Physical functioning and health-outcomes following hospitalisation with COVID-19: a longitudinal cohort study

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Declaration

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List of Abbreviations

Abbreviation	Full Term
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
WHO	World Health Organisation
SARS-CoV	Severe Acute Respiratory Syndrome Coronavirus
MERS-CoV	Middle Eastern Respiratory Syndrome Coronavirus
SpO2	Oxygen Saturation
PaO2	Partial Pressure of Oxygen
FiO2	Fraction of Inspired Oxygen
mmHg	Millimetres of Mercury
ARDS	Acute Respiratory Distress Syndrome
RAAS	Renin-Angiotensin-Aldosterone System
V/Q	Ventilation/Perfusion
FDA	Food and Drug Administration
DMARD	Disease Modifying Anti-Rheumatic Drug
HIV	Human Immunodeficiency Virus
AIDS	Acquired Immune Deficiency Syndrome
CRRT	Continuous Renal Replacement Therapy
CPAP	Continuous Positive Airway Pressure
NIV	Non-Invasive Ventilation
IMV	Invasive Mechanical Ventilation
COPD	Chronic Obstructive Pulmonary Disease
SPPB	Short Performance Physical Battery
DLCO	Diffusion Capacity for Carbon Monoxide
PFTs	Pulmonary Function Tests

HrQOL	Health Related Quality of Life
SF-36-II	Short-Form-36 Version 2
FEV1	Forced Expiratory Volume
6MWT	6-Minute Walk Test
6MWD	6-Minute Walk Test Distance
PTSD	Post-Traumatic Stress Disorder
RT-PCR	Reverse Transcription–Polymerase Chain Reaction
MRC Scale	Medical Research Council Scale
HRCT	High-Resolution CT
ICU	Intensive Care Unit
EQ-5D-5L	Eurquol-5 Dimension
PACS	Post-Acute COVID-19 Syndrome
PICS	Post-Intensive Care Unit Syndrome
BMI	Body Mass Index
MSc	Master of Science
NPHET	National Public Health Emergency Team
CMO	Chief Medical Officer
PUP	Pandemic Unemployment Payment
HSE	Health Service Executive
CCO	Chief Clinical Officer
CEO	Chief Executive Officer
IT	Information Technology
T1	Timepoint 1
T2	Timepoint 2
T3	Timepoint 3

EU	European Union
DCC	Digital Covid Certificate
mRNA	Messenger Ribonucleic Acid
NIAC	National Immunisation Advisory Committee
TUH	Tallaght University Hospital
SJH	St. James's Hospital
MDT	Multidisciplinary Team
PIL	Patient Information Leaflet
ICC	Intraclass Correlation Coefficient
CI	Confidence Interval
MBD Scale	Modified Borg Dyspnoea Scale
NCCN	National Comprehensive Cancer Network
SD	Standard Deviation
IQR	Interquartile Range
TA	Thematic Analysis
IPA	Interpretative Phenomenological Analysis
GT	Grounded Theory
PF	Physical Functioning
RP	Role Limitations due to Physical Problems
RE	Role Limitations due to Emotional Problems
VT	Vitality
MH	Mental Health
SF	Social Functioning
BP	Bodily Pain
GH	General Health

HC	Health Change
NS	Not Significant
A & E	Accident & Emergency
FVC	Forced Vital Capacity
PEM	Post-Exertion Malaise
PESE	Post-Exertion Symptom Exacerbation
ME	Myalgic Encephelomyelitis
CFS	Chronic Fatigue Syndrome
HSCP	Health and Social Care Professional

Summary

Introduction: A novel coronavirus (severe acute respiratory syndrome coronavirus 2; SARS-CoV-2) emerged in Wuhan, China in late 2019, causing an outbreak of viral pneumonia. Initial studies published focused on the management of acute COVID-19 and the containment of the virus. The wide range of clinical presentations of acute COVID-19 is well-documented from asymptomatic infection to death. Published studies suggest short-term physical recovery from COVID-19 is complex, with many individuals experiencing persistent symptoms. There is a paucity of data investigating the longer-term trajectory of physical recovery from COVID-19. There have been no studies to-date investigating physical recovery from hospitalisation with COVID-19 amongst an Irish cohort.

Methods: This study was conducted in St. James's Hospital, Dublin. Participants were recruited from the hospital's Post-Acute COVID-19 Multidisciplinary Clinic from May to November 2020. For Project 1 a prospective longitudinal design was utilised to investigate the impact COVID-19 has on physical functioning at 10-weeks (T1), 6-months (T2) and 1-year (T3) post-hospital discharge. Objective measures of recovery included 6-Minute Walk Test Distance (6MWTD), frailty (Clinical Frailty Scale), quantification of falls following hospital-discharge, return to work status and exercise levels. Subjective markers included symptoms (COVID-19-Specific Patient Concerns Assessment), fatigue (Chalder Fatigue Score) and health-related quality of life (HrQOL) (Short-Form-36 Health Survey Questionnaire). Univariate analysis was performed using t-test, Wilcoxon rank-sum, and Chi-squared test, paired analysis using one-way analysis of variance and Kruskal-Wallis testing and correlation analysis with Spearman correlation tests.

At T2 a subset of participants was recruited to participate in Project 2. Project 2 sought to gain a deeper understanding of the lived experience of recovering from hospitalisation with COVID-19 through individual interviews. A total of 18 participants were interviewed. Interviews were

recorded and transcribed verbatim. Reflexive thematic analysis was used to interpret and analysis the interview data.

Results Project 1: Sixty-one subjects participated. Assessments were conducted at a median of 55 days(T1), 242 days(T2), and 430 days(T3) following hospital-discharge. 6MWD improved significantly overtime ($F = 10.3$, $p < 0.001$) from 365(209) m at T1 to 447(85)m at T3, however remained below population norms (572m for males and 538m for females) and with no associated improvement in perceived exertion (as assessed by the Modified Borg Scale). Approximately half (n = 27(51%)) had returned to pre-diagnosis exercise levels at T3. At least one concern/symptom was reported by 74%, 59% and 64% participants at T1, T2 and T3 respectively. Fatigue was the most frequently reported symptom at T1(40%) and T2(49%), while issues with memory/concentration was the most frequently reported at T3(49%). SF-36-II scores did not change significantly in any domain over the study period, and scores remained lower than population norms in the domains of physical functioning, energy/vitality, role limitations due to physical problems and general health. Return-to-work rates are low, with 55% of participants returning to work in some capacity, and 31% of participants don't feel back to full-health at 1-year following infection.

Results Project 2: Participants gave varying accounts of recovery with several over-arching themes emerging including a) *a complex recovery experience characterised by persistent symptoms, often which are unpredictable and confusing*, b) *positive recovery experience with little effect on physical function*, c) *the effects of the global pandemic and government mandated restrictions on recovery*, d) *follow-up care* and e) *return-to-work*. Results from Project 2 highlighted the importance of the patient narrative in understanding the complex and individual nature of recovery from COVID-19.

Conclusion: Hospitalised COVID-19 survivors report persistent symptoms, particularly fatigue and breathlessness, low health-related quality of life scores, sub-optimal exercise levels and

continued work absenteeism 1-year following infection, despite some objective recovery of physical functioning. Findings suggest those who returned to exercise within 1-year may have less fatigue and breathlessness. Future research on the impact of exercise, and other rehabilitative strategies is warranted to explore rehabilitation goals to optimise patient outcomes during recovery from COVID-19.

Outputs

Publications

O'Brien K, Townsend L, Dowds J, Bannan C, Nadarajan P, Kent B, Murphy N, Sheill G, Martin-Loeches I, Guinan E. (2022) 1-year quality of life and health-outcomes in patients hospitalised with COVID-19: a longitudinal cohort study. Respiratory Research 23(1); 115 doi: 10.1186/s12931-022-02032-7.

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Conference Presentations:

Conference: The Annual Scientific Meeting of the Irish Thoracic Society 2021

Platform/Location: Zoom

Lead Presenter: Kate O'Brien

Title: Physical functioning and health-outcomes in individuals hospitalised with COVID-19: a longitudinal cohort study

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Conference: The Annual Conference of the Psychology Society of Ireland

Platform/Location: Recording Studio in Dublin City Centre

Lead Presenter: Kate O'Brien

Title: Physical functioning and health-outcomes in individuals hospitalised with COVID-19: a longitudinal cohort study and the potential role of Clinical Psychology in Long COVID.

Date: November 2021

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Platform/Location: Lisbon, Portugal

Lead Presenter: Kate O'Brien

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Date: April 2022

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Lead Presenter: Kate O'Brien

Title: Physical functioning and health-outcomes in individuals hospitalised with COVID-19: a longitudinal cohort study

Date: May 2022

Conference: The St. James's Hospital Multidisciplinary Annual Conference

Platform/Location: St. James's Hospital, Dublin

Lead Presenter: Kate O'Brien

Title: Physical functioning and health-outcomes in individuals hospitalised with COVID-19: a longitudinal cohort study

Date: September 2022

Other (Media): The findings of this research were also discussed by the lead researcher on The Pat Kenny Show (Newstalk) in April 2022 and will be discussed on the Real Health Podcast with Karl Henry in September 2022.

Chapter 1 Introduction

1.1 Defining COVID-19

A novel coronavirus (severe acute respiratory syndrome coronavirus 2; SARS-CoV-2) emerged in Wuhan, China in late 2019, causing an outbreak of viral pneumonia. It has been named Coronavirus Disease or COVID-19 (Lv et al., 2020). It is classified as a highly contagious infectious disease and is transmitted from person to person through respiratory secretions (Thomas et al., 2020). After the first cases were reported in Wuhan, the SARS-CoV-2 virus spread rapidly across the world. The World Health Organisation (WHO) declared a global pandemic on March 11th, 2020. Due to efforts of researchers worldwide over the last 2 years, there is growing understanding of the virology, epidemiology and clinical management of COVID-19, however stopping the spread of the virus is still a major issue of concern with many countries enduring multiple waves of outbreaks which is mainly attributed to the emergence of new mutant variants of the RNA virus (Cascella et al., 2022). Variants of concern to-date include Alpha, Beta, Gamma, Delta and Omicron (Cascella et al., 2022).

Since being declared a global pandemic by the WHO, SARS-CoV-2 has spread to 223 countries with more than 579 million cases, and almost 6.5 million deaths reported globally as of August, 2022 (WHO, 2022a). Other epidemics caused by viruses in the last 20 years include severe acute respiratory syndrome coronavirus (SARS-CoV) from 2002 to 2003, H1N1 influenza in 2009, and the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) in 2012 and were considered to have significant impact on global health. However, the COVID-19 pandemic is considered to be the most consequential global health crisis since the influenza pandemic in 1918 (Cascella et al., 2022). In Ireland, as of the 29th of August 2022, there have been over 1.6 million confirmed cases of COVID-19 with 7,820 associated deaths.

1.2 COVID-19 Levels of Severity

COVID-19 has many clinical presentations and is often categorised in terms of its severity. The following categories are cited from the National Institutes of Health COVID-19 Treatment Guidelines 2021 are commonly used:

- Asymptomatic infection: Individuals who test positive for SARS-CoV-2 but who display no symptoms consistent with COVID-19.
- Mild illness: Individuals who display the signs and symptoms of COVID-19 (e.g., fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhoea, loss of taste and smell) but who do not have shortness of breath, dyspnoea, or abnormal chest imaging.
- Moderate illness: Individuals who show evidence of lower respiratory disease during clinical assessment or imaging and who have an oxygen saturation (SpO_2) ≥94% on room air at sea level.
- Severe illness: Individuals who have SpO_2 <94% on room air at sea level, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO_2/FiO_2) <300 mm Hg, a respiratory rate >30 breaths/min, or lung infiltrates >50%.
- Critical illness: Individuals who have respiratory failure, septic shock, and/or multiple organ dysfunction.

COVID-19 severity has also been classified using a 7-item ordinal scale. This was originally proposed by Cao and colleagues when investigating the use of Lopinavir-Ritonavir for the treatment of severe COVID-19 (Cao et al., 2020). This scale has been used by other researchers including Huang and colleagues (Huang et al., 2021b). The COVID-19 severity scale can be seen in the table below.

Table 1: The 7-category COVID-19 severity ordinal scale as proposed by Cao and colleagues (Cao et al., 2020).

Severity categories	Clinical manifestation
Category 1	Not hospitalised with a resumption of normal activities.
Category 2	Not hospitalised, but unable to resume normal activities.
Category 3	Hospitalised, but not requiring supplemental oxygen.
Category 4	Hospitalised, requiring supplemental oxygen.
Category 5	Hospitalised, requiring nasal high-flow oxygen therapy, non-invasive mechanical ventilation, or both.
Category 6	Hospitalised requiring invasive mechanical ventilations, extracorporeal membrane oxygenation, or both.
Category 7	Death.

COVID-19 is primarily considered a viral respiratory illness as the SARS-CoV-2 virus predominantly targets the respiratory system (Cascella et al., 2022). The pathogenesis of SARS-CoV-2 in the lungs is explained in two phases (Cascella et al., 2022). Firstly, the early phase which is characterized by viral replication resulting in direct virus-mediated tissue damage (Wang et al., 2020). This is then followed by the late phase when the infected host cell triggers an immune response with the recruitment of various white blood cells (lymphocytes, monocytes and neutrophils) which in turn release cytokines (e.g., tumour necrosis factor-α (TNF α) and

interleukin-6 (IL-6)) (Wang et al., 2020). In severe COVID-19 the immune system's overactivation results in a 'cytokine storm', releasing high levels of these cytokines into the circulation, which results in local and systemic inflammation (Azkur et al., 2020). Within the pulmonary vasculature there is increased permeability and patients with severe COVID-19 can develop pulmonary oedema, this can be explained by a number of mechanisms. These mechanisms and processes lead to lung inflammation (pneumonitis) until the development of fibrosis, or lung tissue scarring (Conti et al., 2020). This lung inflammation affects the lung's oxygen carrying capacity, resulting in respiratory failure and leads to hypoxia or hypoxaemia. For a small percentage of patients this will develop into the critical COVID-19 associated Acute Respiratory Distress Syndrome (ARDS).

While the lungs are the primary target for SARS-CoV-2, it can affect other organ systems including the gastrointestinal tract, hepatobiliary, cardiovascular, renal and central nervous systems (Coopersmith et al., 2021). Such organ dysfunction can be explained by one or a combination of mechanisms such as direct viral toxicity, ischaemic injury caused by inflammation of blood vessels (vasculitis), thrombosis (clotting), thrombo-inflammation, immune dysregulation, and renin-angiotensin-aldosterone system (RAAS) dysregulation (Coopersmith et al., 2021).

1.3 Treatment of acute COVID-19

The severity of COVID-19 disease determines the treatment approach. Those with mild illness are advised to self-isolate, monitor their symptoms and treat them accordingly. For example, a fever should be treated with paracetamol and increasing oral intake of fluids, or a cough can be treated with over-the-counter medications from one's local pharmacy (Health Service Executive ((HSE)), 2022). Individuals are also advised to rest and contact their general practitioner should they become concerned about any of their symptoms or should they experience chest pain or breathlessness (HSE, 2022).

There have been and continues to be valiant efforts from researchers worldwide to identify different treatment options for those who are hospitalised with COVID-19, in the form of clinical trials. One of the largest of these was the WHO Solidarity trial which took place in 600 hospitals across 52 countries (WHO, 2022b). This is a worldwide collaborative series of trials carried out to identify life-saving treatments for COVID-19 (WHO, 2022b). This trial series investigated the efficacy of a number of drugs in treating COVID-19, with varying outcomes. Drugs trialled include Remdesivir (an antiviral FDA-approved medication), hydroxychloroquine (a disease modifying anti-rheumatic drug normally used to prevent and treat malaria), lopinavir/ritonavir (a combination antiretroviral drug often use for the treatment and prevention of HIV/AIDS) and interferon (an immunomodulator used for the treatment of a variety of conditions including hepatitis B and C and lymphoma) (WHO, 2021a).

More recent studies have shown that Remdesivir has had favourable outcomes in those with severe COVID-19, including reduced risk of mortality and more favourable recovery (Olender et al., 2021). It has also been shown to be effective in the prevention of progression of severe COVID-19 in high risk patients (Gottlieb et al., 2021). Dexamethasone is a corticosteroid which is commonly used in the hospital setting and has been proven to reduce the length of time COVID-19 patients require invasive mechanical ventilation (WHO, 2021a). It is now used as a first line treatment for those who show COVID-19 pneumonitis on chest X-rays to prevent escalation to critical care and/or ventilation (WHO, 2021a). It has been shown to save lives of those with severe and critical illness.

Another recent study conducted in 2022 has shown that Remdesivir plus Dexamethasone versus Dexemethasone alone is effective in reducing mortality, hospital length of stay, and faster clearance of the Sars-CoV-2 virus in those with COVID-19. Care of those with moderate to severe COVID-19 also focuses largely on the treatment of the sequelae / symptoms of the virus (HSE, 2022). These sequalae may be managed with oxygen therapy and other supportive

therapies including intravenous fluids, and for some, non-invasive ventilation. Supportive care for the critically ill with COVID-19 associated ARDS includes (Murthy, Gomersall and Fowler, 2020):

- Conservative intravenous fluids
- Empirical intravenous antibiotics for suspected bacterial coinfection
- Consideration for early, invasive endotracheal intubation and ventilation to maintain adequate oxygenation and carbon dioxide elimination
- Lung protective ventilation strategies, such as limiting tidal volumes and inspiratory pressures
- Periods of prone positioning while mechanically ventilated to decrease the risk of mechanical lung injury and to optimise V/Q (ventilation/perfusion) matching
- Consideration of extracorporeal membrane oxygenation

In-hospital physicians also use other therapies for the treatment of the sequelae or complications caused by severe COVID-19 including the use of antibiotics to treat secondary bacterial infections and interventions for multi-organ failure as a result of septic shock including continuous renal replacement therapy (CRRT) for kidney failure and the use of inotropes and vasopressors for those in cardiogenic shock/heart failure.

The clinical manifestations and severity of COVID-19 vary greatly. Male gender, the presence of pre-existing conditions, increasing age, pregnancy in women, compromised immune systems, lower socioeconomic status, certain ethnic backgrounds (black and south-Asian) and increased viral load exposure increase the risk for developing severe COVID-19 (Gao et al., 2021).

1.4 The effects of acute COVID-19 on physical function

For some, acute COVID-19 will affect one's physical function, particularly those who are hospitalised with moderate to severe illness. The factors contributing to physical dysfunction are multifactorial.

Patients in a hospital setting with moderate to severe COVID-19 experience a significant reduction in mobility due to the isolation requirement (Welch et al., 2020). Patients who were hospitalised during the first and the beginning of the second wave of the outbreaks in Ireland were required to isolate in a single-room or small 6-bed bay for at-least 14-days, before this requirement was reduced to 10-days. The only form of activity these patients would be achieving would likely have been mobilising to and from the toilet and perhaps one physiotherapy session per day, perhaps in-between sessions of self-proning. Patients who were in respiratory failure and required high levels of high flow oxygen therapy, non-invasive ventilation (E.g., continuous positive airway pressure (CPAP)) or invasive mechanical ventilation in the critical care setting, as treatment for COVID-19 during hospital admissions were as a consequence, completely immobile for extended periods of time. Immobility leads to muscle wasting or sarcopenia (Welch et al., 2020). Sarcopenia is a condition of extreme muscle insufficiency, defined by reduced muscle strength with reduced muscle quantity and/or muscle quality (Cruz-Jentoft, 2016), and occurs most commonly in hospitalised patients (Welch et al., 2020). Sarcopenia is associated with limitations in physical function and reduced quality of life in community-dwelling adults over the age of 65 (Beaudart et al., 2015). Although it is associated more-so with the elderly, is increasingly recognised that it can occur at any age, particularly amongst those with chronic conditions including Chronic Obstructive Pulmonary Disease and other cardiorespiratory disorders. It has also been linked with reduced diaphragmatic strength in hospitalised patients and can therefore contribute to respiratory failure, causing a requirement for prolonged ventilation in critically unwell patients (Deniz et al., 2021). Previous

studies have shown that previously 'robust' individuals can develop acute sarcopenia after hospitalisation with severe illness (Welch et al., 2018).

In addition to this sudden decrease in physical activity, COVID-19 survivors may also be at risk of developing sarcopenia for a variety of other reasons. These include the occurrence of cytokine release leading to a state of anabolic resistance. Anabolic resistance is defined by a weakened stimulation of muscle protein synthesis rates to common anabolic stimuli in skeletal muscle tissue such as dietary protein and exercise (Paulussen et al., 2021). This in turn creates a requirement for higher protein intake to stimulate muscle protein synthesis, leading to increased nutritional demand, however during a period of reduced oral intake (Welch et al., 2020). Other contributing factors to the development of sarcopenia include the use of steroids including dexamethasone, and in some critically unwell patients the use of paralysing agents such as actracurium, and muscle relaxants like midazolam also increase the risk of developing sarcopenia (Welch et al., 2020). Sarcopenia has been associated with increased rehabilitation needs in surgical populations (Reisinger et al., 2015) and this will be no different for the COVID-19 population.

In those with moderate to severe COVID-19, whereby the respiratory system has been targeted, exercise tolerance during and immediately following acute illness will be profoundly affected, with those who required ventilation during their acute illness in particular experiencing respiratory muscle weakness (Nava, 1998). This sarcopenia and reduced exercise tolerance results in impaired physical function and will affect one's ability to carry out the simplest activities of daily living (Nava, 1998; Beaudart et al., 2015).

A number of studies have investigated patients' physical functioning status soon after resolution of acute infection with COVID-19. Belli and colleagues investigated the physical functioning of hospitalised COVID-19 patients on entering a rehabilitation facility in Northern Italy, from the acute hospital setting and at the time of their discharge home (Belli et al., 2020).

One of the main outcome measures used was the Short Physical Performance Battery (SPPB). This test includes three functional tests, standing balance, 4-meter gait speed, and 5-repetition sit-to-stand motion (Paneroni et al., 2021). On entry to this rehabilitation setting almost 80% of 103 patients were in the low performance group of the SPPB, 67% of patients scored poorly on the Barthel Index while almost half were bedridden (Belli et al., 2020). For reference the Barthel Index (BI) assesses disability in patients with neuromuscular and musculoskeletal conditions receiving inpatient rehabilitation (Sainsbury et al., 2005). The BI is an ordinal scale which assesses ten different activities of daily living including feeding, dressing and toilet use, and is often used in the older population (Sainsbury et al., 2005). Despite having received early mobilisation/bedside physiotherapy while in the rehabilitation hospital, more than half of the patients still had suboptimal PPB scores and just under half scored poorly on the Barthel Index while issues with feeding, toileting, bathing and dressing were identified (Belli et al., 2020). A similar study was conducted again in Italy by Paneroni and colleagues where patients who were admitted to a subacute unit following their management in the acute setting for respiratory failure caused by COVID-19 and were assessed for impaired physical functioning (Paneroni et al., 2021). Normal physical function was detected in only 12% of patients on admission to this subacute unit (Paneroni et al., 2021). These studies, and experience with other similar hospitalised patient cohorts highlight the importance of rehabilitation in the acute hospital setting.

1.5 Recovery at 3-months post-infection

When one considers the impact COVID-19 has on physical functioning during the acute phase it is not unreasonable to assume that symptoms and problems may persist after resolution of acute infection. Findings from research on recovery from other coronaviruses such as Sars showing that patients experienced incomplete recovery 1-2 years following infection validate this theory (Rooney, Webster and Paul, 2020). Extraordinary efforts have been made by researchers worldwide to understand recovery from COVID-19 with many studies being

published initially on recovery or lack thereof up to 3-months after acute infection with COVID-19.

A number of European studies investigated health-outcomes and functional status of patients hospitalised during their acute COVID-19 illness 1-2 months following hospital-discharge have been published (de Graaf et al., 2021, Carenzo et al., 2021, van der Sar-van der Brugge et al., 2021).

A study conducted by De Graaf and colleagues in the Netherlands found that most (67%) hospitalised patients (both those who required critical care and those who did not) suffered some form of functional limitation, scoring 2 or above on the Post-COVID-19 Functional Status Score when presenting to an outpatient clinic 6-weeks post hospitalisation (de Graaf et al., 2021). A score of 2 on this scale indicates that daily activities are performed at a lower intensity, patients who scored 3 are forced to modify their activities due to symptoms, pain or anxiety and those who score 4 require assistance with activities of daily living because due to functional limitations (Klok et al., 2020). Dyspnoea on exertion was the most commonly reported symptom, which may be reflective of the reduced diffusion capacity for carbon monoxide (DLCO) noted on patients' pulmonary function tests (PFTs) at this timepoint (de Graaf et al., 2021). A similar 6-week follow-up Dutch study looked at PFTs, health-related quality of life using the short-form-36 survey (SF-36-II) and persistent symptoms in those who suffered moderate or severe COVID-19 pneumonia during their hospitalisation (van der Sar-van der Brugge et al., 2021). Similarly, reduced DLCO was found in 71.7 % of cases, and was particularly lower in those who had severe pneumonia during acute illness (van der Sar-van der Brugge et al., 2021). Significant impairment was observed across all domains of the SF-36 and most importantly there was a significant positive correlation with the presence of reduced DLCO and Forced Expiratory Volume (FEV1) and breathlessness scores as assessed by the Borg Scale and Modified Medical Research Council Score (mMRC) and many of the SF-36 domains, particularly physical

functioning (van der Sar-van der Brugge et al., 2021). Another early Italian study investigating COVID-19 recovery found that patients who suffered severe COVID-19 requiring invasive mechanical ventilation presented with mild to moderate functional impairment (as denoted by impaired 6-minute walk test distance) 2-months after hospital discharge and reported a large number of symptoms of post-traumatic stress disorder symptoms at the same time-point (Carenzo et al., 2021).

The shorter-term studies mentioned above have primarily investigated those who were hospitalised with COVID-19 pneumonia soon after their hospital-discharge. Impairments observed on PFTs, leading to breathlessness and in turn reduced physical function are to be expected at this timepoint. However, it is important that such impairments are investigated over a longer period.

Several studies investigated recovery following COVID-19 in the sub-acute phase (2-3 months following initial infection) (Carfì, Bernabei and Landi 2020; Arnold et al., 2021; Chopra et al., 2021; Garrigues et al., 2020 and Xiong et al., 2021). An Italian study assessed 143 patients 60 days after initial onset of symptoms. Seventy two percent of the study's cohort had evidence of COVID-19 pneumonia during their hospitalisation, with 15% requiring non-invasive ventilation and 5% requiring invasive mechanical ventilation (Carfì et al., 2020). Concerningly, at time of assessment, 32% of patients had 1-2 symptoms including fatigue and breathlessness, while 55% had 3 or more symptoms, with a high proportion of patients reporting fatigue, dyspnoea, joint pain and chest pain (Carfì et al., 2020). Similarly, a UK based study found that most (74% of 110) patients who attended a follow-up outpatient clinic had persistent symptoms up to 12-weeks post hospital-admission with the most notable symptoms being fatigue and breathlessness (Arnold et al., 2021). However, in this cohort abnormalities in chest radiographs, blood tests, spirometry and exercise tests were less frequent (35%) perhaps suggesting resolution of pulmonary abnormalities as time progresses (Arnold et al., 2021).

While the aforementioned studies investigated recovery in those who were hospitalised with COVID-19, it is important to assess recovery in those with milder acute infection, to understand the broad spectrum of COVID-19-associated illness. This importance was recognised by researchers of a large multistate study in the United States and of a single-centred study in France (Tenforde et al., 2020; Carvalho-Schneider et al., 2021). In the first study, telephone interviews were conducted with non-hospitalised respondents 2-3 weeks after their positive reverse transcription–polymerase chain reaction (RT-PCR) test for SARS-CoV-2. Of the 292 respondents, 94% reported experiencing one or more symptoms at the time of their positive RT-PCR test, and 35% of these reported not having returned to their usual state of health at the time of the interview with the most common persistent symptoms being breathlessness, fatigue and persistent cough (Tenforde et al., 2020), however this study is very limited by its short follow-up time. In the latter study which followed-up both those who were hospitalised and those who were not during their acute illness with non-critical COVID-19, it was found that 66% of 150 patients had symptoms at 3-months with 30% reporting ongoing dyspnoea and 40% reported asthenia (Carvalho-Schneider et al., 2021).

A comprehensive review and meta-analysis exploring the various longer-term effects of COVID-19 among both hospitalised and non-hospitalised patients with COVID-19 from 14 to 110 days following infection was published in 2021 (Lopez-Leon et al., 2021). The review only included studies that had 100 patients or more. A total of 47, 910 patients were included across the 15 included studies with an age range of 17-87 years. Ten studies collected information from the patients using self-reported surveys, two studies collected data from medical records and three by a clinical evaluation. Fifty-five potential long-term effects were identified with the most common being fatigue (58%), headache (44%), attention disorder (27%), hair loss (25%), and dyspnoea (24%) (Lopez-Leon et al., 2021).

It is clear from reviewing the literature published to-date that recovery from mild to critical acute COVID-19 up to 3-months following acute infection is suboptimal and the need for longer-term follow-up studies was identified.

1.6 Recovery at 6-months and 12-months following infection

Several studies have been published which have investigated outcomes at 6-months following acute infection (Romero-Duarte et al., 2021, Huang et al., 2021a, Wu et al., 2021, Hodgson et al., 2022). A multi-centred Spanish study demonstrated that 63.9% of 797 who survived hospitalisation with COVID-19 reported some sequelae during their first 6-months of recovery (Romero-Duarte et al., 2021). The most frequent were respiratory (42.0%), systemic (36.1%), neurological (20.8%), mental health (12.2%) and infectious (7.9%) (Romero-Duarte et al., 2021). Although authors did not specify what percentage of participants were still experiencing these sequelae at 6-months, they did endeavour to understand the impact these sequelae had on the health-care system, reporting on the percentage of participants who presented to the emergency department during this 6-month period (20.1%), how many were re-admitted to hospital (4.4%) and how many died (1%) during the study period (Romero-Duarte et al., 2021).

Preliminary results from Huang and colleagues' year-long, comprehensive, follow-up study showed that 76% of 1655 patients reported at least one persistent symptom at 6-months after hospital-discharge (Huang et al., 2021a). Those that had more severe initial infection were more likely to have a persistent symptom and the most commonly reported symptoms were fatigue, muscle weakness or sleep difficulties (Huang et al., 2021a). In the same study those who had more severe illness more likely to score higher on the mMRC scale for breathlessness and to report issues with anxiety/depression, mobility and pain and performed worse in the 6MWT (Huang et al., 2021a). Authors of the study further analysed PFT results with respect to severity of initial COVID-19 illness using the COVID-19 severity scale (see Table 1). They found that the proportion of participants with lung diffusion impairment was 22% (18 of 83) for category 3,

29% (48 of 165) for category 4, and 56% (48 of 86) for category 5–6. These PFT findings are consistent with findings of abnormalities on chest high resolution CT (HRCT) and authors suggest that further follow-up is warranted in search for resolution of these abnormalities (Huang et al., 2021a). These findings are in keeping with that of another study which solely investigated respiratory outcomes at 6-months following hospitalisation with COVID-19; reduced DLCO was observed in 54% of 83 participants' PFTs and radiological abnormalities on HRCT persisted in 48% at 6-months (Wu et al., 2021). Despite these persistent abnormalities researchers did observe a significant improvement in 6MWTD between 3- and 6-months and the number of patients with various levels of dyspnoea symptoms progressively and significantly decreased between these two timepoints also (Wu et al., 2021). This improvement in 6MWT and symptoms despite a persistent reduction in DLCO might suggest that the observed deficit in DLCO might not be clinically significant, as frequently observed in clinical practice.

From the abundance of research that has been conducted on physical functioning and health-outcomes in those who have survived COVID-19, it is apparent that recovery is sub-optimal at both 3-months and 6-months. However, comparison with COVID-19 hospitalised cohorts and other hospitalised cohorts (such as those admitted to critical care for other causes of respiratory failure) has not been frequently investigated. Researchers in Australia set out to fill this gap in the literature, investigating 6-month outcomes of patients who required invasive mechanical ventilation in ICU amongst COVID-19 and non-COVID-19 survivors (Hodgson et al., 2022). Those in the non-COVID-19 cohort were admitted to ICU for acute respiratory failure between 2017 and 2019 (Hodgson et al., 2022). At 6-months, there was no difference in the incidence of death or new disability between patients with COVID-19 compared with non–COVID-19 acute respiratory failure (58/93 [62.4%] vs. 99/150 [66.0%]), however it is worth noting that the incidence and severity of pre-existing disability was significantly lower in patients with COVID-19 at baseline (Hodgson et al., 2022). The EQ-5D-5L Utility Scale is an self-administered questionnaire comprising of 5-dimensions with one item per dimension; mobility, self-care,

usual activities, pain/discomfort, and anxiety/depression, each dimension has response levels ranging from 'no problems' to 'inability to perform the task' (Feng et al., 2021). At baseline the median EQ-5D-5L utility scale was considerably higher in patients with COVID-19 across all domains, the number of patients reporting no problems was higher in patients with COVID-19 (Hodgson et al., 2022). From this, and from clinical experience, it is clear that many of those who were hospitalised with COVID-19 had no previous comorbidities or limitations in activity of daily living. For such individuals there must be a period of adjustment; those who were once well with no issues with physical function must adjust to life with persistent symptoms and impaired function. This clarifies the need for comprehensive multi-disciplinary outpatient clinics to holistically support those in their recovery from COVID-19.

