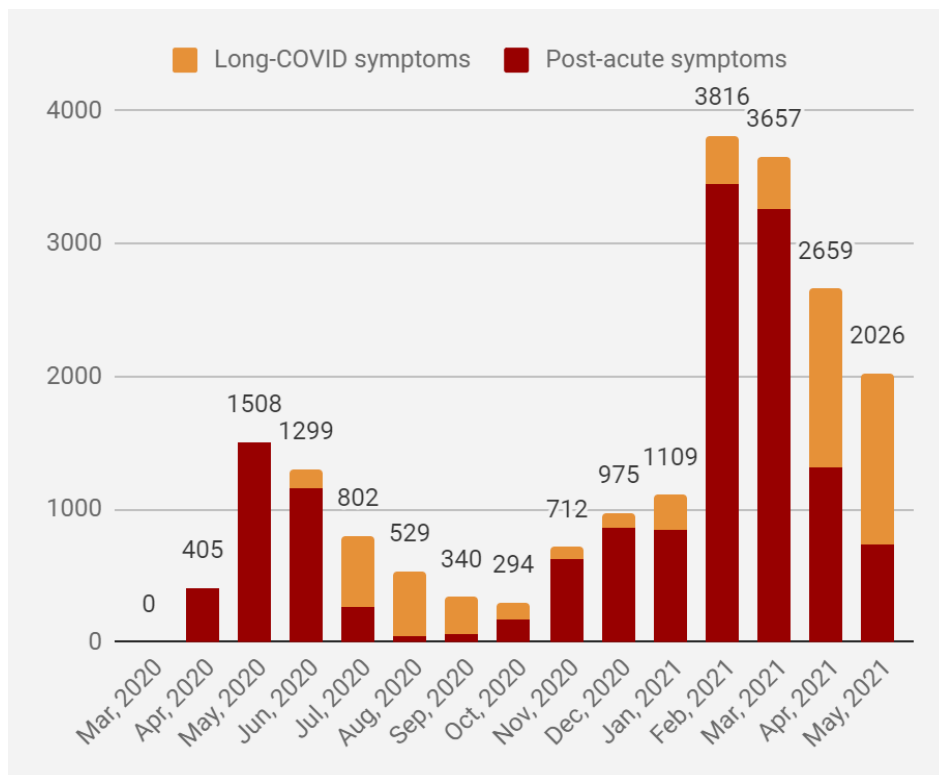


Figure 8. Ward Patients with post-acute and long-COVID



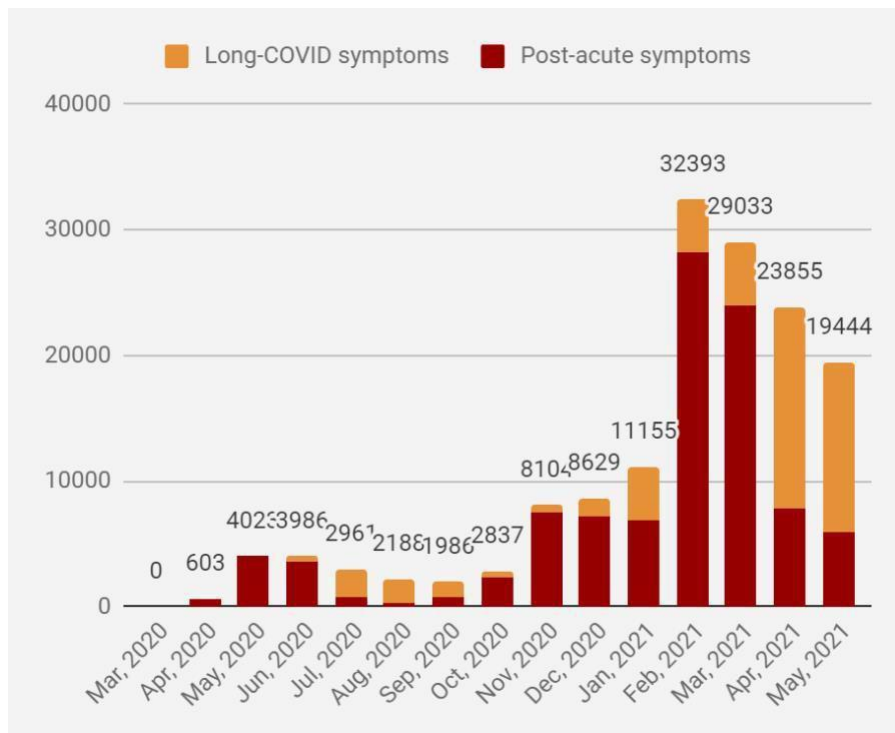


Figure 9. Post-acute and long-COVID in the community

Based on a further analysis and the assumption that new cases will remain relatively constant for the months of May to July. We can expect the number of people experiencing both post acute and long-COVID symptoms to drop significantly in the coming months.

While we are expecting the current number of people with lingering symptoms (Approx 22,000 for may 2021) especially after the peak of new cases in January, we forecast the numbers to halve by July 2021 and keep dropping thereafter. (See chart below)

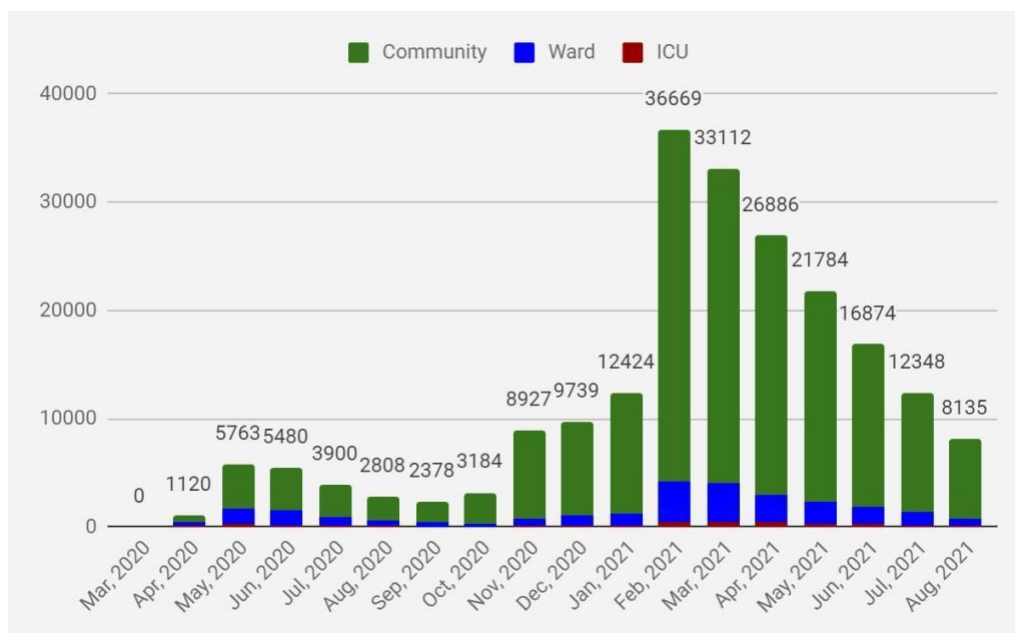


Figure 10. Forecast for total post-acute & long COVID persons

## 4.2 Estimates of need at a county level

There is considerable geographic variation in the incidence of laboratory confirmed COVID-19 cases since the start of the pandemic. As such the demand for Long COVID services will vary considerably across the country. In order to determine which counties had the biggest burden of disease over time we calculated both the absolute number of cases since the start of wave 3 and the number of cases at a county level adjusted for their respective population.

Below is a map detailing the cases per 100,000 population for each county from December 2020 up to April 2021. The numbers were calculated using 2021 CSO population projections and the total number of cases since December 2020 up to May 2021. The counties were then ranked in the chart below.

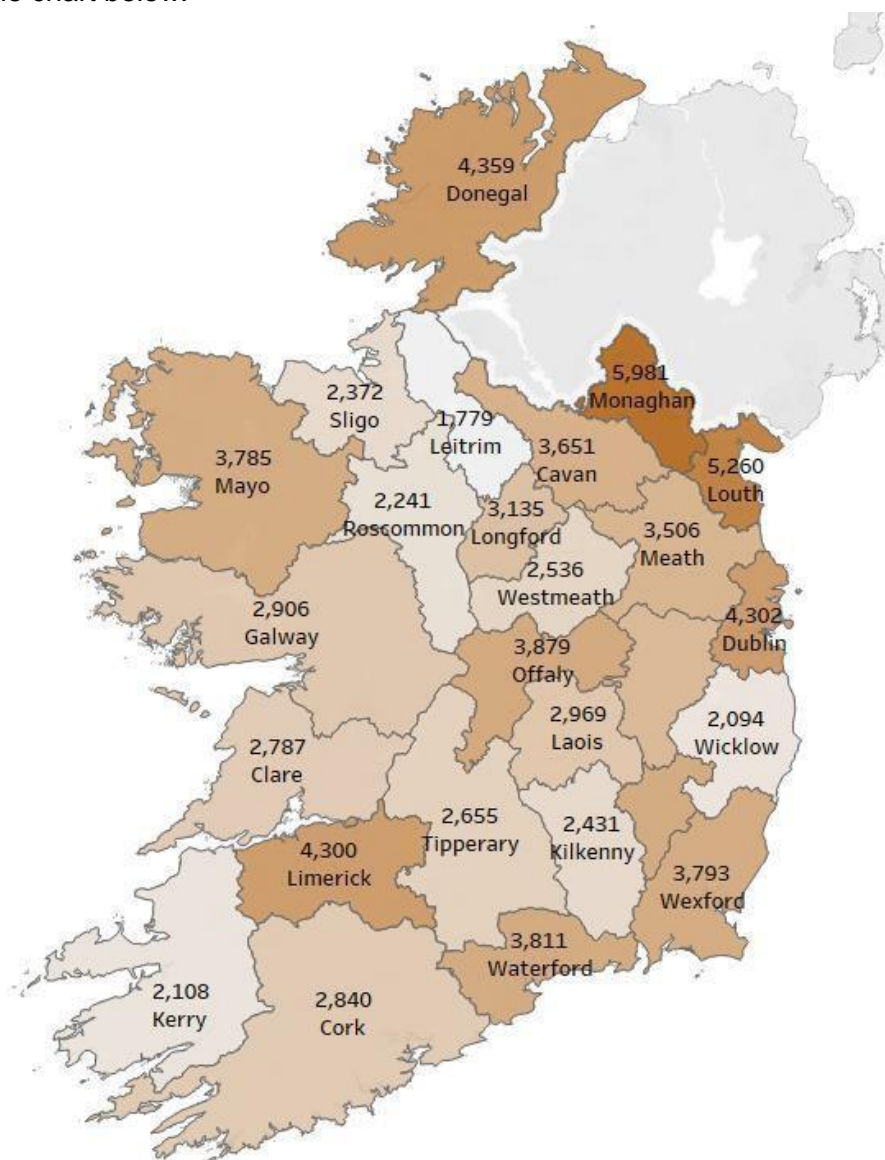


Figure 11. Cases per 100,000 by county since December 2020

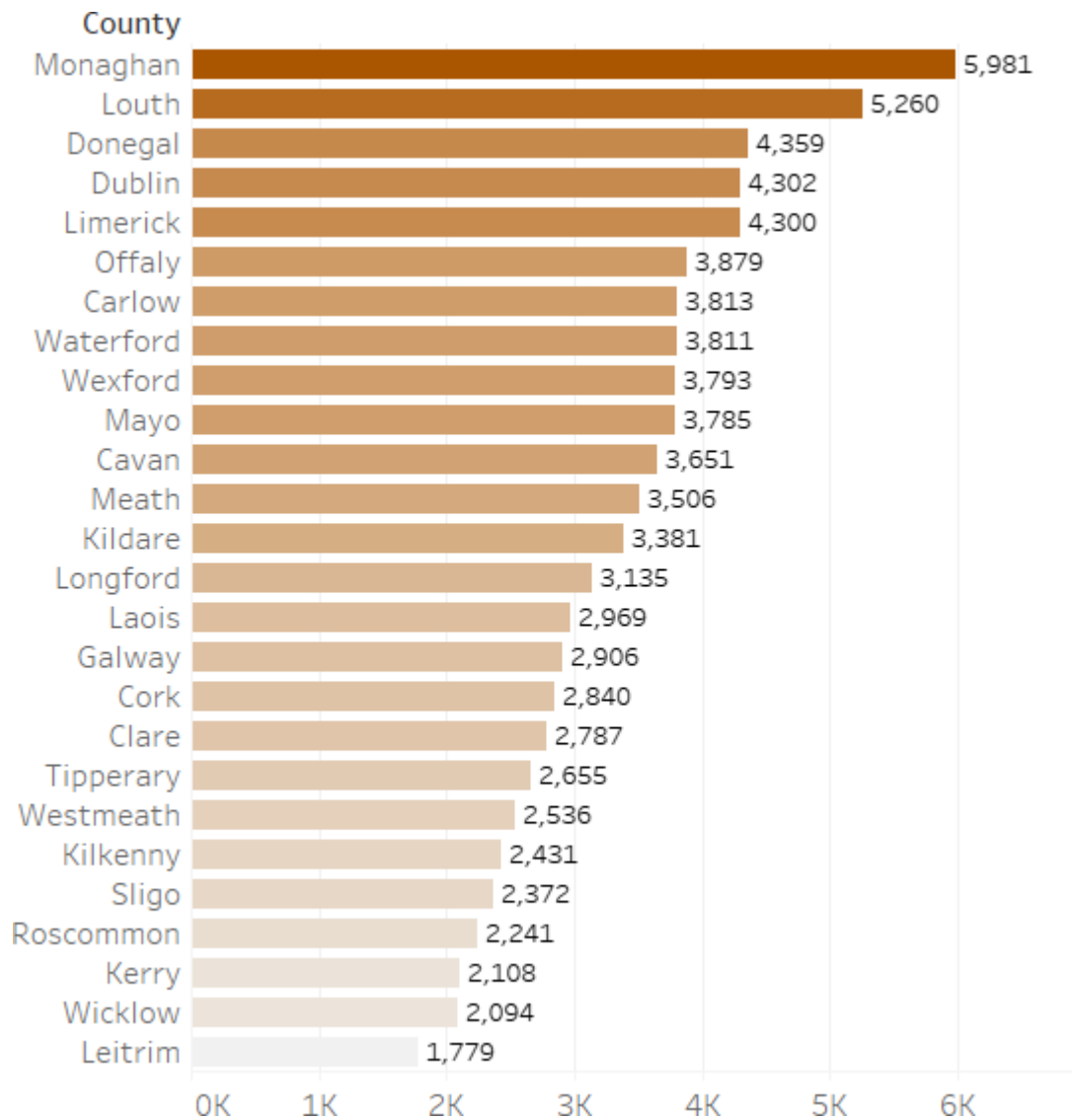


Figure 12. Cases per 100,000 by county ranked since December 2020

Since the beginning of the pandemic the top five counties with the highest number of cases per 100,000 population adjusted for their respective populations were Monaghan, Louth, Donegal, Dublin & Limerick.

In terms of absolute numbers the top counties for cases of COVID-19 since December 2020 were Dublin, Cork, Limerick, Kildare and Galway. See chart below.

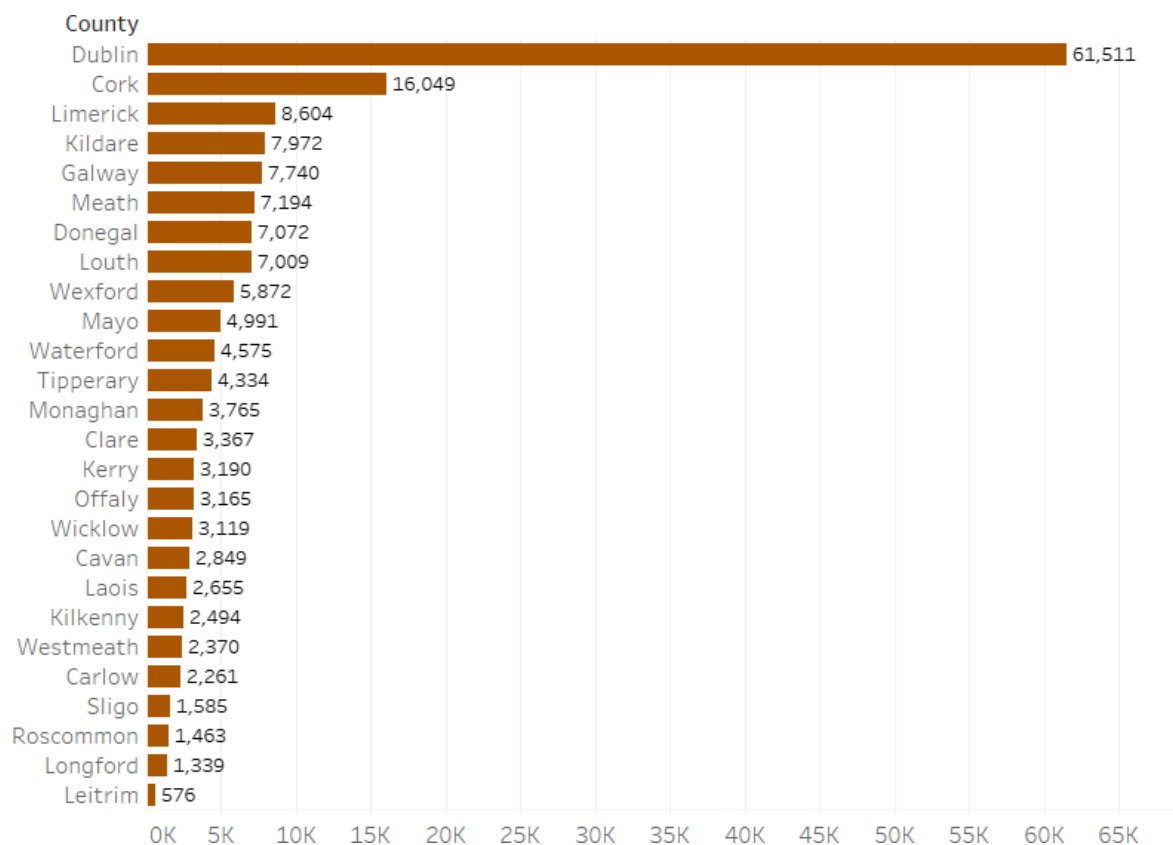


Figure 13. Cases by county ranked since December 2020

## 5. Model of care for Long COVID service

A three pillar approach to a national post COVID service is proposed.

1. Patient led rehabilitation and recovery
  - Online support and education platform to manage symptoms at home
2. General assessment, support and rehabilitation
  - General Practice and primary care rehabilitation
3. Specialist assessment support and rehabilitation
  - Specialist acute hospitals clinics supported by primary care HSCPs with early discharge back to primary care for ongoing follow up where appropriate

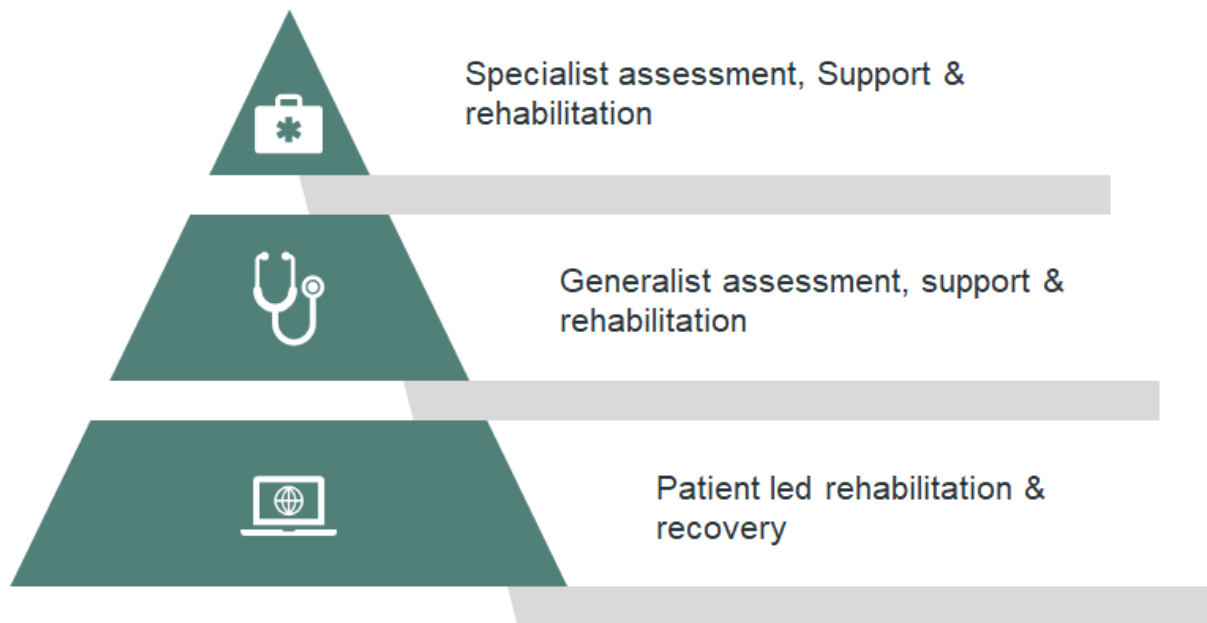


Figure 14. 3 Services for model of care for Long COVID

The national Long COVID service would focus on delivering care as close to home as possible for people who are still experiencing symptoms 4 weeks post-acute infection. Within this group, we know that those who were admitted to ICU will require specialist follow up and a proportion of hospitalised non- ICU patients will require specialist follow up. Given our current understanding of the disease it is anticipated that the vast majority of people in the community can be self managed by the provision of evidence based educational material and support. Those who have persistent and debilitating ongoing symptoms will be advised to contact their GP who will perform an assessment and determine if:

1. Symptoms can be self managed with additional reassurance and guidance
2. Referral to community rehabilitation services are needed
3. Investigations are required
4. Referral to a specialist clinic is required.

## 5.1 Patient Led Rehabilitation and Recovery

Patient education is key to ensuring people are empowered with the accurate information to self manage symptoms that do not require medical intervention and aid their recovery and rehabilitation in their own homes.