Due to the persistent symptomology and sub-optimal physical recovery identified in COVID-19 survivors at 3- and 6-months after infection, inevitably researchers identified the need to investigate recovery 1-year following infection. When Project 1, presented in this thesis, was submitted for publication there were only 4 other studies that had investigated recovery at the 1-year time-point. One of the studies focused solely on recovery in those who developed COVID-19-related ARDS, finding that COVID-19-associated ARDS results in persisting impairment in performance-based measures of physical function at 1-year but reassuringly ADL, cognitive and mental health status, and health-related quality of life may be less impaired (Latronico et al., 2021). Two concentrated solely on respiratory outcomes focusing on radiological abnormalities (on high resolution CT) and persistent impairments in pulmonary function tests at 1-year following COVID-19 pneumonitis (Wu et al., 2021; Yan et al., 2021). The fourth was a comprehensive study conducted by Huang and colleagues in China, preliminary findings from their 6-month assessments are discussed above (Huang et al., 2021a).

Huang and colleagues reported an improvement in the percentage of participants reporting persistent symptoms between 6-months (68%) and 1-year (49%), however persistent symptoms

were still very prevalent and the percentage of those who reported persistent dyspnoea increased from 26% at 6-months to 30% at 1- year (p=0.014) (Huang et al., 2021b). This slight increase in reporting of breathlessness occurred alongside a lack of improvement in DLCO impairment from 6 months to 12 months and no overall improvement in median 6MWTD between the two timepoints (Huang et al., 2021b). Thirty-five percent of 243 participants had persistent reduced DLCO, with a higher incidence among those who were sicker during acute illness (Huang et al., 2021b). Reassuringly the proportion of patients with abnormal CT decreased significantly from 6 months to 12 months, as did the severity of ground glass opacities on these CTs (Huang et al., 2021b). Despite the persistent symptoms reported by many, 88% of those who were employed prior to having COVID-19 had returned to work 1-year following their hospitalisation (Huang et al., 2021b). These symptoms included fatigue, which was the most reported symptom at both time-points but decreased considerably from an incidence of 52% at 6-months to 20% at 1-year (Huang et al., 2021b). Despite an observation of resolution of some symptoms including sleep difficulties, hair loss and smell and taste disorders, more patients had anxiety or depression at 1-year (Huang et al., 2021b). Again, the reason for this may be multifactorial with pandemic stressors being a contributing factor. This, along with findings from Mazza and colleagues that there is a high prevalence of psychiatric sequelae at 1-year following COVID-19 confirm the need to provide integrated multidisciplinary services to properly address long-lasting mental health sequelae of COVID-19 and to treat them with the aim of reducing the disease burden (Gennaro Mazza et al., 2021).

Recently more studies have been published investigating physical recovery from COVID-19 1-year following initial infection. Similar to Latronico and colleagues' work, who found that COVID-19-associated ARDS leads to persisting impairment in performance-based measures of physical function (Latronico et al., 2021), two studies investigated outcomes only of those who required invasive mechanical ventilation during their acute battle with COVID-19 (Bels et al., 2022; Zangrillo et al., 2022). Findings from both these studies were reassuring. Of 116 patients who

were admitted to ICU in a hospital in Italy, 61 (56%) survived to hospital discharge and 56 completed assessments at 1-year following infection (Zangrillo et al., 2022). Despite participants in this study having severe initial illness requiring invasive mechanical ventilation, authors report an overwhelmingly positive recovery with over 80% reporting good recovery and no issues with usual activities and 93% had no issues with dyspnoea at rest, and at 1-year psychological tests confirmed low rates of anxiety, depression, PTSD, insomnia, and cognitive impairment (Zangrillo et al., 2022). Like Huang and colleagues' cohort, 30% of individuals reported breathlessness on exertion and abnormalities on chest CTs improved over-time with only 4 out of 36 (13.8%) having fibrotic like changes at 1-year (Zangrillo et al., 2022). These positive outcomes meant that 32 out of the 38 participants (84%) were able to return to work at 12-months following acute illness (Zangrillo et al., 2022). Bels and colleagues also observed a similar survival rate of 55% of 94 patients who were admitted to their ICU in the Netherlands, and 90% of survivors completed 1 year follow-up assessments (Bels et al., 2022). In contrast to findings by Huang and colleagues however, the proportion of patients with ground glass opacities and other radiological abnormalities on chests CT remained largely unchanged at 12-months from 3-months, but the extent of the abnormalities was less (Bels et al., 2022). However most other findings are in keeping with the other two studies including improvement in DLCO over-time along with health-related quality of life but dyspnoea and fatigue remaining unaltered (Bels et al, 2022). In contrast to findings by Huang and colleagues, the authors of the study in the Netherlands found that physical performance as assessed by the 6MWT improved from 3-months to 1-year, this discordance may be due the Huang and colleagues comparing median 6MWTD between 6-months and 1-year rather than 3-months. Authors did not comment on return-to-work rates amongst their cohort.

While the studies described above assessed both subjective and objective physical recovery, some researchers focused solely on subjective recovery used self-reported questionnaires and telephone interviews to gain an insight into persistent symptoms experience by COVID-19

survivors 1-year after infection (Heesakkers et al., 2022; Pauley et al., 2021, Shivani et al., 2022, Zhang et al., 2021). In all studies persistent symptoms were common and included physical symptoms such as fatigue, dyspnoea, deconditioning, joint pain, muscle weakness; and mental symptoms such as anxiety and depression (Heesakkers et al., 2022; Pauley et al., 2021; Shivani et al., 2022; Zhang et al., 2021).

The overall consensus from the studies that have investigated both subjective and objective recovery from COVID-19 at 1-year following infection, is that recovery appears to be complex and unpredictable. While some trends may appear in terms of predictors for better or worse outcomes, it is evident that many people are still living with persistent symptoms, radiological abnormalities and functional impairments, which in turn affects their mental health status. With that being said, the need for longer-term follow-up studies is evident. This is necessary so the correct infrastructure, services and staffing are allocated towards COVID-19 recovery.

1.7 Terminology to describe COVID-19 Recovery (Post-acute COVID-19 Syndrome, Post-COVID-19 Syndrome and Long COVID)

1.7.1 Post-Acute COVID-19 Syndrome / Post-COVID-19 Syndrome

Due to the impaired physical functioning and persistent symptomology experienced by many for some time following acute infection with COVID-19, and the stigma associated with it, some new terms have been penned to label these clusters of symptoms/sequelae as syndromes or conditions. The first was Post-Acute COVID-19 Syndrome or PACS (Nalbandian et al., 2021). PACS is a syndrome characterized by persistent symptoms and/or delayed or long-term complications beyond 4 weeks from the onset of symptoms of COVID-19 (Nalbandian et al., 2021). Nalbandian and colleagues presented a detailed review of the literature on PACS, it's pathophysiology and organ-specific sequelae (Nalbandian et al., 2021). The main purpose of this review was to provide an in-depth understanding of patients' care needs beyond the acute phase. PACS has been divided into two categories (Greenhalgh et al., 2020, Shah et al., 2021b):

1. Subacute or ongoing symptomatic COVID-19 which includes symptoms and abnormalities present from 4-12 weeks beyond acute COVID-19.
2. Chronic or post-COVID-19 syndrome which includes symptoms and abnormalities persisting or present beyond 12 weeks of the onset of acute COVID-19 and not attributable to alternative diagnosis.

Common symptoms of PACS include (Nalbandian et al., 2021):

- Fatigue
- Muscular weakness
- Joint pain
- Dyspnoea
- Persistent cough
- Persistent oxygen requirements
- Anxiety / Depression
- Sleep disturbances
- Post-traumatic stress disorder
- Cognitive disturbances
- Headaches
- Palpitations
- Chest pain
- Thromboembolism
- Chronic kidney disease
- Hair loss

After conducting a comprehensive review of the literature, Nalbandian and colleagues provided a summary of PACS by organ system including (Nalbandian et al., 2021):

- Pulmonary (including symptoms such as dyspnoea and decreased exercise capacity which may be explained by hypoxia, reduced diffusion capacity, restrictive pulmonary physiology, and ground-glass opacities and fibrotic changes on imaging).
- Hematologic (thromboembolic events)
- Cardiovascular (including symptoms such as palpitations, chest pain and dyspnoea which may be explained by myocardial fibrosis or scarring detectable via cardiac MRI, arrhythmias, tachycardia, and autonomic dysfunction).
- Neuropsychiatric (including symptoms such as fatigue, brain fog, myalgia, headache, anxiety, depression and sleep disturbances which may be explained by a number of diverse mechanisms including immune dysregulation, inflammation, microvascular thrombosis, iatrogenic effects of medications and psychosocial impacts of infection).
- Renal (including persistent reduced estimated glomerular filtration rate despite resolution of acute kidney injury in most COVID-19 survivors).
- Endocrine (including worsening control of existing diabetes mellitus, subacute thyroiditis and bone demineralisation).
- Gastrointestinal & hepatobiliary (prolonged viral faecal shedding despite negative nasopharyngeal swab testing)
- Dermatologic (including hair loss)
- Multi-system inflammatory syndrome in children

Based on the emerging literature available Nalbandian and colleagues also proposed detailed organ system-specific pathophysiological processes and mechanisms to explain the persistent sequalae experienced by survivors (Nalbandian et al., 2021). In short, the potential pathophysiological mechanisms contributing to PACS include a) virus specific pathophysiological changes; b) immunologic aberrations and inflammatory damage in response to the acute infection; and c) expected sequelae of post-critical illness such as Post-ICU Syndrome (PICS) (Nalbandian et al., 2021).

1.7.2 Long COVID and risk factors for Long COVID

The second term that has becoming increasingly recognised is Long-COVID. While PACS may be more associated with more severe acute illness or initial recovery, studies have shown that increasing numbers of patients with mild initial illness experience prolonged symptoms (Davis et al., 2021). Patients recognised this trend and identified themselves as 'long-haulers' or having Long-COVID (Callard and Perego, 2021). Long COVID is therefore a 'patient made' term referring to symptoms persisting greater than 4-weeks after acute COVID-19 infection, and not explained by any other diagnosis (Shah et al., 2021b). Long Covid was the first illness created through patients finding one another on Twitter: it moved from patients, through various media, to formal clinical and policy channels in just a few month (Callard and Perego, 2021). The WHO use post-COVID-19 condition or Long COVID interchangeably, and state that it can affect approximately 10-20% of people who have had COVID-19 (WHO, 2021b). There are over 200 (many the same as mentioned for PACS) symptoms which are associated with Long COVID, and fatigue is the most common one (David et al., 2021; WHO, 2021b). Symptoms may persist after initial infection, or they may be new ones and may fluctuate and flare-up in response to triggers (Raveendran, Jayadevan and Sashidharan, 2021). Diagnosing Long COVID or Post-COVID Syndrome has its challenges, including defining the cut-off time for diagnosis, as severity and therefore length of initial illness is so variable (Raveendran, Jayadevan and Sashidharan, 2021). Making a diagnosis of Long-COVID when someone doesn't have a previous diagnosis of confirmed SARS-CoV-2 infection is difficult, which is a case for many who contracted the virus during the worst waves of the pandemic and testing was largely unavailable for the general public.

Long COVID is a condition that was initially misunderstood, with many patients struggling experiencing the stigma associated with it. Some patients describe not being believed by family members and friends about their ill-health and persistent symptoms (Ladds et al., 2020), as the

condition was not recognised health-care providers particularly in the early pandemic months (Callard and Perego, 2021). Long COVID is now being recognised by clinicians as a condition, and measures are being put in place to support patients both in their assessment/investigation of symptoms and interventions are being developed to manage and improve these symptoms which lead to such impaired physical function. In Ireland, over the last year, work has commenced on the development on six Post-Acute COVID and seven Long COVID clinics nationally. The aim of these clinics is to investigate persistent symptoms experienced by patients and to signpost them to pathways or provide the most appropriate rehabilitative interventions to those who need it. The ultimate goal is to improve post-COVID-19 recovery and to alleviate and improve many of the persistent symptoms experienced by survivors, to improve their physical function and overall quality of life.

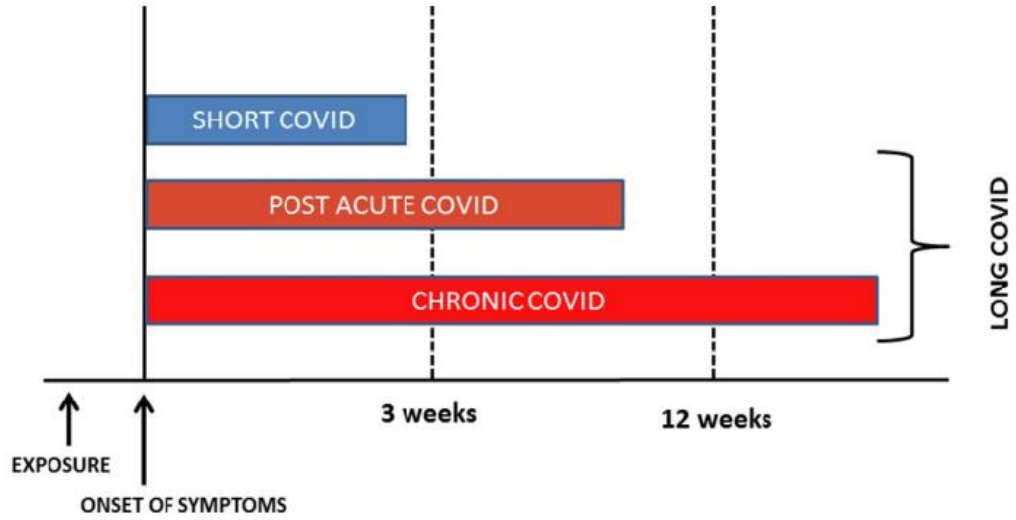

Figure 1 Classification of Long COVID ***(Raveendran, Jayadevan and Sashidharan, 2021).*** *Permission has kindly been granted by Professor Raveendran to use this figure in this thesis (Appendix 1). A copyright license was also granted to use this figure by the publishing company, Elsevier (Appendix 2).*

Risk factors for developing Long-COVID include (Fernández-de-Las-Peñas et al., 2021):

- Female gender
- Aged 35-69 years
- Lower socioeconomic status
- Increased BMI
- The presence of other chronic diseases

Researchers have attempted to cluster symptoms into patterns or 'phenotypes'. As with PACS there are many proposed mechanisms driving the condition which are best summarised in Figure 2 below.

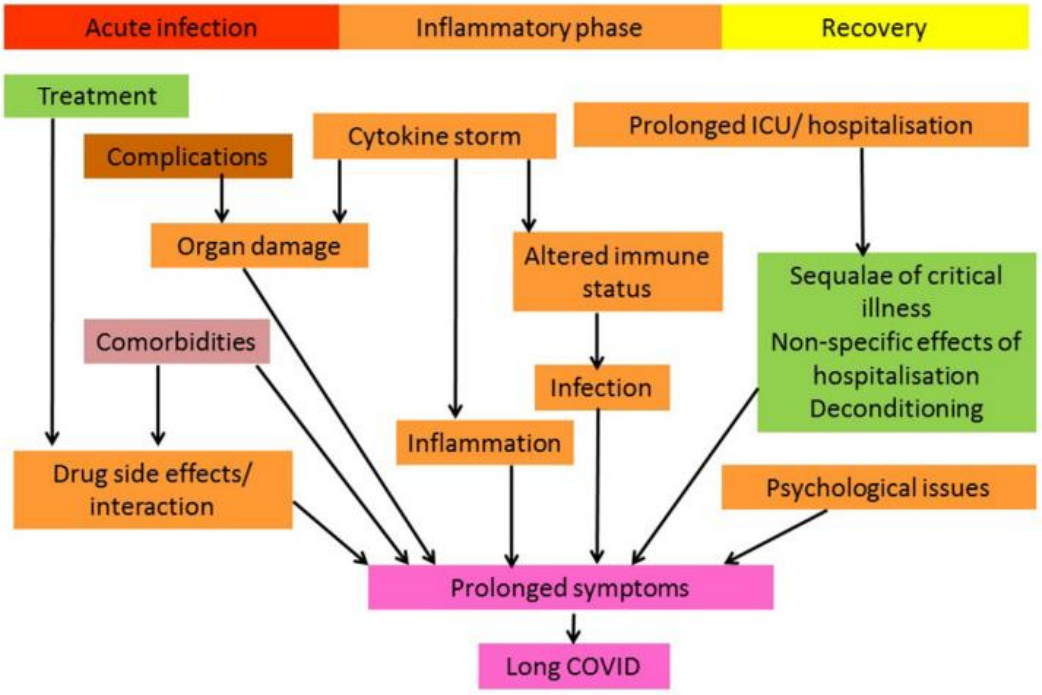

Figure 2 Various pathophysiological mechanisms of Long COVID (Raveendran, Jayadevan and Sashidharan, 2021). Permission has kindly been granted by Professor Raveendran to use this figure in this thesis (Appendix 1). A copyright license was also granted to use this figure by the publishing company, Elsevier (Appendix 2).

1.7.3 Research on Long COVID

Two studies have explored the lived experience of those who are living with Long COVID (Ladds et al., 2020; Wurz et al., 2022). The first was conducted by Ladds and colleagues in the UK and

comprised of 55 individual interviews and 8 focus groups made up primarily of females (70% of 114), the majority of whom experienced mild initial illness (Ladds et al., 2020). Eight of the 114 individuals who participated were hospitalised during their acute illness and 51 were healthcare professionals (Ladds et al., 2020). Participants in this study described a 'confusing' illness, leaving participants with a heavy sense of loss and stigma (Ladds et al., 2020). Participants spoke of the wide variety of symptoms they experienced including fatigue and cognitive deficits, many of which were unpredictable and debilitating. This difficult experience was worsened as individuals found navigating services challenging and felt at times that they were not taken seriously, by family, friends, and even health-care providers (Ladds et al., 2020). Something which was apparent was the disparity in satisfaction with follow-up care reported by participants, some satisfied with the therapeutic relationships and access to services and some not (Ladds et al., 2020).

The second study used open ended survey responses to explore individuals' experiences with Long COVID across a number of countries including Canada, the United Kingdom and the United States of America (Wurz et al., 2022). Similarly, a high proportion (88.2%) of the 169 survey respondents self-identified as female and whether or not participants were hospitalised during acute illness was not stated (Wurz et al., 2022). Over-arching themes identified were similar to that of the previous study and included the wide variety of debilitating symptoms and the difficult experience of feeling unheard or not listened to (Wurz et al., 2022). Interestingly the challenge of returning to physical activity due to post-exertion malaise (PEM) was discussed by participants, with them mourning their previous exercise capabilities, with some avoiding physical activity completely to avoid symptom exacerbation (Wurz et al., 2022). PEM is described in detail below. Participants also spoke about losing a sense of themselves in general. Both studies primarily recruited individuals from Long COVID support groups on social media (Twitter and Facebook). There has been no qualitative research conducted investigating the recovery experience solely of those who were hospitalised with COVID-19.

PEM It is defined by the following characteristics (Carruthers et al., 2011):

- marked, rapid physical or cognitive fatigability in response to exertion
- symptoms that worsen with exertion
- post-exertional exhaustion
- exhaustion is not relieved by rest and
- Substantial reduction in pre-illness activity level due to low threshold of physical and mental fatigability

A study of 213 individuals living with Long-COVID showed most were experiencing Post-Exertion Symptom Exacerbation (PESE), with 58.7 % meeting PEM scoring thresholds (Twomey et al., 2022). Symptoms such as fatigue and PEM/PESE may overlap with that experienced by other patient populations such as Myalgic Encephalomyelitis (ME) or Chronic Fatigue Syndrome (CFS) (Cuesta-Vargas, 2022).

Research is currently being conducted on the potential underlying pathophysiology which may cause the symptoms like PEM, breathlessness and fatigue in those suffering from Long-COVID. Authors of a comprehensive review published in Infectious Diseases give some putative pathophysiological drivers and are separated into two main categories long-term tissue damage and pathological inflammation (Yong, 2021).

1. Long-term tissue damage

The first type of damage discussed is in the lungs with persistent radiological abnormalities observed on convalescent chest x-rays and CT Thoraxes months following acute infection with COVID-19, alongside gas exchange issues identified in pulmonary function tests and xenon gas radiological techniques (Yong, 2021). This may be the cause of post-COVID-19 dyspnoea. The second organ proposed that may have been subjected to long-term damage is the brain as authors report on a short-term study which identified neurological abnormalities in those who

suffered mild acute COVID-19 but reported ongoing issues with memory loss, anosmia and fatigue (Yong, 2021).

The third proposed organ to suffer long-term damage is the heart with authors quoting studies of both hospitalised and asymptomatic COVID-19 patients who presented with myocardial inflammation (Yong, 2021). Lastly authors of the review suggest the possibility of multi-organ damage. Research is very much in its infancy with many of the studies included in the review having limitations including small sample sizes and short-term follow-up.

The other potential pathophysiological driver for the persistent symptoms experienced by those with Long-COVID is pathological inflammation (Yong, 2021).

2. Pathological Inflammation

Some preliminary studies have shown that SARS-CoV-2 can persist in the body (prolonged positive RT-PCR tests and extended shedding of SARS-CoV-2 in respiratory and gastrointestinal tracts) inducing some sort of immune activation contributing to Long COVID (Yong, 2021). It is also suggested that T-cell dysfunction may be an underlying cause of Long-COVID (Yong, 2021), which conflicts with the work mentioned above by Townsend et. al (Townsend et al., 2020). There is also a suggestion that multisystem inflammation syndrome denoted by elevated levels of systemic pro-inflammatory markers including CRP, interleukin-6 and D-dimers, could lead to Long-COVID, however studies are limited to short follow-up of between 2-6 weeks post initial infection (Yong, 2021). We know that longer-term studies looking at the presence of absence of the same pro-inflammatory markers at 10-weeks following initial assessment do not show any association between the presence of the common symptom of fatigue in Long-COVID and pro-inflammatory markers (Townsend et al., 2020).

1.8 The effects of the COVID-19 Pandemic in Ireland

Like other countries, Ireland experienced huge healthcare, economic and social consequences as a result of the pandemic. This MSc project was conducted during the 2-year pandemic. Appendix 3 gives a brief timeline of the pandemic in Ireland, mapped against the project timeline (HSE, 2022).

1.9 Overall conclusion of the literature on COVID-19 recovery

Overall, it is apparent that recovery from COVID-19, whether patients experience mild, moderate, severe or critical illness, is complex. Many researchers have endeavoured to report on outcomes at various timepoints after infection and draw conclusions from their findings. Some have concluded that unfavourable outcomes are associated with more severe initial illness, older age, the existence of pre-COVID-19 comorbidities, female gender and the presence of abnormalities on various investigations to name just a few. Some have found the persistent symptoms, reduced exercise capacity, pulmonary abnormalities etc. resolve over time, some have not. What is certain is that the spectrum of persistent symptoms and issues experienced by survivors is broad and unpredictable. COVID-19, irrespective of severity of initial illness, affects everyone differently. There have been efforts to provide terms to acknowledge individuals' experience of recovery such as Long COVID or PACS. For many, contracting COVID-19 may have been their first reason for hospital admission, and as seen in the literature, many of those who were sick with the virus were highly functioning beforehand. There has been, and continues to be, a period of adjustment for those who are trying to navigate their way through recovery, and it is imperative that patients are listened to, believed, and supported by the appropriate healthcare professionals during this navigation.

1.10 Gap in the literature surrounding COVID-19 recovery

When work on this thesis commenced in September 2020, there were only 4 other studies that had investigated COVID-19 recovery at the 1-year time-point (Latronico et al., 2021; Huang et al., 2021b; Yan et al., 2021; Wu et al., 2021). One of the studies focused solely on recovery in those who developed COVID-19-related ARDS (Latronico et al., 2021) and two concentrated solely on respiratory outcomes (Wu et al., 2021; Yan et al., 2021). At the commencement of this work there were also no published studies investigating recovery of physical function following COVID-19 amongst an Irish cohort.

Aims and Objectives

Therefore, the aim of this thesis was to investigate physical recovery from COVID-19 amongst a heterogeneous group of patients who were hospitalised in an acute Irish hospital, all of whom had varying degrees of initial illness.

The specific objectives of this thesis were:

1. To investigate change in physical recovery over time by conducting comprehensive subjective and objective physical functioning assessments with participants at 10-weeks (Timepoint 1), 6-months (Timepoint 2) and 12-months (Timepoint 3) following their hospitalisation with COVID-19.

2. To gain a deeper understanding of individuals' own perceptions of their recovery from COVID-19 by conducting interviews with a subset of participants.

Chapter 2 Methods

2.1 Thesis Overview

This work consists of two related projects. Project 1 uses quantitative research methods to prospectively examine physical functioning outcomes at 10-weeks (T1), 6-months (T2) and 1-year (T3) following hospitalisation with COVID-19. While conducting assessments at T1, the lead researcher noted that while patients were demonstrating objective clinical recovery from COVID-19, subjectively participants felt they were very far from their pre-COVID physical baseline and reported persistent symptoms. Therefore, a second project, Project 2, was added which used qualitative methods to gain a deeper insight and understanding of recovery from COVID-19 from a sub-set of participants in the form of interviews. Semi-structured interviews were conducted with this sub-set of participants at 8-10 months following hospitalisation with COVID-19.

2.2 Ethical Approval

Ethical approval for both projects was obtained from the Tallaght University Hospital (TUH)/St James's Hospital (SJH) Joint Research Ethics Committee as part of a larger programme of work examining recovery following COVID-19, which was submitted by Dr Grainne Sheill (REC: 2020-11 List 43 – Amendment (24)) (Appendix 4).

The following sections will describe the study design, participants and measures utilised in Project 1.

2.2.1 Quantitative Study Design

This project utilised a prospective longitudinal design to investigate the impact COVID-19 has on long-term physical functioning at 10-weeks (T1), 6-months (T2) and 1-year (T3) post-hospital discharge. T1 was established at 10-weeks as this was the average follow-up time patients attending the post-COVID-19 clinic in St. James's Hospital (where recruitment, and T1 assessments took place) were offered appointments. As this study was commenced early on in

the pandemic, Long COVID was not defined when this study commenced, and so 12-weeks was not an important cut-off point. The patients were not assessed at 12-weeks or 3-months as this would be too close to their assessment at 10-weeks. Longitudinal studies employ repeat measures to follow particular individuals over a prolonged period of time and prospective studies follow the same participants over a period of time (Edward Joseph Caruana, 2015). In these types of studies data is collected from individuals within a predefined group, and in this case, as mentioned, from those who were hospitalised in St. James's Hospital with moderate to severe COVID-19. Appropriate statistical testing was used to analyse change over time for that group. When conducting longitudinal studies, researchers must ensure that data collection and data recording methods are identical, consistent and standardised at each time-point (Caruana et al., 2015). Longitudinal studies can be difficult to conduct, with many researchers challenged by incomplete and interrupted follow-up of individuals, and the temporal and financial demands associated with this study design.

2.2.2 Participants

Project 1 included a consecutively enrolled prospective cohort of patients hospitalised with COVID-19 in St. James's Hospital, Dublin, Ireland. A convenience sampling method was used to recruit participants from the hospital's Post-Acute COVID-19 Clinic. In convenience sampling, participants are recruited as they are 'in the right place at the right time' (Acharya et al., 2013). While widely used in quantitative research, convenience sampling is not without its limitations, with the inability to control or measure bias and the inability for the data to be generalised beyond the sample being the main two (Acharya et al., 2013).

At discharge from hospital, patients were automatically referred to the Post-COVID-19 Multidisciplinary Clinic, which was located on hospital site. Patients were referred to this clinic at time of discharge, and to the clinic physiotherapy service for assessment of persistent issues with physical functioning on the day of their clinic appointment. All patients who were referred

to the clinic physiotherapy service between May and November 2020 were invited to participate in the study by a gatekeeper, a physiotherapist in the clinic. After their physical functioning assessment was complete, participants were provided with a Patient Information Leaflet (Appendix 5) containing details of the study. They were given time to read the PIL and were given a 'cooling off' period in the waiting room. After the 'cooling off' period, participants were asked if they would like to participate. Those who consented signed a Consent Form (Appendix 6) and were advised to take the PIL home. They were informed that if they changed their mind about participating in the study they could contact the researcher via telephone, the number of which was provided in the PIL.

Patients were eligible for enrolment in the study if they were hospitalised in St. James's Hospital for COVID-19 (confirmed by positive SARS-CoV-2 Polymerase Chain Reaction test), were able to complete study questionnaires in English and were ≥ 18 years of age. Participants were excluded if they could not commence a 6-Minute Walk Test at the time of their physical functioning assessment, at T1. The same PIL was provided to participants at their 6-month assessment (T2) to remind them of the details of the study and to inform them of their right to withdraw from the study at any time. A sub-set of participants were recruited to complete qualitative interviews for Project 2 using purposive sampling methods. Sampling and recruitment for Project 2 will be described in Section 2.4.

2.2.3 Data collection and outcome measures

Clinical data pertaining to the acute hospital stay were obtained through electronic chart reviews.

At the initial clinic appointment (T1), two physiotherapists (one being the lead researcher) assessed aerobic capacity and endurance using the 6-Minute Walk Test (6MWT) and frailty using the Clinical Frailty Score. Information on return to work, pre- and post-morbid activity/exercise levels and prevalence of falls was also collected through direct interviews with participants using standardised subjective assessments. Fatigue, health-related quality of life and persistent symptoms were assessed using self-reported questionnaires which are discussed below in detail. This full assessment was repeated by the lead researcher at T2 and T3.

2.2.4 6-Minute Walk Test (6MWT)

The 6MWT is a sub-maximal exercise test used to assess aerobic capacity and endurance, by measuring the distance an individual can walk in 6-minutes, usually at a quick pace, on a flat surface (2002). It is a practical simple test that requires a 30-metre hallway and very little equipment. It evaluates the global responses of all bodily systems involved during exercise (American Thoracic Society (ATS) 2002). As most activities of daily living are performed at a submaximal level of exertion, it is commonly used as a one-time measure of functional status of patients with COPD (Bernstein et al., 1994; Hajiro et al., 1998), heart failure (Bittner, 1997; Peeters and Mets, 1996; Zugck et al., 2000), fibromyalgia (King et al., 1999) and in the elderly population (Enright et al., 2003). The intra-rater and inter-rater reliability of the test has is strong with an ICC of 0.98 (lower limit 95% CI: 0.94) and 0.96 (lower limit 95% CI: 0.94) respectively, when used in COPD patients (Hansen et al., 2018). Similarly, the test is highly reliable over time (ICC = 0.96) when used to assess exercise capacity in patients with congestive heart failure (Lans et al., 2020).

The Modified Borg Dyspnoea Scale (MBS) was also used during the test to assess perceived exertion (range, 0–10). The MBS has been widely used in both healthy and diseased states (Borg et al., 2010, Bausewein et al., 2007).

6MWT Protocol

The 6MWT recording sheet can be found in Appendix 7. Participants were asked to walk continuously up and down a 30-metre hallway between two cones at either end, for 6-minutes. Participants were instructed to walk at a brisk pace, as fast as possible without running. Participants' heart rate and oxygen saturation levels were monitored and documented at 1-minute intervals throughout the test. Participants were asked to rate their breathlessness using the Modified Borg Dyspnoea Scale (Appendix 9) at 1-minute intervals also. Participants were informed they could take a standing or seated rest if required at any stage during the test and they could terminate the test at any time. If participants required a rest during the test, the timepoint at which the rest was taken, and the duration of the rest was documented. A stopwatch was used to record time, and after the 6-minutes participants were asked to sit on a chair at the end of the corridor. Participants' heartrate, oxygen saturation levels and breathlessness scores were documented at 1-minute intervals for 3-minutes following the walk while the participant remained seated, the test therefore took 9-minutes to conduct in total.