There is a need to provide trusted and reliable information to the public about Long COVID to (1) raise awareness of the condition (2) reassure people that people can have prolonged symptoms and what they can expect as part of their recovery (3) empower patients to self manage post-COVID symptoms by providing them with the knowledge and tools to assist in their recovery (4) signpost services that are available for patients who require clinical assessment and referral pathways to rehabilitation and/or specialist clinics (5) inform patients how to get support from other services such as social care .

It is proposed that a dedicated area on the HSE website is established providing clear advice and information on Long COVID symptoms and how to get help if needed. Clinically generated

content would be shared with the public and promoted through media campaigns by the existing communications digital team.

## 5.2 General assessment, support and rehabilitation in Primary Care

General practice plays a key part in the delivery of a national Long COVID service. The initial role of general practitioners is to exclude acute or life-threatening complications and other unrelated diagnoses. An assessment should be carried out by the GP, using a holistic, person centred approach. This should include a comprehensive clinical history and appropriate examination that involves assessing physical, cognitive, psychological and psychiatric symptoms, as well as functional abilities. Investigations should be tailored to each individual in order to rule out acute or life-threatening complications and determine if symptoms are due to post-acute or Long COVID. If another diagnosis unrelated to COVID-19 is suspected, offer investigations and referral in line with relevant local or national guidelines.

### History and Examination

- Detail the history of the acute disease and subsequent clinical course
- Enquire about red flag symptoms e.g. chest pain, breathlessness, confusion
- Review medications
- Explore the social history including issues affecting the person's wellbeing e.g. isolation, economic hardship, pressure to return to work, bereavement or loss of personal routines
- Face-to-face assessment usually required to review functional status
- Check oxygen saturations above 95%. If above 96% at rest check for desaturation on exertion e.g. 40 steps around the room or supervised one minute sit and stand test). If more than 3% drop, then further assessment required.

### Exercise Testing

**One minute sit-to-stand test** ask the patient to go from sitting to standing as many times as they can in one minute

**40 step test** ask the patient to take 40 steps on flat ground

The test should be terminated if the patient becomes distressed

A 3% drop in oxygen saturations is a cause for concern and hospital assessment should be considered

\*The NICE guide recommends the above tests but emphasises the importance of clinical judgement as the effectiveness of these tests has not been reviewed

### Investigations

Offer investigations tailored to the symptoms the patient is presenting with considering possibility of ongoing symptomatic COVID-19, post-COVID-19 syndrome or a new diagnosis

Blood tests recommended include FBC, kidney and liver function tests, C-reactive protein test, ferritin, B-type natriuretic peptide (BNP) and thyroid function tests. Consider performing an ECG.

- Offer a chest X-ray by 12 weeks after acute COVID-19 if the person has not already had one and they have continuing respiratory symptoms. Chest X-ray appearances alone should not determine the need for referral for further care as a chest X-ray alone may not be sufficient to rule out severe disease.
- If postural symptoms, for example palpitations or dizziness on standing, carry out lying and standing blood pressure and heart rate recordings.

## **Management**

Provide people with COVID-19 advice on the likelihood of developing long COVID, the common symptoms which can occur and symptoms that would require contact with their GP. Patients often recover with holistic support, rest, symptomatic treatment and a gradual increase in activity.

- Rule out acute/life-threatening complications or an alternative diagnosis then consider referring people for multidisciplinary assessment any time from 4 weeks after the start of acute COVID-19.
- Those with persistent cough and breathlessness may benefit from simple breathing exercises (slow, diaphragmatic breathing with a 1:2 inspiration to expiration ratio several times per day). Formal rehabilitation is often helpful if the initial respiratory illness was severe, but not for milder illness 30
- Consider psychiatric assessment if presenting with suicidal ideation or severe psychiatric symptoms
- Work with the person to develop a personalised rehabilitation and management plan that is recorded in a rehabilitation prescription including
  - Areas of rehabilitation and interventions based on their assessment
  - Helping the person to decide and work towards goals
  - Patients should be advised to pace themselves carefully and cut back if symptoms worsen with exercise. (Pace, plan, prioritise approach recommended
  - for rehabilitation. See occupational therapy guidance for patients here)
  - Symptom management for all presenting symptoms, for example advice and education on managing breathlessness, fatigue and 'brain fog'.
  - The HSE provide a Patient information leaflet on management of breathlessness
  - Sports Ireland have produced guidance on advising patients on return to play for sporting activities.

## **Severe complications COVID-19 include**

- Pulmonary embolus
- Heart failure
- Stroke
- Myocardial infarction, ventricular dysfunction
- Lung fibrosis
- Neurologic derangement

- Severe deterioration in mental health
- Acute kidney injury

**Urgent referral to secondary care required if:**

- Severe hypoxaemia or oxygen desaturation on exercise
- Signs of severe lung disease
- Cardiac chest pain
- Multisystem inflammatory syndrome (in children)

Research to evaluate the long-term health and psychosocial effects of COVID-19 is continuing. After excluding serious ongoing complications or comorbidities, and until the results of long term follow-up studies are available, patients should be managed pragmatically and symptomatically with an emphasis on holistic support while avoiding over-investigation

**GP Guidelines**

Clear guidelines will be developed to ensure that GPs know how and when to refer patients for specialist opinion. A series of webinars on Long COVID are proposed to support general practitioners in the management of Long COVID patients in primary care and help to ensure that where possible care is delivered in the community.

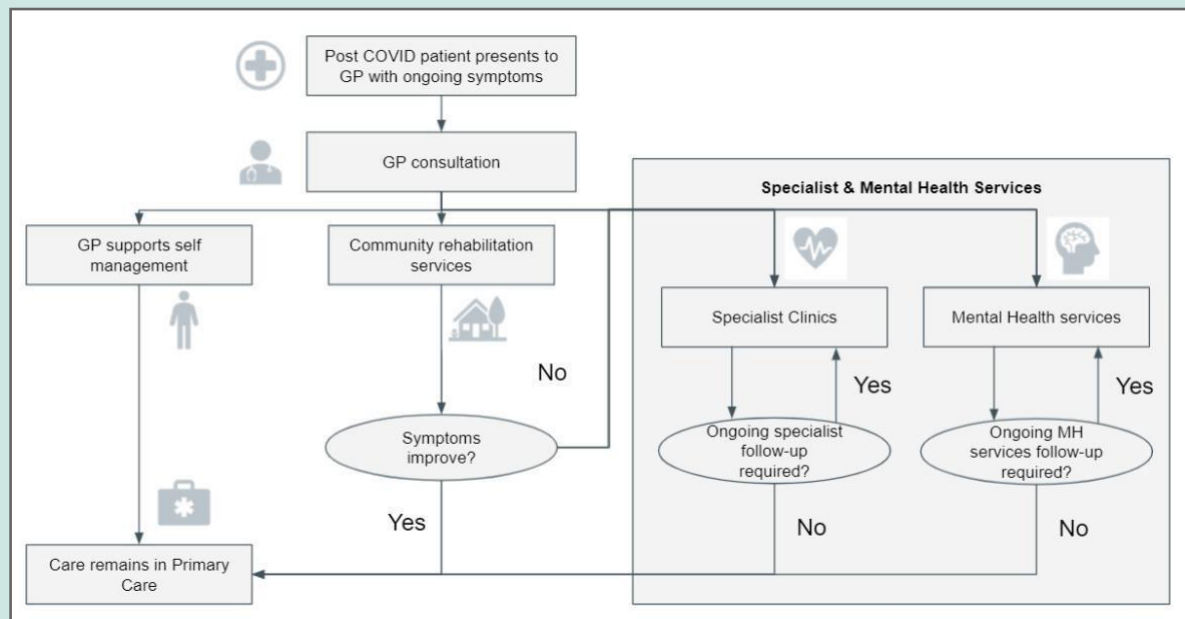


Figure 18. Proposed GP guideline for patient pathway

**5.2.2 Primary care services and resources**

From the limited current evidence, we anticipate that many patients whose COVID-19 illness is prolonged will recover without specialist input through a holistic and paced approach. Much can be achieved through interprofessional, community-facing rehabilitation services which embrace patient self-management and peer support and harness the potential of video and other remote technologies. Given the immediate need to establish community services to support Long COVID patients and enable their recovery and rehabilitation in the community, it is proposed that we leverage existing and additional capacity which is currently being



recruited as part of the Winter and Pandemic plan. Active recruitment campaigns are underway to recruit additional nursing and Health and Social Care Professionals (HSCPs) for the Community Health Networks and Specialist teams (ICPOP and CDM). Therefore a number of staff would be immediately available to direct their workload towards supporting the recovery and rehabilitation of Long COVID patients in the community.

### Staffing recruitment progress (as of week ending May 7th, 2021)

#### CHN staff recruitment progress

Grade	Phase I Requirement	Recruited / In Process	Remaining requirement
Chiropodist/ Podiatrist	57	2.6	54.4
Dietitian	57	7.5	49.5
Nursing	513	3	510
Occupational Therapist	57	27	30
Physiotherapist	171	42	129
Speech & Language Therapist	114	23	91

#### ICPOP Staff recruitment progress

Grade	Phase I Requirement	Recruited / In Process	Remaining requirement
Dietitian	8.5	2.5	6
Nursing	43.5	4	39.5
Occupational Therapist	11.5	2	9.5
Physiotherapist	11.5	5.5	6
Social Worker	15	1	14
Speech & Language Therapist	9	1	8

#### CDM staff recruitment progress

Grade	Phase I Requirement	Recruited / In Process	Remaining requirement
Chiropodist/ Podiatrist	54	7	47
Dietitian	121	5	116
Nursing	283	4	279
Physiotherapist	80	7	73

## 5.3 Specialist assessment support and rehabilitation

### 5.3.1 Post acute COVID clinics

#### **Proposal:**

Given the limited resources available and the time taken to recruit new staff, it is proposed that the 7 approved integrated Respiratory care Consultants, newly appointed as part of the Chronic Disease Management Programme, direct their workload towards establishing and leading the post-acute COVID clinics in the short to medium term. Additional staff are required to support these multidisciplinary outpatient clinics. The staff required include respiratory fellows, administrative staff, specialist respiratory physiotherapists, clinical nurse specialists and a psychologist. It is proposed that any occupational therapy and dietitian supporting services are delivered in the community by the Community Health Network staff.

**Aims:** The aim of a Post COVID-19 Assessment and Recovery Clinic is to ensure that patients who have recovered from the acute phase of COVID-19 are followed up in a timely and appropriate fashion taking into account factors such as disease severity, likelihood of long term respiratory symptoms and functional disability. As the recovery phase from COVID-19 may at times be unpredictable, clinical follow-up of this patient group should remain mindful of the possibility of additional, emerging issues.

Figure 19 illustrates the proposed patient pathway. All patients admitted to hospital with COVID-19 should be reviewed in clinic 4-6 weeks post discharge for patients with severe disease or those that required ICU admission. Mild to moderate cases should be reviewed at 12 weeks post discharge. Additionally, patients referred from Primary Care with ongoing, concerning, respiratory symptoms should be seen within an appropriate time frame.

General Practitioners should refer patients with ongoing, concerning respiratory symptoms who have an abnormal CXR and/or restrictive spirometry (FVC <80%) and/or unexplained desaturation on exercise testing and/or elevated D-dimers.

## Proposed pathway

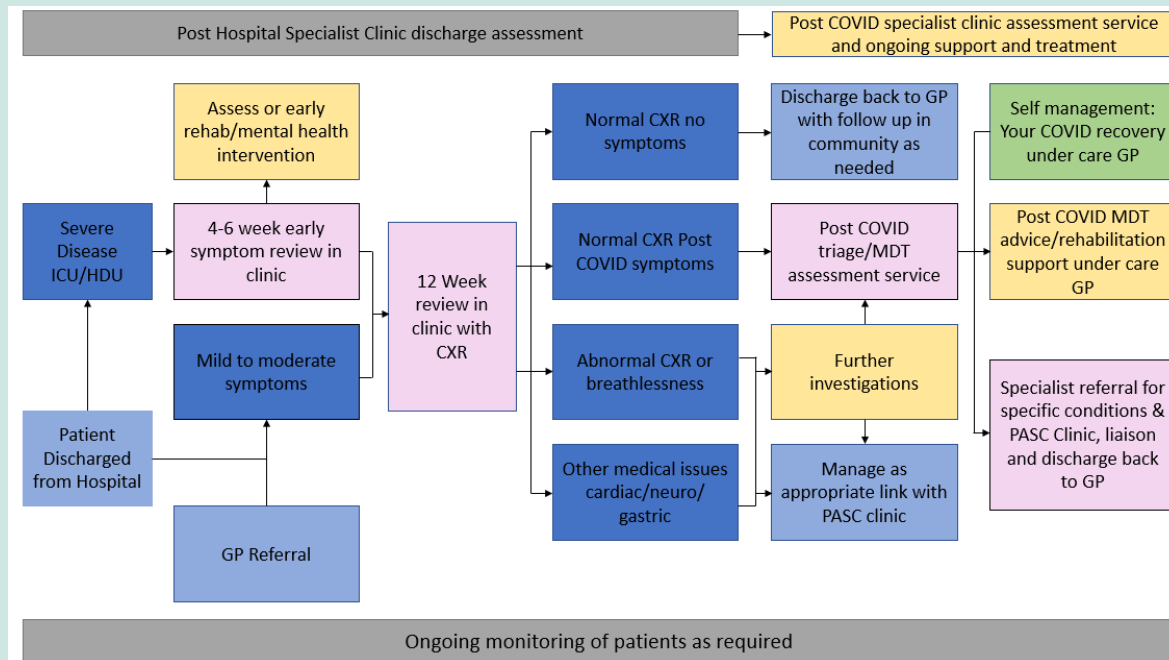


Figure 19. Proposed guideline for post acute patient pathway

### Assessment to include:

- Assessment and management of breathlessness.
- Assessment and management of oxygen requirements.
- Consideration of rehabilitation needs and onward referral where required.
- Psychosocial assessment and onward referral where required.
- Assessment and management of anxiety.
- Assessment and management of dysfunctional breathing.
- Consideration of a new diagnosis of venous thromboembolic disease (VTE).
- Symptom screen- mood, fatigue, quality of life, SF36.
- Neurophysiology

### Diagnostics

- All patients attending the clinic may require diagnostic testing which will include the following (with the potential requirement for additional testing if deemed clinically necessary);
- Cardiac diagnostics: ECG, +/-ECHO.
- Radiology: Chest X-ray +/- CT thorax
- Blood tests
- Full lung function includes Spirometry +/-bronchodilator response, Lung Volumes,
- Diffusing capacity +/- ((based on presenting symptoms and an agreed pathway).
- 6 MWTs.
- EMG

### Governance

- Governance of the post acute COVID clinics will be governed by the hospitals existing

### 5.3.2 Long COVID clinics / Post Acute Sequelae of COVID(PASC)

#### Proposal

Hospital Group provision of care with six specialist sites to which patients with undifferentiated symptoms for > 12 weeks post COVID diagnosis can be referred. Subject to further discussion, engagement and agreement with management and colleagues, there is the potential for three current ID consultant Locums to quickly establish the clinics at three sites, as outlined below. The three Locums could be made permanent to support services at:

- (1) University Hospital Galway
- (2) St James's Hospital and
- (3) Vincent's University Hospital

For the remaining three hospitals, there is the potential of restructuring GIM workload, ideally with a GIM locum, pending the appointment of permanent colleagues. This would support the establishment of services at

- (4) University Hospital Limerick (currently there is only one consultant in post and a second consultant in post would be a prerequisite for the service)
- (5) Beaumont Hospital and
- (6) Cork University Hospital

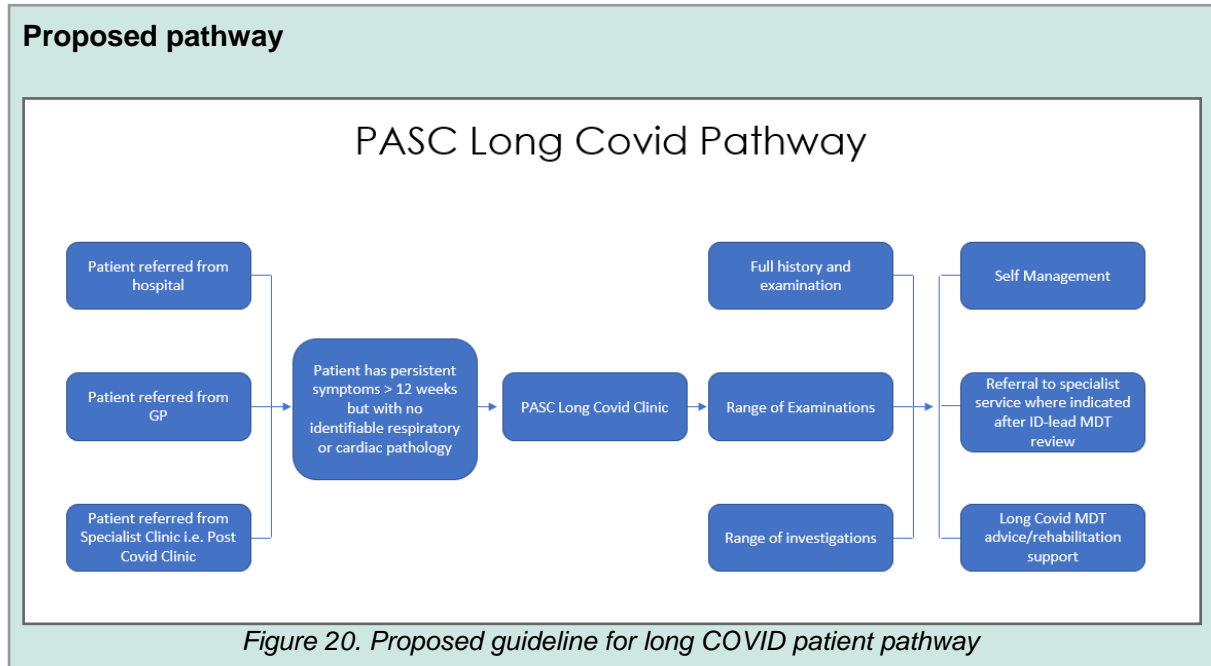
Any revised model would be contingent on the Multidisciplinary Team (MDT) recruitment and appointment, with at minimum a designated clerical officer and CNS or allied health care professional in posts. Access to neurocognitive and psychiatry/psychology services will be required to support the clinics. There will need to be flexibility in the approach to ensure development of the service meets the clinical needs. It is proposed that a full time temporary (1 year) Consultant Neurology post is appointed in St James Hospital to support both service delivery and research. This post will need 0.6 WTE Grade V support.

The clinics may be located on a single site, delivered across multiple sites or where appropriate virtually. Accessibility should be a priority both in terms of geographical location and service delivery model. Given the geographical variation in case incidence across the country the service delivery model will include an outreach and virtual clinics to ensure equitable provision of services at a national level.

As a minimum the post-COVID Specialist Assessment Clinics should:

- Be available, following clinician referral, to all affected patients, whether hospitalised or not
- Have access to a multidisciplinary team of professionals to account for the multi-system nature of post-COVID syndrome
- Support collaboration across localities
- Have age appropriate arrangements in place for managing children and young people with post-COVID syndrome including support for psychological needs
- Have access to diagnostic tests
- Have a plan for ensuring equity of access (bearing in mind many population groups have been disproportionately affected by COVID-19)
- Have a local communications plan for raising awareness within the clinical community

- Have an external communication plan for informing and raising awareness with patients



#### Referral criteria:

- Signs and symptoms which develop during or following an infection consistent with COVID-19, continue for more than 12 weeks and are not explained by an alternative diagnosis.
- Symptoms that are worsening or not improving and are having a significant impact on psychological well-being and/or causing significant delay to physical recovery in the absence of other explanatory diagnoses/pathology and/or limiting the person's ability to return to normal activities.
- Common Long COVID symptoms and signs include fatigue, breathlessness, anxiety/depression, problems with memory & concentration (brain fog), chest pain, heart palpitations, dizziness, joint pain, earache, high temperature, rashes
- Do not exclude people from referral to a multidisciplinary assessment service or for further investigations or specialist input based on the absence of a positive SARS-CoV-2 test or hospital admission

#### Exclusions:

- Acute COVID-19 symptoms
- Acute severe or worrisome symptoms or deterioration in physical or mental health causing clinical concern with imply needs for urgent assessment
- Patients with previous diagnosis of functional illness unless there is clear evidence of COVID-19 infection and change in symptoms in the context of the pandemic.

#### Assessment to include:

The British Thoracic society guidance identified that the post COVID syndrome holistic

assessment should at least include the following

- Assessment and management of breathlessness
- Assessment and management of oxygen requirements
- Consideration of rehabilitation needs and onward referral where required
- Psychosocial assessment (depression, anxiety disorders, PTSD, traumatic bereavement, psychosis screen, risk to self and/or others, COVID related life stresses such as debt, unemployment, relationship issues) and onward referral where required
- Assessment and management of dysfunctional breathing
- Cognitive function
- Consideration of a new diagnosis of venous thromboembolic disease (VTE)
- Post-exertion malaise, fatigue and neurological symptoms
- Symptom or palliative care management where required

Whilst some issues can be addressed immediately in the post-Covid assessment clinic if the right specialist is present, many patients will need further therapeutic input

Clinics should have clear pathways to ensure referral into appropriate services which may include rehabilitation, psychological support, specialist investigation or treatment, or to social care support services or the voluntary, community and social enterprise sector.