The instructions given to the participants before, during and after the 6MWT are provided in Appendix 8.

2.2.5 Clinical Frailty Scale

Frailty was assessed using the Clinical Frailty Score (CFS) (Mendiratta and Latif, 2021). The CFS is a judgement-based frailty tool that evaluates specific domains including comorbidity, function, and cognition to generate a frailty score ranging from 1 (very fit) to 9 (terminally ill) (Church et al., 2020). The scale focuses on items that can be readily observed including mobility, balance, use of walking aids, and the abilities to eat, dress, shop, cook, and bank; scoring should

match the description, and should not be based solely on the pictures that accompany each level. The CFS has been used in multiple settings and is a good predictor for mortality, comorbidity, function, mobility and more. A large study looking at the reliability of the CFS (n= 1923 pairs of assessors) demonstrated that inter-rater reliability is strong (weighted kappa 0.86) (Flaatten et al., 2021). The tool is easy to use, with no space or equipment necessary. As the cohort of patients in this study include the elderly, some adults who had been admitted to critical care, and all of whom had experienced significant insult in the form of the Sars-CoV-2 virus, frailty is a key concern in this growing patient population.

Clinical Frailty Scale Protocol

The Clinical Frailty Scale can only be administered by a health-care professional (Appendix 10). The lead researcher, a physiotherapist, who conducted the physical functioning assessments at each timepoint scored participants' frailty using the scale by watching the participant mobilise, inquiring about their habitual physical activity and ability. Through questioning, the lead researcher assessed whether the participant could independently perform tasks such as bathing, dressing, housework, going upstairs, going out alone, going shopping, taking care of finances, taking medications, and preparing meals. Based on this assessment the researcher scored the participants' frailty between 1 to 9 as appropriate.

2.2.6 Chalder Fatigue Scale

Fatigue was assessed using the validated Chalder Fatigue Scale (Jackson, 2015). At each time-point participants are asked to answer the questions with reference to the past month in comparison with their pre–COVID-19 baseline. It is a self-administered, 11-item questionnaire which has been used both clinical and non-clinical populations with a straightforward answering system (Jackson, 2015). Each of the 11 items are answered on a 4-point scale ranging from the asymptomatic to maximum symptomology. For all items, the least symptomatic answers are on the left of the response-set, providing an easy-to-understand checklist for respondents.

Participants can score between 0-33 spanning two dimensions (physical and psychological fatigue) with higher scores suggesting worse fatigue. This method is validated and closely resembles other fatigue questionnaires (Morriss, Wearden and Mullis, 1998; Loge, Ekeberg and Kaasa, 1998; Jackson, 2015). When considering the sample population in this study the Chalder Fatigue Scale was chosen as it has been shown to be valid when assessing fatigue in the general population (Fong et al., 2015) and in those who suffer from Chronic Fatigue Syndrome (Morriss, Wearden and Mullis, 1998). In this study the same researchers scored the responses, the Chalder Fatigue Scale seemed the most appropriate measure due to the scale's good internal reliability (Jing et al., 2016).

Chalder Fatigue Scale Protocol

As described above Chalder Fatigue Scale (Appendix 11) is a self-administered questionnaire. Participants filled out this questionnaire independently during their physical functioning assessment at each timepoint. All participant questions about how to use the scale were answered by the lead researcher. If the patient was unable to read or write, the lead researcher explained the scale clearly to the participant and read each question aloud, asking the patient to say 'yes' to whichever answer was most applicable to them. The lead researcher summed the scores out of 33 after the assessment.

2.2.7 Short-form 36 Health Survey Questionnaire Version 2 (SF-36-II).

This study investigated the effect COVID-19 has had on the participants' quality of life at standardised time-points during their recovery using the Short-form 36 Questionnaire Version 2 (SF-36-II).

The SF-36-II is a patient-reported questionnaire that assessed health-related quality of life across eight different health domains: physical functioning (10 items), bodily pain (2 items), role limitations due to physical health problems (4 items), role limitations due to personal or emotional problems (4 items), emotional well-being (5 items), social functioning (2 items),

energy/fatigue (4 items), and general health perceptions (5 items). Scores for each domain range from 0 to 100, with a higher score defining a more favorable health state (Brazier et al., 1992). Patients enrolled in this study experienced varying degrees of the acute virus with some requiring short hospital admission and others requiring longer stays and critical care admission. Results of a study whereby 9332 respondents between the ages of 18 and 64 years completed the SF-36 provides strong evidence for the survey's use in groups reporting varying extents of ill-health (Jenkinson, Wright and Coulter, 1994). The measure has also been shown to be valid and reliable in assessing health-related quality of life amongst various population cohorts including patients recovering from critical care admission (Chrispin et al., 2003) and amongst the general population (Thumboo et al., 2013).

SF-36-II Protocol

The SF-3-II tool (Appendix 12) is a self-administered tool, which participants completed independently at the time of their physical functioning assessment. It takes between 5 and 15-minutes to complete. If a participant was unable to read or write, the lead researcher explained the tool clearly to the participant and read each question aloud, asking the participant to say 'yes' to whichever response was most applicable to them at the time.

The lead researcher scored each participants questionnaire response after the time of the assessment using an online SF-36-II calculator (the link for which can be seen in Appendix 13).

2.2.8 Covid-19 Specific Patient Concerns Assessment

Patient concerns assessment tools have been widely used amongst different patient populations in recent times including general practice, internal medicine, cardiology, oncology, paediatrics, surgery (orthopaedics, maxillofacial), orthodontics and pain (Nilan, Doltani and Harmon, 2018). The tool used in this study was adapted from the NCCN Clinical Practice Guidelines in Oncology for Distress Management (V.2.2013) (Snowden et al., 2015). This 'concerns checklist' is currently being used as part of a holistic needs assessment in a

randomised-controlled trial by Snowden et al investigating the efficacy of this type of assessment and intervention in cancer patients (Snowden et al., 2015). It comprises of a list of concerns or symptoms which participants can 'tick' if these are still bothersome for them at each time-point during their recovery from COVID-19. In this patient group it was initially used as a framework for patient-centred discussion of symptoms and then subsequently to count the number of symptoms experienced by patients at each time-point.

COVID-19 Specific Patient Concerns Assessment protocol

The COVID-19 Specific Patient concerns assessment tool can be seen in Appendix 14. This was a self-administered survey, where participants were provided with a list of potential concerns or symptoms and were asked to put a tick beside any symptom they were experiencing at the given time.

2.3 Statistical Analysis

Statistical analysis for Project 1 was carried out using STATA v15.0 (Texas, USA). Data visualisation was performed using GraphPad Prism v9.0 (California, USA). Descriptive statistics are reported as means with standard deviations (SD) and median with interquartile ranges (IQR) following Shapiro-Wilks testing for normality. Univariate analysis was performed using t-test, Wilcoxon rank-sum, and Chi-squared test as appropriate. Paired analysis between matched samples from the same patients were carried out using one-way analysis of variance (ANOVA) with post-hoc Tukey testing as appropriate. Comparison of SF-36 scores with normative data was performed using Kruskal-Wallis testing with Dunn's multiple comparisons test. Multivariable linear regression is reported as beta-coefficients with corresponding 95% confidence intervals and *p* values. Variables included in regression analyses are stated in the relevant results section and table legends. Correlation analysis between parameters was performed using Spearman correlation tests. Specific tests used and adjusted significance levels are stated in the relevant figure/table legends. Statistical significance was considered $p<0.05$.

2.4 Project 2

The following sections will describe the study design, participants and recruitment methods utilised in Project 2.

2.4.1 Qualitative Study Design

Qualitative research is defined is as 'an iterative process in which improved understanding to the scientific community is achieved by making new significant distinctions by getting closer to the phenomenon studied' (Aspers and Corte, 2019). This type of research involves the collection of a variety of different materials including personal experiences, life stories, interviews, interactions and visual texts that describe routine and problematic moments and meanings in individuals' lives (Denzin and Lincoln, 2005). When highlighting the difference between qualitative and quantitative research, Braun and Clarke state that qualitative research is broadly focused on meaning and it aims to generate contextualised and situated knowledge (Braun and Clarke, 2021). The purpose is often to gain rich, in depth understanding of a particular phenomenon and often smaller samples are valued (Braun and Clarke, 2021). In this thesis, the researcher wanted to gather quantitative data to understand how individuals recover from COVID-19 over time, and qualitative data to understand what recovery means to individuals and the challenges associated with it. Therefore, this thesis uses a mixed methods approach, meaning the researcher used both quantitative data collection and qualitative data collection. These approaches were used concurrently, rather than sequentially. This has its advantages as the collection and analysis of embedded qualitative responses can add deeper understanding to the findings of the quantitative research (Driscoll et al., 2007).

Considering the complexity of recovery from COVID-19 reported in published literature to-date, having participants detail their recovery experience in their own words may explain this

complex experience and perhaps the discordance between objective physical recovery data and subjective recovery data which researchers are discovering.

Project 2 used a qualitative approach to explore the participants' experiences of recovering from COVID-19 through semi-structured interviews, completed individually with participants by telephone.

Reflexive thematic analysis was used to analyse the data collected. An explanation of reflexive thematic analysis can be found in section 2.4.5.

2.4.2 Participants

A sub-set of participants from Project 1 were invited to participate in Project 2. At the T2 assessment, participants were informed of Project 2. Purposive sampling was used to recruit participants into Project 2. Purposive sampling is the deliberate choice of a participant due to the qualities the participant possesses, it is a non-random technique and does not need a set number of participants (Etikan et al., 2016). It is typically associated with qualitative research and involves the identification of individuals or groups of individuals who are available and willing to participate and have the ability to communicate experiences and opinions in an articulate, expressive and reflective manner (Etikan et al., 2016). Participants were provided with a separate patient information leaflet (Appendix 15) providing a summary of the nature and rationale of this part of the study. Participants were also provided with a separate consent form (Appendix 16).

Of the 61 participants Project 1, 20 were selected, and the lead researcher contacted participants via telephone call at 7-months following hospital-discharge and asked participants if they would like to participate in the telephone interviews. All participants who were contacted 1 by 1 and those that agreed to the telephone interviews were asked to post back their signed consent form they had received at T2. A telephone interview was organised for the following month.

2.4.3 Data collection

An interview guide (Appendix 17) seeking to explore individuals' lived experience of recovery, containing 5 open-end questions was devised. It sought to explore this recovery across multiple domains including the persistent symptoms experienced by these individuals, the pattern and nature of these symptoms, how symptoms affected their ability to return to previous levels of function, if there were activities participants had not yet returned following their illness with COVID-19 and how, in their opinion, follow-up care for this cohort could be improved. The iterative review of the guide was conducted by the multidisciplinary team which consisted of Consultant Physicians in Infectious Diseases and Respiratory Medicine and physiotherapists working with COVID-19 patients. It was discussed at length over a number of meetings until a general consensus was met. A copy of this interview guide can be found in Appendix 17. This guide was used to create a narrative, and conversational prompts (such as *"can you tell me more about that?"* or *"and what happened next?"*) were used to maintain the narrative. All interviews were conducted via telephone by lead researcher, KOB. All interviews were recorded/audiotaped using a Dictaphone. All interviews were transcribed verbatim by KOB directly afterwards.

Participants were assured that all data would be de-identified and stored and handled anonymously, and that if they changed their mind about anything they said, they could contact a named researcher and withdraw that section of the data.

The lead researcher who conducted the interviews works in the acute hospital setting and also in the post-acute COVID-19 clinic, clinically. Therefore, she may have encountered the participants in the clinical setting previously. To overcome this potential conflict of interest, the researcher informed and explicitly states to participants that this research is unrelated to the researcher's clinical role.

2.4.4 Data management

Interviews were conducted and all were transcribed in full. Transcripts and notes were de-identified by removing reference to real names and by deleting the audio recordings immediately after transcription. Each participant was allocated a random code/number to protect their identity. Paper based data was stored in locked cabinets at the Physiotherapy Department at St James's Hospital. Consent forms were stored separately. Coded information was stored on a secure, password protected encrypted computer. The key was stored separately on a password protected file. An anonymised password protected excel repository was maintained.

All interview transcripts were inputted into NVivo software, version 12.

Data analysis took place at St. James's Hospital, Dublin.

2.4.5 Data analysis and theoretical framework

Data collected through qualitative research methods is analysed to identify themes which occur within the collected data. This searching for themes is called Thematic Analysis (TA). Braun and Clarke state that there are many varieties of TA one of which being the selected reflexive TA, used in this research project. Reflexive TA is an approach to analysing qualitative data to answer either broad or narrow research questions about people's experiences, views and perceptions (Braun and Clarke, 2021). It involves a six-step process, as proposed by Braun & Clarke. These steps of the process should not be seen as a set of 'rules', but rather a guide, as reflexive TA should be flexible, while still being systematic and rigorous. The 6 phases of the reflexive TA are outlined below, with an overview of how these 6 phases were followed by the researcher of this study (*Table 2*).

2.5 Steps: 1-6 of Reflexive Thematic Analysis

Table 2 Steps 1-6 of reflexive thematic analysis and how each step was applied by the lead researcher in analysis data collect in Project 2.

The 6-step process of Reflexive Thematic Analysis as proposed by Braun & Clarke & how these steps were adhered to by the lead researcher of the study.		
Reflective TA Steps	Definition	Application in this Project
1. Data familiarisation	The researcher becomes deeply and intimately familiar with the content of their dataset. It involves reading and re-reading the data and if working with transcripts of audio data, listening to recordings of transcripts at least once.	The lead researcher not only conducted the interviews with all 18 participants, but she also transcribed all the interviews immediately afterwards, allowing for an initial understanding of the data collected. The lead researcher then read the transcripts multiple times prior to analysis to further familiarise herself with the data.
2. Data coding	This involves working through the data systematically and identifying segments that appear potentially interesting or meaningful for the research question. The researcher begins to add descriptions in the form of code labels. Coding is not just about summarising and condensing down the content, it's about capturing one's 'analytic take' of the data. The entire dataset is coded systematically and thoroughly. When this is complete code labels are collated and the relevant segments of data are compiled for each code.	Both the lead researcher and a second data coder used the NVivo 12 software to code the data into sub-themes called nodes. This was done by the lead researcher and the second coder separately to allow for rich and rigorous interpretation of the data. The second coder had experience in TA. Her clinical subject area is not in COVID19 specifically but as a physiotherapist she has a broad understanding of the key concepts presented.
3. Initial theme generation	Clusters of codes that share a core idea/concept are compiled. These may provide meaningful answers to the research question. Once potential/candidate themes that capture the data and address the research question are identified, all coded data relevant to each candidate theme is collated.	The lead researcher and the second coder met on multiple occasions to discuss sub-themes/nodes identified and to categorise them into initial over-arching themes, of which 8-10 were identified.
4. Theme development	The researcher must assess the initial 'fit' of the potential/candidate themes to the data by going back to the full dataset. Development of themes involves checked that themes	On subsequent meetings, the lead researcher and the second coder settled on 5 over-arching themes which best represented the data collected through the interviews. At this stage the lead researcher re-

	make sense in relation to the coded extracts and to the full dataset. The themes must highlight the most important patterns across the dataset in relation to the research question. At this stage candidate themes can be collapsed together or split up. Some may need to be disregarded. Here the researcher must start considering the relationship between themes.	read all the interview transcripts. The 5 over-arching candidate themes were discussed in detail with the lead researcher's supervisor.
5. Theme refining, defining & naming	Here the researcher must ensure that each theme is clearly demarcated and is built around a strong core concept. The themes must fit into the narrative of the data. At this stage, the researcher must decide on concise and informative names for each theme.	The lead researcher then spent some time defining and naming each theme to best represent the essence of the interviews conducted, and to best represent the most poignant points made by participants on their recovery from COVID-19.
6. Writing-up	This phase must start early on. Some researchers may start writing as early as phase 3, the informal writing of reflexive journaling will feed into the more formal writing in phase 6. In writing up, you are finishing the writing process. The researcher is aiming to weave together their analytic narrative and vivid data extracts to tell the reader a persuasive story about the dataset that addresses their research question.	The lead researcher conducted the write-up phase in stages, discussing each theme identified in detail, contextualising each theme and supporting each theme with the relevant participant quotes.

There are many reasons why reflexive TA was chosen as the most appropriate analytic method for this research. Braun & Clarke encourage researcher subjectivity and highlight it as the primary tool for reflexive TA. This method does not see the researcher's subjectivity as a problem, but rather as a resource for analysis. This suggests the notion of 'researcher bias' is not something which should be considered as a weakness in this type of analysis. The lead researcher, who not only conducted the interviews, but also carried out analysis of the data collected, works clinically in the area of COVID-19 recovery, therefore this method of analysis is a perfect fit as she can draw on her experience from working closely with this patient cohort to

interpret the data in an informed, understanding and open-minded manner. Not only is researcher subjectivity essential for successful reflexive TA, as suggested in the name – reflexivity is also imperative. Roni Berger defines reflexivity as 'taking responsibility for one's own situatedness within research and the effect it may have on the people being studied, data being collected and it's interpretation' (Berger, 2015). The use of reflexive TA has many benefits including the ability to shift from inductive to deductive analysis, it allows for flexibility, yet, with clear guidelines, it works especially well for a single researcher and works well for a wide range of datasets of varying sizes.

Chapter 3 Results

3.1 Project 1: Quantitative Results

The results of this study were published in the Journal of *Respiratory Research* in May 2022 (O'Brien et al., 2022).

Between May and November 2020, 61 patients were referred to physiotherapy and consented to take part in this study (*Figure 3)*. Assessments were conducted at three timepoints; Timepoint 1 (T1) at median 55 days (IQR 41.26 – 63) post-discharge, Timepoint 2 (T2) at median 242 days (IQR 219.75 – 261.25) post-discharge, and Timepoint 3 (T3) at median 430 days (IQR 398 – 458) following discharge. Demographics for the study cohort can be found in *Table 3.*

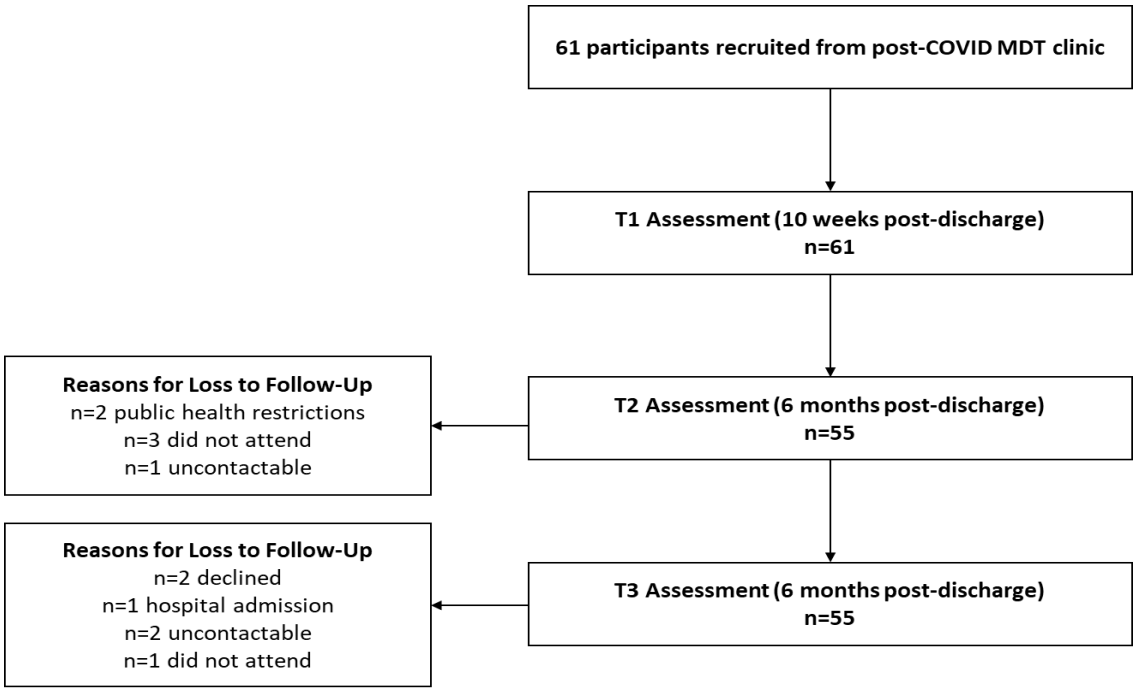

Figure 3 Study Flowchart. Of 61 participants enrolled in the study, all 61 were assessed at least once. 3 (4.91%) patients were assessed only once (all at 3-months post hospital discharge). 7 (11.45%) patients were assessed twice only (3 patients at 3 and 6-months, 1 patient at 6 and 12-months and 3 patients at 3 and 12-months) and the remaining 51 (83.6%) patients were assessed 3 times.

Table 3: Patient demographics for the study cohort.

Demographic	Total (n=61)
Male sex – *n (%)*	35 (57)
Age years *mean (SD)*	58.6 (13.1)
Occupation	
Retired pre COVID – *n (%)*	22 (36)
Unemployed – *n (%)*	6 (9.8)
Working pre COVID – *n (%)*	33 (54.1)
Healthcare worker pre COVID – *n (%)*	17 (27.9)
Other characteristics	
Co-morbidities – *median (IQR)*	1 (0-3)
Hospital length of stay – *median (IQR)*	13.1 (5.8-18.1)
Acute illness characteristics	
Required admission to ICU – *n (%)*	16 (26)
Required IMV – *n (%)*	10 (16)
Required supplemental oxygen – *n (%)*	46 (75)

Received inpatient physiotherapy – *n (%)*	35 (57)
Received steroid therapy – *n (%)*	19 (32)
COVID-19 Severity	
3 (hospital admission not requiring supplemental oxygen) *n – (%)*	15 (25)
4 (hospital admission requiring supplemental oxygen) *n – (%)*	46 (75)
5 (hospital admission requiring high-flow oxygen / NIV *n – (%)*	6 (10)
6 (critical care admission requiring IMV) *n – (%)*	10 (16)
Total	61

3.1.1 Objective Measures of Recovery

Physical recovery was assessed at all three timepoints using the 6MWT, return to work rates, prevalence of falls and the Clinical Frailty Score. Return to pre-COVID-19 exercise levels was also assessed at T2 and T3. The median 6MWD covered at each timepoint is shown in *Table 4*. There was a significant improvement in distance covered across these timepoints (F=10.3, p<0.001) and this improvement was independent of illness severity, age and sex. Despite the improvement in distance covered, there was no significant change in perceived exertion, as assessed by MBS (*Table 4*). Mean 6MWD were considerably less than that of population norms (e.g. average 6MWD at T3 was 447m compared to population norms of 572m for males and 538m for females) (33).

Thirty-three participants had been employed prior to their hospitalization. Of those, 13 (39%), 15 (45%) and 18 (55%) returned to work full-time at T1, T2 and T3, respectively. Of the 17 health-

care workers enrolled, 71% had returned to work fully, 11 % had returned on reduced hours, while 18% had not returned at all at 1-year.

Prior to hospitalization with COVID-19, 53 (87%) of participants had undertaken regular exercise. There was no difference between return to exercise at T2 and T3 (*n*=24 and *n*=27, *F*=0.08, *p*=0.78; *Table 4*). Those who had returned to pre-COVID-19 exercise levels at T3 had significantly lower breathlessness scores during the 6MWT (p=0.02) than those who had not.

At T1, 5 (8.3%) participants reported having at least one fall since their discharge from hospital, with a further 4 (7.27%) reporting falls at T2. No further falls were reported at T3. There was a significant association between the prevalence of falls and increasing frailty scores (p=0.002) (R^2 = 0-39). The median frailty scores were 3, 2 and 2 at T1, T2 and T3 respectively.

Table 4 Physical functioning outcomes of hospitalised COVID-19 survivors

OUTCOME	TIMEPOINT 1 (N=60)	TIMEPOINT 2 (N=55)	TIMEPOINT 3 (N=55)	P VALUE	F VALUE
OBJECTIVE MEASURES OF RECOVERY					
6MWTD *(MEAN, SD)*	365 (209)	421 (92)	447 (85)	0.0001	10.13
MBS *(MEAN, SD)*	3.5 (2.4)	3.2 (2.6)	2.5 (2.4)	0.15	1.93
RETURN TO WORK N=33					
FULL EMPLOYMENT, *N (%)*	13 (39)	15 (45)	18 (55)	0.32	1.17
REDUCED HOURS, *N (%)*	1 (3)	3 (9)	4 (12)		
NO RETURN TO WORK, *N (%)*	19 (58)	15 (46)	11 (33)		
EXERCISE (N=53)					
SAME EXERCISE LEVELS PRE- AND POST-COVID-19, *N (%)*	N/A	24 (45)	27 (51)	0.78	0.08
LOWER EXERCISE LEVELS PRE- AND POST-COVID-19, *N (%)*	N/A	29 (54)	26 (49)		
FALLS					
PARTICIPANTS REPORTING FALLS FOLLOWING HOSPITAL DISCHARGE, *N (%)*	5 (8) (between DC and T1)	4 (7) (between T1 and t=T2)	0 (between T2 and T3)		
FRAILTY					
CLINICAL FRAILTY SCORE *(MEDIAN)*	3	2	2		
SUBJECTIVE MEASURES OF RECOVERY					
FATIGUE					

CHALDER FATIGUE SCORE *(MEAN, SD)*	17.5 (6.5)	16.7 (5.9)	16.7 (5.6)	0.73	0.32
HEALTH-RELATED QUALITY OF LIFE, SHORT-FORM 36 SCORES					
PF *(MEAN, SD)*	62 (24)	61 (25)	64 (25)	0.85	0.17
RP *(MEAN, SD)*	39 (39)	50 (43)	54 (45)	0.20	1.65
RE *(MEAN, SD)*	58 (43)	64 (41)	65 (44)	0.70	0.36
VT *(MEAN, SD)*	47 (24)	52 (22)	49 (21)	0.50	0.70
MH *(MEAN, SD)*	70 (23)	74 (18)	73 (19)	0.60	0.52
SF *(MEAN, SD)*	66 (29)	76 (26)	77 (26)	0.10	2.29
BP *(MEAN, SD)*	65 (30)	65 (27)	68 (26)	0.82	0.20
GH *(MEAN, SD)*	61 (20)	55 (19)	54 (19)	020	1.65
HEALTH CHANGE *(MEAN, SD)*	44 (28)	40 (25)	61 (31)	0.0005	8.04
PATIENT CONCERNS					
NUMBER OF CONCERNS REPORTED *(MEDIAN, IRQ)*	4 (7)	3 (7)	4 (7)		
PARTICIPANTS REPORTING FATIGUE, *N (%)*	24 (40)	27 (49)	21 (38)		
PARTICIPANTS REPORTING ISSUES WITH MEMORY/CONCENTRATION, *N (%)*	22 (37)	19 (35)	27 (49)		

Unknown or missing data: Chalder Fatigue Score: 0 (10-weeks), 1 (6-months) and 1 (12-months). 6MWTD: 0 (10-weeks), 4 (6-months) and 3 (12-months). SF-36-II: 9 (10-weeks), 2 (6-months) and 1 (12-months). Return to work: 0 (10-weeks), 0 (6-months) and 0 (12-months). Patient concerns/symptoms: 0 (10-weeks), 0 (6-months) and 1 (12-months). Exercise levels: N/A at 10-weeks, 0 (6-months) and 0 (12-months). Falls: 0 (10-weeks), 0 (6-months) and 0 (12-months). SD = standard deviation. N/A = not assessed. IQR = Interquartile range. HrQOL = Health-related quality of life. PF = physical function. RP = role limitations due to physical problems. RE = role limitations due to emotional problems. VT = energy/vitality. MH = emotional well-being. SF = social functioning. BP = bodily pain. GH = general health. †P values are calculated for comparisons across the 3-month, 6-month and 12-month assessments using linear mixed models for continuous variables or cumulative link mixed models for ordinal variables.

3.1.2 Subjective Measures of Recovery

Participants were asked to identify persistent symptoms/concerns from a list of potential COVID-19-related concerns (Appendix 14). At least one concern was reported by 44 (74%), 32 (59%) and 35 (64%) participants at T1, T2 and T3 respectively, while the median number of concerns reported per participant across timepoints were 4, 3 and 4 (*Table 4*). Fatigue was the most frequently reported symptom at T1, n=24 (40%) and T2, n=27 (49%), while issues with memory/concentration was the most frequently reported at T3, n=27 (49%). Breathlessness was reported by 23 (38%), 14 (25%) and 11 (20%) participants at T1, T2 and T3 respectively. A further breakdown of participant-reported concerns can be seen in *Figure 5.*

Fatigue was formally assessed using the Chalder Fatigue Score. The median fatigue scores are shown in *Table 4*. Twenty-eight (46%) participants met the case definition for fatigue at T1, with 29 (48%) meeting it at 2 and 26 (43%) at T3. Fatigue scores for the cohort as a whole did not significantly differ across timepoints (*Table 4*). However, of the 28 participants who met the case definition for fatigue at T1, fatigue scores demonstrated significant improvement at both T2 and T3 ($\chi 2$ 12.88, $p<0.01$). Those who had returned to self-reported pre-COVID-19 exercise levels had significantly lower fatigue scores at time-point 2 ($p=0.0249$). At T1, T2 and T3, 18 (30%), 18 (33%) and 23 (42%) participants reported new sleep problems since infection with COVID-19.

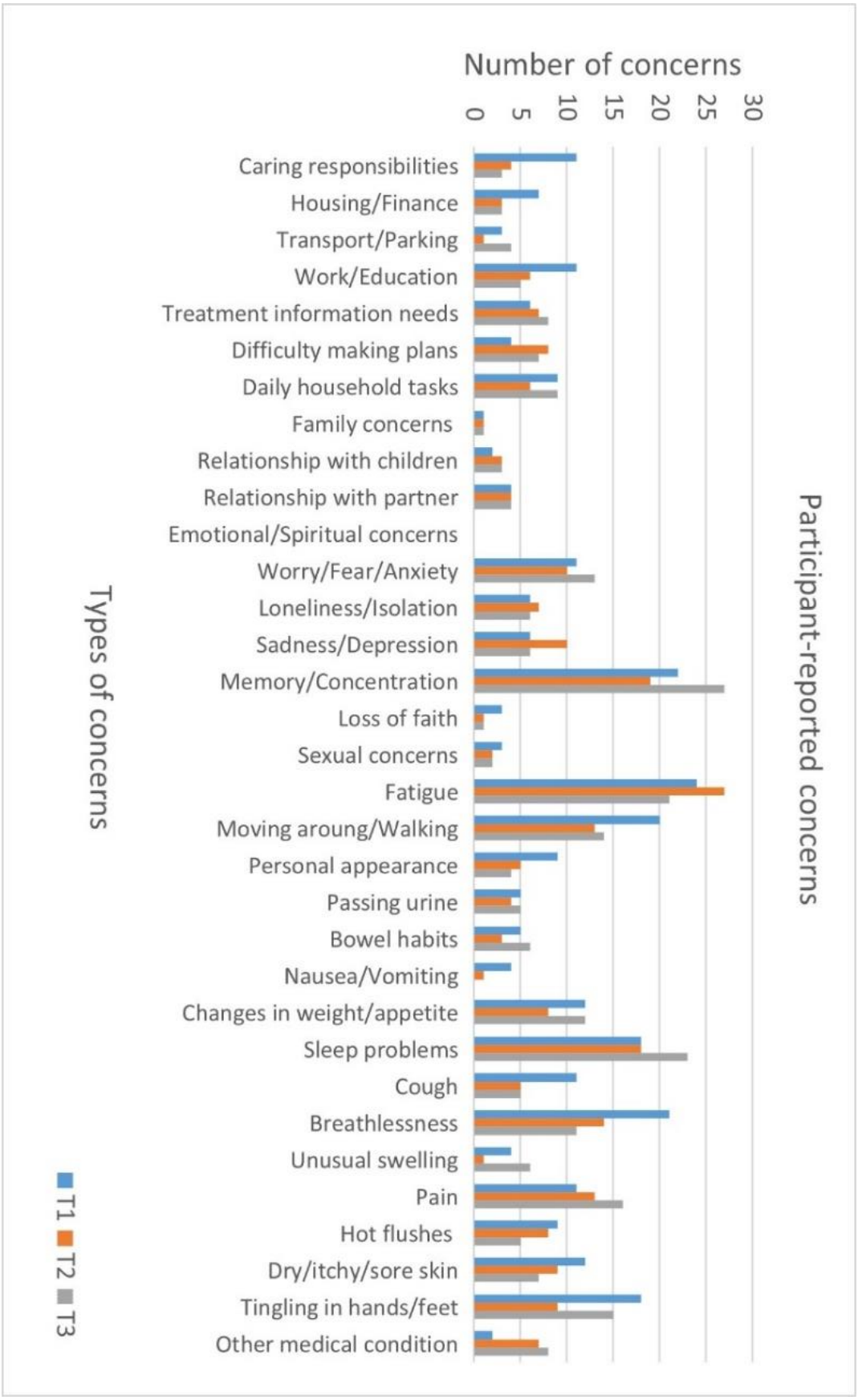

Figure 4 Participant-reported concerns at each timepoint.