## 6. Map of suggested Locations

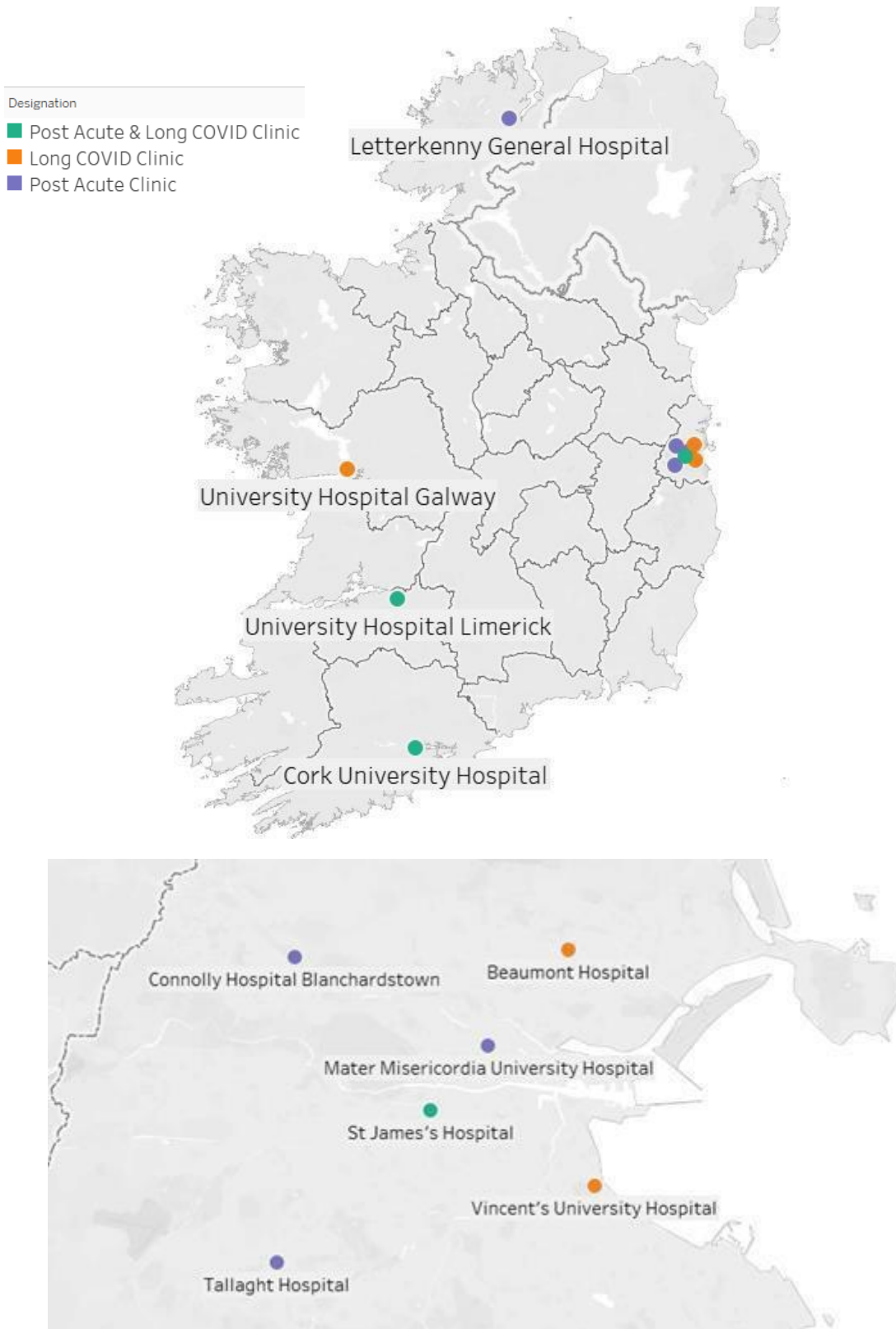
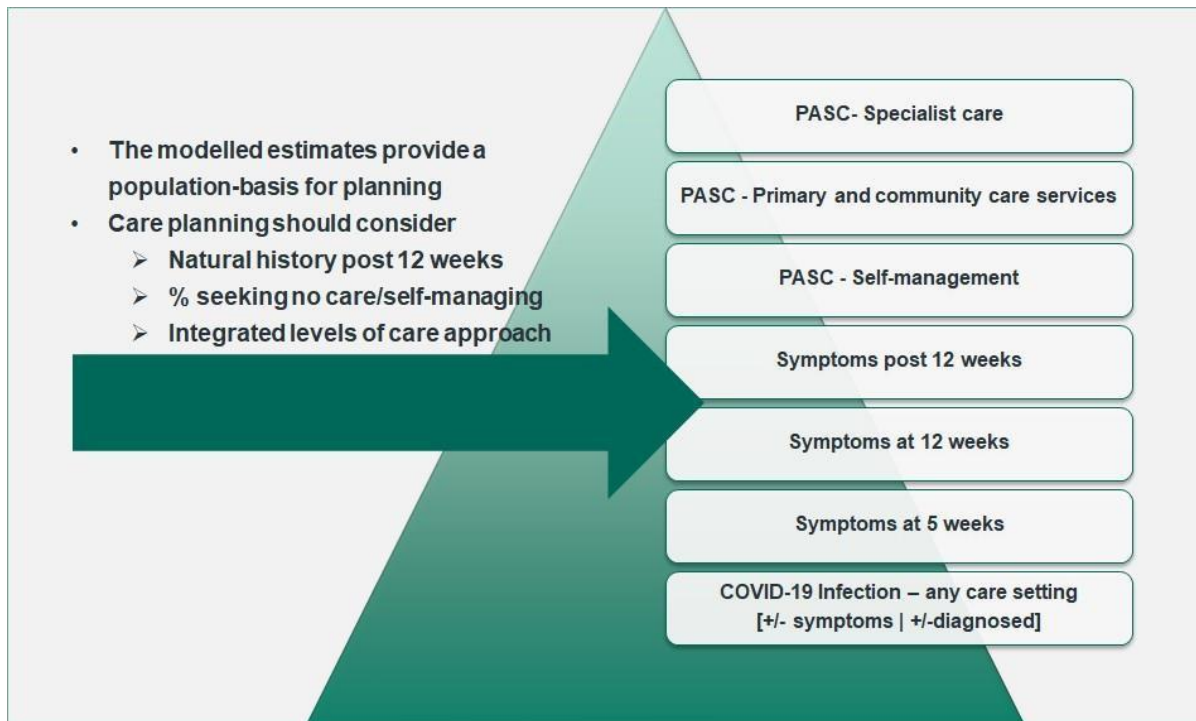


Figure 21. Maps for proposed sites for post-acute and long COVID clinics

## 7. Future study

### Population-based Long COVID/PASC care planning - ecology of care approach



In order to gain an understanding of the prevalence of Long COVID in Ireland and plan for service provision to meet the needs of patients it is proposed to conduct a retrospective cohort study.

### Potential Approach - Methods

#### Retrospective cohort study design

Sample population drawn from database of incident CIDR cases maintained by HPSC – simple probability sample designed to take account of time-to-event nature of study [~800 to measure 10% (+/- 2%) at 95% CI. Baseline information on COVID infection and symptoms at time of infection onset available in enhanced surveillance accessed via HSE COVIDCARETRACKER (CCT)

**Outcome** – self reported symptom status, functional status assessed, post-acute health service utilisation and perceived health needs measure with validated and reliable items and scales (cf Literature e.g. ISARIC baseline tool with permission)

**Data collection** – Telephone administered questionnaire completed by trained clinical personnel in HSE Contact Tracing Centre, information collated in HSE CCT through a specially designed form [similar forms currently in place for collection of other case information] and final dataset [baseline information and outcome information] extracted in conjunction with HSE OoCIO.



**Data analysis** – Prevalence of various outcome measures at follow-up; survival analysis (for ongoing symptoms); regression analysis (including cox proportional hazards regression) to identify factors associated with various outcome measures.

### Potential extensions

Participants could also

- be invited to participate in nested physical examination/functional assessment;
- be invited to participate in qualitative exploration of experience and perceived needs
- Provide access to healthcare records for record review;
- Agree to further follow up over time by telephone interview;

Nested study of HCW with boosted sample – link with PRECISE study

### Potential Approach – Project governance, management and resources

- Project Steering Group - membership drawn from current Long COVID/PASC working group – extend to include patient representatives and HPSC
- Project Group led by HSE HIU/R&E
  - external academic support – research collaboration with collaborative grant agreement managed by HSE R&E (Dr Ana Teres)
  - HPSC
  - Contact Tracing / COVIDCARETRACKER
- Patient reference group
  - Link with Dr Philip Crowley / QID
- Support on research ethics and data protection via Dr Ana Teres agreed – potential to expedite given nature of study
- Support on partnering with HSE Test and Trace via Dr Stephanie O’Keeffe agreed – one CTC Lead (Seconded Research Manager/PhD) identified to coordinate



## 8. Costing

Indicative Costs for Post acute COVID-19 Clinics

Priority	Requirements	WTE/No. per Clinic	Cost per Clinic	WTE/No. for 7 Clinics	Cost for 7 clinics
1	Integrated Respiratory Consultant contract B	1	Cost Neutral	7	Cost Neutral
	Clinical Fellow Registrar in Respiratory <b>OR</b>	1	€105,301	7	€737,107
	ANP/CS Physio	1	€77,830	7	€544,810
	Clinical Nurse Specialist	1	€64,648	7	€452,536
	Clinical Specialist Physiotherapist	0.5	€35,934	3.5	€251,538

	Grade IV Clerical staff	0.5	€21,670	3.5	€151,690
	Sub Total	3	€227,553	21	€1,592,871
2	Respiratory Physiologist	1	€57,844	7	€404,908
	Procurement of 1 Pulmonary Function Testing (PFT) machine	1	€44,878	7	€314,146
	Sub Total	2	€102,722	14	€719,054
3	Senior Dietitian	0.5	Community delivered	3.5	Community delivered
	Senior Occupational Therapist	0.5	Community delivered	3.5	Community delivered
	Sub Total	1	0	7	0
4	Cardiac Physiologist	1	€57,844	7	€404,908
	Cardiac monitoring equipment (x2 Holter monitors and x2 BP monitors)	4	€9,508	28	€66,556
	Medical Scientist	1	€45,150	7	€316,050
	Sub Total	6	€112,502	42	€787,514
<b>Total</b>		<b>12</b>	<b>€442,777</b>	<b>84</b>	<b>€3,099,439</b>

#### Indicative Costs for Long COVID Clinics

Requirements	WTE	Cost per Clinic	WTE for 6 clinics	Cost for 6 Clinics
ID Consultant	1	€229,744	6	€1,378,464
Clinical Fellow Registrar in ID	1	€105,301	6	€631,806
Clinical Nurse Specialist	1	€66,721	6	€400,326
Grade V/VI Clerical Staff/Data Manager	1	€60,078	6	€360,468
Neurocognitive / Psychology/Psychiatry	0.67	€70,200	4	€421,204
<b>Total</b>	<b>4.67</b>	<b>€532,044</b>	<b>28</b>	<b>€3,192,268</b>

#### Indicative costs for epidemiological survey

- Much of the overhead for study already available to the HSE through re-organisation of current workplans within HSE HIU/R&E, use of CCTs for interviews etc
- €150,000 - X2 postdocs plus senior biostatistical advice, some consumables
- Full time temporary Neurology Consultant €229,744 and a grade V 0.6 WTE €27,000

#### Total Indicative Costs

Requirement	Total Costing
7 Post acute COVID-19 Clinics	€3,099,439
6 Long COVID Clinics	€3,192,268
Epidemiological survey	€406,744
<b>Total</b>	<b>€6,698,451</b>

## 9. Implementation Plan

The HSE will form an implementation committee, to be led by the Integrated Operational Team and will include membership from other divisions within the HSE, including CCO office.

Key items for consideration by the implementation team will be:

- Liaison with modelling team to align service development with emerging need,
- Consideration of a pathway of care for those under 16 years old,
- Formalise pathways to neurocognitive clinic,
- Continued engagement with stakeholder groups e.g. Enhanced Community Care Steering Committee, ICGP etc.

## 10. Appendix

### 10.2. Summary of studies

1	<b>Carfi, A.,</b> Bernabei, R. and Landi, F. (2020). Persistent symptoms in patients after acute COVID-19. <i>Jama</i> , 324(6), pp.603-605.
2	Davis, H.E., Assaf, G.S., McCorkell, L., Wei, H., Low, R.J., Re'em, Y., Redfield, S., Austin, J.P. and Akrami, A., (2020) *PREPRINT* Characterizing Long COVID in an International Cohort: 7 Months of Symptoms and Their Impact. medRxiv.
3	D'Cruz, R.F., Waller, M.D., Perrin, F., Periseleris, J., Norton, S., Smith, L.J., Patrick, T., Walder, D., Heitmann, A., Lee, K. and Madula, R., (2020). Chest radiography is a poor predictor of respiratory symptoms and functional impairment in survivors of severe COVID-19 pneumonia. ERJ Open Research
4	Dennis, A., Wamil, M., Kapur, S., Alberts, J., Badley, A., Decker, G.A., Rizza, S.A., Banerjee, R. and Banerjee, A., (2020) *PREPRINT* Multi-organ impairment in low-risk individuals with long COVID. medrxiv.
5	Hampshire, A., Trender, W., Chamberlain, S., Jolly, A., Grant, J.E., Patrick, F., Mazibuko, N., Williams, S., Barnby, J.M., Hellyer, P. and Mehta, M.A., (2020)*PREPRINT* Cognitive deficits in people who have recovered from COVID-19 relative to controls: An N= 84,285 online study. MedRxiv
6	Arnold, D.T., Hamilton, F.W., Milne, A., Morley, A.J., Viner, J., Attwood, M., Noel, A., Gunning, S., Hatrick, J., Hamilton, S. and Elvers, K.T. (2020) Patient outcomes after hospitalisation with COVID-19 and implications for follow-up: results from a prospective UK cohort. Thorax
7	Mandal, S., Barnett, J., Brill, S.E., Brown, J.S., Denny, E.K., Hare, S.S., Heightman, M., Hillman, T.E., Jacob, J., Jarvis, H.C. and Lipman, M.C. (2020) 'Long-COVID': a cross-sectional study of persisting symptoms, biomarker and imaging abnormalities following hospitalisation for COVID-19. Thorax.
8	Raman, B., Cassar, M.P., Tunnicliffe, E.M., Filippini, N., Griffanti, L., Alfaro-Almagro, F., Okell, T., Sheerin, F., Xie, C., Mahmood, M. and Mózes, F.E.,(2021). Medium-term effects of SARS-CoV-2 infection on multiple vital organs, exercise capacity, cognition, quality of life and mental health, post-hospital discharge. <i>EClinicalMedicine</i> , 31, p.100683.
9	Halpin, S.J., McIvor, C., Whyatt, G., Adams, A., Harvey, O., McLean, L.,

	Walshaw, C., Kemp, S., Corrado, J., Singh, R. and Collins, T., (2021) Postdischarge symptoms and rehabilitation needs in survivors of COVID-19 infection: A cross-sectional evaluation. <i>Journal of medical virology</i> , 93(2), pp.1013-1022.
10	Venturelli, S., Benatti, S.V., Casati, M., Binda, F., Zuglian, G., Imeri, G., Conti, C., Biffi, A.M., Spada, S., Bondi, E. and Camera, G., (2021). Surviving COVID-19 in Bergamo Province: a post-acute outpatient re-evaluation. <i>Epidemiology &amp; Infection</i> , 149, e32, pp.1-9
11	Buonsenso, D., Munblit, D., De Rose, C. Sinatti, D., Ricchiuto, A. Carfi, A., Valentini, P (2021) *PREPRINT* Preliminary Evidence on Long COVID in children. medRxiv
12	Xiong, Q., Xu, M., Li, J., Liu, Y., Zhang, J., Xu, Y. and Dong, W., (2021) Clinical sequelae of COVID-19 survivors in Wuhan, China: a single-centre longitudinal study. <i>Clinical Microbiology and Infection</i> , 27(1), pp.89-95
13	Moreno-Pérez, O., Merino, E., Leon-Ramirez, J.M., Andres, M., Ramos, J.M., Arenas-Jiménez, J., Asensio, S., Sanchez, R., Ruiz-Torregrosa, P., Galan, I. and Scholz, A. (2021) Post-acute COVID-19 Syndrome. Incidence and risk factors: a Mediterranean cohort study. <i>Journal of Infection</i>
14	Tomasoni, D., Bai, F., Castoldi, R., Barbanotti, D., Falcinella, C., Mulè, G., Mondatore, D., Tavelli, A., Vegni, E., Marchetti, G. and d'Arminio Monforte, A. (2021). Anxiety and depression symptoms after virological clearance of COVID-19: a cross-sectional study in Milan, Italy. <i>Journal of Medical Virology</i> , 93(2), pp.1175-1179
15	Tenforde, M.W., Kim, S.S., Lindsell, C.J., Rose, E.B., Shapiro, N.I., Files, D.C., Gibbs, K.W., Erickson, H.L., Steingrub, J.S., Smithline, H.A. and Gong, M.N. (2020) Symptom duration and risk factors for delayed return to usual health among outpatients with COVID-19 in a multistate health care systems network—United States, March–June 2020. <i>Morbidity and Mortality Weekly Report</i> , 69(30), p.993
16	Sudre, C.H., Murray, B., Varsavsky, T., Graham, M.S., Penfold, R.S., Bowyer, R.C., Pujol, J.C., Klaser, K., Antonelli, M., Canas, L.S. and Molteni, E. (2020) *PRE PRINT* Attributes and predictors of Long-COVID: analysis of COVID cases and their symptoms collected by the Covid Symptoms Study App. medRxiv.
17	Vaes, A.W., Machado, F.V., Meys, R., Delbressine, J.M., Goertz, Y.M., Van Herck, M., Houben-Wilke, S., Franssen, F.M., Vijlbrief, H., Spies, Y. and Van't Hul, A.J. (2020) Care dependency in non-hospitalized patients with COVID-19. <i>Journal of Clinical Medicine</i> , 9(9), p.2946.act
18	Cirulli, E., Barrett, K.M.S., Riffle, S., Bolze, A., Neveux, I., Dabe, S., Grzymiski, J.J., Lu, J.T. and Washington, N.L. (2020) *PRE PRINT* Long-term COVID-19 symptoms in a large unselected population. medrxiv
19	Huang, C., Huang, L., Wang, Y., Li, X., Ren, L., Gu, X., Kang, L., Guo, L., Liu, M., Zhou, X. and Luo, J., (2021) 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study. <i>The Lancet</i> .
20	Logue, J.K., Franko, N.M., McCulloch, D.J., McDonald, D., Magedson, A., Wolf, C.R. and Chu, H.Y. (2021) Sequelae in adults at 6 months after COVID-19 infection. <i>JAMA Network Open</i> 4(2), pp.e210830-e210830
21	Garrigues E, Janvier P, Kherabi Y, et al. Post-discharge persistent symptoms and health-related quality of life after hospitalization for COVID-19. <i>J Infect.</i> 2020;81(6):e4-e6. doi:10.1016/j.jinf.2020.08.029
22	Ayoubkhani D, Khunti K, Nafilyan V, Maddox T, Humberstone B, Diamond I

	et al. Post-covid syndrome in individuals admitted to hospital with covid-19: retrospective cohort study BMJ 2021; 372 :n693 doi:10.1136/bmj.n693
23	Office for National Statistics, Prevalence of ongoing symptoms following coronavirus (COVID-19) infection in the UK: 1 April 2021
24	Chopra V, Flanders SA, O'Malley M, Malani AN, Prescott HC. Sixty-Day Outcomes Among Patients Hospitalized With COVID-19. <i>Ann Intern Med.</i> 2021;174(4):576-578. doi:10.7326/M20-5661

Study	<b>Carfi, A.,</b> Bernabei, R. and Landi, F. (2020). Persistent symptoms in patients after acute COVID-19. <i>Jama</i> , 324(6), pp.603-605.
Date, Country	July 2020, Italy
No. of participants	143
Follow up	60 days
Description	In one of the first clinical reports on symptoms of Long Covid, Carfi et al. (2020) describe outcomes from a post acute outpatient service for people discharged from an Italian hospital after Covid19. In addition to medical examination, 143 patients were asked to retrospectively reflect on which symptoms they had experienced during their acute illness, and whether those symptoms had continued until the follow-up appointment (on average around two months after symptom onset). A <b>high proportion (87%)</b> reported persistence of at least one symptom. The study was limited by a lack of detail on the symptoms and severity early in the patients' experience

Study	Davis, H.E., Assaf, G.S., McCorkell, L., Wei, H., Low, R.J., Re'em, Y., Redfield, S., Austin, J.P. and Akrami, A., (2020) *PREPRINT* Characterizing Long COVID in an International Cohort: 7 Months of Symptoms and Their Impact. medRxiv.
Date, Country	December 2020, International (56 countries)
No. of participants	3,762
Follow up	28 days
Description	In a patient-led study, an international survey was distributed via online support groups and social media. It collected data from 3,762 people who had ongoing symptoms at least 28 days after confirmed (27%) or suspected COVID-19 infection. More than 200 symptoms of varying severity were reported, with some lasting seven months or more, and sometimes following a relapsing-remitting trajectory. Survey respondents describe the disabling nature of their condition,

	<p>with many feeling unable to return to previous levels of work even after six months. The most frequent symptoms reported after month 6 were: fatigue (77.7%, 74.9% to 80.3%), post-exertional malaise (72.2%, 69.3% to 75.0%), and cognitive dysfunction (55.4%, 52.4% to 58.8%). These three symptoms were also the three most commonly reported overall.</p> <p>There are several limitations to this study. First, the retrospective nature of the study exposes the possibility of recall bias. Second, as the survey was distributed in online support groups, there exists a sampling bias toward Long COVID patients who joined support groups and were active participants of the groups at the time the survey was published.</p>
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Study	D'Cruz, R.F., Waller, M.D., Perrin, F., Periselneris, J., Norton, S., Smith, L.J., Patrick, T., Walder, D., Heitmann, A., Lee, K. and Madula, R., (2020). Chest radiography is a poor predictor of respiratory symptoms and functional impairment in survivors of severe COVID-19 pneumonia. ERJ Open Research
Date, Country	October 2020, UK
No. of participants	119
Follow up	35 days
Description	This single-centre observational cohort study focused on radiological outcomes from 119 patients with severe Covid19 pneumonia, when assessed four to six weeks after discharge from a UK hospital. Despite radiographic resolution of pulmonary infiltrates in 87%, mMRC breathlessness scores were above pre-COVID baseline in 46% and patients reported persistent fatigue (68%), sleep disturbance (57%) and breathlessness (32%). Screening thresholds were breached for post-traumatic stress disorder (25%), anxiety (22%) and depression (18%).