A broader quality of life assessment was performed using the SF-36. There was no significant difference in mean scores of the eight domains of HrQOL over the 1-year period, however, there was significant improvement in the single-item health-change score (p=0.0005, *F*=8.04). Improvement in this score were observed between T2 (when participants compared their general health to pre-COVID-19) and T3 (when participants compared their general health to the time of their acute infection with COVID or just after). Nonetheless, 30 (55%) participants at T2, and at 17 (31%) at T3, felt their general health was worse than 1-year prior. To further contextualise the SF-36 results, they were compared to normative population data as seen in *Figure 6.* Post-COVID-19 patients demonstrated significantly lower scores in physical functioning and energy/vitality at all three timepoints, as well as role limitations due to physical problems at T1 and T2 and general health domains at T2 and T3 (34).

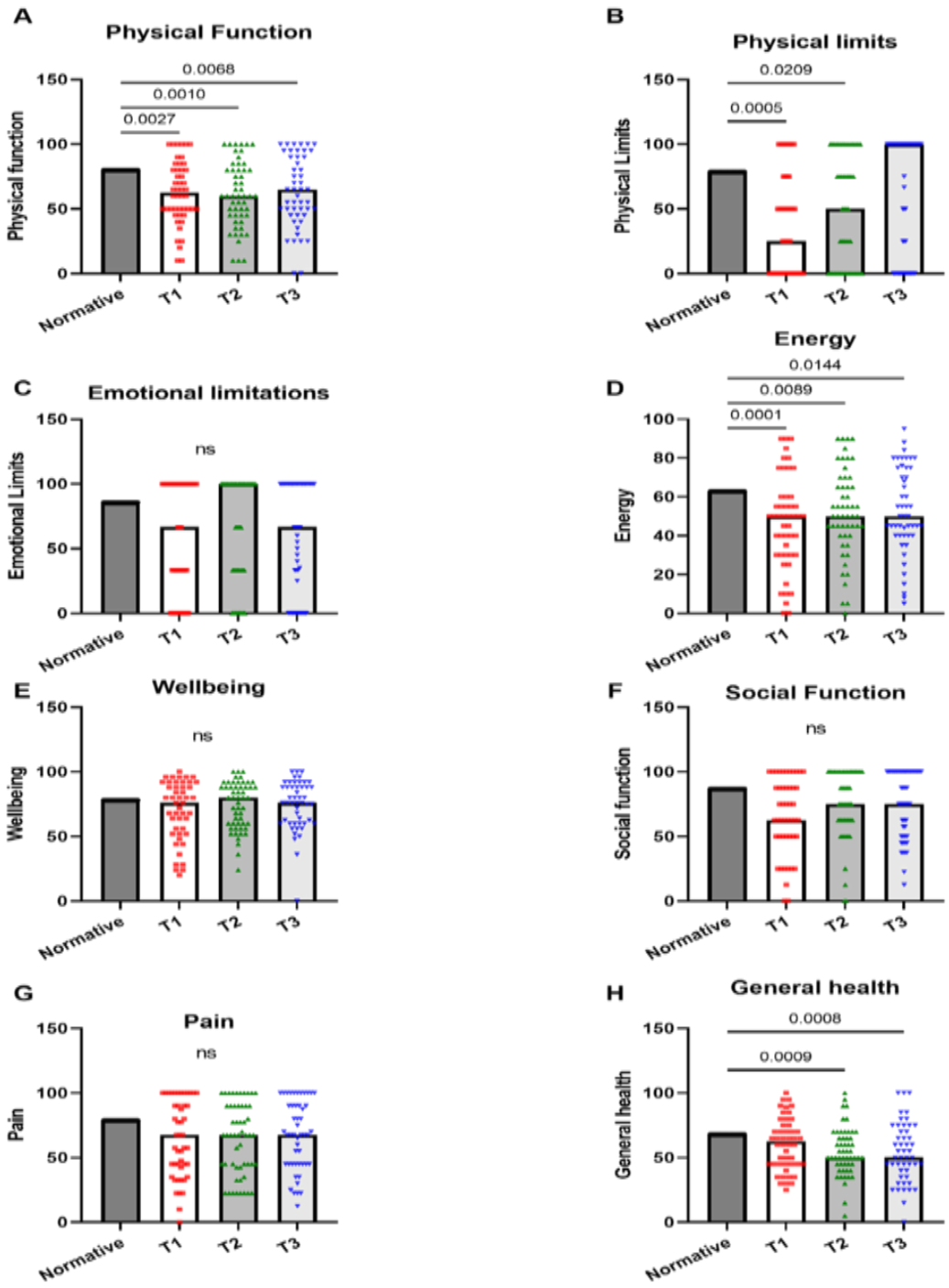

Figure 5 Results across 8 SF-36 domains compared with normative population data (Jenkinson, Coulter and Wright, 1993) at T1, T2 and T3. Kruskal-Wallis test with post-hoc Dunn's multiple comparison test used to assess differences. ns=not significant.

Finally, the associations between failure to return to functional baseline and subjective measures of health were investigated *(Figure 7)*. Scores across the 8 SF-36 domains were compared between those who had returned to work (n=18) and those who had not (n=15), as well as those who had returned to pre-COVID-19 exercise levels (n=27) and those who had not (n=26), at T3. Participants who had not returned to employment at 1-year reported worse physical function (PF) and general health (GH) measures. Those who had not returned to pre-COVID-19 exercise levels also demonstrated worse physical function (PF), as well as significantly lower scores on physical and emotional impact on their life (RP and RE respectively), worse social functioning (SF), and worse pain scores (*Figure 7*). These results remained significant when adjusted for sex, age and severity of initial infection.

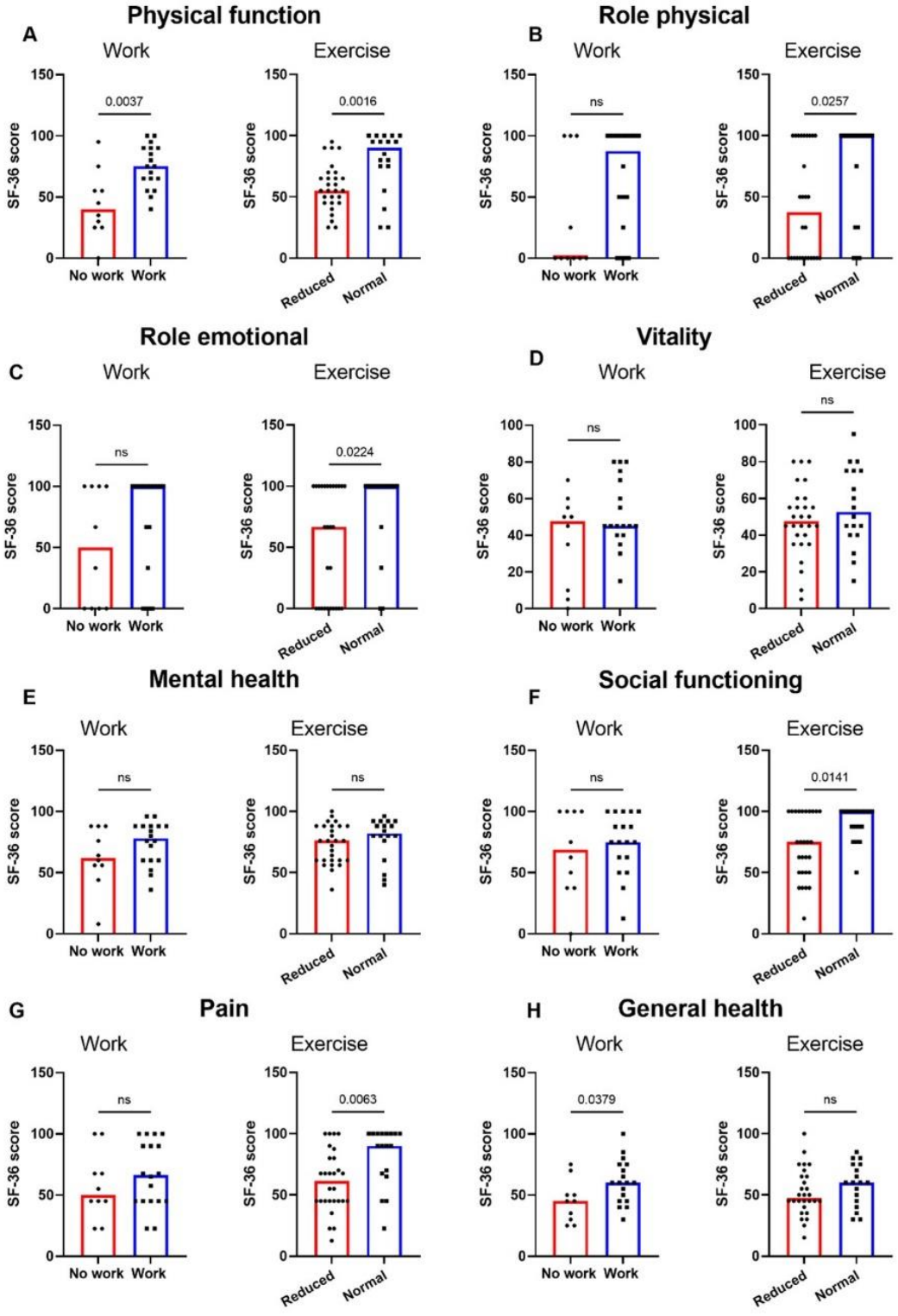

Figure 6 Comparison of those returned to work and those returned to exercise and those who have not across the SF-36 domains (A) Physical function, (B) Role physical, (C) Role emotional, (D) Vitality, (E) Mental health, (F) Social functioning, (G) Pain, and (H) General health. Differences assessed using Wilcoxon rank-sum. ns=not significant

3.2 Project 2: Qualitative Results

3.2.1 Description of dataset

A total of 20 participants were invited to interview, but after 15 interviews, no new themes were emerging, and so, 3 more were conducted for completeness. Still no more new themes emerged, so the final 2 were not conducted and therefore a total of 18 interviews were carried out. Of the participants, 66% (n=12) were male. Mean age of interviewees was 60.4 years (*SD = 12.5).* During their acute illness the average hospital length of stay for this cohort was 14.3 days (*SD = 10.9).* Of the 18 interviewees, 7 required admission to critical care and 16 required oxygen therapy during their inpatient stay. Prior to having contracted COVID-19, 72 % (n=13) were still working, with the remaining 5 participants in retirement pre-COVID -19 diagnosis.

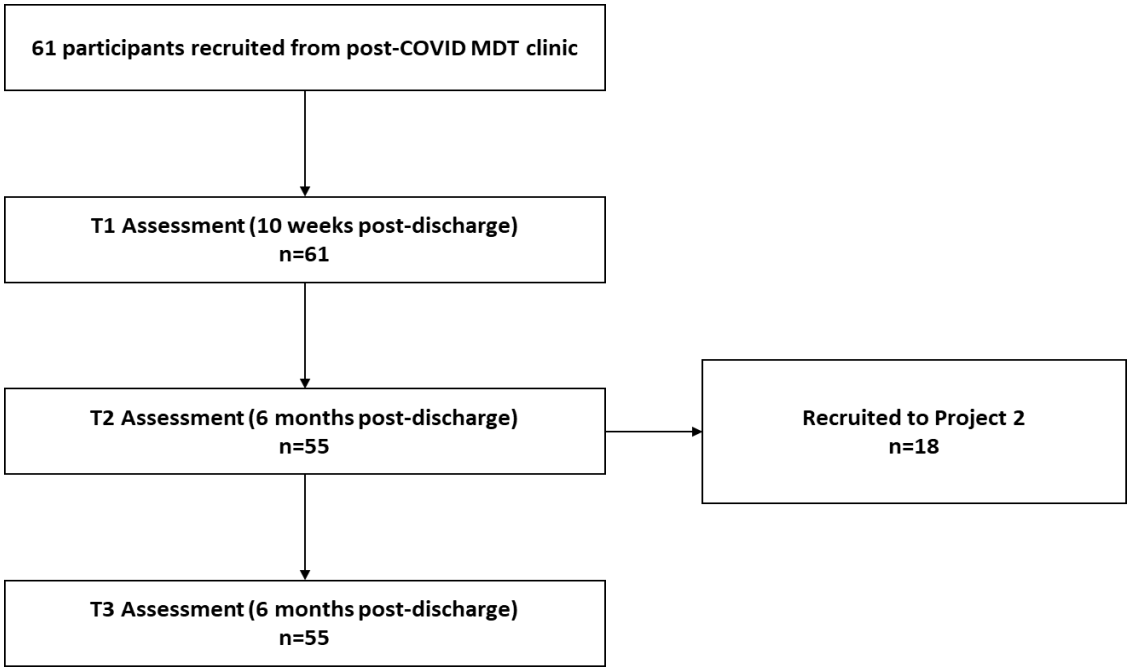

Figure 7 Study Flowchart including participant flow through Project 1 and Project 2.

Demographics and occupational details of the participants are shown in Table 1.

A table of thematic analysis (Appendix 18) was put together by the lead researcher and the second coder, containing themes, subthemes and supporting quotes.

The 18 interviews produced just over 50 pages of transcripts. Data analysis surfaced themes which we have been divided into 5 categories which will be discussed in further detail below, these include favourable recovery following COVID-19, poor recovery following COVID-19, the effects on the global pandemic on recovery, follow-up care and return to work.

Table 5: Interview Themes

Theme	Sub-theme
1. Complex Recovery	Persistent symptoms Not feeling back to baseline function Recovery is very slow / losing patience Fear/anxiety Symptoms are unpredictable Period of adjustment Knowing how to manage symptoms
2. Positive Recovery Experience	Accepting recovery takes time Different things that helped with recovery Back to functional baseline No lasting effect of COVID-19
3. Effects of Pandemic on Recovery	Restrictions to GP and hospital access Lockdown affecting mood and motivation Fear of re-infection and COVID-19 spikes Closure of gyms, leisure facilities and sports clubs
4. Follow-up Care	Adequate /satisfaction Inadequate The desire for investigations Recommendations for improved care
5. Return-to-Work	Returning to work on reduced hours Some spoke about returning to work Changing the type of work they do

	Some spoke about not returning to work at all

3.2.2 Theme 1: Complex recovery characterised by persistent symptoms

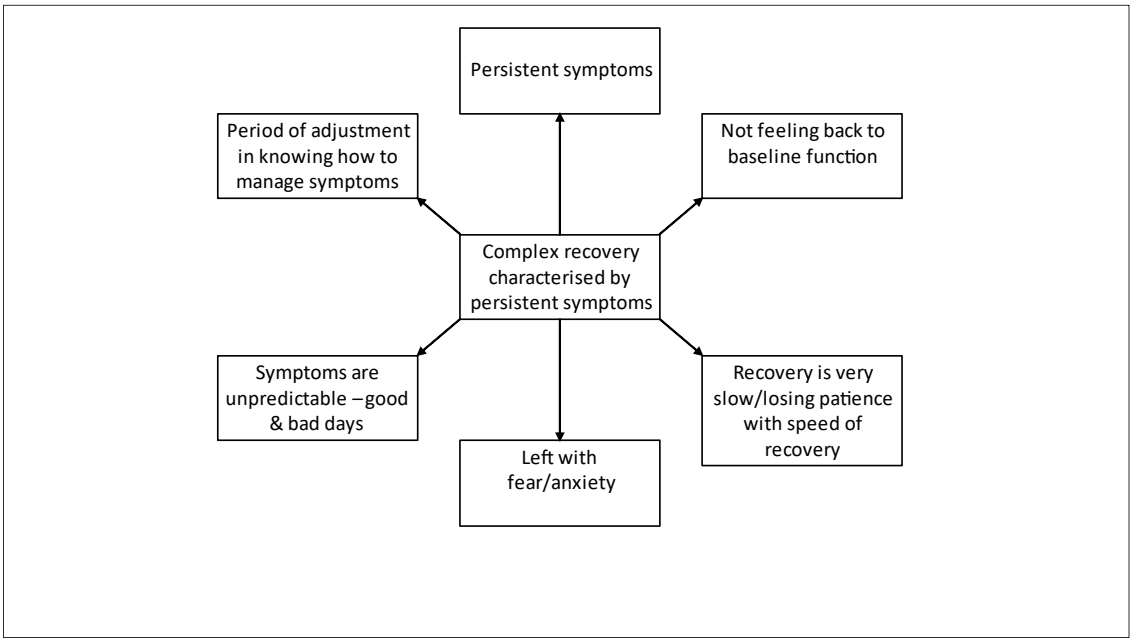

Figure 8: Theme 1 - Complex recovery characterised by persistent symptoms

Figure 8 outlines the first over-arching them, which is that recovery from COVID-19 is complex, with many patients experience persistent symptoms. Some sub-themes were identified within the over-arching theme. The overwhelming majority of participants did not feel they were back to their baseline function at the time of interview, which were held between 8-10 months following hospital-discharge. Persistent symptoms experienced by participants varied but are in keeping with what has been published in the literature to-date. One of the common symptoms reported by participants is fatigue and with one woman saying:

"it's just like a fatigue over me… I just get this tiredness, I sit there and I'm yawning and yawning, but it's only you know if I kind of over-do it on the walking and things like that…"

(Participant 14).

Others spoke about how their breathing has been affected, with one participant describing:

"As I said, I know my breathing is affected, I know I can't seem to – whenever I feel I want to breathe deeply I can feel a restriction in my chest. The breathing is the worst because that restricts everything else I do" (Participant 18).

Unsurprisingly, as many describe these persistent symptoms of fatigue and breathlessness, they touch on experiencing reduced fitness or exercise tolerance, with one participant, who was once a keen runner, running 40 kilometres on average per week, detailed her experience of "*ending up in A&E with ST depression*" after attempting to run 5 kilometres. When one participant was asked about her ability to exercise, she simply laughed and reported her exercise to be "*very minimal*" now. Other participants speak about the activities they used to enjoy and their inability to return to these, and one gentleman described his difficulty with the stairs.

"Well ability (to exercise) as in I don't have any (laughs). And I'm now – my exercise is very, very minimal" (Participant 5)

"Okay my ability to exercise is zero. I just cannot. My thing was- I used to do walks, I used to do hill walks. I can walk on a flat but if I start walking on an incline or for any length of time – I just can't. I end up limping because of it" (Participant 13)

Other physical symptoms experienced by patients included aches and pains, specifically joint pain for many participants and for others pain in their lungs.

"I still have pains in my lungs and in my back, every day I have the pains" (Participant 12)

Some participants reported issues with their throat, with one gentleman detailing his concern:

"But I have an issue internally with the throat. That really hasn't gone away and I'm worried now coming into the winter that it's going to be sort of worse again, because it was worse during the winter than it was during the summer. So I don't know what the hell is going to happen with that but sure it is what it is" (Participant 17)

Other non-physical symptoms reported by participants included forgetfulness, with one gentleman struggling during conversation:

"Do you know I'll tell you one thing – forgetfulness, not being able to pick a word or a name, it's like, even a system I can't even get the word out sometimes of what it's called. And that's definitely a feature of COVID" (Participant 6)

Others spoke about the issues with sleep with one man detailing his experience of what he called "insomnia":

"I don't know if that's something people are getting but I'm kind of- almost insomnia sometimes, like sometimes I just can't get to sleep again after I wake up. I might wake up at two o'clock in the morning and I end up just going downstairs and you know turning on the telly" (Participant 6)

While one participant linked an exacerbation of their symptoms with an increase in activity, after reporting feeling *"banjaxed for 2 days after a day of cycling yesterday"* (Participant 9), others reported these exacerbations to be somewhat random, and not knowing "*what each day is bringing*" in terms of recovery (Participant 5).

As seen in Figure 9, one of the sub-themes which emerged was the speed at which participants recovered. As many participants were still experiencing symptoms 8-10 months following hospital discharge, they acknowledged their slow recovery, and, while it may have been easy for them to feel frustrated by this, some participants showed acceptance; an acceptance that recovery from COVID-19 is "*complex and takes time to heal"* (Participant 13).

"And it took me a really long time to start coming around a good bit, that I could start feeling even that I could walk a little better and breathe a little better" (Participant 14)

"I suppose now, I just know its not going to get better in a day, once you accept that you kind of can get on with it, do you know? That kind of a way" (Participant 11)

While some participants demonstrated acceptance and patience, for others it affected their overall sense of well-being. It is apparent in some interview transcripts that there was an air of losing their identity and a longing for their former selves to return, one participant said the fatigue she is experiencing meant *"I just didn't feel that I was 'me' ever really after wards"* (Participant 14)

"Between you and me, sometimes when I'm on my own I get a bit down. I think, Jesus, I am only half the man now, that's how I feel sometimes" (Participant 18)

"It has robbed me of a lot of my life. I just don't have that energy anymore, that energy buzz that I used to have" (Participant 4)

As per inclusion criteria for this project, all participants required hospital admission during their acute illness, all hospitalised during the 1st wave of the pandemic, when little was known about the severity of COVID-19 and its aftermath, participants reported increased anxiety and fear, the fear of re-infection is also evident when reading the transcripts. While it is important that the fear these participants must have experienced as being amongst the first patients hospitalised with COVID-19 in the country is acknowledged, with one gentleman saying he will *"never go near a hospital again"* (Participant 3), it is also important the effect that this traumatic experience had on their recovery is not underestimated.

"I said to him (the doctor) "have I got COVID?" and he said "yes"- ehm, I asked him "will I get better?" and he said "I don't know, you're the wrong side of eighty and you

have a compromised immune system'. So that was the one time that I felt "eugh"-maybe this going to be serious" (Participant 2)

"The scariness and the fear of getting it again. You can't really put that into words. It's just so scary. Getting it as severe as I got it. There are just no words to describe that you know" – Participant 9

3.2.3 Theme 2: Positive recovery experience

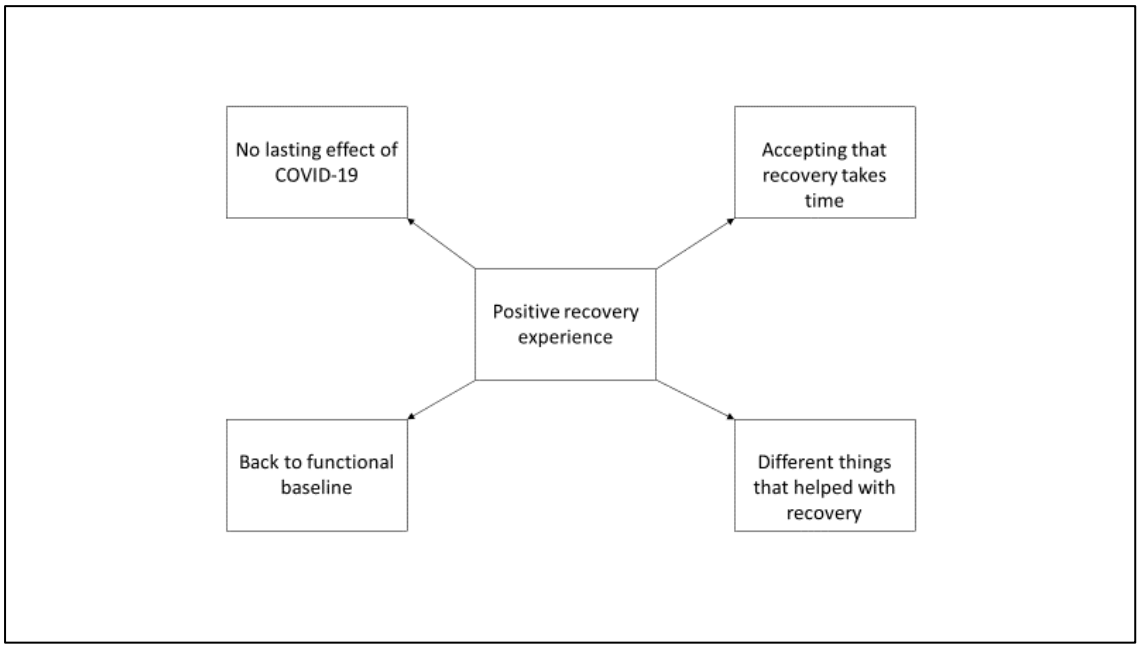

Figure 9: Theme 2 - Positive recovery experience

Figure 9 outlines the second theme identified from the interviews. The recovery trajectory described in the interviews appears to be complex, with some participants experiencing debilitating persistent symptoms, and others experiencing few, speaking about an uncomplicated or favourable recovery journey (as outlined in Figure 9), with one participant even feeling back to normal, physically. A small number of participants report having no lasting effects of COVID-19 and report returning to their previous functional baseline and with one gentleman detailing his experience:

"I went for a 25/30-minute run, and I feel fine, eh I walk to work every day, which is an hour walk and an hour back you know. And I cycle, so physically I'm pretty well. When the gym was open, I was swimming lengths, so I feel back to normal physically you know. My recovery has been remarkable" (Participant 3)

Despite being hospitalised during their acute illness, one participant felt COVID-19 hadn't affected him at all. Some participants attributed their enhanced recovery to family support with one participant remembering vividly *"barely being able to make it up the stairs*" of his house when he came out of hospital initially but praised his wife and children for "*pushing him into*" recovery (Participant 6).

"And I suppose I had good family support and ehm yeah. Family support was good, you know my family has been very good" (Participant 7)

Other participants felt that access to physiotherapy enhanced their recovery with one participant reporting *"getting himself going*" with the exercise sheets he was provided with by the physiotherapist, finding the *"literature around exercise very helpful*". Other participants attributed their improvement in recovery to the passage of time.

"Oh, the physio, I was doing physio ehm.. two eh.. virtually, I had been referred to the community from … and I did an assessment in … and then they were..it was just virtual twice a week, I found that very good" (Participant 7)

"When I came out of hospital, I was very weak, but within two weeks I was walking a couple of miles and within four weeks I was walking six or seven miles you know. Like I just gradually got better with time" (Participant 3)

3.2.4 Theme 3: Effects of pandemic on recovery

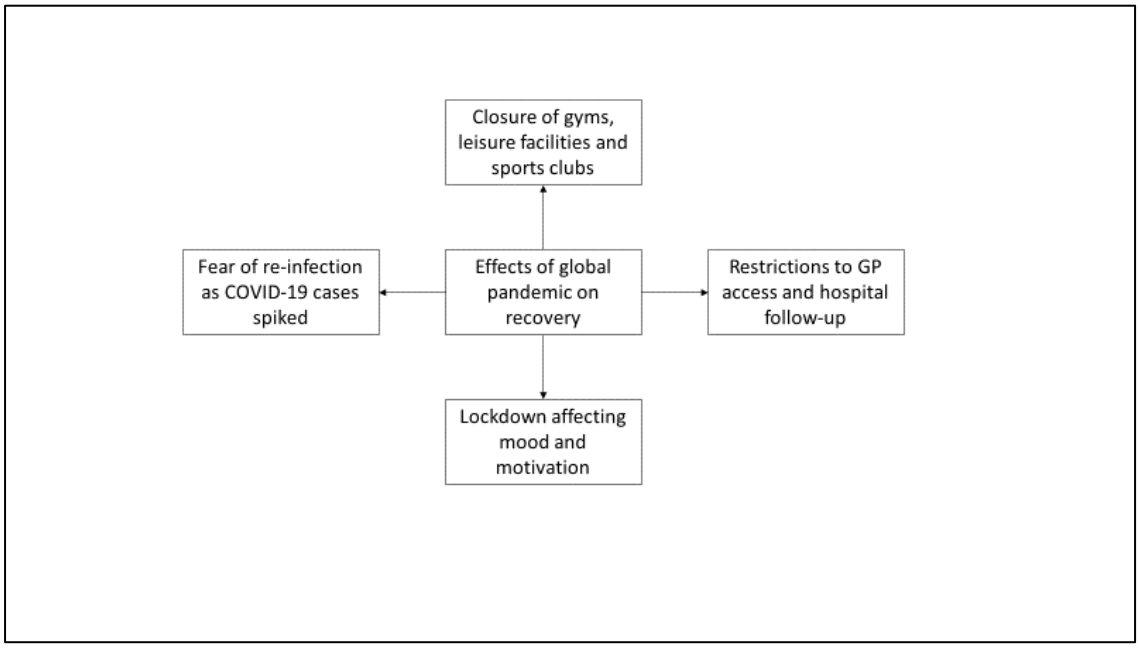

Figure 10: Theme 3 Effects of global pandemic on recovery

Consistently, participants described the effects the ongoing global pandemic had on their recovery, with many participants referencing government-mandated restrictions as barriers. These pandemic effects are detailed in Figure 10. It is worth noting that interviews were conducted in January and February 2021, during the worst wave of the COVID-19 pandemic in Ireland. While there was hope, with the administration of the country's first Pfizer/BioNTech COVID-19 vaccine, Ireland still had the highest daily number of newly confirmed COVID-19 cases in the world for every million people. Each day there were newly reported deaths and there was national unease as the Alpha and Beta variants of COVID-19 were detected in the country. Panic and unease heightened as the overriding message from the National Public Health Emergency Team (NPHET) and the Irish government was to 'stay at home'. These restrictions were extended until May2021. Not only did the level 5 restrictions result in the closure of gyms and leisure centres, impeding physical activity, but this national state of emergency must have been a triggering and terrifying time for those who were hospitalized with COVID-19 at earlier timepoints during the pandemic.

Participants report that the closure of leisure facilities such as gyms and pools affected their ability to return to normal exercise.

> *"You know? And obviously swimming, we can't do that and I was hoping to do a bit of swimming that I could get that done. And it's hard at the moment because everything is closed, all the pools and everything so that makes things 10 times more difficult" (Participant 4)*

> *"Ehm, well it's just the running because obviously the gyms and everything are closed, I haven't tried anything like that" (Participant 11)*

Some participants felt that restrictions hindered their ability to access hospital follow-up (considering the national state of emergency mentioned above they were most likely correct in this assumption). Some participants were understanding of the pressure the healthcare system was and hospitals were "*very restricted in what they could do*", others felt frustrated, stating that *"even a call to see how they were would halve the battle of the day*".

> *"I know it could be different every other time, these were emergency circumstances, but it felt like -treat the condition, not the patient" (Participant 17)*

Lastly, when considering the effects the global pandemic had on patients' recovery, some acknowledged that recovering in a lockdown-situation affected their anxiety levels, mood and motivation, with one gentleman speaking of how 'it's too easy to "*fall into those sorts of mindsets*" (Participant 6). Again, considering the national state of unease at the time, and the traumatising experience endured by these participants this increased anxiety of 'not wanting to ever go back there', there being the Intensive Care Unit in St. James's Hospital, is unsurprising. One lady who required critical care "*worries an awful lot*" about her family and friends "*ending up there*" (Participant 9).