Study	Dennis, A., Wamil, M., Kapur, S., Alberts, J., Badley, A., Decker, G.A., Rizza, S.A., Banerjee, R. and Banerjee, A., (2020) *PREPRINT* Multi-organ impairment in low-risk individuals with long COVID. medrxiv.
Date, Country	October 2020, UK
No. of participants	201
Follow up	140 days
Description	<p>Assessment 140 days after initial symptoms, prevalence of pre-existing conditions was low and only 18% had been hospitalised with COVID-19 .</p> <p>Fatigue (98%), muscle aches (88%), breathlessness (87%), and headaches (83%) were the most frequently reported symptoms. Ongoing cardiorespiratory (92%) and gastrointestinal (73%) symptoms were common, and 42% of individuals had ten or more symptoms.</p> <p>There was evidence of mild organ impairment in heart (32%), lungs (33%),</p>

	kidneys (12%), liver (10%), pancreas (17%), and spleen (6%). Single (66%) and multi-organ (25%) impairment was observed, and was significantly associated with risk of prior COVID-19 hospitalisation ( $p < 0.05$ ).
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Study	Hampshire, A., Trender, W., Chamberlain, S., Jolly, A., Grant, J.E., Patrick, F., Mazibuko, N., Williams, S., Barnby, J.M., Hellyer, P. and Mehta, M.A., (2020)*PREPRINT* Cognitive deficits in people who have recovered from COVID-19 relative to controls: An N= 84,285 online study. MedRxiv
Date, Country	October 2020, UK
No. of participants	84,285
Follow up	
Description	<p>Analysed cognitive test data from 84,285 Great British Intelligence Test participants who completed a questionnaire regarding suspected and biologically confirmed COVID-19 infection. 60 reported being put on a ventilator, a further 147 were hospitalised without a ventilator, 176 required medical assistance at home for respiratory difficulties, 3466 had respiratory difficulties and received no medical assistance and 9201 reported being ill without respiratory symptoms.</p> <p>People who had recovered, including those no longer reporting symptoms, exhibited significant cognitive deficits when controlling for age, gender, education level, income, racial-ethnic group and pre-existing medical disorders.</p>

Study	Arnold, D.T., Hamilton, F.W., Milne, A., Morley, A.J., Viner, J., Attwood, M., Noel, A., Gunning, S., Hatrick, J., Hamilton, S. and Elvers, K.T. (2020) Patient outcomes after hospitalisation with COVID-19 and implications for follow-up: results from a prospective UK cohort. Thorax
Date, Country	October 2020, UK
No. of participants	110
Follow up	70 days
Description	<p>A primary observational cohort study at a single NHS centre in Bristol, UK. Consecutive patients admitted with COVID-19 (confirmed by a positive PCR test result or clinical/radiological diagnosis) were prospectively recruited. All survivors who had been discharged from hospital were invited to an outpatient clinic review, and 110 people attended 8-12 weeks after their acute infection. Outcomes were based on medical review, physiological tests, chest imaging, and a quality of life questionnaire. Results were reported separately according to the severity of initial illness (mild, moderate or severe). The study investigators observed that those patients with mild Covid19 (not requiring supplemental oxygen) had a low likelihood of having abnormalities detected on chest x-ray at follow-up (14% abnormal) . However they did note that most participants (74%) reported at least one persistent symptom or limited physical ability, including those originally admitted with mild disease. (39% breathless, 39% fatigue, 24% insomnia)</p>

Study	Mandal, S., Barnett, J., Brill, S.E., Brown, J.S., Denny, E.K., Hare, S.S., Heightman, M., Hillman, T.E., Jacob, J., Jarvis, H.C. and Lipman, M.C. (2020) 'Long-COVID': a cross-sectional study of persisting symptoms, biomarker and imaging abnormalities following hospitalisation for COVID-19. Thorax.
Date, Country	September 2020, UK
No. of participants	384
Follow up	60 days
Description	<p>Around two months (on average) after discharge from any of three London hospitals, 384 Covid19-positive patients were followed up by telephone or in person to enquire about persistent symptoms. 53% reported persistent breathlessness, 34% cough and 69% fatigue. 14.6% had depression.</p> <p>At the time of discharge 224 had abnormalities detected in blood test or scan results; this subgroup was invited to undergo repeat testing. 30.1% and 9.5% had persistently elevated d-dimer and C reactive protein, respectively. 38% of chest radiographs remained abnormal with 9% with 9% showing significant post-discharge deterioration suggestive of pulmonary fibrosis.</p>

Study	Raman, B., Cassar, M.P., Tunnicliffe, E.M., Filippini, N., Griffanti, L., Alfaro-Almagro, F., Okell, T., Sheerin, F., Xie, C., Mahmood, M. and Mózes, F.E.,(2021). Medium-term effects of SARS-CoV-2 infection on multiple vital organs, exercise capacity, cognition, quality of life and mental health, post-hospital discharge. EClinicalMedicine, 31, p.100683.
Date, Country	November 2020, UK
No. of participants	58
Follow up	75 days
Description	<p>Around two to three months after onset of symptoms, outcomes from 58 patients hospitalised with moderate to severe Covid19 were compared with matched controls. 64% of patients experienced breathlessness and 55% reported fatigue. On MRI, abnormalities were seen in lungs (60%), heart (26%), liver (10%) and kidneys (29%). Patients exhibited changes in the thalamus, posterior thalamic radiations and sagittal stratum on brain MRI and demonstrated impaired cognitive performance, specifically in the executive and visuospatial domains. Exercise tolerance (maximal oxygen consumption and ventilatory efficiency on CPET) and six-minute walk distance were significantly reduced. The extent of extra-pulmonary MRI abnormalities and exercise intolerance correlated with serum markers of inflammation and acute illness severity. Patients had a higher burden of self-reported symptoms of depression and experienced significant impairment in all domains of quality of life compared to controls (<math>p &lt; 0.0001</math> to <math>0.044</math>).</p>

Study	Halpin, S.J., McIvor, C., Whyatt, G., Adams, A., Harvey, O., McLean, L.,
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	Walshaw, C., Kemp, S., Corrado, J., Singh, R. and Collins, T., (2021) Postdischarge symptoms and rehabilitation needs in survivors of COVID-19 infection: A cross-sectional evaluation. <i>Journal of medical virology</i> , 93(2), pp.1013-1022.
Date, Country	July 2020, UK
No. of participants	100
Follow up	42 days
Description	This publication from early in the pandemic describes symptoms and impact on daily life 4-8 weeks after UK hospital discharge, in a purposively sampled group of 100 Covid19 survivors (who had been diagnosed using a PCR swab test). Prevalence of Long Covid symptoms was higher in those who required ICU care when compared with those who were managed on the ward. A clinically significant reduction in quality of life was found in 69% of the ICU group, and 46% of the ward group.

Study	Venturelli, S., Benatti, S.V., Casati, M., Binda, F., Zuglian, G., Imeri, G., Conti, C., Biffi, A.M., Spada, S., Bondi, E. and Camera, G., (2021). Surviving COVID-19 in Bergamo Province: a post-acute outpatient re-evaluation. <i>Epidemiology &amp; Infection</i> , 149, e32, pp.1-9
Date, Country	January 2021, Italy
No. of participants	767
Follow up	84 days
Description	767 patients discharged from the emergency department or inpatient wards of an Italian hospital, Covid19 patients underwent their first post-discharge multidisciplinary assessment 12 weeks later. 51.4% still complained of symptoms, most commonly fatigue and exertional dyspnoea, and 30.5% were still experiencing post-traumatic psychological consequences. Impaired lung diffusion was found in 19%. D-dimer levels consistent with pulmonary thromboembolism were detected in 17% of people.

Study	Buonsenso, D., Munblit, D., De Rose, C. Sinatti, D., Ricchiuto, A. Carfi, A., Valentini, P (2021) *PREPRINT* Preliminary Evidence on Long COVID in children. medRxiv
Date, Country	January 2021, Italy
No. of participants	129 children
Follow up	120 days
Description	This cross-sectional study in Italy prospectively recruited 129 children with laboratory-confirmed COVID- 19 (included hospitalised and non-hospitalised) . Interviews with caregivers indicated persistence of one or more symptoms in 53% children 120 days after Covid19 diagnosis, with 43% reporting an impact on activities of daily living. The authors intend to continue monitoring this group of children, and to compare findings with a control group (not having been

	diagnosed with Covid19).
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Study	Xiong, Q., Xu, M., Li, J., Liu, Y., Zhang, J., Xu, Y. and Dong, W., (2021) Clinical sequelae of COVID-19 survivors in Wuhan, China: a single-centre longitudinal study. <i>Clinical Microbiology and Infection</i> , 27(1), pp.89-95
Date, Country	January 2021, China
No. of participants	538
Follow up	97 days
Description	Longitudinal study based on a telephone follow up survey of 538 patients with COVID discharged from hospital. Follow up took place 97 (95-102) days later. Clinical sequelae were common, including general symptoms (n = 267, 49.6%), respiratory symptoms (n = 210, 39%), cardiovascular-related symptoms (n = 70, 13%), psychosocial symptoms (n = 122, 22.7%) and alopecia (n = 154, 28.6%). We found that physical decline/fatigue (p < 0.01), postactivity polypnoea (p= 0.04) and alopecia (p < 0.01) were more common in female than in male subjects.

Study	Moreno-Pérez, O., Merino, E., Leon-Ramirez, J.M., Andres, M., Ramos, J.M., Arenas-Jiménez, J., Asensio, S., Sanchez, R., Ruiz-Torregrosa, P., Galan, I. and Scholz, A. (2021) Post-acute COVID-19 Syndrome. Incidence and risk factors: a Mediterranean cohort study. <i>Journal of Infection</i>
Date, Country	January 2021, Mediterranean
No. of participants	277
Follow up	84 days
Description	Prospective cohort study of PCR positive patients attending ED. Patients were classified depending on the presence of pneumonia. 277 included in study: 20% no pneumonia, 15% non-severe and 66% severe. Assessment was performed 10 to 14 weeks after infection.  50% patients had post acute COVID-19 Syndrome ( 58% in severe pneumonia, 37% in mild pneumonia and 37% in no pneumonia.) The most frequent symptoms were dyspnea and fatigue. These symptoms were mostly mild general (fatigue), respiratory (dyspnea) or neurological complaints, but were not found to be associated with other pathological findings in the examinations performed. Radiological and spirometric changes were observed in less than 25%. PCS entails a high psychological distress influencing the quality of life. However, respiratory and neurological symptoms drastically improve 16–18 weeks after disease onset.

Study	Tomasoni, D., Bai, F., Castoldi, R., Barbanotti, D., Falcinella, C., Mulè, G., Mondatore, D., Tavelli, A., Vegni, E., Marchetti, G. and d'Arminio Monforte, A. (2021). Anxiety and depression symptoms after virological clearance of COVID-19: a cross-sectional study in Milan, Italy. <i>Journal of Medical Virology</i> , 93(2), pp.1175-1179
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Date, Country	August 2020, Italy
No. of participants	105
Follow up	60 days
Description	A cross-sectional study which followed up patients hospitalised with COVID- 19 in Italy. Patients were required to have a history of documented clinical recovery and virological clearance (two consecutive negative PCR tests within 24-48 hours). After one to three months, 105 patients underwent a clinical examination, completed a Hospital Anxiety and Depression Scale (HADS) questionnaire, and underwent mini mental state examination to evaluate potential cognitive disorders. 1-3 months after clinical and virological recovery from symptomatic COVID-19 disease, 30% and 52.4% of patients still presented psychological and physical symptoms, respectively. Persistence of anxiety and depression was independently associated with ongoing physical symptoms.