"I think people, a lot of people will only really start to recover when they can start living normally. If you want to stay locked up in the house, those four walls moving in on you are terrible, it's a tough place to be. The problem with COVID, it gives you the excuse to do that" *(Participant 6)*

3.2.5 Theme 4: Follow-up care following hospitalisation with COVID-19

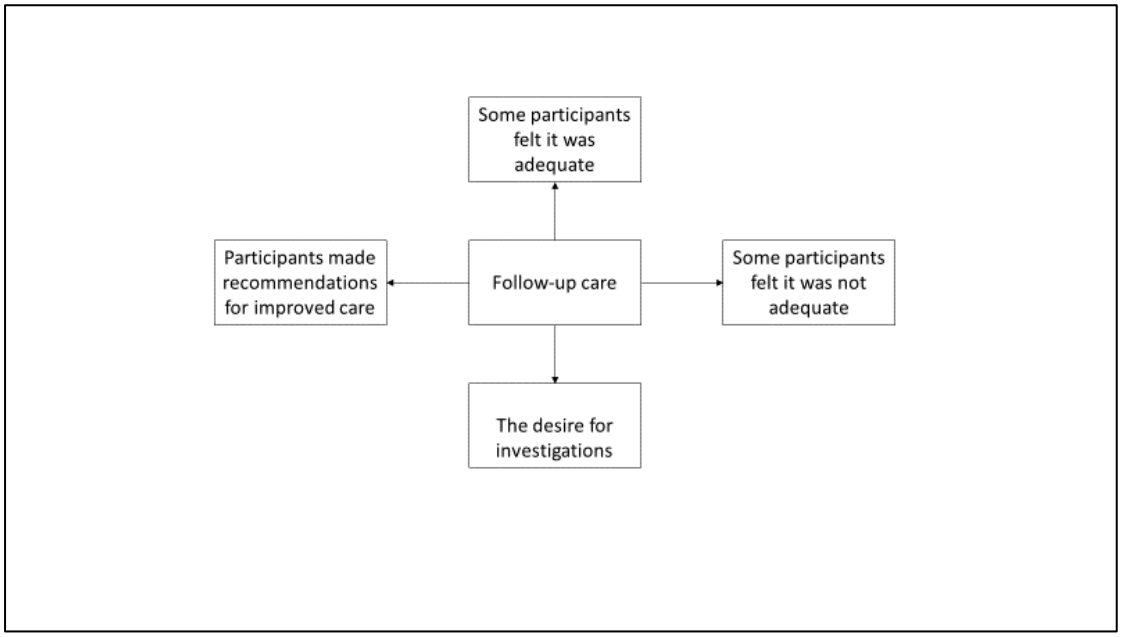

Figure 11: Theme 4 - Follow-up care

Theme 4 deals with follow-up care for these hospitalised patients, the details of which are outlined briefly in Figure 11. Some felt hospital outpatient follow-up was required to aid their recovery and to provide them with information on this new disease phenomenon which has devastated health-care systems globally. During the first and second waves, resources and staffing were limited and therefore were allocated to the management and containment of the virus in the acute setting. Very little was known about recovery from COVID-19. For this reason, there is a wide variety of accounts regarding follow-up, with some participants feeling their follow-up was adequate, with one participant thanking the post-COVID-19 clinic at St. James's Hospital, and reporting that *"without it I wouldn't be where I am now*", however others felt

differently. It is worth mentioning that a post-acute COVID-19 clinic was set up in St. James's Hospital in a timely fashion, to offer some form of follow-up to all patients and staff who tested positive for COVID-19 in our institution. All participants in this study were recruited from this clinic. It should be acknowledged that such clinics were not set up as quickly in other hospitals and many patients, both hospitalised and not, did not, and still do not, have access to these specialised clinics.

Participants appreciated receiving information from who they perceived to be experts in the area of COVID-19 in the Post-COVID-19 Multidisciplinary clinic, one lady felt *"it might mean nothing to the doctors, but they had the answers I couldn't get anywhere else*" (Participant 9).

> *"Well, I know that I can always contact somebody in St. James's Hospital if I have some symptom or anything that bothers me because I have found that St. James's Hospital has been absolutely amazing in following-up" (Participant 9)*

> *"You know taking into account the fact that there was a pandemic going on and the resources were needed elsewhere, I genuinely feel I got a good back-up in James's so yeah" (Participant 6)*

While most participants were appreciative of the follow-up care they received from the hospital, some did highlight areas for improvement for follow-up for future patients who would be hospitalised with COVID-19. One gentleman who suffered multi-organ failure during his acute illness felt that "*more than one outpatient follow-up*" was needed and suggested a multidisciplinary approach as he spoke about his complex recovery from respiratory and renal failure, requiring mechanical ventilation and dialysis acutely for each respective issue. Although participants did have access to assessment by physiotherapists in this clinic, some felt "*physiotherapy should be more involved*" and made some suggestions to add respiratory physiotherapy into their rehabilitation/recovery journey. Another gentleman suggested the

provision of a device to track activity levels by the physiotherapists, as part of the patients' *'packing up out of hospital routine'*, noting *"I felt that (the activity-tracking device) really helped, ehm it really helped me anyway..."* (Participant 6).

One participant made the valuable suggestion of incorporating a patient advocate, who might take patient feedback and bring it back to the hospital and suggest ways in which to improve follow-up for patients.

As seen in Figure 11, when speaking about follow-up, many participants focused on investigations they had done, or would have liked to have done. Again, when you consider that all participants interviewed were hospitalised during the 1st wave of the pandemic, with a disease even the most experienced clinicians knew very little about, you can understand their desire to investigate their persistent symptoms. Some participants were happy that they "*had been tested for everything*" (Participant 11), and others spoke about having their symptoms investigated alleviated some of their worry.

> *"I suppose there is a lot of research out there now on long COVID, knowing you're not on your own, like it doesn't worry me if I have a chest pain or it doesn't worry me as much as before because it's being investigated, you know that kind of a way?"*
>
> *Participant 11*

Some participants discussed the lack of correlation of results of investigations with their persistent symptoms. This both caused confusion and a lack of validation of how debilitating symptoms were.

> *"Ehm, I think the way COVID is showing up now, because your x-ray is okay or as you say you medically look okay even though you still have symptoms… ehm, there was kind of no – I felt like I was lost to follow-up" (Participant 5)*

Other participants felt they required more investigations in the search for answers as to why they did not feel fully recovered, particularly those who had some changes on previous scans of their lungs during their acute illness, with one participant wanting another chest x-ray:

"Yeah, the only other thing I would say is that I would love to get another scan on my lungs, just to see how they are coming on because I remember seeing the last one, eh, there was still some damage on the lungs. I'd love to see whether they're clearing, or what's happening with them really, that's the only other thing that concerns me you know" (Participant 12)

3.2.6 Theme 5: Return to work

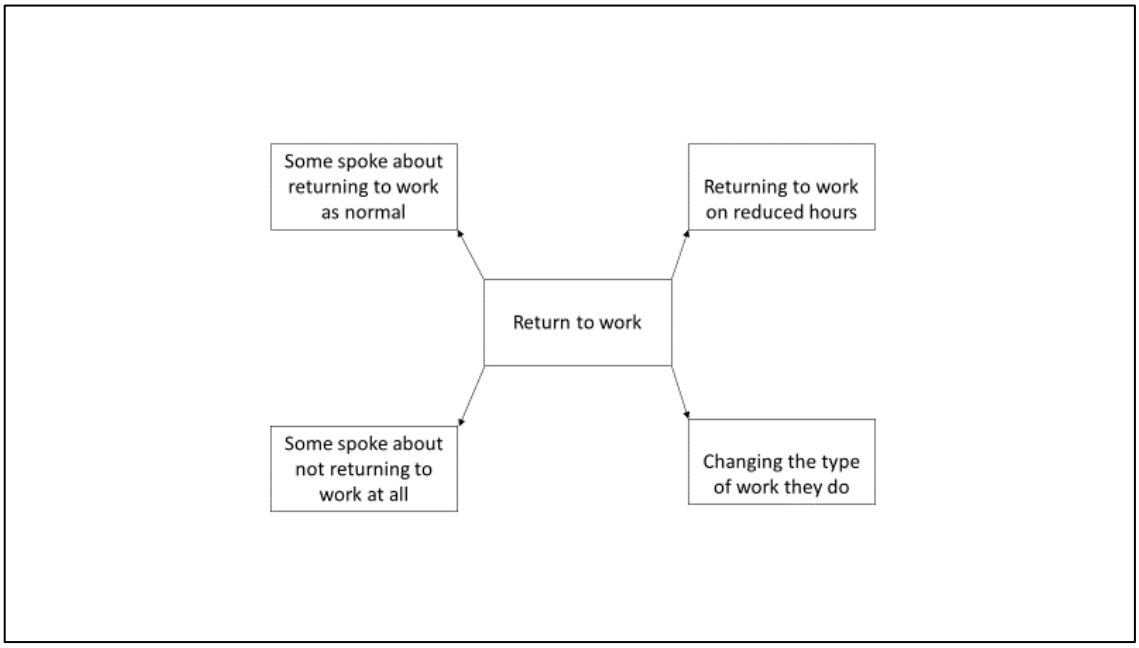

Figure 12: Theme 5 - Return to work

As described above, 72% of participants interviewed were working prior to their admission to hospital with COVID-19, the remainder were in retirement. A large, and important benchmark of recovery is often one's ability to return to work, to the same type of work and same hours. As summarised in Figure 12, some participants spoke about returning to work on reduced hours and splitting up their working days as they are simply 'too tired' to work on consecutive days.

A number of participants spoke about changing the type of work they do, this especially applied for healthcare workers. One participant described "*stepping away from the ward*", to give herself a chance to 'build up a little bit more strength' (Participant 11).

"Like I am able to work but it's definitely different" (Participant 11)

"I tried to get back flying and what not. I had to take various steps in a formal way sort of directed me back into getting back to fitness or being fit again. I've only done like since November- I've done 4 flights" (Participant 6)

Some participants had not returned to work at all but were hopeful that they might soon return 'if at all possible' and used it as 'something to focus on' in their recovery.

"Well, I'm still out of work, I'm hoping to go back to work in the next few weeks, I'm going to go back part-time'. When asked how long they were off work for participant replied – 'ehm, since April so will be 10 months or 11 months" (Participant 5)

Chapter 4 Discussion

This thesis examined recovery following hospitalisation for COVID-19 over a 1-year period. Longitudinal data collection prospectively investigated physical recovery and self-reported well-being at 10-weeks, 6-months and 1-year following hospital discharge. Semi-structured interviews were completed to gain further insights and deeper understanding of recovery through detailed accounts of the lived experience.

Overall, while participants experienced some recovery as demonstrated objectively by improvements in 6MWD, many reported ongoing symptoms. When compared to population norms (Jenkinson, Coulter and Wright, 1993), HrQOL amongst our cohort were lower, with fatigue, breathlessness and issues with memory/concentration persisting long after hospital-discharge. Return to work rates were low amongst our cohort, with just over half of participants returning to work in some capacity, and a substantial percentage of participants do not feel back to full-health at 1-year following infection. Several themes emerged from the patient interviews. The most pertinent themes included the less common positive recovery experience, while a larger theme of complex recovery characterised by persistent symptomology reported by participants came to the fore. Other interesting themes identified and explored included the complexity of recovering from illness necessitating hospital admission during a global pandemic, amidst government-mandated restrictions, follow-up care for those recovering from COVID-19 and return to work.

The purpose of conducting this research was to add to the growing body of evidence investigating recovery from COVID-19 and to inform best practice for the management and treatment of patients during their recovery. Findings from the first quantitative part of this study have been peer-reviewed and published in the journal of Respiratory Research. To disseminate our findings with clinicians working in their area of COVID-19 recovery, findings

from both the quantitative and qualitative parts of the study have also been presented at conferences both nationally and internationally (see pages 13 & 14).

4.1 Physical Recovery

4.1.1 Physical fitness

Participants in Project 1 demonstrated some improvement in physical measures of recovery, as observed in 6MWT results. A statistically significant improvement in mean 6MWD was observed over time (p=0.0001), with the most significant improvement occurring between 10-weeks and 6-months and less significant between 6-months and 1-year. Despite this improvement however, 6MWD were considerably less than that of population norms (E.g., average 6MWD at T1 was 365m compared to population norms of 572m for males and 538m for females) (Chetta et al., 2006). There was a slight, non-significant decrease in MBS breathlessness scores during the 6MWT over time. The symptom of breathlessness seemed to resolve for some participants over time. However, despite this reduction in the incidence of reported breathlessness, it is still a prevalent symptom experienced by our cohort at 1-year following infection (20%), which would inevitably affect one's exercise capacity and physical fitness.

When analysing the data collected from the individual participant interviews, it became apparent that participants' perception of their return to pre-COVID physical fitness varied greatly. A small number of participants reported having no lasting effects of COVID-19 and reported returning to their previous functional baseline and physical fitness. Participants attributed this to a number of different reasons including the passage of time, support from family and access to physiotherapy. However, the majority of patients who were interviewed did not feel as physically fit as they were before hospitalisation with COVID-19 and many attributed this decrease in fitness to an inability to exercise due to their persistent symptoms they were still experiencing long after hospital discharge, these included debilitating fatigue and issues with breathing.

The initial objective improvement in physical fitness observed in our cohort is in keeping with 6MWT outcomes observed amongst other studied COVID-19 survivors (Bels et al., 2022), as is the tapering off of improvement between 6-months and 1-year (Huang et al., 2021b). However, this contrasts with findings from an Italian cohort of COVID-19 associated ARDS survivors who observed no improvement in median 6MWD over time at all (Latronico et al., 2021). The most common abnormality observed in pulmonary function tests of those who developed COVID-19 pneumonitis during acute infection with SARS-CoV-2 is reduced diffusion capacity of the lungs (DLCO) (Huang et al., 2021b, Wu et al., 2021). In a cohort of 47 COVID-19 survivors who required mechanical ventilation due to this pneumonitis during their acute illness, a significant improvement in impaired DLCO was observed between 3-months and 1-year following infection. Similar improvements were observed in a study of 73 patients who were hospitalised with COVID-19 in Canada in pulmonary function results, including FEV1, FVC and DLCO between 3 and 6-months following discharge from hospital (Shah et al., 2021a). A small percentage of participants in Project 1 experienced COVID-19 related ARDs and the reason for this improvement in 6MWTD may be multifactorial. It is noteworthy that 75% of our patient cohort required at least oxygen therapy during acute illness suggesting a pulmonary involvement. Unfortunately, Project 1 did not include pulmonary function test findings and/or results of CT THORAX so it is impossible to establish a relationship between 6MWTD and persistent breathlessness with PFT results. Like findings in an Italian cohort where 6MWTD were 80% of predicted (Latronico et al., 2021), 6MWTD in Project 1 was lower than population norms at each time-point following discharge from hospital. T1 assessments were conducted at a median of 55 days following hospital discharge and considering how debilitated patients are during their acute infection during hospitalisation, it is unsurprising that they experience such functional impairment as denoted by 6MWTD so soon after hospital-discharge. Similar impairments in physical function were observed in an Italian cohort

in results of the Short Physical Performance Battery and 1-Minute Sit-To-Stand test on discharge from a step-down rehabilitation facility following acute COVID-19.

This theory is echoed by participants during their interviews with one participant stating that when he came out of hospital, he was very weak, but within two weeks he was walking a couple of miles and within four weeks he was walking six or seven miles, he remembers gradually getting better with time. It is concerning however that 6MWTD at 1-year were still significantly lower than that of population norms persists for up to 1-year following hospital discharge (e.g. 447m compared to population norms of 572m for males and 538m for females) (Chetta et al., 2006). As physical impairments are still observed 1-year down the line, it is important that COVID-19 survivors are followed-up over a longer period, to assess for resolution of such impairments. This is echoed by authors of a large Chinese study investigating outcomes of hospitalised COVID-19 survivors; a longitudinal study is needed to describe the natural history of lung structural and functional abnormality after COVID-19, and to explore the effect of these persistent abnormalities on physical function and quality of life (Huang et al., 2021b). To our knowledge, no other qualitative research studies have explored return to physical fitness and previous exercise capacity following COVID-19.

4.1.2 Physical activity levels

One contributing factor to impaired submaximal exercise capacity may be suboptimal exercise levels during their recovery from COVID-19. Prior to hospitalization with COVID-19, 53 (87%) of participants had undertaken regular exercise. Only 45% and 51% of these participants had returned to their pre-COVID-19 levels of exercise at 6-months and 1-year following discharge respectively. Further analysis was conducted, and it was found that those who had returned to self-reported pre-COVID-19 exercise levels had significantly lower fatigue scores at time-point 2 ($p=0.0249$). Similarly, participants who had returned to pre-COVID-19 exercise levels at T3 had significantly lower breathlessness scores during the 6MWT ($p=0.02$) than those who had not.

This then poses the question, does participating in physical activity aid recovery and possibly reduce persistent symptoms, or simply do those who experience less breathlessness or fatigue following COVID-19 feel more able to return to exercise? This is something which should be explored in future research in an attempt to identify rehabilitative strategies which may improve outcomes in this growing patient group.

As the percentage of participants returning to their previous activity/exercise levels was low, the reasons surrounding this inability to return to such were explored further during the interviews. Some potential reasons were proposed by participants. Participants were hospitalized during the 1st wave of the pandemic and were recovering when government mandated restrictions were in place in the year following their hospitalization. Participants reported that the closure of leisure facilities such as gyms and pools at various timepoints during their first year of recovery affected their ability to return to normal exercise.

Persistent symptomology seemed to be a barrier in returning to exercise. Many participants gave detailed accounts of persistent symptoms they are still experiencing 8-10 months following hospital-discharge and were fearful of the effect exercising or increasing physical activity may have on these symptoms. Some participants spoke of previous experiences of attempting to get back into exercise but being deterred by a worsening their fatigue. One participant, who was once an avid runner, running 40 km per week pre-COVID, detailed her experience of ending up in A&E with ST depression after attempting to run just 5km. Throughout the interviews, participants seemed to mourn their pre-COVID-19 exercise capabilities and this is something that was observed in survey responses of a Canadian Long-COVID cohort in a study conducted by Wurz and colleagues, with participants in their qualitative research 'expressing a sense of loss' over their pre-COVID physical activity behaviour (Wurz et al., 2022). Some participants who were interviewed felt access to physiotherapy enhanced their physical recovery, while some participants touched on a lack of motivation, getting out of the routine of

exercising and fear/anxiety surrounding symptom exacerbation as barriers to returning to exercise. One of the principal goals of physiotherapy is to promote and encourage physical activity amongst patients, and this is no different for COVID-19 survivors, one could suggest physiotherapy should play a large role in re-integrating patients back into exercise in a safe, controlled, and gradual manner without exacerbating any persistent symptoms. Unfortunately, many participants in this study did not have access to physiotherapeutic interventions during their recovery. Attempts are now being made to develop rehabilitative pathways in post-acute and long COVID-19 clinics nationally, ensuring that those recovering from COVID-19 have access to physiotherapy, occupational therapy and other relevant specialities to improve their outcomes.

While there was limited research exploring the physical activity habits of COVID-19 survivors at the time this thesis was written, the reasons identified in patient interviews for participants not returning to exercise during their recovery are similar to that experienced amongst a cancer cohort during the COVID-19 pandemic. Three-hundred and seventy-seven participants with cancer were surveyed and reported a decrease in physical activity levels during restrictions, citing isolation; declining health/fitness; lack of access and motivation (Brown et al., 2021). This solidifies the idea that pandemic associated factors may have influenced exercise behaviours amongst our COVID-19 cohort and thus contributed to suboptimal recovery of physical fitness.

4.1.3 Return to work

As stated previously, an important benchmark of recovery is often one's ability to return to work, to the same type of work, at the same intensity. Therefore, physical recovery was also assessed by return-to-work rates. The return-to-work rates amongst our cohort is considerably lower than that observed in other studies of hospitalised COVID-19 patients which report that up to 88% of participants return to work at 12-months following infection (Latronico et al., 2021, Huang et al., 2021b). Fifty-five percent of our participants had returned to work in some

capacity at 1-year following discharge. Of the 17 health-care workers in our study, 71% had returned to work fully, 11 % had returned partially, while 18% had not returned at all. It is difficult to say why such stark differences occur between the return-to-work rates in our study and the two studies aforementioned. One which is worth considering is the location in which the study was conducted, that the first in Italy (Latronico et al., 2021), and the other in China (Huang et al., 2021b). Perhaps socioeconomic and cultural reasons should be considered, for example different illness benefit terms etc. The second point to consider is the type of work carried out by participants across the different studies. In the other studies, the type of work undertaken by participants pre-COVID is not specified. Seventeen of the 33 participants in our study who were working pre-COVID-19 hospitalisation were healthcare workers, all of whom were patient-facing in their roles. It should be considered that returning to work to care for others in the hospital where you were once cared for, returning to a physically demanding job and returning to an environment where your risk of re-infection is high would be very difficult and may offer some explanation as to why many of our cohort did not return to work within 6-months or 1-year of their hospital discharge.

With an already under-pressure health-care system, with many of its employees contracting COVID-19 in the workplace, having just over 70% of these employees returning to previous levels of work is not ideal. As many health-care workers were infected in the workplace, this brings its own set of challenges and complexities to their recovery and subsequently their return to work. Of those who had not returned to work at 1-year, 70% reported persistent issues with memory and concentration at this time, which along with physical limitations must contribute to work absenteeism. One's ability to return-to-work is vital for their overall sense of achievement and purpose, therefore when comparing scores across the eight SF-36 domains between those who had returned to work (n=18) and those who had not (n=15), it is unsurprising that participants who had not returned to employment at 1-year reported significantly worse physical function (PF) and general health (GH) measures. Appropriate follow-

up in the form of vocational rehabilitation with the appropriate members of the MDT such as an Occupational Therapist should be prioritised. This process involves enabling individuals to overcome barriers faced when returning to work following an injury or illness.

Return to work was also explored in the participants interviews. As observed by Wurz and colleagues (Wurz et al., 2022), some participants in Project 2 spoke about returning to work on reduced hours and breaking up the days they work with a day off in between, as they are simply 'too tired' to work on consecutive days. A number of participants spoke about changing the type of work they do, this especially applied for those working in healthcare or doing physical jobs, which would justify the point made above. The challenge of returning to work with long COVID was also described by Greenhalgh et al. in focus groups and interviews, with some participants speaking of having to leave work and being unable to imagine applying for new jobs while dealing with debilitating fatigue and brain fog (Ladds et al., 2020). However, despite the wealth of knowledge that has been published on COVID-19 in the last two years, few studies have evaluated the effects of this illness on occupational health, this is surprising considering illness affects a significant number of individuals who are working-age (Santos-Paz et al., 2020). Work and occupation give individuals a sense of purpose, so it is obvious why returning to work is a goal which was mentioned by a number of participants in the interviews. The inability to return to work will have knock-on consequences on mental health of survivors as they may struggle to identify their sense of purpose, be faced with financial difficulties and the stigma associated with long-term sick leave (Santos-Paz et al., 2020).

4.2 Persistent symptoms

4.2.1 Overview

There was a clear discordance between objective measures of recovery from COVID-19 and subjective measures of recovery in Project 1, with many of our cohort experiencing persistent symptoms at each time-point during their first year of recovery. A breakdown of the persistent

symptoms experienced by participants at each time-point can be seen in Figure 5. Overall, 72%, 56% and 60% of participants report at least one persistent symptom at 10-weeks, 6-months and 1-year respectively. Commonly reported symptoms included fatigue, breathlessness, issues with memory and concentration, worry/fear/anxiety and many more. Similar trends have been observed in other studied COVID-19 cohorts. Bels and colleagues found that physical recovery in the form of 6MWD, radiological changes on CT thorax and diffusion capacity of the lungs as assessed by pulmonary function tests all improved between 3-months and 1-year following discharge from critical care, but participants reported no improvement in symptoms such as breathlessness and fatigue (Bels et al., 2022). This persistent symptomology was observed in another large study of 2433 COVID-19 survivors with 45% experiencing at least 1 persistent symptom at 1-year following acute infection, one of the most commonly experienced being fatigue (Zhang et al., 2021). Consistent with the results presented in this thesis, Huang and colleagues observed a decrease in persistent symptomology reported between 6-months and 1-year following acute infection, but an increase in reporting of worry/fear/anxiety at 1-year. The mechanism underpinning these symptoms is not entirely understood. However, it is important that indirect effects of the COVID-19 pandemic are considered too, including recovering from hospitalisation during a lockdown, reduced social contact, inability to return to work due to ongoing illness or government mandated restrictions and living in a period of uncertainty to name just a few.

To test these theories and to attempt to understand the mechanisms underpinning these persistent symptoms, participants were asked to give a detailed account of their persistent symptoms during the participant interviews. Some participants identified particular triggers or activities which may worsen their symptoms including joint pain and fatigue, while some felt that there was no pattern and their symptom onset can be completely unpredictable, making it difficult for patients to understand their symptoms themselves. This idea of a ‘confusing’ illness emerged as a theme in qualitative research conducted by Ladds and colleagues investigating

persistent symptoms experienced by those with Long COVID through interviews and focus groups (Ladds et al., 2020). Consistent with the results presented in Project 2, participants in their study reported symptoms in 'every part of the body' which were 'fluctuating' with many unable to make sense of their suffering (Ladds et al., 2020).

4.2.2 Fatigue

Consistent with the broader literature, post-COVID-19 fatigue was very common. Fatigue was the most reported symptom/concern amongst our cohort at T1 (49%) and T2 (38%), and despite being surpassed by issues with memory and concentration at T3, it was still extremely common with 34% of participants experiencing it 1-year following hospitalisation. Overall, 47%, 53% and 49% of patients who completed Chalder Fatigue Scales met case definition for fatigue or reported substantial fatigue at time-point 1, 2 and 3, this is much higher than that of the general population (9.7%) (Kocalevent et al., 2011). Unfortunately, there was no overall improvement in fatigue scores over-time, unless participants were considerably fatigued at time-point 1. These findings were mirrored in the energy/vitality domain of the SF-36-II, with participants scoring substantially lower than population norms in this domain at all three timepoints. Unsurprisingly post-COVID fatigue was discussed at length by many participants during interviews. Some participants reported general fatigue or tiredness which prevented them from doing certain activities they used to enjoy. However, more often, participants reported trying or carrying out the activities as they felt they are physically capable but then would be severely debilitated by fatigue for some time (up to days) afterwards.

While it is possible that the fatigue experienced by some participants in our cohort may be attributable to the sleep problems patients are reporting post-COVID-19, extensive research is ongoing by multiple study groups to attempt to understand the mechanisms driving post-COVID-19 fatigue. In this thesis, those who reported substantial fatigue during interviews were not necessarily those who experienced more severe initial infection necessitating intensive

care. This idea is solidified by work carried out by Townsend et al who set out to identify predictors of worse fatigue following infection with SARS-CoV-2 (Townsend et al., 2020). They found that there was no association between COVID-19 severity (need for inpatient admission, supplemental oxygen or critical care) and fatigue following COVID-19 (Townsend et al., 2020). Similarly, there was no association between routine laboratory markers of inflammation and cell turnover (leukocyte, neutrophil or lymphocyte counts, neutrophil-to-lymphocyte ratio, lactate dehydrogenase, C-reactive protein) or pro-inflammatory molecules (IL-6 or sCD25) and fatigue post COVID-19 (Townsend et al., 2020). What they did find was that female gender and those with a pre-existing diagnosis of depression/anxiety were more likely to be fatigued. Due to the modest sample size, it was not possible to say whether female gender was a predictor for the persistent fatigue amongst our cohort.

As described in the literature review, Long COVID is the collective term to denote persistence of symptoms in those who have recovered from SARS-CoV-2 infection (Raveendran, Jayadevan and Sashidharan, 2021). Fatigue is one of the listed symptoms of Long COVID. The data collection for T1 and T2 of this study took place before the term Long COVID was created or known, and the term was only emerging at the time of the interviews. Therefore, participants in this study did not really identify as having Long-COVID and so was not something that was mentioned very frequently during participant interviews. Fatigue however was mentioned multiple times during interviews. Similarly, Post- Exertion Malaise or PEM has recently been identified as another key feature of Long-COVID, which is described in detail above. This term was well-known in the Chronic Fatigue Syndrome cohort prior to the Long COVID cohort. Although not labelled as PEM during interviews, is something which some participants appeared to experience, referencing debilitating fatigue and feeling generally unwell following any kind of activity, including exercise.

When one considers the traumatic experience COVID-19 patients faced when hospitalised during a pandemic with an unknown novel virus, it is not surprising that many patients experience fatigue and other symptoms like PEM during recovery. As 27% of SARS survivors met the criteria for chronic fatigue syndrome 4 years following acute illness (Lam et al., 2009), it is important that COVID-19 survivors are followed up over the same prolonged timescale to better understand the trajectory and recovery of fatigue.

4.3 Follow-up care

When the many persistent symptoms reported by participants are considered, the topic of follow-up care surfacing as a theme during participant interviews was to be expected. Some participants were satisfied with the follow-up care they received through the hospital's post-acute COVID-19 MDT follow-up clinic, some, however, highlighted areas for improvement. One suggestion was the ordering of investigations to identify causes for these persistent and debilitating symptoms. This was discussed by participants in a study by Ladds and colleagues during interviews and focus groups when researching persistent symptomology experienced by Long-COVID patients, as the authors explored patients accessing and navigating services (Ladds et al., 2020). Participants in their study found the process of looking for follow-up exhausting, and participants went to extreme lengths to access investigations. This exhausting process was not mentioned by participants in our study. Extensive investigations were likely not carried out on their cohort as 93% of participants in their study were not hospitalised during their acute infection with COVID-19, with the assumption they had mild COVID-19 and therefore deemed at lower risk for abnormal findings on investigations. All participants in our study were hospitalised with moderate to severe COVID-19 and therefore follow-up investigations were seen as routine care.

Something which surfaced as a theme in the research by Ladds et al was the concern about safety and quality of care, with the majority of participants believing their clinician did not

recognise their condition (Long COVID), did not acknowledge their suffering , did not know how to manage it and refused to test or re-refer (Ladds et al., 2020). Thankfully, the experience by our cohort appeared to be different. Many participants praised the clinicians in the post-acute COVID-19 clinic in St. James's Hospital, referring to them as experts and who had the answers they felt their General Practitioners did not, perhaps due to the clinical experience they had in the area of COVID-19 recovery. The general feeling was that participants could rely on the hospital's clinic, referring to it as 'back-up' and 'supportive'.

4.4 Psychological impact of COVID-19 on recovery

The psychological burden of COVID-19 and its recovery appears to be substantial and remains substantial over time. The results presented in this thesis report an increase in participants experiencing issues with anxiety/depression between 6-months and 1-year, in conjunction with participants scoring lower than population norms in the emotional well-being domain of the SF-36-II at 1-year following discharge. As in Sars survivors, Mazza and colleagues also observed a high prevalence of psychiatric sequelae at 6- and 12-months following infection with COVID-19, with 44% of 216 participants and 45 % of 192 participants self-rating above the clinical threshold in at least one of the psychopathological dimensions (Mazza et al., 2021). They identify the need to provide integrated multidisciplinary care services to properly address the needs of this growing patient population. The semi-structured interviews in Project 2 in this thesis, sought to gain a deeper understanding of the mental health burden that is associated with COVID-19.

As mentioned above trauma from participants' experience of acute COVID-19 must be considered. Participants spoke about the trauma of their experience in the acute hospital setting, with one participant giving a detailed account of receiving her diagnosis and the thought process that came thereafter, that there was a strong possibility she may not survive this illness. During their hospitalisation between March and May 2020 participants in this study would have been isolated in single rooms or 6-bed bays for at least 14-days, being cared for by health-

professionals in full personal protective equipment with no visitors permitted onto the wards. Some of the participants spoke about the health-care staff limiting their time in the patient areas to reduce their exposure to the virus, resulting in patients spending hours alone. One patient even mentioned how now hearing a beep which slightly resembles hospital equipment takes him back to his time in hospital.

Secondly, fear of re-infection surfaced as a sub-theme throughout patient interviews. Given the ordeal participants suffered not only during their acute illness, but in the months after, fear of re-infection amongst participants was inevitable. As seen in Table 1, interviews were conducted in January and February 2021, during the 3rd and worst wave of the COVID-19 pandemic in Ireland. Daily incidence was at an all-time high, with the government and the National Public Health Emergency Team urging people to stay at home, imposing strict restrictions, there was certainly an air of unease throughout the interviews. One general practitioner who participated in Project 2 said he would avoid hospitals after his experience.

Thirdly, recovering from any kind of illness during a lockdown situation is difficult and reduced motivation is something which was mentioned by a number of participants during interviews. Many found it difficult to get back into the routine of exercising. One participant provided an insightful analysis on how he felt people were not going to recover fully until they were allowed to live normally again and touched on how restrictions and negativity in the media can affect one's motivation, which is something he experienced early on in his recovery. He credited his family for helping him out of this mental headspace and focused on things he could do to help his recovery. Trying to navigate your recovery during a global pandemic must have been challenging for all those who required hospital admission during their acute infection with COVID-19, and capturing this unique experience is important, to determine how it might affect long-term recovery. However, this is not unique to just those who are recovering from COVID-19, but also to those who had to recover from other illnesses and hospital admissions during

the global pandemic, and perhaps outcomes, including mental well-being between COVID-19 survivors and other patient cohorts should be explored in future research. Huang and colleagues found that there was an increase in reporting of anxiety or depression between 6-months and 1-year following acute infection with COVID-19, and they propose some reasons for this, citing several hypotheses including aberrant immune responses, but they too mention some of the indirect effects of the pandemic including reduced social interaction and loneliness, incomplete recovery of physical health and loss of employment (Huang et al., 2021b).

4.5 Complexity of recovery

Findings from this study demonstrate the complexity of recovery from COVID-19, with participants giving varied accounts of their recovery journey. There results of this thesis, and the work of researchers mention above, shows that many people experience persistent symptoms long after initial infection. These symptoms experienced by participants in this study lead to reduced health-related quality of life, impact individuals' ability to return to previous levels of function including work and exercise, and inevitably effect individuals' mental health. Recovery is further complicated by the novelty of the virus, the fear of re-infection and particularly during the first wave, the lack of expertise surrounding the management and treatment of those infected. The controversy in the media surrounding infection rates, government-mandated restrictions, and the lack of adequate follow-up care for survivors will add to the complexity, not to mention the social isolation experienced by many during the pandemic.

Throughout the individual participant assessments and interviews, what was apparent to the lead researcher was the appreciation all participants had for St. James's Hospital and the staff who cared for them during their acute illness. Although the sample size was relatively modest, retention rates were high with over 90% of participants being re-assessed at both 6-months and 1-year. Participants often mentioned wanting to give back to St. James's Hospital in any way

that they could, even in the form of participating in research. Participants travelled from different parts of the country to participate in the study and were generous with their time to give interviews detailing their experiences. Phone interviews were facilitated to increase accessibility for participation. Not only did participants want to give back to the hospital, but they were desperate to improve follow-up care for those who were to come after them, contracting other variants of the virus and requiring hospital admission during subsequent waves of the pandemic. Throughout participant interviews, suggestions were made on how to improve care for those who were still to contract the virus. Through researchers investigating recovery from COVID-19 and disseminating their findings, like researchers of this study have, we are hopefully one step closer to developing comprehensive care pathways for those recovering from mild, moderate and severe COVID-19 in this country.

Efforts are being made nationally to ensure individuals' needs are met country-wide with the roll-out of 6 national post-acute- and 7 national long- COVID-19 clinics, with the essential personnel with relevant expertise in the field staffing such clinics. It is important that the body of evidence grows to inform best practice for the management of the sequelae of COVID-19, and this is only possible through patients participating in research projects like this one. The ultimate goal of this research is to improve care for those recovering from COVID-19 in Ireland.

4.6 Conclusion

Recovery from COVID-19 is complex, particularly for those who were hospitalised with moderate to severe COVID-19. Individuals are left with persistent symptoms including debilitating fatigue, issues with breathing and memory and concentration issues to mention just a few, along with impaired mental health in the form of increased depression and anxiety. When compared to healthy populations, those recovering from COVID-19 demonstrate impaired exercise tolerance and reduced health-related quality of life. Many of the participants

in this cohort are unable to get back to exercise and work, two important benchmarks of recovery. Recovery from COVID-19 is further complicated by pandemic factors which should not be underestimated. Individuals who do not feel fully recovered are looking for more, more investigations, more answers and more follow-up.

Since the publication of Project 1 of this study (O'Brien et al., 2022), many more studies on this topic have been published, and this paper has added to this growing body of literature. As it stands there are very few qualitative papers published whereby individuals are asked to speak about recovery from COVID-19 in their own words. The lead researcher of this study hopes to publish the qualitative part of this research project in Autumn 2022, to disseminate the knowledge she has gained from interviewing individual participants.

This growing body of quantitative and qualitative literature will hopefully spark innovation amongst researchers to investigate rehabilitative strategies which may improve outcomes amongst this growing patient group.

4.6.1 Implications for practice

The main aim of this research was to gain an understanding of how individuals who were hospitalised with COVID-19 recover over time, with the hope that gaining a deeper understanding of recovery would inform health-care providers' clinical practice in the management of this patient group going forward. The lead researcher who conducted this research works as a physiotherapist with those who are recovering from COVID-19 every day. She has huge clinical interest in the area and by conducting this research, she has improved her assessment and management of her patients.

1. **Identification of rehabilitation needs for this group:** Shortly after this research commenced the lead researcher began her role as a Clinical Specialist Physiotherapist in post-COVID-19 recovery in St. James's Hospital. Based on her findings from this research she developed a service that would offer interventions and management

strategies addressing many of the potential symptoms and physical functioning issues she knew her patients may experience. This service includes the provision of online exercise classes for those presenting with exertional dyspnoea and reduced exercise tolerance, who express fear and anxiety over exercising alone and unsupervised. She has also incorporated breathing re-education for those who have developed breathing pattern disorders. She has set up links with other speciality services including generic pulmonary rehabilitation, cardiac rehabilitation and community and day hospital services. Based on her research findings, that many individual experience debilitating fatigue, memory and concentration issues and subsequently results in work absenteeism, she successfully advocated for Occupational Therapy as an essential component of the post-COVID-19 multidisciplinary team, who now offer fatigue management and vocational rehabilitation to those who require it. Based on her findings of increased anxiety and depression amongst this cohort she also included psychology sessions as part of her online recovery programme, developing strong links with the psychology service in St. James's Hospital, and similarly advocated for funding to be allocated towards clinical psychology as part of this multidisciplinary team.

2. **The importance of the patient voice:** Through doing the patient interviews for Project 2, the qualitative part of this research, the lead researcher learned just how important the patient voice is. While it can be easy to focus on outcome measures, hard data and objective findings, in healthcare the patient experience is the most important outcome. Learning how difficult some individuals both in this research and in the research of others found recovery and how some felt unsupported by their friends, colleagues, even healthcare professionals, as they navigated their way through this recovery, often longing for someone just to listen to their experience, this taught the lead researcher the importance of empathy. It also taught her the effect that simply listening has on validating patients' concerns. Doing the interviews taught the lead researcher that the

patient is often the expert, and it should be patient feedback that inform changes to practice. She now asks all patients who come through her post-COVID-19 service to fill-out a feedback form, to ensure that she is providing the highest quality service to her patients.

3. **Application to other conditions:** What the lead researcher has learned from the participants in this study about the trauma of an acute hospital experience, the difficulties of recovering from hospitalisations, the rehabilitation that is required for recovery thereafter, the importance of listening and empathy and much more, can be applied to individuals who are recovering from other acute illnesses and who have chronic health conditions.

4.6.2 Strengths of the research project

A comprehensive physical functioning assessment battery was included in the assessment of both objective physical recovery and subjective self-reported recovery. Validated outcome measures were used to assess recovery across multiple domains. Two methods of data collection were incorporated, firstly quantitative; to assess for improvement in recovery over-time, and then qualitative; when an opportunity to learn more about COVID-19 recovery through participants' own words of their lived experience was identified. The lead researcher conducted all standardised/identical assessments personally at all three timepoints and used measures that had strong intra-rater reliability. The rigour of the qualitative data analysis was strengthened through the involvement of a second independent coder.

Despite the relatively modest sample size, retention rates were high with over 90% pf participants being assessed at 6-months and 1-year. There were likely a number of factors which contributed to this. Firstly, the lead researcher developed a good rapport with participants during assessments. Secondly, participants were eager to participate in research, in their own words to 'give back' to the hospital in which they were cared for, and to improve care for those

who would contract the virus after them. The novelty of the virus also sparked interest and many participants mentioned wanting to be part of the growing body of evidence surrounding recovery from COVID-19.

This work was conducted as part of a collaborative, multidisciplinary team of respiratory, infectious diseases and intensive care doctors, along with physiotherapists in critical care (respiratory), cancer rehabilitation and post-COVID-19 rehabilitation. Feedback was sought from the research team at every stage throughout the project; on protocol, preparation, data analysis and manuscript preparation, to ensure applicability to a broad range of health professionals.

As seen in Table 1, this research was also conducted in a timely manner, the first case of COVID-19 in Ireland was identified on the 27th of February 2020, data collection for this study commenced in May 2020. Data collection was completed 1-year later. Data analysis and writing commenced immediately and the first publication detailing the study's findings was published in the journal of Respiratory Research 1-year later, on the 4th of May 2022.

4.6.3 Limitations of the research project

This study is single-centred and uses a small sample size. Data collection took place between May and November 2020, patients who attended the clinic and consented to participating in research were consecutively enrolled. Recruitment ceased in November 2020 when physiotherapists could no longer attend the post-COVID-19 MDT clinic and recruit participants, due to increasing inpatient caseloads and high numbers of COVID-19-related absenteeism, thus resulting in a small sample size.

The literature highlights female gender as a risk factor for developing long COVID. The sample size in this thesis was too small to complete thorough sub analysis of the impact of gender on outcomes measured however future work should examine the impact of gender on early post-COVID recovery to gain insights into how this may translate into long COVID presentations.

No pre COVID-19 physical functioning data was available for the participants in this study and due to the research being conducted during a global pandemic, most other outpatient clinics were cancelled or virtual and therefore it was not possible to enrol/recruit participants recovering from hospitalisation with other illnesses as a control group.

Participants were enrolled consecutively, and all had moderate to severe covid and therefore were likely representative of those attending an acute hospital post-COVID-19 clinic. However, the generalisability of the results outside of this setting needs to be confirmed. We acknowledge that the sample recruited for Project 2 was a subset of those in Project 1. This approach was appropriate to fulfil the aims of exploring the quantitative results more in-depth, however, a larger sample independent of Project 1 would inform the external validity of the findings.

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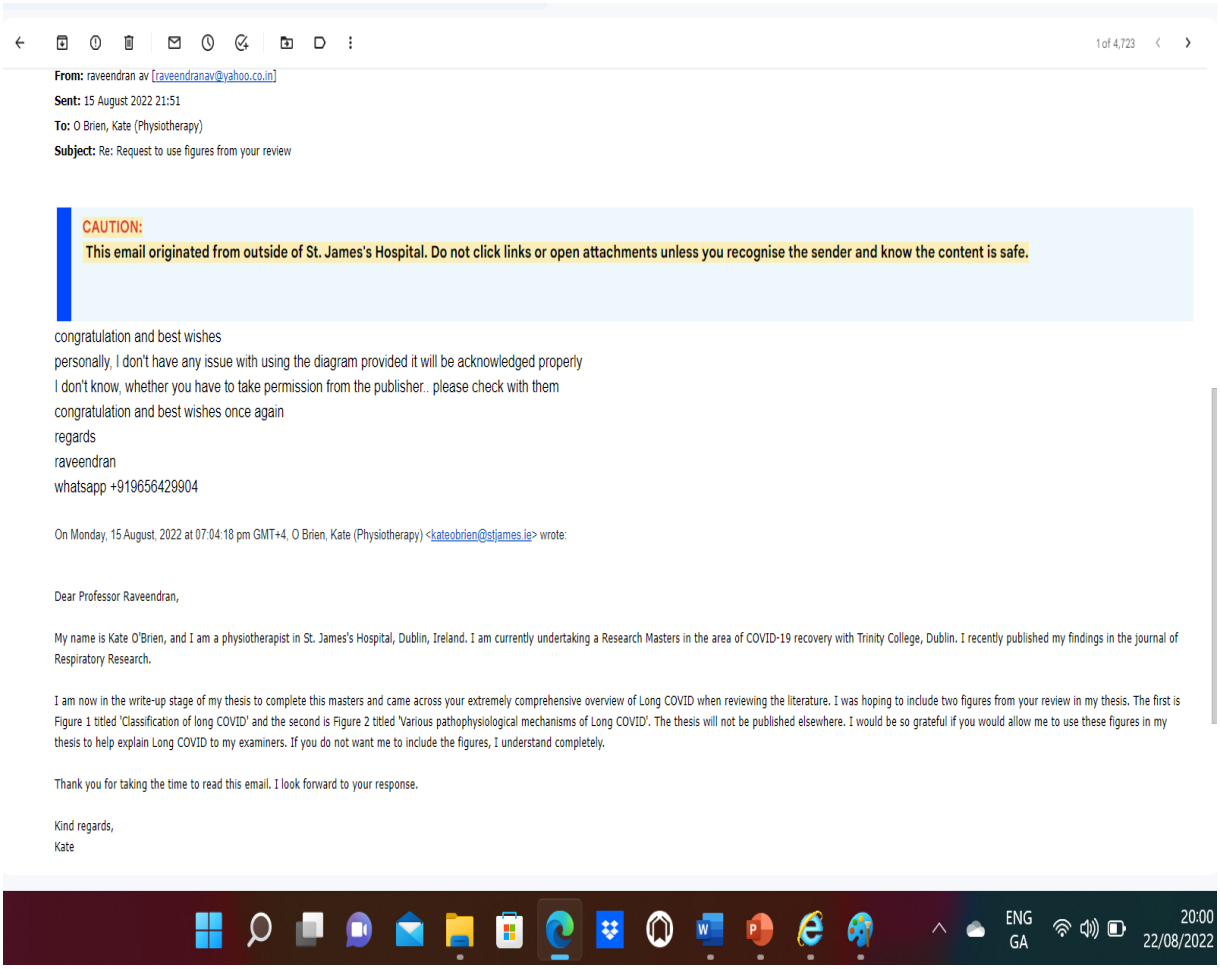
Email thread seeking permission to use Figures 1 and 2 from Long COVID Overview from Professor Raveendran



1 of 4,723

From: raveendran av [raveendranav@yahoo.co.in]
Sent: 15 August 2022 21:51
To: O Brien, Kate (Physiotherapy)
Subject: Re: Request to use figures from your review

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On Monday, 15 August, 2022 at 07:04:18 pm GMT+4, O Brien, Kate (Physiotherapy) <kateobrien@stjames.ie> wrote:

Dear Professor Raveendran,

My name is Kate O'Brien, and I am a physiotherapist in St. James's Hospital, Dublin, Ireland. I am currently undertaking a Research Masters in the area of COVID-19 recovery with Trinity College, Dublin. I recently published my findings in the journal of Respiratory Research.

I am now in the write-up stage of my thesis to complete this masters and came across your extremely comprehensive overview of Long COVID when reviewing the literature. I was hoping to include two figures from your review in my thesis. The first is Figure 1 titled 'Classification of long COVID' and the second is Figure 2 titled 'Various pathophysiological mechanisms of Long COVID'. The thesis will not be published elsewhere. I would be so grateful if you would allow me to use these figures in my thesis to help explain Long COVID to my examiners. If you do not want me to include the figures, I understand completely.

Thank you for taking the time to read this email. I look forward to your response.

Kind regards,
Kate

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Portions

Figure 1: Classification of Long COVID page 870 Figure 2: Various pathophysiological mechanisms of Long COVID page 871

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Appendix 3 – An overview of the COVID-19 Pandemic in Ireland and of the Research Project Timeline

Date	Event/Restrictions	Study Timeline
27th January 2020	The National Public Health Emergency Team (NPHET) was created.	
29th February 2020	1st case of COVID-19 in Ireland was confirmed.	
11th March 2020	1st COVID-19 related death of an elderly person in Ireland.	
11th March 2020	The WHO declared a global pandemic. Taoiseach of Ireland announced the closure of all schools, colleges and childcare facilities until 29th of March 2020.	Participants who were recruited into the study began being hospitalised with acute COVID-19 in March 2020.
23rd March 2020	Over 1000 COVID-19 confirmed cases in Ireland with 6 associated deaths.	
27th March 2020	Taoiseach of Ireland announced a national 'stay-at-home' order.	
2nd April 2020	A total of 148 patients had been admitted to ICUs across Ireland with COVID-19.	
10th April 2020	The national 'stay-at-home' order was extended to May 2020.	
18th April 2020	The Chief Medical Officer reported the 'curve had flattened' but recommended the restrictions remained in place.	
1st May 2020	A roadmap to easing restrictions in Ireland that includes five stages was adopted by the government on 1 May 2020 and subsequently published online.	Study recruitment and timepoint 1 or 10-week physical functioning assessments for Project 1 commenced in the hospital's post-acute COVID-19 clinic in May 2020.
18th May 2020	The Government of Ireland confirmed that phase one of easing the COVID-19 restrictions would begin on Monday 18 May.	

5th June 2020	The Taoiseach announced a series of changes to the government's roadmap of easing COVID-19 restrictions in Ireland, which he summed up as 'Stay Local'.	
8th June 2020	Phase 2+ of easing of the COVID-19 restrictions commenced.	
12th June 2020	Taoiseach announced travel restrictions remain in place and nobody should leave Ireland for the purpose of tourism or leisure.	
25th June 2020	Minister for Health announced face coverings were mandatory on public transport.	
29th June 2020	Hairdressers, barbers, gyms, pubs serving food, hotels, cinemas and churches were allowed to re-open.	
12th July 2020	5 key priority areas were announced by the government of Ireland 1. Face coverings to be worn in all shops. 2. Pubs, hotel bars, nightclubs and casinos would remain closed until 10 August. Pubs currently serving food can remain open. 3. Social visits to people's homes should be limited to a maximum of ten people from no more than four different households. 4. Social visits to people's homes should be limited to a maximum of ten people from no more than four different households. 5. Social visits to people's homes should be limited to a maximum of ten people from no more than four different households.	
20th July 2020	A green list of countries safe to travel to was published, but only essential travel was recommended.	

23rd July 2020	The Government of Ireland launched a 7.4 billion July jobs stimulus package to get people back to work, with the COVID-19 Pandemic Unemployment Payment and the Temporary COVID-19 Wage Subsidy Scheme extended until April 2021.	
4th August 2020	The Government of Ireland announced more key priority areas: 1. Phase four of easing COVID-19 restrictions will not go ahead on 10 August. 2. Pubs, bars, hotel bars, nightclubs and casinos will remain closed. 3. Restaurants and pubs serving food will now have to close by 11pm. 4. Current restrictions of 50 people in indoor gatherings, 200 at outdoor gatherings will remain in place.	
7th August 2020	Various strict measures and restrictions were put in place for certain counties who experienced spikes in cases.	
10th August 2020	Face coverings were made mandatory in all shops, shopping centres, libraries, cinemas, museums, nail salons, hairdressers, dry cleaners, betting stores, tattooists and travel agents, with fines of up to €2,500 or a prison sentence of six months to people who do not comply.	
12th August 2020	It was announced that the Government intended to move away from the phases of re-opening the country, and switch to a colour-coded system planned by the National Public Health Emergency Team to indicate how counties, regions and the country as a whole are currently affected by COVID-19.	
15th August 2020	Acting Chief Medical Officer announced that Ireland was having multiple clusters with secondary spread of disease and rising numbers of cases in many parts of the country.	

18th August 2020	The Government announced six new measures because of the growing number of confirmed cases, which would remain in place until at least 13 September: 1. All outdoor events will be limited to 15 people. 2. All indoor events will be limited to 6 people. 3. Gardaí will be given new powers to enforce rules around social gatherings. 4. Restaurants and cafés can remain open with closing times of 11.30pm. 5. People will be advised to work from home and to avoid using public transport. 6. Sports events and matches will revert to behind closed doors with strict avoidance of social gatherings.	
5th September 2020	Church bells rang out across the country as the Minister for Justice and 14 other people attended an outdoor, socially distanced ceremony at Collins Barracks, Dublin to celebrate National Services Day in Ireland, remembering all those in the frontline who lost their lives.	
7th September 2020	Ireland was officially in recession after the economy shrank by 6.1% between April and June as the impact of COVID-19 brought the largest quarterly drop on record.	
9th September 2020	The Government of Ireland announced that measures introduced on 18 August would be extended until Tuesday 15 September as a new roadmap for "living with COVID-19" would be announced, which would include a colour-coded, five-level system to indicate what public health measures are in place in different areas of the country at any given time	

14th September 2020	The self-isolation period for patients who test positive for COVID-19 was reduced from 14 days to 10 days	
15th September 2020	The Government of Ireland announced a medium-term plan for living with COVID-19 that included five levels of restrictions, with the entire country at Level 2 and specific restrictions in Dublin including the postponement of the reopening of pubs not serving food.	
23rd September 2020	Following a meeting of the Oireachtas Special Committee on COVID-19 Response, a specialist in infectious diseases warned that Ireland is at the beginning of a second wave of COVID-19.	
25th September 2020	Minister for Further and Higher Education, Research, Innovation and Science Simon Harris announced that all higher education institutions had been asked to deliver lectures remotely where possible for the next two weeks.	
1st October 2020	The National Public Health Emergency Team recommended to Government that a maximum of six people only from a single household should be allowed visit another home across the entire country, and that no counties were expected to see an upgrade in their level of COVID-19 restrictions.	Recruitment of participants ceased in the post-acute COVID-19 clinic at the beginning of October 2020. Timepoint 2 or 6-month follow-up assessments of physical functioning for Project 1 commenced in October 2020.
5th October 2020	The Government rejected the NPHET's recommendation to place the entire country under Level 5 restrictions, and instead moved every county in Ireland to Level 3 COVID-19 restrictions, which would come into effect from the midnight of 6 October until 27 October at the earliest.	

6th October 2020	Large-scale garda checkpoints were mounted across the entire country as 'Operation Fanacht' recommenced following the imposition of Level 3 restrictions.	
14th October 2020	The Government agreed a nationwide ban on all household visits from the night of Thursday 15 October, except for essential reasons such as childcare and on compassionate grounds. Some counties moved to level 4 restrictions which included the closure of all gyms and lesire facilities.	
19th October 2020	The Government agreed to move the entire country to Level 5 lockdown restrictions from midnight on Wednesday 21 October for six weeks until 1 December. Such restrictions included: 1. People must stay at home. 2. People will be permitted to exercise within a radius of 5 km of their home. 3. Non-essential businesses and services will close. 4. Public transport will operate at 25% capacity for the purposes of allowing those providing essential services to get to work. 5. Pubs, cafés and restaurants may provide takeaway and delivery services only. 6. Schools, early learning and childcare services will continue to remain open. 7. There should be no organised indoor or outdoor events.	
24th November 2020	Tánaiste stated in Dáil Éireann that a third wave of restrictions may be required in the new year after the Christmas holiday.	

27th November 2020	The Government agreed the approach for easing restrictions, including a phased move to Level 3 restrictions nationally from midnight on Tuesday 1 December, with a number of exceptions in place for the Christmas period from 18 December.	
1st December 2020	1. Non-essential retail, hairdressers, gyms, leisure centres, museums, galleries, libraries, cinemas and places of worship will reopen. 2. Households should not mix with any other households outside those within their bubble. 3. People should stay within their county apart from work, education and other essential purposes. 4. Face coverings will be recommended to be worn in crowded workplaces, places of worship and in busy or crowded outdoor spaces where there is significant congregation.	
4th December 2020	1. Restaurants, gastropubs and hotel restaurants may reopen for indoor dining with additional restrictions. 2. Pubs not serving food will remain closed except for takeaway and delivery.	
18th December 2020	1. Households can mix with up to two other households until 6 January 2021. 2. Travel outside your county to be permitted until 6 January 2021.	Timepoint 2 or 6-month physical functioning assessments for Project 1 were completed by the 18th of December 2020.
22nd December 2020	The Government agreed to move the entire country to Level 5 lockdown restrictions with a number of adjustments from Christmas Eve until 12 January 2021 at the earliest.	

23rd December 2020	The Chair of the NPHET Coronavirus Expert Advisory Group announced that the new variant of COVID-19 in the United Kingdom was now present in the Republic of Ireland, based on a selection of samples analysed from the weekend	
29th December 2020	A 79-year-old woman became the first person in the Republic of Ireland to receive the Pfizer/BioNTech COVID-19 vaccine at St. James's Hospital, Dublin after the first shipment of 10,000 Pfizer/BioNTech COVID-19 vaccines arrived in the Republic of Ireland on the 26th of December.	
30th December 2020	The government announced the extension of level 5 restrictions to 31st January 2021 at the earliest, schools were to remain closed until the 11th of January at the earliest.	
31st December 2020	The Health Service Executive (HSE) announced that close contacts of confirmed cases of COVID-19 are no longer being advised to get tested due to current widespread levels of infection.	
1st January 2021	A further 1,754 cases and 11 deaths were reported, bringing the totals to 93,532 cases and 2,248 deaths.	Telephone interviews with a subset of participants for Project 2 took place in January & February 2021.
6th January 2021	The Government of Ireland agreed a number of new lockdown measures including the closure of all schools until February with Leaving Certificate students allowed to attend school for three days a week, the closure of all non-essential construction sites with certain exceptions at 6pm on 8 January, the requirement from 9 January for all passengers from the UK and South Africa to have a negative PCR test that they acquired within 72 hours of travelling and the prohibition of click-and-collect services for non-essential retail.	

8th January 2021	In a statement from NPHET, Chief Medical Officer confirmed that three cases of the South African variant of COVID-19 had been detected in the Republic of Ireland.	
11th January 2021	Figures revealed by the Our World in Data organisation showed that Ireland had the highest daily number of new confirmed COVID-19 cases in the world for every million people.	
11th January 2021	Gardaí received new COVID-19 enforcement powers, including the power to fine people €100 in breach in the 5 km travel limit.	
18th January 2021	The number of patients with COVID-19 being treated in hospitals around the country reached a record 2,023, with 200 in ICUs and over 400 people receiving high-grade ventilation and respiratory support	
22nd January 2021	Chief Clinical Officer of the Health Service Executive (HSE) stated that COVID-19 transmission levels remained too high for schools to reopen in February. Meanwhile the vaccine roll out continued.	
30th January 2021	Chief Medical Officer announced that more cases had been confirmed in one month than throughout 2020 with over 1,000 deaths and more than 100,000 cases confirmed in January.	
1st February 2021	Throughout February numbers of confirmed COVID-19 cases remained steady while level 5 restrictions were still in place. The vaccine rollout continued for the month of February	
11th February 2021	Taoiseach stated that the majority of the current Level 5 lockdown restrictions were set to be extended until the Easter period, with only schools and the construction sector likely to be allowed to reopen before Easter. The CEO of the HSE suggested that healthcare workers who refused to take the COVID-19 vaccine may be removed from their frontline duties.	

15th February 2021	Minister for Health Stephen Donnelly confirmed locations for 37 vaccination centres across all counties as part of the country's COVID-19 vaccination programme.	
19th February 2021	Deputy Chief Medical Officer confirmed that three cases of the Brazilian variant of COVID-19 had been detected in the Republic of Ireland all associated with travel from Brazil.	
23rd February 2021	Taoiseach announced the extension of Level 5 lockdown restrictions until 5 April (Easter Monday) at the earliest as the Government of Ireland published its new revised Living with COVID-19 plan called "The Path Ahead", which includes the phased reopening of schools and childcare and the extension of the COVID-19 Pandemic Unemployment Payment and the Employment Wage Subsidy Scheme.	
26th February 2021	Latest figures showed that as of 25 February, Gardaí had issued over 9,800 fines to people breaching COVID-19 regulations, with over 7,566 fines issued for non-essential travel and 1,386 fines issued for attending or hosting house parties.	
28th February 2021	Ireland officially marked one year since the first case of COVID-19 in the country was confirmed on 29 February 2020.	
6th March 2021	Taoiseach announced that Ireland had reached the milestone of half a million COVID-19 vaccines administered	T3 or 12-month physical functioning assessments for Project 1 commenced in March 2021 and were completed in June 2021.
26th March 2021	Ireland's mandatory hotel quarantine system for all passengers arriving into the country from high-risk countries came into force at 4 am	

8th April 2021	The CEO of the Health Service Executive (HSE) announced that Ireland had reached the milestone of one million COVID-19 vaccines administered.	
12th April 2021	The phased easing of Level 5 restrictions began with the 5 km travel limit lifted, the resumption of all residential construction work, two households could meet up outdoors and the full reopening of all schools.	
19th April 2021	The Director of the National Virus Reference Laboratory confirmed that three cases of the B.1.617 variant of COVID-19, first identified in India, had been detected in the Republic of Ireland.	
26th April 2021	The further easing of Level 5 restrictions came into effect with all sports pitches, golf courses, tennis courts, zoos, pet farms and heritage sites reopening. Minister for Health announced that Ireland was to donate 700 oxygen concentrators to India as part of efforts to assist with the COVID-19 outbreak in the country.	
29th April 2021	The Government of Ireland announced a reopening plan for the country throughout May and June.	
10th May 2021	Inter-county travel allowed, the reopening of all hairdressers, libraries, museums and galleries, up to 50 people allowed to attend religious services, the resumption of click-and-collect services and the allowances of three households to meet outdoors (including in private gardens) and a vaccinated household to meet an unvaccinated household indoors.	

14th May 2021	The Health Service Executive (HSE) shut down all of its IT systems after a major ransomware attack, with Ireland's GP and Close Contact referral system and the COVID-19 vaccine registration portal down, while the COVID-19 vaccination programme had not been affected by the attack. The Department of Health announced that there would be no daily COVID-19 figures update provided due to the Health Service Executive cyberattack, with backdated figures being published "when possible". The Chief Executive of the Health Service Executive (HSE) Paul Reid stated that the cost of the cyber-attack on its IT systems could exceed €100 million.	
17th May 2021	All retail could re-open.	
2nd June 2021	Hotels, B&Bs, self-catering and hostels could reopen but services must be restricted to overnight guests and residents	
7th June 2021	1. The numbers permitted at organised outdoor events could increase to a maximum of 100 for the majority of venues, with a maximum of 200 for outdoor venues with a minimum accredited capacity of 5,000 2. Reopening of all cinemas, theatres, gyms, swimming pools and leisure centres 3. Outdoor services in restaurants and bars could recommence, with groups limited to a maximum of 6 people 4. Resumption of outdoor sports matches	
1st June 2021	According to a new study published by the Irish Medical Journal, medics reported what they believed to be the first case of COVID-19 reinfection in Ireland in a 40-year-old female healthcare worker.	

1st June 2021	The Government of Ireland launched a €3.5 billion Economic Recovery Plan to achieve rapid job creation and economic growth after the pandemic, with the COVID-19 Pandemic Unemployment Payment and the Employment Wage Subsidy Scheme extended until September 2021, when gradual reductions would begin.	
21st June 2021	Chief Medical Officer stated that the latest data showed a "concerning increase in transmission" of the Delta variant of COVID-19 in Ireland.	
29th June 2021	Due to the rapidly increasing incidence of the Delta variant, the Government of Ireland announced that the planned reopening of indoor dining and drinking in restaurants and pubs on 5 July would be delayed until at least 19 July when a system to verify vaccination or immunity would be implemented, while 50 guests would be permitted to attend wedding celebrations as an exception from July.	T3 or 12-month physical functioning (and over all data collection) for Project 1 was completed by the end of June 2021.
1st July 2021	Chief Medical Officer announced that a fourth wave of COVID-19 was beginning in Ireland following an increase in cases caused by the Delta variant.	Data analysis of the physical functioning assessments of Project 1 commenced in July 2021.
3rd July 2021	Over 3,500 people attended a pilot music festival featuring Gavin James, Denise Chaila and Sharon Shannon in Dublin, with antigen testing used for entry.	
5th July 2021	In a statement, Chief Medical Officer stated that more than 70% of all cases were now accounted for by the Delta variant, as it continued to present a risk to those who were unvaccinated or waiting for a second dose of vaccine.	
5th July 2021	Over 500 pharmacies around the country began administering the Janssen COVID-19 vaccine to people aged 18 to 34 who opted-in to receive it.	

12th July 2021	Fully vaccinated people began receiving their EU Digital COVID-19 Certificates via email or post. The Government of Ireland approved legislation for the resumption of indoor hospitality, with proofs of vaccination needed for those who were vaccinated or recovered from COVID-19, while those under 18 would be required to be accompanied by a fully vaccinated person.	
19th July 2021	Ireland joined the rest of the EU in implementing the Digital COVID-19 Certificate as travel restrictions into and out of the country eased	
26th July 2021	Indoor dining in pubs and restaurants resumed for the first time since December 2020 for fully vaccinated and COVID-19 recovered people. Under the guidelines, the EU Digital COVID Certificate (DCC) would be the primary evidence for proof of immunity, all customers would have to show photo ID and contact tracing details for all customers would have to be taken, with an online QR code scanner developed to verify people's DCCs.	
31st July 2021	Taoiseach announced that Ireland had more adults fully vaccinated than the UK, with 72.4% of adults in Ireland fully vaccinated compared to 72.1% in the UK.	
6th August 2021	Following a meeting of the Cabinet COVID-19 sub-committee, it was announced that the Government would publish a roadmap by the end of August for the easing or ending of remaining COVID-19 restrictions.	
12th August 2021	The Chief Executive of the HSE said the vaccination programme was in "the final leg" after more than 50,000 people aged 12 to 15 registered to receive the COVID-19 vaccine, with 90% of adults partially vaccinated and 80% fully vaccinated.	