Study	Tenforde, M.W., Kim, S.S., Lindsell, C.J., Rose, E.B., Shapiro, N.I., Files, D.C., Gibbs, K.W., Erickson, H.L., Steingrub, J.S., Smithline, H.A. and Gong, M.N. (2020) Symptom duration and risk factors for delayed return to usual health among outpatients with COVID-19 in a multistate health care systems network— United States, March–June 2020. <i>Morbidity and Mortality Weekly Report</i> , 69(30), p.993
Date, Country	July 2020, US
No. of participants	292
Follow up	2 weeks
Description	292 adults who had previously tested positive for COVID-19 at a US outpatient clinic (milder illness) were followed up in a telephone interview around two weeks later. 94% (274) reported experiencing one or more symptoms at the time of testing; 35% of these symptomatic respondents reported not having returned to their usual state of health by the date of the interview (median = 16 days from testing date), including 26% among those aged 18–34 years, 32% among those aged 35–49 years, and 47% among those aged ≥50 years. Among respondents reporting cough, fatigue, or shortness of breath at the time of testing, 43%, 35%, and 29%, respectively, continued to experience these symptoms at the time of the interview. These findings indicate that COVID-19 can result in prolonged illness even among persons with milder outpatient illness, including young adults.

Study	Sudre, C.H., Murray, B., Varsavsky, T., Graham, M.S., Penfold, R.S., Bowyer, R.C., Pujol, J.C., Klaser, K., Antonelli, M., Canas, L.S. and Molteni, E. (2020) *PRE PRINT* Attributes and predictors of Long-COVID: analysis of COVID cases and their symptoms collected by the Covid Symptoms Study App. medRxiv.
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Date, Country	October 2020, UK
No. of participants	4,182
Follow up	28 days, 56 days and 84 days
Description	<p>The Covid Symptoms Study ('Zoe') app collected self-reported symptom data from a subset of 4,182 participants with Covid19 positive tests. Comparisons were made with matched symptomatic test-negative controls. Findings were characterised according to different periods of follow-up: up to 28 days, eight weeks or more, and those persisting for at least 12 weeks.</p> <p>558 (13.3%) had symptoms lasting &gt;28 days, 189 (4.5%) for &gt;8 weeks and (2.3%) for &gt;12 weeks. Long-COVID was characterised by symptoms of fatigue, headache, dyspnoea and anosmia and was more likely with increasing age, BMI and female sex.</p> <p>Fatigue (97.7%) and headache (91.2%) were the most reported symptoms in those with Long COVID, followed by anosmia and lower respiratory symptoms. Notably, while fatigue was reported continuously, other symptoms such as headache are reported intermittently</p> <p>While this study provides important insights into the disease presentation, any generalisation should be considered carefully. Our study was limited by being confined to app users who were disproportionately female and under-represented those &gt;70years which could increase or decrease our estimate of the extent of Long-COVID respectively.</p>

Study	Vaes, A.W., Machado, F.V., Meys, R., Delbressine, J.M., Goertz, Y.M., Van Herck, M., Houben-Wilke, S., Franssen, F.M., Vijlbrief, H., Spies, Y. and Van't Hul, A.J. (2020) Care dependency in non-hospitalized patients with COVID-19. Journal of Clinical Medicine, 9(9), p.2946.act
Date, Country	September 2020, Netherlands and Belgium
No. of participants	1,837 non hospitalised
Follow up	77 days
Description	<p>Members of two Facebook groups for COVID-19 patients with persistent complaints in The Netherlands and Belgium, and from a panel of people who registered at a website of the Lung Foundation Netherlands, were assessed for demographics, pre-existing comorbidities, health status, and symptoms. In addition, patients were asked about their dependence on others for personal care before and after the infection.</p> <p>Around 11 weeks after symptom onset, participants reported an increased need for personal care when reflecting on changes in their condition before and after infection. Despite few needing help previously, almost one third considered themselves to be at least partially dependent on others at follow-up.</p>

Study	Cirulli, E., Barrett, K.M.S., Riffle, S., Bolze, A., Neveux, I., Dabe, S., Grzymiski, J.J., Lu, J.T. and Washington, N.L. (2020) *PRE PRINT* Long-term COVID-19 symptoms in a large unselected population. medrxiv
Date, Country	December 2020, US
No. of participants	357 COVID-19+ cases, 5,497 SARS-CoV-2-negative controls, and 19,095 non-tested individuals.
Follow up	N/A
Description	<p>Prospective research study of the general population. Because the assessed period covered a timeframe of ten months (January - October 2020), most individuals had been sick at least once during the period and thus reported at least one symptom. Though several of the surveyed symptoms were common to seasonal flu, the common cold, and allergies, we found that nearly all symptoms were statistically significant in their association with a positive COVID-19 test</p> <p>The majority of COVID-19+ cases were mild (2.5% hospitalised) , 36.1% of COVID-19+ cases have symptoms lasting longer than 30 days, compared to 11.7% for those with negative tests and 8.4% for those with no test. At 60 and 90 days, these numbers were 25.3% and 14.8% for COVID-19+ cases, 8.5% and 7.0% for COVID-19-controls, and 6.3% and 4.8% for those with no tests.</p> <p>These numbers were higher for COVID-19+ cases who were initially more ill. Individuals who have an initial symptom of dyspnea are significantly more likely to develop long-term symptoms.</p> <p>The long-term symptoms most enriched in those with COVID-19 are anosmia, ageusia, difficulty concentrating, dyspnea, memory loss, confusion, chest pain, and pain with deep breaths.</p>

Study	Huang, C., Huang, L., Wang, Y., Li, X., Ren, L., Gu, X., Kang, L., Guo, L., Liu, M., Zhou, X. and Luo, J., (2021) 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study. The Lancet.
Date, Country	China
No. of participants	January 2021, 1,733
Follow up	186 days
Description	<p>1,733 patients (severity scale 1 to 7) admitted to hospital enrolled for questionnaire interview, physical examination, laboratory tests, and a 6-min walking test. The median follow-up time after symptom onset was 186 days. Patients requiring HFNC, NIV, or IMV (severity scale <math>\geq 5</math>) were all invited to receive the pulmonary function test, ultrasound, and HRCT of chest. 76% of patients reported at least one symptom at 6 months after symptom onset, and the proportion was higher in women.</p> <p>The most common symptoms were fatigue or muscle weakness and sleep difficulties. Additionally, 23% of patients reported anxiety or depression at follow-up.</p> <p>516 (30%) patients were ascertained as eligible for PFTs, HRCT and USS but 126 lost to follow up.</p> <p>The results of lung function assessment in this study showed that a considerable proportion (22–56% across different severity scales) of</p>

	<p>participants had a pulmonary diffusion abnormality 6 months after symptom onset</p> <p>13% of patients without acute kidney injury and with normal eGFR at the acute phase had decreased eGFR at follow-up</p> <p>Patients who were more severely ill during their hospital stay had more severe impaired pulmonary diffusion capacities and abnormal chest imaging manifestations.</p>
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Study	Logue, J.K., Franko, N.M., McCulloch, D.J., McDonald, D., Magedson, A., Wolf, C.R. and Chu, H.Y. (2021) Sequelae in adults at 6 months after COVID-19 infection. <i>JAMA Network Open</i> 4(2), pp.e210830-e210830
Date, Country	February 2021, US
No. of participants	177
Follow up	169 days
Description	<p>A longitudinal cohort study of 177 US adults with laboratory-confirmed Covid19. Overall, 11 (6.2%) were asymptomatic, 150 (84.7%) were outpatients with mild illness, and 16 (9.0%) had moderate or severe disease requiring hospitalization. The follow-up survey was completed a median (range) of 169 (31-300) days after illness onset among participants with COVID-19. Among participants with COVID-19, persistent symptoms were reported by 17 of 64 patients (26.6%) aged 18 to 39 years, 25 of 83 patients (30.1%) aged 40 to 64 years, and 13 of 30 patients (43.3%) aged 65 years and older. The most common persistent symptoms were fatigue (24 of 177 patients [13.6%]) and loss of sense of smell or taste (24 patients [13.6%])</p> <p>Participants were asked to complete a single follow-up questionnaire between three and nine months of symptom onset (averaging around five to six months). Impact on activities of daily living and on quality of life was assessed, and around 30% of both hospitalised and non-hospitalised people reported Long Covid symptoms (despite most having experienced mild acute illness).</p>

Study	Garrigues E, Janvier P, Kherabi Y, et al. Post-discharge persistent symptoms and health-related quality of life after hospitalization for COVID-19. <i>J Infect.</i> 2020;81(6):e4-e6. doi:10.1016/j.jinf.2020.08.029
Date, Country	August 2020, France
No. of participants	120
Follow up	111 days
Description	<p>We included 120 patients after a mean (<math>\pm</math>SD) of 110.9 (<math>\pm</math>11.1) days following admission. The most frequently reported persistent symptoms were fatigue (55%), dyspnoea (42%), loss of memory (34%), concentration and sleep disorders (28% and 30.8%, respectively). Comparisons between ward- and ICU patients led to no statistically significant differences regarding those symptoms. In both group, EQ-5D (mobility, self-care, pain, anxiety or depression, usual activity) was altered with a slight difference in pain in the ICU group.</p>

Study	Ayoubkhani D, Khunti K, Nafilyan V, Maddox T, Humberstone B, Diamond I et al. Post-covid syndrome in individuals admitted to hospital with covid-19: retrospective cohort study BMJ 2021; 372 :n693 doi:10.1136/bmj.n693
Date, Country	March 2021, UK
No. of participants	47,780
Follow up	140 days
Description	<p>47 780 individuals (mean age 65, 55% men) in hospital with covid-19 and discharged alive by 31 August 2020, exactly matched to controls from a pool of about 50 million people in England for personal and clinical characteristics from 10 years of electronic health records.</p> <p>Over a mean follow-up of 140 days, nearly a third of individuals who were discharged from hospital after acute covid-19 were readmitted (14 060 of 47 780) and more than 1 in 10 (5875) died after discharge, with these events occurring at rates four and eight times greater, respectively, than in the matched control group. Rates of respiratory disease (<math>P&lt;0.001</math>), diabetes (<math>P&lt;0.001</math>), and cardiovascular disease (<math>P&lt;0.001</math>) were also significantly raised in patients with covid-19, with 770 (95% confidence interval 758 to 783), 127 (122 to 132), and 126 (121 to 131) diagnoses per 1000 person years, respectively. Rate ratios were greater for individuals aged less than 70 than for those aged 70 or older, and in ethnic minority groups compared with the white population, with the largest differences seen for respiratory disease (10.5 (95% confidence interval 9.7 to 11.4) for age less than 70 years v 4.6 (4.3 to 4.8) for age <math>\geq 70</math>, and 11.4 (9.8 to 13.3) for non-white v 5.2 (5.0 to 5.5) for white individuals).</p> <p>Individuals discharged from hospital after covid-19 had increased rates of multiorgan dysfunction compared with the expected risk in the general population.</p>