31st August 2021	The Government of Ireland announced a further reopening plan for the country, with all remaining COVID-19 restrictions to be eased by 22 October, including the two-metre social distancing rule depending on the requirement of individual sectors, while masks would still be required in the health and retail sectors and on public transport.	Data analysis for Project 1 was complete in by the end of August 2021.
1st September 2021	Taoiseach announced that the NPHET would cease to exist as a separate body over time and that their role and the vaccine taskforce would be transitioned into the normal functions of the Department of Health and the HSE.	Write-up of paper detailing findings of Project 1 was commenced in September 2021.
3rd September 2021	According to the European Centre for Disease Control, Ireland had the highest incidence of COVID-19 in the EU, which put the country firmly in the red zone as hospitalisations rise.	
6th September 2021	Organised indoor and outdoor events and mass gatherings returned and live music and dancing were permitted at weddings, as the further easing of COVID-19 restrictions took place.	
8th September 2021	Minister for Health Stephen Donnelly announced an update to Ireland's COVID-19 vaccination programme, with residents aged 65 years and older living in long term residential care facilities and people aged 80 years and older living in the community to receive a booster dose of an mRNA COVID-19 vaccine.	
19th September 2021	Latest figures showed that over 90% of Irish people over the age of 16 were now fully vaccinated against COVID-19, the highest rate in the EU	
25th September 2021	Ireland's mandatory hotel quarantine system ended immediately following an announcement by Minister for Health Stephen Donnelly, with all countries removed from the list of "high-risk" countries for international travel.	

22nd October 2021	Easing of restrictions continued with nightclubs allowed to reopen, the return of normal trading hours in pubs and restaurants, no attendance limits on weddings and religious ceremonies and 100% capacity allowed at sporting venues, while the continued use of masks, vaccine certificates and social distancing measures would remain in place until at least February 2022.	
1st November 2021	Following new advice from the National Immunisation Advisory Committee, Minister for Health Stephen Donnelly authorised the use of booster vaccines for healthcare staff.	
16th November 2021	The Government announced a series of measures in a bid to curb the spread of COVID-19, with a closing time for bars, restaurants and nightclubs to be midnight, household contacts of a person with COVID-19 to restrict movements for five days and take three antigen tests, people required to work from home where possible and vaccination certificates required for cinemas and theatres.	
26th November 2021	Minister for Health Stephen Donnelly announced that COVID-19 booster vaccines would be offered to everyone aged 16 and over, starting with pregnant women aged over 16, those aged 40 to 49 and those aged 16 to 39, following new recommendations from NIAC.	
29th November 2021	Minister for Health Stephen Donnelly said it was likely that the new Omicron variant was in Ireland after the Department of Health confirmed that 11 suspected cases of the new variant were sent for whole genome sequencing.	

30th November 2021	The Government announced additional measures in a bid to curb the spread of COVID-19, with parents of children aged 12 and under urged to reduce socialisation indoors, a negative test required for people arriving into Ireland from Friday 3 December, the re-establishment of mandatory hotel quarantine, the wearing of face coverings for children aged 9 years and over on public transport, in retail and for children in third class and above.	
3rd December 2021	The Government reintroduced a series of measures that would commence from 7 December to 9 January amid concerns of the Omicron variant, with nightclubs to close, bars and restaurants to revert to six adults per table and no multiple table bookings allowed, indoor cultural and sporting events to operate at 50% capacity, a maximum of four households allowed to meet indoors, the Pandemic Unemployment Payment to be reinstated and the requirement of vaccination certificates extended to gyms, leisure centres and hotel bars.	
17th December 2021	With an increase in the number of Omicron variant cases and to curb the spread of COVID-19 over the Christmas period, the Government announced an 8pm closing time for bars, restaurants, live events, cinemas and theatres that would commence from 20 December to 30 January.	
23rd December 2021	Minister for Health Stephen Donnelly announced that booster vaccines would be offered to everyone aged 30 and over from 29 December and to all remaining age groups from 10 January.	
6th January 2021	People who received a third or booster vaccine dose began receiving an updated Digital COVID Certificate.	
11th January 2021	Chief Medical Officer estimated that up to 500,000 people (10% of Irish population) contracted COVID-19 in the previous week.	

19th January 2021	The Government agreed a plan to give frontline healthcare workers a once-off €1,000 tax free payment for their work during the pandemic and also agreed on an extra public holiday on 18 March in remembrance of people who died due to COVID-19.	
22nd January 2021	Taoiseach announced the easing of almost all COVID-19 restrictions from 6am on 22 January, with the requirements of vaccine certificates and social distancing to end, restrictions on household visits and capacity limits for indoor and outdoor events to end, nightclubs to reopen and pubs and restaurants to resume normal trading times, while rules on isolation and the wearing of masks would remain.	
28th January 2022	The Department of Health confirmed that daily COVID-19 figures would no longer be released at weekends.	Write-up of paper detailing findings of Project 1 was complete mid-January 2022 and submitted to the journal Respiratory Research on the 20th of January 2022.
22nd February 2022	The Government agreed to end almost all remaining COVID-19 restrictions from 28 February, with mask wearing in schools, indoor retail settings and on public transport to be voluntary, restrictions in schools to end and testing to be scaled back.	Data analysis of interview transcripts for Project 2 commenced at the beginning of February 2022.
21st March 2022	Ireland entered a new wave of the Omicron variant, as latest figures showed that 63,954 people had tested positive for COVID-19 since St Patrick's Day, while hospitalisations were at its highest level in nearly a year at 1,308.	Data analysis of interview transcripts for Project 2 was completed by the end of March 2022.
8th April 2022	Minister for Health Stephen Donnelly announced the establishment of a new COVID-19 advisory group, replacing the National Public Health Emergency Team.	The paper detailing findings from project 1 was accepted by the journal Respiratory Research on 7th April 2022.

26th April 2022	The number of people who died with COVID-19 in Ireland surpassed 7,000, while hospitalisations reached their lowest level since December.	Write up of methods and results of Project 2 was carried out in April 2022.
29th April 2022	The Department of Health announced that updates on the number of new COVID-19 cases in Ireland would no longer be published daily.	The paper detailing the findings was Project 2 was published online on the 4th of May 2022.
12th June 2022	COVID-19 hospitalisations continued to increase with warnings from Ireland's leading medical professionals that a summer wave was likely to be on the way.	Write up of the thesis detailing Projects 1 and 2 commenced in May 2022.
27th July 2022	A recommendation from Interim Chief Medical Officer Professor Breda Smyth that all Health Service Executive COVID-19 testing facilities be stood down from the autumn and to end free COVID-19 tests was accepted by Government.	

Appendix 4 – Letter of Ethics Approval

SJH/TUH Research Ethics Committee Secretariat
email: researchethics@tuh.ie

JREC Reference: 2020-11 List 43 – Amendment (24)

Dr Grainne Sheill,
St James's Hospital,
James' Street,
Dublin 8

30th November 2020

REF: Profiling of Physical Recovery of Patients Admitted to an Acute Hospital with COVID-19 (REPATH)

REC: 2020-11 List 43 – Amendment (24)
(Please quote reference on all correspondence)

Date of Valid Submission to REC: 29.09.2020
Date of Ethical Review: 06.11.2020

Dear Dr Sheill,

The Chairman, Prof. Richard Deane, on behalf of the Research Ethics Committee, has reviewed the amendment you submitted to the SJH/TUH JREC for the above named study and has given **FULL APPROVAL** for this amendment.

The following documents were reviewed:

- 22_09_20 Amendment COVID REPATH Cover Letter.docx
- 220920 Appendix 2 REPATH_Consent_Form_Version 2.docx
- 220920 Appendix 3 REPATH_PIL_Form_Version 2.docx
- 220920 Appendix 5 REPATH_Qual Interview_PIL_Form_Version 1.docx
- 220920 Appendix 6 REPATH Consent Form Pt Interview Study_Version1.docx
- 220920 Appendix 7 REPATH Interview Guide.docx
- TUH-SJH_REC_Standard_Application_V5-6_GDPRUpdate-Sept 2020- REPATH.doc

Please note that ethical approval for this study is only active under the following conditions:

1. *Applicants must submit an annual report for ongoing projects.*
2. *Applicants must submit an end of study declaration/end of study report upon completion of the study.*
3. *All adverse events must be reported to the JREC.*
4. *All changes (minor and substantial) to documentation/study must be submitted to the JREC using the amendment request form and the changes must be tracked/highlighted clearly. Approval from the JREC is required before implementation of the changes.*

It is the responsibility of the researcher/research team to ensure all aspects of the study are executed in compliance with the General Data Protection regulation (GDPR), Health Research Regulations and the Data Protection Act 2018.

Yours sincerely,

Sadhbh O'Neill

REC Officer – Dr Sadhbh O'Neill
SJH/TUH Research Ethics Committee

The SJH/TUH Joint Research and Ethics Committee operates in compliance with and is constituted in accordance with the European Communities (Clinical Trials on Medicinal Products for Human Use) Regulations 2004 & ICH GCP guidelines.

Appendix 5 – Patient Information Leaflet Project 1

PARTICIPANT INFORMATION LEAFLET

'Profiling the Recovery of Patients Admitted to an Acute Hospital with COVID-19'

Principal Investigator:	Dr Ignacio Martin Loeches	Consultant Anaesthetist
Co-investigators:	Joanne Dowds	Clinical Specialist Physiotherapist
	Dr Grainne Sheill	Postdoctoral Researcher
	Dr Ciaran Bannan	Consultant in Infectious Disease
	Kate O Brien	Chartered Physiotherapist

You are being invited to take part in a research study. Before you decide whether or not you wish to take part, you should carefully read the information provided below. Please take your time to make your decision. You may wish to discuss this with your family, friends, or healthcare team. If you have any questions, you can ask a member of the research team. You should clearly understand the risks and benefits of participating in this study so that you can make a decision that is right for you. This process is known as Informed Consent.

PART 1 – THE STUDY

Why is this study being done?

Treatment for COVID-19 often has long lasting effects. We are aiming to examine the long term effects of a diagnosis of COVID -19 on a person's physical function and overall quality of life.

Why am I being asked to take part?

You are being asked to participate in this study as you attended St James's Hospital due to a diagnosis of COVID-19.

Do I have to take part? What happens if I say no? Can I withdraw?

No, participation is voluntary. It is up to you whether or not you take part.

If you decide not to take part it won't affect your current or future medical care. You can change your mind about taking part in the study and opt out at any time even if the study has started. If you decide to opt out, it won't affect your current or future medical care. You don't have to give a reason for not taking part or for opting out. If you withdraw from the study after agreeing to take part, data collected up to the point of withdrawal will be retained and will continue to be processed.

If you wish to opt out, please contact Dr Gráinne Sheill (email: sheillg@tcd.ie, telephone: +353 01-4162503), who will be able to organise this for you.

How will the study be carried out?

This study will begin in June 2020 and will continue for 18 months. A total of 80 participants will be recruited. The study will take place at St James's Hospital, Dublin. This study is a **cohort study**, a quality form of research where participants who share a characteristic (i.e. patients with a certain medical condition) complete measures to assess their health.

What will happen to me if I agree to take part?

If you decide to join the study you will attend St James's Hospital, Dublin for an initial assessment. The assessment components are detailed below.

Physical Performance

- You will perform a walking test where the research team measure your oxygen levels. The physiotherapist will also use your information to complete a measure of frailty.
- We will assess any **fatigue** you may experience with a questionnaire.

Quality of Life

- **Quality of Life** with a questionnaire

Healthcare Needs

- You will be given a form and be asked to identify any healthcare needs you have.

As part of this assessment, we will also collect information about your medical history. Information from your hospital stay (eg. length of stay, rehabilitation received in hospital, level of care required) will be collected by the research team and used when examining your physical recovery after hospital discharge. The total time needed to

complete this assessment is 30 minutes. The research team may invite you to attend a repeat assessment after 6 and 12 months in St James's Hospital where the measures listed above will be repeated.

Are there any benefits to me or others if I take part in the study?

If you take part in the study and share your medical information, you may help scientists and doctors understand the long term physical effects of COVID-19. This may improve treatment for patients diagnosed with COVID-19.

Are there any risks to me or others if I take part in the study?

We do not anticipate adverse effects during the assessments. You may feel a little tired after the walking test, but this should pass quickly. You will only be invited to join the study if your doctors feel that you are well enough to complete the assessments.

What will happen if something goes wrong when I'm taking part in the study?

Your safety while taking part in the study is most important. All study assessments will be carried out by Professionals with expertise in this area. The clinical areas where the research assessments will take place have trained medical professionals on site and are covered by the hospital emergency team. In the event of you becoming unwell during the assessment you will be evaluated and referred for appropriate treatment. If you experience any adverse effects as a result of the study assessments it is important that you inform a member of the research team immediately.

Will I be told the outcome of the study? Will I be told the results of any tests or investigations performed as part of this study that relate to me?

When the results of the study are known, we will be able to provide you with an individual summary of your personal results on request. Results will be shared with healthcare professionals at an education seminar hosted by the research team. Overall findings will also be presented at relevant conferences and published in a relevant peer-reviewed journal.

PART 2 – DATA PROTECTION

What information about me (personal data) will be used as part of this study? Will my medical records be accessed?

The following **clinical data** will be recorded at your first assessment.

- **Age**
- **Gender**
- **Height and weight**
- **Information related to your COVID-19 diagnosis**
- **Past Medical History**
- **Medications**
- **Smoking status**

Access to your healthcare records at St James's Hospital will be required to gather this information. In addition, your healthcare records will be accessed to record information on your length of stay in hospital and the care you received in hospital (including physiotherapy).

Study data also includes information collected during your assessments; physical performance measures, fatigue and quality of life.

What will happen my personal data?

If you consent to take part in this study, your personal details and your responses to the questionnaire will remain strictly confidential at all times. Personal data will be processed **only as is necessary** to achieve the objectives of the health research.

You will be allocated a study number, which will be used as a code to identify you on all documentation. Your name and contact details will not be passed to anyone other than members of the research team. Your information will be kept filed securely for up to 10 years and then it will be destroyed. Your data will not be transferred outside the EU.

Who will access and use my personal data as part of this study?

Members of the research team will access and use your personal data as part of the study. Research team members will only be granted access to your data when they have completed training in data protection.

Will my personal data be kept confidential? How will my data be kept safe?

Your personal data will be kept confidential. We will keep it in a secured file. Your study data will be identified with a code number which will not include your name or other information that directly identifies you. Your data will not be identifiable in any future presentations/publications on the study. To protect the security of data collected for this study

a Data Protection Impact Statement has been completed. A Data Management Plan is also in place and will be reviewed on a monthly basis throughout the study.

What is the lawful basis to use my personal data?

The legal basis for processing of your personal data is under Article 6(1)(e) of GDPR, this is research in the public interest. The legal basis for processing sensitive personal data is under Article 9(2)(j), this is processing data for scientific purposes.

What are my rights?

You have the following rights regarding your **data**.

- Right to access data held
- Right to restrict the use of the data held
- Right to correct inaccuracies
- Right to have information deleted
- Right to data portability

PART 3 – COSTS, FUNDING & APPROVAL

Will it cost me anything if I agree to take part?

You will not be charged for participation in this study.

Who is funding this study?

There is no funding for this research.

Has this study been approved by a research ethics committee?

Ethical approval has been sought from the Tallaght University Hospital/ St James's Hospital Research Ethics Committee (researchethics@tuh.ie).

PART 4 – FUTURE RESEARCH

Will my personal data and/or biological material be used in future studies?

When consenting to this study you will only give permission for your data to be used for this current study. In the final section of the consent form you will be asked if you are happy for your data to be used in possible future studies to help answer future research questions.

PART 5 – FURTHER INFORMATION

Where can I get further information?

Principal Investigators:		
Dr Martin Loches		Email: IMARTINL@tcd.ie
Dr Grainne Sheill	+353 01-4162503	Email: sheillg@tcd.ie
Data Controller: St James's Hospital Dublin		
Data Processors:	St James's Hospital Dublin	Phone: +353 01-4162503
	RE-PATH Research Team Members	Email: sheillg@tcd.ie
Data Protection Officer, Trinity College Dublin		Email: dataprotection@stjames.ie
Mr Cathal Kinsella		

If you have any questions or would like more information about the study please contact ***a member of the research team*** *(Dr Grainne Sheill)*, Monday – Friday from 8.00 am to 5.00pm (telephone: 01-4162503, email: sheillg@tcd.ie).

What happens if I wish to make a complaint?

Complaints regarding this study should be directed to the Principal Investigator Dr Martin Loches (contact details above). Complaints regarding data protection should be directed to the Data Protection Officer (email address above).

Will I be contacted again?

The research team may wish to contact you in the future. In particular they may wish to contact you with regards participation in future studies. In the consent form you will be explicitly asked to consent to receiving information about future research studies.

Informed Consent Form

'Profiling the Recovery of Patients Admitted to an Acute Hospital with COVID-19' The REPATH Study

To be completed by the **PARTICIPANT**:

I have read and understood the information leaflet.	YES ☐	NO ☐
I have had the opportunity to discuss the study, ask questions about the study and I have received satisfactory answers to all my questions.	YES ☐	NO ☐
I have received enough information about this study.	YES ☐	NO ☐
I understand that I am free to withdraw from the study at any time without giving a reason and this will not affect my future medical care.	YES ☐	NO ☐
I agree to allow the researchers use my information (personal data) as part of this study as outlined in the information leaflet.	YES ☐	NO ☐
I agree to allow the researchers access my medical records, including medical information from my hospital stay, as part of this study.	YES ☐	NO ☐
I agree to be contacted by researchers as part of this study to participate in further study assessments	YES ☐	NO ☐
I agree to take part in the study	YES ☐	NO ☐
I understand and agree to allow my data to be used for future research. Before any future research is carried out the ethics committee must agree with the research.	YES ☐	NO ☐
I am happy to be contacted in the future about future research projects by the research team.	YES ☐	NO ☐

Participant's Name (Block Capitals):	
Participant's Signature:	
Date:	

Appendix 7 - 6-Minute Walk Test Recording Sheet

Post-COVID-19 6 Minute Walk Test Recording Sheet

Patient name:

MRN:

Time	SpO2	HR	BORG
Min 0			
Min 1			
Min 2			
Min 3			
Min 4			
Min 5			
Min 6			
Rest 1			
Rest 2			
Rest 3			

Appendix 8 – 6-Minute Walk Test Instructions

Appendix 9 – Modified Borg Breathlessness Scale

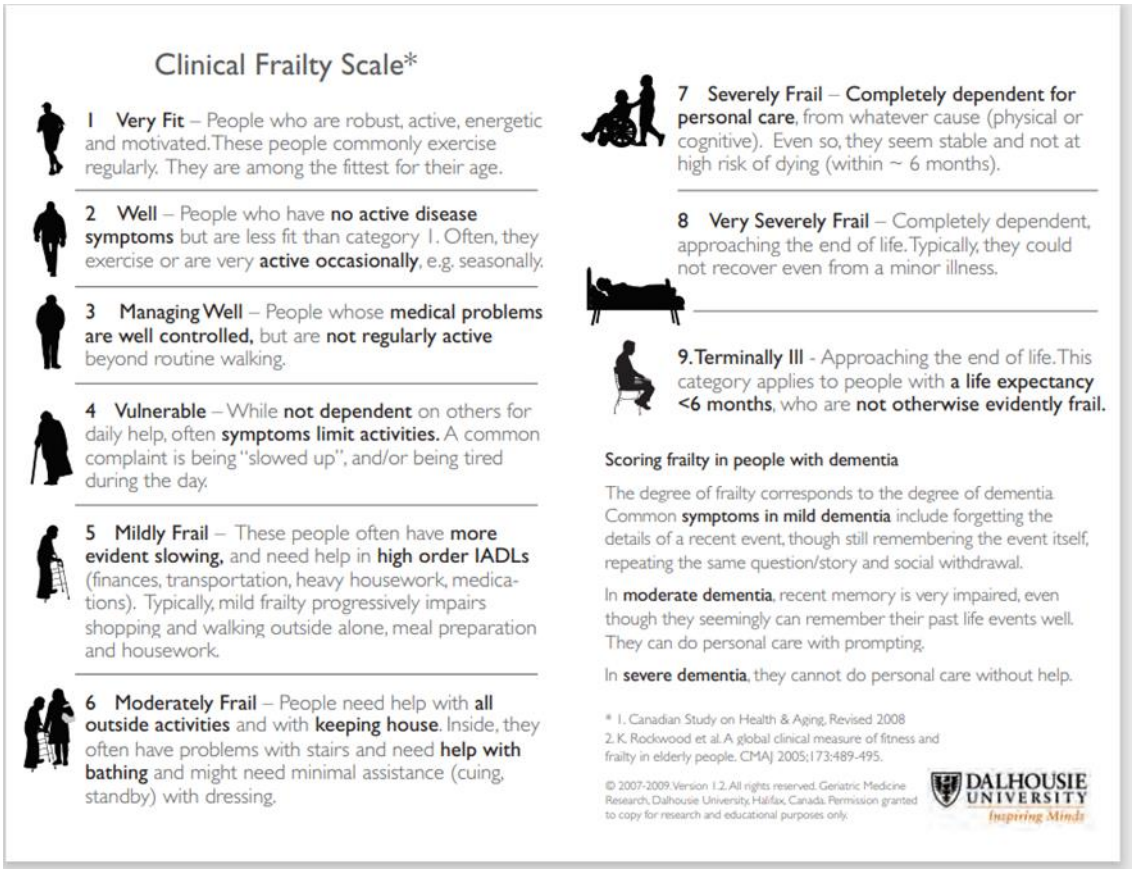
A **Modified Borg scale – Burdon et al[22]**

0	Nothing at all
0.5	Very, very slight (just noticeable)
1	Very slight
2	Slight
3	Moderate
4	Somewhat severe
5	Severe
6	
7	Very severe
8	
9	Very, very severe (almost maximal)
10	Maximal

B **Modified Borg scale – Kendrick et al[23]**

0	No breathlessness at all
0.5	Very, very slight (just noticeable)
1	Very slight
2	Slight breathlessness
3	Moderate
4	Somewhat severe
5	Severe breathlessness
6	
7	Very severe breathlessness
8	
9	Very, very severe (almost maximal)
10	Maximal

Appendix 10 – Clinical Frailty Scale



Clinical Frailty Scale*

1 **Very Fit** – People who are robust, active, energetic and motivated. These people commonly exercise regularly. They are among the fittest for their age.

2 **Well** – People who have **no active disease symptoms** but are less fit than category 1. Often, they exercise or are very **active occasionally**, e.g. seasonally.

3 **Managing Well** – People whose **medical problems are well controlled,** but are **not regularly active** beyond routine walking.

4 **Vulnerable** – While **not dependent** on others for daily help, often **symptoms limit activities.** A common complaint is being "slowed up", and/or being tired during the day.

5 **Mildly Frail** – These people often have **more evident slowing,** and need help in **high order IADLs** (finances, transportation, heavy housework, medications). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation and housework.

6 **Moderately Frail** – People need help with **all outside activities** and with **keeping house**. Inside, they often have problems with stairs and need **help with bathing** and might need minimal assistance (cuing, standby) with dressing.

7 **Severely Frail** – **Completely dependent for personal care**, from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~ 6 months).

8 **Very Severely Frail** – Completely dependent, approaching the end of life. Typically, they could not recover even from a minor illness.

9. **Terminally Ill** - Approaching the end of life. This category applies to people with **a life expectancy <6 months**, who are **not otherwise evidently frail.**

Scoring frailty in people with dementia

The degree of frailty corresponds to the degree of dementia. Common **symptoms in mild dementia** include forgetting the details of a recent event, though still remembering the event itself, repeating the same question/story and social withdrawal.

In **moderate dementia**, recent memory is very impaired, even though they seemingly can remember their past life events well. They can do personal care with prompting.

In **severe dementia**, they cannot do personal care without help.

* 1. Canadian Study on Health & Aging, Revised 2008
2. K. Rockwood et al. A global clinical measure of fitness and frailty in elderly people. CMAJ 2005;173:489-495.

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Appendix 11 – Chalder Fatigue Scale

chalderfatiguescale

name: _____ date: _____

We would like to know more about any problems you have had with feeling tired, weak or lacking in energy in the last month. Please answer ALL the questions by ticking the answer which applies to you most closely. If you have been feeling tired for a long while, then compare yourself to how you felt when you were last well. Please tick only one box per line.

	less than usual	***no more than usual***	***more than usual***	***much more than usual***
do you have problems with tiredness?				
do you need to rest more?				
do you feel sleepy or drowsy?				
do you have problems starting things?				
do you lack energy?				
do you have less strength in your muscles?				
do you feel weak?				
do you have difficulties concentrating?				
do you make slips of the tongue when speaking?				
do you find it more difficult to find the right word?				
	better than usual	***no worse than usual***	***worse than usual***	***much worse than usual***
how is your memory?				

This scale can be scored "bimodally" with columns representing 0, 0, 1 & 1 and a range from 0 to 11 with a total of 4 or more qualifying for "caseness". Alternatively it can be scored in "Likert" style 0, 1, 2 & 3 with a range from 0 to 33. Mean "bimodal" score for CFS sufferers was 9.14 (SD 2.73) and for a community sample 3.27 (SD 3.21). Mean "Likert" score was 24.4 (SD 5.8) and 14.2 (SD 4.6).

total (0-33) =

Cella, M. and T. Chalder (2010). *"Measuring fatigue in clinical and community settings."* J Psychosom Res 69(1): 17-22. This study involved 361 CFS sufferers and 1615 individuals from the community. Average age was in the 30's. Fatigue levels were similar for males and females. A score of 29 discriminated between CFS sufferers and the community sample in 96% of cases and a score in the 30's discriminated in 100% of cases. The CFS sufferers also scored a mean of 26.99 on the Work & Social Adjustment Scale (W&SAS) with a SD of 8.6 (i.e. about 70% scoring between 18.4 and 35.6).

Appendix 12 – Short-Form-36-II

SF-36 QUESTIONNAIRE

Name:_____ **Ref. Dr:**_____ **Date:**_____

ID#: _____ **Age:** _____ **Gender: M / F**

Please answer the 36 questions of the **Health Survey** completely, honestly, and without interruptions.

GENERAL HEALTH:
In general, would you say your health is:

○ Excellent ○ Very Good ○ Good ○ Fair ○ Poor

Compared to one year ago, how would you rate your health in general now?

○ Much better now than one year ago
○ Somewhat better now than one year ago
○ About the same
○ Somewhat worse now than one year ago
○ Much worse than one year ago

LIMITATIONS OF ACTIVITIES:
The following items are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports.
○ Yes, Limited a lot ○ Yes, Limited a Little ○ No, Not Limited at all

Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf
○ Yes, Limited a Lot ○ Yes, Limited a Little ○ No, Not Limited at all

Lifting or carrying groceries
○ Yes, Limited a Lot ○ Yes, Limited a Little ○ No, Not Limited at all

Climbing several flights of stairs
○ Yes, Limited a Lot ○ Yes, Limited a Little ○ No, Not Limited at all

Climbing one flight of stairs
○ Yes, Limited a Lot ○ Yes, Limited a Little ○ No, Not Limited at all

Bending, kneeling, or stooping
○ Yes, Limited a Lot ○ Yes, Limited a Little ○ No, Not Limited at all

Walking more than a mile
○ Yes, Limited a Lot ○ Yes, Limited a Little ○ No, Not Limited at all

Walking several blocks
○ Yes, Limited a Lot ○ Yes, Limited a Little ○ No, Not Limited at all

Walking one block
○ Yes, Limited a Lot ○ Yes, Limited a Little ○ No, Not Limited at all

Bathing or dressing yourself

Yes, Limited a Lot | Yes, Limited a Little | No, Not Limited at all

PHYSICAL HEALTH PROBLEMS:

During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

Cut down the amount of time you spent on work or other activities

Yes | No

Accomplished less than you would like

Yes | No

Were limited in the kind of work or other activities

Yes | No

Had difficulty performing the work or other activities (for example, it took extra effort)

Yes | No

EMOTIONAL HEALTH PROBLEMS:

During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

Cut down the amount of time you spent on work or other activities

Yes | No

Accomplished less than you would like

Yes | No

Didn't do work or other activities as carefully as usual

Yes | No

SOCIAL ACTIVITIES:

Emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?

Not at all | Slightly | Moderately | Severe | Very Severe

PAIN:

How much bodily pain have you had during the past 4 weeks?

None | Very Mild | Mild | Moderate | Severe | Very Severe

During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

Not at all | A little bit | Moderately | Quite a bit | Extremely

ENERGY AND EMOTIONS:
These questions are about how you feel and how things have been with you during the last 4 weeks. For each question, please give the answer that comes closest to the way you have been feeling.

Did you feel full of pep?
- All of the time
- Most of the time
- A good Bit of the Time
- Some of the time
- A little bit of the time
- None of the Time

Have you been a very nervous person?
- All of the time
- Most of the time
- A good Bit of the Time
- Some of the time
- A little bit of the time
- None of the Time

Have you felt so down in the dumps that nothing could cheer you up?
- All of the time
- Most of the time
- A good Bit of the Time
- Some of the time
- A little bit of the time
- None of the Time

Have you felt calm and peaceful?
- All of the time
- Most of the time
- A good Bit of the Time
- Some of the time
- A little bit of the time
- None of the Time

Did you have a lot of energy?
- All of the time
- Most of the time
- A good Bit of the Time
- Some of the time
- A little bit of the time
- None of the Time

Have you felt downhearted and blue?

- All of the time
- Most of the time
- A good Bit of the Time
- Some of the time
- A little bit of the time
- None of the Time

Did you feel worn out?

- All of the time
- Most of the time
- A good Bit of the Time
- Some of the time
- A little bit of the time
- None of the Time

Have you been a happy person?

- All of the time
- Most of the time
- A good Bit of the Time
- Some of the time
- A little bit of the time
- None of the Time

Did you feel tired?

- All of the time
- Most of the time
- A good Bit of the Time
- Some of the time
- A little bit of the time
- None of the Time

SOCIAL ACTIVITIES:
During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)?

- All of the time
- Most of the time
- Some of the time
- A little bit of the time
- None of the Time

GENERAL HEALTH:
How true or false is each of the following statements for you?

I seem to get sick a little easier than other people

Definitely true | Mostly true | Don't know | Mostly false | Definitely false

I am as healthy as anybody I know

Definitely true | Mostly true | Don't know | Mostly false | Definitely false

I expect my health to get worse

Definitely true | Mostly true | Don't know | Mostly false | Definitely false

My health is excellent

Definitely true | Mostly true | Don't know | Mostly false | Definitely false

Appendix 13 – Short-Form-36-II Calculator Link

Free online SF-36 score calculator - OrthoToolKit

Appendix 14 - COVID-19 Patient Concerns Assessment

Patient Concerns Assessment

Please also tick **discuss** if any of the following items have been a concern since having COVID19.

Practical concerns	**Discuss**	**Physical concerns**	**Discuss**
Caring responsibilities	☐	Sexual concerns	☐
Housing or finances	☐	Fatigue	☐
Transport or parking	☐	Moving around/walking	☐
Work or education	☐	Personal appearance	☐
Treatment information needs	☐	Passing urine	☐
Difficulty making plans	☐	Bowel habits	☐
Daily household tasks	☐	Nausea and/or vomiting	☐
Family concerns	☐	Changes in weight/appetite	☐
Relationship with children	☐	Sleep problems	☐
Relationship with partner/ spouse	☐	Cough	☐
Emotional/Spiritual concerns		Breathlessness	☐
Worry, fear or anxiety	☐	Unusual swelling	☐
Loneliness or isolation	☐	Pain	☐
Sadness or depression	☐	Hot flushes	☐
Memory or concentration	☐	Dry, itchy or sore skin	☐
Loss of faith or other spiritual concerns	☐	Tingling in hands or feet	☐
		Other medical condition	☐

Appendix 15 – Patient Information Leaflet Project 2

PARTICIPANT INFORMATION LEAFLET

Feedback Interview

'Profiling the Recovery of Patients Admitted to an Acute Hospital with COVID-19'

Principal Investigator:	Dr Ignacio Martin Loeches	Consultant Anaesthetist
Co-investigators:	Joanne Dowds	Clinical Specialist Physiotherapist
	Dr Grainne Sheill	Postdoctoral Researcher
	Dr Ciaran Bannan	Consultant in Infectious Disease
	Kate O Brien	Chartered Physiotherapist

You are being invited to take part in a research study. Before you decide whether or not you wish to take part, you should carefully read the information provided below. Please take your time to make your decision. You may wish to discuss this with your family, friends, or healthcare team. If you have any questions, you can ask a member of the research team. You should clearly understand the risks and benefits of participating in this study so that you can make a decision that is right for you. This process is known as Informed Consent.

PART 1 – THE STUDY

Why is this study being done?

Treatment for COVID-19 often has long lasting effects. We are aiming to examine the long term effects of a diagnosis of COVID -19 on a person's physical function and overall quality of life. To do this, we are keen to talk to you about the effect of COVID-19 on your physical function. This information will be used to improve how we provide care for patients recovering from COVID-19 in future. We will gather this information through a one to one semi-structured interview.

What is a Semi-Structured Interview and what will we discuss?

During the semi-structured interview you will meet with a member of our research team. The researcher will ask you a series of open questions regarding your physical recovery from COVID-19. The researcher may explore your answers to some questions in more detail and may enquire about how COVID-19 has impacted your health and wellbeing.

The researcher will make an **audio-recording** of your interview. You will have access to the transcripts of the interview if you wish and you can request change to be made to your personal comments if you are unhappy with the content. The interview will take in a quiet private room at St James's Hospital. If you wish a family member or friend may accompany you for your interview. The interview will last approximately 15 minutes.

Why am I being asked to take part?

You are being asked to participate in this study as you received medical care from St James's Hospital due to a diagnosis of COVID-19.

Do I have to take part? What happens if I say no? Can I withdraw?

No, participation is voluntary. It is up to you whether or not you take part.

If you decide not to take part it won't affect your current or future medical care. You can change your mind about taking part in the study and opt out at any time even if the study has started. If you decide to opt out, it won't affect your current or future medical care. You don't have to give a reason for not taking part or for opting out. If you withdraw from the study after agreeing to take part, data collected up to the point of withdrawal will be retained and will continue to be processed.

If you wish to opt out, please contact Dr Gráinne Sheill (email: sheillg@tcd.ie, telephone: +353 01-4162503), who will be able to organise this for you.

Are there any benefits to me or others if I take part in the study?

If you take part in the study and share your medical information, you may help scientists and doctors understand the long term physical effects of COVID-19. This may improve treatment for patients diagnosed with COVID-19.

Are there any risks to me or others if I take part in the study?

We do not anticipate adverse effects during the assessments.

PART 2 – DATA PROTECTION

What information about me (personal data) will be used as part of this study? Will my medical records be accessed?

For this study we will use the audio recording and transcript of your interview.

What will happen my personal data?

If you decide to take part in this study, you give the researcher permission to collect an audio of your discussion during your individual interview. Your data will be identified with a code number which will not include your name or other information that directly identifies you. Your personal details will be kept confidential. All data will be filed and stored securely. At any time, you may ask to see your personal information. Your data will be processed **only as is necessary** to achieve the objectives of this research. Your information will be kept filed securely for up to 10 years, after which it will be destroyed. The results of the study may be used in presentations or published in scientific reports. You will not be identified in any presentation or publication.

Who will access and use my personal data as part of this study?

Authorised members of the research team will have access to and use your personal data for analysis as part of this study.

Will my personal data be kept confidential? How will my data be kept safe?

Your personal data will be kept confidential. We will keep it in a secured file. Your study data will be identified with a code number which will not include your name or other information that directly identifies you. Your data will not be identifiable in any future presentations/publications on the study. To protect the security of data collected for this study a Data Protection Impact Statement has been completed. A Data Management Plan is also in place and will be reviewed on a monthly basis throughout the study.

What is the lawful basis to use my personal data?

The lawful basis for processing of your personal data is covered by Article 6(1)(a) and Article 9(2)(j) of GDPR.

Article 6(1)(a) states processing shall be lawful if the data subject has given consent to the processing of his or her personal data for one or more specific purposes.

Article 9(2)j) states that processing is necessary for scientific research purposes in accordance with Article 89(1) based on Union or Member State law which shall be proportionate to the aim pursued, respect the essence of the right to data protection and provide for suitable and specific measures to safeguard the fundamental rights and the interests of the data subject.

What are my rights?

You have the following rights regarding your **data**.

- Right to access data held
- Right to restrict the use of the data held
- Right to correct inaccuracies
- Right to have information deleted
- Right to data portability

PART 3 – COSTS, FUNDING & APPROVAL

Will it cost me anything if I agree to take part?

You will not be charged for participation in this study.

Who is funding this study?

There is no funding for this research.

Has this study been approved by a research ethics committee?

Ethical approval has been sought from the Tallaght University Hospital/ St James's Hospital Research Ethics Committee (researchethics@tuh.ie).

PART 4 – FUTURE RESEARCH

Will my personal data and/or biological material be used in future studies?

When consenting to this study you will only give permission for your data to be used for this current study. In the final section of the consent form you will be asked if you are happy for your data to be used in possible future studies to help answer future research questions.

PART 5 – FURTHER INFORMATION

Where can I get further information?

Principal Investigators:		
Dr Martin Loches		Email: IMARTINL@tcd.ie
Dr Grainne Sheill	+353 01-4162503	Email: sheillg@tcd.ie
Data Controller: St James's Hospital Dublin		
Data Processors: St James's Hospital Dublin		Phone: +353 01-4162503
RE-PATH Research Team Members		Email: sheillg@tcd.ie
Data Protection Officer, Trinity College Dublin		Email: dataprotection@stjames.ie
Mr Cathal Kinsella		

If you have any questions or would like more information about the study please contact ***a member of the research team*** *(Dr Grainne Sheill)*, Monday – Friday from 8.00 am to 5.00pm (telephone: 01-4162503, email: sheillg@tcd.ie).

What happens if I wish to make a complaint?

Complaints regarding this study should be directed to the Principal Investigator Dr Martin Loches (contact details above). Complaints regarding data protection should be directed to the Data Protection Officer (email address above).

Will I be contacted again?

The research team may wish to contact you in the future. In particular they may wish to contact you with regards participation in future studies. In the consent form you will be explicitly asked to consent to receiving information about future research studies.

Appendix 16 – Consent Form Project 2

CONSENT FORM

Feedback Interview

'Profiling the Recovery of Patients Admitted to an Acute Hospital with COVID-19'

To be completed by the **PARTICIPANT**:

I have read and understood the information leaflet.	YES ☐	NO ☐
I have had the opportunity to discuss the study, ask questions about the study and I have received satisfactory answers to all my questions.	YES ☐	NO ☐
I have received enough information about this study.	YES ☐	NO ☐
I understand that I am free to withdraw from the study at any time without giving a reason and this will not affect my future medical care.	YES ☐	NO ☐
I agree to allow the researchers use my information (personal data) as part of this study as outlined in the information leaflet.	YES ☐	NO ☐
I agree to be contacted by researchers as part of this study. I consent to take part in this research study having been fully informed of the risks, benefits and purpose of the study.	YES ☐ YES ☐	NO ☐ NO ☐
I give my explicit consent to have my data processed as part of this research study.	YES ☐	NO ☐
I agree to have the interview recorded so that it can be transcribed by the research team.	YES ☐	NO ☐
I agree to be contacted by the researchers about other research activities in the future.	YES ☐	NO ☐
I give my explicit consent to have my data processed as part of this research study'	YES ☐	NO ☐

Participant's Name (Block Capitals):	
Participant's Signature:	
Date:	

Appendix 17 – Interview Guide for Project 2

Qualitative Interview Guide

'Profiling the Recovery of Patients Admitted to an Acute Hospital with COVID-19'

Aim: To explore patients' perceptions of the impact of COVID19 on their physical function

1. How do you feel COVID19 has affected you physically?
2. Tell me about your physical recovery from COVID19
   Prompts: Activity levels, ability to exercise, ability to do work, ongoing symptoms
3. Are there any activities that you have not returned to or have difficulty completing since having COVID19?
4. What have you found useful in terms of recovery?
   Prompts: Any resources / access to services
5. What further supports, if any, did you feel you required in assisting with your recovery from COVID19?
   Prompts: community supports / advice from healthcare professionals / access to services

   Any further comments

Appendix 18 – Table of Thematic Analysis Project 2 (Code Book)

Theme	Code	Quote	Narrative
Persistent symptoms	Fatigue	*"It's only you know if I kind of over-do it on the walking and things like that, I just get this tiredness, I sit there and I'm yawning and I'm yawning, it's just like a fatigue over me"- 14* *"Ehm, I would have felt tiredness in the mornings, eh a lot. That would have been the main thing. At night, I would, I kind of nod off a bit – which I would never have done before COVID really. Just a kind of a tiredness"- 15* *"Eh, it has caused me fatigue"- 17* *"Ehm.. tiredness, worn out" – 4*	Many patient report general fatigue or tiredness which can prevent them from doing certain activities but more often they do the activities as they feel they are physically able but then will fatigued for some time (up to days) after.
	Breathing difficulties	*"I still have chest pain and shortness of breath" – 11* *"Ehm I feel it has affected my.. eh my lungs- I don't breathe as good as I used to". – 12* *"Sometimes I feel like my chest is full, even though it's not. Sometimes-it's like a heavy feeling on your chest sometimes, ya know? It's not all the time, just sometimes"- 14* *"I would say breathlessness would be the main thing- when I walk" – 15* *"As I said, I know my breathing is affected, I know I*	While some patients touch on shortness of breath or lung pain, many describe an altered breathing pattern / dysfunctional breathing pattern whereby they feel they don't have capacity to take a deep breath / feel restricted / can't get enough air in.

		can't seem to – whenever I feel I want to breathe deeply I can feel a restriction in my chest" – 18 *"The breathing- because that restricts everything else I do" – 18* *"You know say if I, the best way to probably explain to you is if I exhale out completely okay, I find it very difficult to get my breath back again. But I'm kind of struggling like *makes panting noise* - I can't breathe even though you are breathing, like I can't get any oxygen into my body" – 4*	
	Reduced exercise tolerance	*"Like, I've two flights of stairs in the house, if I go up the two flights of stairs, by the time I get to the top of the second flight I'm absolutely breathless" – 4* *"And I'm not as physically fit. Like I don't run anymore. Yeah, I would have ran about 40 km per week. I actually went for a run last month, I ran 5k for the first time, and I felt great after it but the next day I ended up in A&E with ST depression and cardiac changes so.. I'm not doing that again." – 11* *"Yeah, well, I was in the gym, on the treadmill- I haven't got back on the treadmill yet, running wise. I'm still just up to walking pace, that's all now, ya know?" – 12* *"Okay my ability to exercise is zero. I just cannot. My thing*	While many of the patients report experiencing a relatively good recovery, many feel their ability to exercise (at same intensity/level) as pre COVID is reduced, for some it's due to their breathing and for others it is due to fatigue. Some seem reluctant/nervous to push themselves.

		was- I used to do walks, I used to do hill walks. I can walk on a flat but if I start walking on an incline or for any length of time – I just can't. I end up limping because of it" – 13 *"Eh it has affected my ability to exercise, if you try to do too much you're paying back for it if you know what I mean, more than you would have normally- the recovery time seems to be an awful lot longer" – 17* *"Okay I can walk. But don't ask me to run for a bus anymore" – 18* *"Well ability (to exercise) as in I don't have any (laughs). And I'm now – my exercise is very, very minimal" – 5*	
	Brain fog	*"Yes, so I have what I call a foggy brain. Memory re-call – not memory re-call, memory-word association" – 4* *"Do you know I'll tell you one thing – forgetfulness, not being able to pick a word or a name, it's like, even a system I can't even get the word out sometimes of what it's called. And that's definitely a feature of COVID " – 6*	The 'brain fog' suggested by participants seems to affect memory and word-finding difficulties which is in keeping with other studies/literature. People who report it feel certain it is new since COVID.
	Pain / MSK issues	*"Yeah. I still have chest pain and shortness of breath, and back pain" – 11* *"I still have pains in my lungs and in my back, every day I have the pains" – 12* *"Joint pain. The other joints have recovered and come back a lot quicker, this one*	No real pattern to pain. Some experience lung pain following COVID which is very plausible following a severe COVID pneumonitis. Other describe joint pain, difficult to

		(knee) is just- whilst it's improving it's very, very slow progress" – 13 *"Joint pain and everything else that has been associated with it, to me has been the worst part of the COVID" – 13* *"And there is a bit of nerve pain from time to time as well" – 17* *"it's mainly muscle strength, still not one hundred percent" – 3* *"The only thing I was suffering from, I think it was from the proning was ulnar nerve compression but it will get sorted out eventually" – 3* *"My fingers, my shoulder, like I hadn't any of these pains (before)" – 4*	differentiate between arthralgia and myalgia. ? some form of post-viral inflammatory process, don't have blood results to confirm this. ? further research warranted on multi-joint pain following COVID. Others have specific MSK complaints such as ulnar nerve injury from proning or reduced muscle strength.
	Poor sleep	*"Ehm, my sleep pattern is completely gone. Now it's not as bad as it was- it is recovering slowly but there would often be nights where I would just sit downstairs, and I just cannot get to sleep. I find some nights very hard to get to sleep, some nights if I do get to sleep, I'd sleep for about 2 hours but then I could be awake for 3 or 4 hours. I can't get an actual sleep pattern back again" – 13* *"I don't know if that's something people are getting but I'm kind of- almost insomnia sometimes, like sometimes I just can't get to sleep again after I wake up. I*	Participants speak about two things when it comes to sleep, difficulty actually falling asleep and then waking after sleeping for only an hour or two. Patients don't mention nightmares which you could expect as part of PTSD following ICU stay or waking up breathing/snoring which would be associated with OSA which has been reported following COVID.

		might wake up at two o'clock in the morning and I end up just going downstairs and you know turning on the telly" – 6	
	Issues with throat/hoarseness	*"but I have an issue internally with the throat. That really hasn't gone away and I'm worried now coming into the winter that it's going to be sort of worse again, because it was worse during the winter than it was during the summer. So I don't know what the hell is going to happen with that but sure it is what it is" – 17* *"Ehm then I get a chesty – or a tightness in my chest, and then I get the phlegmy cough and then I have a constant kind of clearing of throat or hoarseness. Like I'm chesty in the morning and the evening so" – 5* *"Ehm, well all the symptoms that I had have gone, there's only eh, well there's two, I get this hoarseness now and again that I wasn't getting before it" – 8*	Of the three patients that reported issues with their throat two were not intubated which would out-rule ETT irritation as a cause for this.
Effects of pandemic on recovery	Gyms/pools being closed	*Ehm, well it's just the running because obviously the gyms and everything are closed, I haven't tried anything like that" – 11 "* *"but that's my own fault maybe, I was going swimming – I was doing quite well but gyms are all closed and everything, it's difficult, ya know?" – 3* *"You know? And obviously swimming, we can't do that*	There are very clear statements made during interviews that would suggest the actual pandemic also impacted on recovery which patients recovering from other illness would not have experienced. These include the closure of facilities such as gyms and pools. Participants also feel that due to the

		and I was hoping to do a bit of swimming that I could get that done. And it's hard at the moment because everything is closed, all the pools and everything so that makes things 10 times more difficult" – 4	pandemic, resources for follow-up within the hospital were limited. One participant who was particularly insightful touched on the effects of lockdowns/restriction on mood/motivation and in turn recovery.
	Restrictions affecting hospital follow-up	*"Yeah I thought that maybe I would have gotten a little bit more help from the hospital, I know with the COVID and everything else they can't, obviously with the COVID, they are very restricted in what they can do" – 12* *"I know it could be different every other time, these were emergency circumstances, but it felt like -treat the condition, not the patient" (when speaking about lack of hospital follow-up) – 17* *"I know with all the restrictions at the moment, you know, you're limited and follow-up – I think some people just need a call just to check in with them to see how they are, that's it – that makes half the battle of a day" – 5* *" There is one (ICU support group) in Vincent's, they are trying to set up post-COVID for people in a group setting. It's not easy because of the lockdown and everything, people can't meet up in, you know, maybe the way they would in a normal situation" – 7*	

	Lockdown affecting mood and motivation	*"I think the way the world is at the moment, the way everybody is locked up, its too easy to fall into those sort of mind-sets. And like I've been in it. And that's why I know, you know I have a support network that wouldn't let you dwell in your own (laughs) stuff for too long" – 6* *"I think people, a lot of people will only really start to recover when they can start living normally" – 6* *"If you want to stay locked up in the house, those four walls moving in on you are terrible, it's a tough place to be. The problem with COVID, it gives you the excuse to do that" – 6*	
Adequate follow-up / satisfaction	Post-COVID-19 follow-up clinic	*"Just thanks, all the support I've got (from the post-COVID-19 clinic) - without it I wouldn't be where I am" (voice shaking) – 13* *"Well yourself – the physio is very good. Eh the long COVID clinic in James's – I was only in there twice but I mean it was worthwhile going in" – 17* *"Well I know that I can always contact somebody in St. James's Hospital if I have some symptom or anything that bothers me because I have found that St. James's Hospital has been absolutely amazing in following-up" -2* *"Well I know that I can always contact somebody in St. James's Hospital if I have some symptom or anything that bothers me because I*	Some people felt they got all the support necessary from the hospital and particularly the COVID clinic. They felt that physicians in this clinic knew more about COVID than perhaps their GPs and they could go there for answers.

		have found that St. James's Hospital has been absolutely amazing in following-up" – 6 *"you know taking into account the fact that there was a pandemic going on and the resources were needed elsewhere, I genuinely feel I got a good back-up in James's so yeah" – 6* *"Ehm the COVID clinic in St. James's was very useful. So it might be nothing to you but it's very important to me. They had the answers. So I found that clinic amazing" – 9*	
	Satisfaction with follow-up investigations	*"I suppose there is a lot of research out there now on long COVID, knowing you're not on your own, like it doesn't worry me if I have a chest pain or it doesn't worry me as much as before because it's being investigated, you know that kind of a way?" – 11* *"No, I think I've been tested for everything in the sense, Fibromyalgia, rheumatology- all of these have been ruled out, and everything has been put back –it's all COVID related" – 13*	Some people touched on having persistent symptoms but weren't as worried about them as they had investigations to out-rule serious causes and they could not accept it was just part of recovering from COVID and it would take time.
Inadequate follow-up	Should have gotten more follow-up from hospital	*"If you just had access or even your GP having access (to results of investigations), that sort of thing. For whatever the reason, this time it didn't happen" – 17*	Some participants felt that their follow-up was inadequate, some touched on being 'lost' to follow-up which some put down to the effects of the pandemic on

		"But maybe the COVID, you know I had quite a traumatic experience, you know, four weeks in ICU, I had one outpatient follow-up and that was it. So I think maybe a little bit more follow –up, yeah. Yeah follow-up by the MDT team, yeah yeah. Yeah, yeah I think so, you know COVID is a systemic illness, I had multi-organ failure, I was on dialysis and everything you know, ehm and I had one follow-up. A normal person I think they probably- like I'm a doctor, I know what I'm doing, a normal person I think 4 weeks in ICU with multi-organ failure and getting one follow-up appointment, I think they need a little bit more maybe you know. To help them get back to normal you know. I think it might be better for them to get a bit more follow-up" – 3 *"Nothing. I got no assistance. Well when I was complaining about my bones, the way I was aching and like when I went back originally for the physio, the first time I went back for the physio, I think it was with yourself, I complained of this. And I would have thought that I would have gotten follow-up on that. And I never got any follow-up on that. You know what I mean? I physically had to get money together and pay for my operation, I don't see why I should have had to do all of that. You know?" – 4* *"You know, I had to kind of chase to get appointments*	resources as mentioned above. Some people felt there was a lack of information on recovery while another participant felt they should have been informed if they had immunity following infection – suggesting they were worried about re-infection. One participant touched on how sick he was in ICU, suffering multi-organ failure and that one appointment in clinic was simply not enough.

		so, you know. That part I found wearing" – 5	
	Lack of information	*"know it's not part of your study but the only thing that I would say from my own experience would be- the lack of follow-up information" – 17* *"Ehm, information to be honest. Some follow-up on some of the stuff I had done. Like I said I got some tests done and they were down to yourself. But I got some tests done but I never got any real answers back and neither did my own GP. So access to information would be a good thing" – 17*	
Time	Initial recovery slow	*"At the start it was breathlessness, chest tightness, I can't breathe. And not even 4 steps I can't take even though I was on 4L of oxygen that was given to me in the hospital. Still my sats (oxygen saturations) were around 88-92, it was very stressful that time" – 10* *"Yeah, after the COVID yeah I found it very hard eh to get back into exercise, although I'm now feeling a lot stronger" – 12* *"And it took me a really long time to start coming around a good bit, that I could start feeling even that I could walk a little better and breathe a little better" – 14* *"Now, not if I walk across the road, I walk to Dame Street to Francis Street and earlier on, maybe some months back, up*	Many participants touched on how impaired physically they were initially after their hospital stay.. some then felt they recovered quite quickly, over a few weeks and other felt recovery was slow. There did not seem to be any pattern and it seemed to vary significantly between individuals.

		to some months back I would feel a shortness of breath half-way, now that might have been a 15-20 minute walk" – 15 *"Up until the end of November- up until I did my first flight sometime in December I would say certainly- I felt like I was still suffering from it, almost in every way. When I went down that answer sheet you had a, the last time I was in the hospital there, you had a question sheet- like I ticked all the boxes, but certainly I can't even remember some of the questions. But if they were put in front of me I'd still probably say I'm ticking some of the boxes for it but I'm trying to be more positive about things" – 6* *"when I came out of hospital I was very weak, but within two weeks I was walking a couple of miles and within four weeks I was walking six or seven miles you know. Like I just gradually got better" – 3* *"ehm, physically. So I'm not 100 %, ehm, I was very bad at the start. I couldn't even walk up the stairs. Ehm I'm getting there, I'd say I'm about 70 % myself" – 9* *"when I came out of hospital- if anyone even in the street asked me how I was I'd just burst out crying, but I'm able*	

		to hold it together a little bit more now" – 9	
	Accepting that recovery takes time	*"I suppose now, I just know its not going to get better in a day, once you accept that you kind of can get on with it, do you know? That kind of a way" – 11* *"it's all COVID related, its just going to take its time to heal" – 13* *"it was just a case of going through what ya had to go through to kind of come out the other side, ya know what I mean? It was part of the whole lot. You know what I mean?" – 14*	There seemed to be a general consensus among this group that you need to accept that recovery takes time. Based on other patients I met, they seem angry or frustrated at the time it takes to recover. However there were one or two indivuals in this cohort who feel 'robbed' of time. General feeling that they don't mind it taking time once they know their investigations are normal and there is nothing more sinister wrong / at play – surmising here.
faComparing their situation to others / feeling thankful	Acute experience	*"So, physically, ehm I'd say my dose was a mild one, I believe, from having read about others and how difficult it was for a lot of people. So I consider my recovery from it in keeping with what was probably – well not probably, but definitely what was a mild dose of it" – 2* *"It must have been quite terrifying for others who had a severe dose of it. So ehm, I'm a kind of a practical person, and I am just so grateful now that I had a mild dose of it" – 2*	Because COVID was so topical around the time of these interviews and these patients are '1st' wave patients, I think people compared themselves massively with others who got COVID and there was a lot more talk about people's experience with this illness than there would be with other illness. Although this group of patients were all hospitalised, it was a common theme that they felt 'lucky' that they weren't as unwell as other people
	Long-term experience	*"But from what I hear people say – now I'm not talking necessarily about people who*	Interestingly most patients who mention 'hearing' of others

		were in intensive care as well, but that they – I think they suffered more than I did ya know?" – 15 *"No I can't think of anything, like I say I've no, my friend of mine locally here, he had COVID as well, it has taken him a long time to recover, my physicality seemed to come back fairly quickly" – 16* *"But what I do know is, from having spoken to other people – and they are far worse than I am now- even though I had a severe dose of it" – 17* *"But I did feel because of having had a mild dose and some many others had the much more serious or severe dose than I had, I honestly felt I didn't want to eh, take up time with valuable resources that others might need and I didn't" – 2* *"Because I have patients here who weren't near a ventilator or ICU but they're struggling so, really, it's what they call the long COVID, and I have nothing at all, mentally I'm strong" – 3* *"And then my wife was just recently looking at it and she was saying 'Jesus, these people are really in the shit'" – 6* *"Oh right, I feel I've been one of the lucky ones that I have escaped the long COVID effects like fatigue. I never, I didn't have the fatigue that*	who are suffering more in the long-term are those who were more severely unwell during the acute phase .. i.e. required critical care ? more perspective ? thankful to be alive

		people have been experiencing" – 7	
Not returning to baseline function	Losing a sense of their former selves	*"I was tired, fatigue, I just didn't feel that I was 'me' ever really after wards" – 14* *"Well I would have been a very fit person, if ya get me. You know I loved walking, I walked everywhere. Everything seems to be an ordeal now" – 14* *"Between you and me, sometimes when I'm on my own I get a bit down. I think, Jesus, I am only half the man now, that's how I feel sometimes" – 18* *"It has robbed me of a lot of my life.* *I just don't have that energy anymore, that energy buzz that I used to have" – 4* *"I feel it has taken nearly a year of my life away basically" – 5* *"I'm definitely not as capable as I was before" – 11*	There was a lot of comparison between themselves and their ability now and pre COVID. Nearly 'mourning' the person they were before. This is characterised by sweeping statements, talking about their overall function/capability.
	Losing time		
Long COVID	Identifying as having long-COVID	*"I suppose looking into the future there would be a need for the long COVID clinics to go on for a lot longer I think. You know that type of way?" – 11* *"Ehm well I've had a difficult recovery in that ehm I suffer with long COVID now" – 5*	These interviews were done just when long COVID was coming about, some few people actually said 'I have long COVID', people talked about it more as hearsay. Whereas I think if you conducted these interviews now it would be much different.

	Speaking about people they have heard of having long-COVID	*"I just think there are some people who if they didn't have long COVID they'd have something else. I'm not trying to belittle it but ehm I just, it's too easy" – 6* *"I'm aware of that, I heard about it recently on the radio. People were talking about long covid effects of fatigue, I haven't had any of those symptoms and I feel I'm one of the lucky ones of you know" – 7* *"There seems to be some sort of- like I know people who weren't hospitalised who are suffering now. Whereas I think with me, it's a follow-on from the severity of it" – 17*	Again, a suggestion from those that were more sick acutely that those who are suffering with long COVID weren't as severely unwell during the acute phase
Support groups	Positive/helpful/beneficial	*"And I think one thing that would benefit me I think is to have.. to talk, to be in a group maybe, maybe that's something to think about. With people who have experienced COVID19 and who have made a recovery " – 7* *"I stumbled across an ICU zoom class online. So I signed up for that and a girl called Barbara set it up about 15 years ago. She was in ICU and she found that when she came- she had no support. So she set it up. So that's brilliant. So I do that once per month, online" – 9*	Could be worth mentioning that those who were in favour of support groups were all female and those who really disagreed (quite strongly) with them and their benefits were male.
	Detrimental	*"But I tell you what I would advise – if you could tell people to never download is, there's these groups on Facebook called 'Long COVID' and like I looked at it once or twice, then I found out I was in the group! And after about*	

		2 weeks, this was in September/October, after about 2 weeks of being bombarded with sob stories and horror stories, I actually got out of the group. *They're (the groups) frightening actually, like it's almost like you know that flu years ago that people used to get where they were constantly run down, you know they couldn't get out of bed and I used to always think that was in their head. And to some extent, everything is in your head, but eh, this could really get under your skin I imagine – if you let it" – 6* *"No I didn't really look at any of these COVIDhelps and all this, I avoided all that type of stuff and just got on with it" – 3*	
Fear/anxiety	Fear of re-infection	*"– now I'm a coward I don't want to go anywhere near the hospital again" – 3* *"They'd be the big things. I'm eh very nervous now, very nervous. If I see anybody doing- like them riots down in town there the other day that has my anxiety through the roof over that. Because, I know what the ICU is like and I just, I just don't want to go back there, I don't want any of my family or friends to end up there- so I kind of worry an awful lot" – 9*	While one or two people touched on the fear of the unknown when they first received their diagnosis as they had no idea how sick they were going to become there was definitely a sense of fear of re-infection. Some people were good at verbalising this fear or anxiety while others it came through in them enquiring about their immunity, and worried that getting the vaccine was like getting COVID again. From working with this patient cohort over the last two years

		"The scariness and the fear of getting it again. You can't really put that into words. It's just so scary. Getting it as severe as I got it. There's just no words to describe that you know" – 9 *"Some people were saying it could be eh, like getting the COVID again, like ya know?" – when talking about the vaccine – 8* *Antibody quote*	– fear of re-infection is HUGE.
	Fear of the unknown during acute illness	*"I'm quite surprised the way the doctor told me I had it though, he ehm, didn't come into the room, the others were coming in, he didn't tell me I got a positive result, he just started going on and I had to say to him "have I got COVID?" and he said "yes"- it was a young doctor and he is not there now any-at the moment. And ehm, I asked him "will I get better?" and he said "I don't know, you're the wrong side of eighty and you have a compromised immune system". So that was the one time that I felt "eugh"- maybe this going to be serious" – 2* *"I was just told it was the COVID, we don't know where this is going or what's happening" – 4* *"no-one really had the answers that I was looking for when I came out of hospital. My doctor or anything, he didn't know" – 9*	
Things that help recovery	Physiotherapy	*"Physio has probably been the biggest involvement in it" – 11 (when speaking about helping recovery)*	Physiotherapy was mentioned on a number of occasions and many attribute their recovery to it. It

		"Well all the physiotherapy that I've been getting, I have to say without a doubt- the physiotherapy, I wouldn't be where I am today without it" – 13 *"So definitely physiotherapy has been my road to recovery" – 13* *"I did some yeah, they gave me some exercise sheet and the physiotherapist came up to help me walk up and down the ward to just ..I also did a lot of it myself with the while I was in the hospital, with the exercises they gave me and there was a handrail and I used to walk back and forward to the toilet. I sort of got myself going that way" – 16* *"As I said they gave me the literature around exercising and stuff like that, that was helpful" – 16* *"Well yourself – the physio is very good" – 17* *"Oh the physio, I was doing physio ehm two eh virtually, I had been referred to the community from Stefanie in Armagh road and I did an assessment in the Tallaght cross and then they were, you probably know of, I don't know the names there – ehm Barry, I think it was Barry Keogh. It was just virtual twice a week, I found that very good" – 7*	would be great if you needed patient advocacy for a business case for a physiotherapy post!

		++ there are many more quotes for physio *"Well what I'd say Kate is without you, I wouldn't have gotten access to these. The 2nd visit I had with (Doctor's name), wasn't down to me ringing the hospital, it was down to you, yourself organising that for me. So I appreciate it. But I know it's not your job, but you have been my point of contact with James's – other than that I would never have heard from them" – 17*	
	Family	*"Oh we have the family support, we definitely have that, which helps" – 18* *"Yeah well when I came out of hospital back in May I was, I couldn't even make it up the stairs of my house initially. I was kind of lucky in so far as, my wife – she's a cop and my kids are quite active as well, they kind of pushed me into you know" – 6* *"And I suppose I had good family support and ehm yeah. Family support was good, you know my family has been very good" – 7*	The other thing that participants touched on in terms of helping recovery was family support.
Good recovery	No lasting effects	*"I don't feel it has affected me at all. I don't feel any effects of it"- 1* *"Not at all, perfectly alright. No problems at all. I am perfect" – 10* *"No I just feel that my recovery was good" – 2*	Again, some people felt they had recovered fully – demonstrating the complexity of recovery and the unpredictable nature of it. This kind of contradicts the

			quantitative findings in terms of overall people felt they had a good recovery, yet when presenting with a list of persistent symptoms, a high % of patients reported at least 1 at 6-months and 1-year. These interviews were conducted between these two timepoints.
	Back to baseline	*"Ehm, no. There is nothing (I have not returned to) I would say in that sense- no" – 15* *"No, I can do most things that I would normally do or that I would want to do" – 16* *"I went for a 25/30-minute run, and I feel fine, eh I walk to work every day, which is an hour walk and an hour back you know. And I cycle, so physically I'm pretty well. When the gym was open, I was swimming lengths, so I feel back to normal physically you know. My recovery has been remarkable" – 3* *There are more++*	
Poor recovery	Link to persistent symptoms and not returning to baseline function	*"Physically I'm still- 9 months later, I'm still suffering from it" – 13* *"When you put it like you ask me, like the difference between prior COVID and now – it's a big difference you know. Dramatically it has affected me physically"- 18* *"Physically, it has wiped me out" – 5*	

Pattern of symptoms	Good & bad days	*"I could have a good day, and then I could have a bad day. It depends – and I don't know what the day is bringing with my recovery basically" – 5*	Only one participant kind of suggested that their good days and bad days were random, whereas most suggested that over-doing it on an activity would lead to 'bad' days or an exacerbation of their symptoms.
	Losing days after	*"It's only you know if I kind of over-do it on the walking and things like that, I just get this tiredness" – 14* *"If I kind of work hard today, now what I call hard wouldn't be hard in terms – I'd have to rest tomorrow" – 4* *"Well for instance yesterday I went out cycling so, I'm banjaxed today. That's kind of the way it goes, so. If I do what he would normally do or what my husband would normally do on a normal day, I'd lose a day or 2 after that" – 9*	
	Knowing now not to push themselves to hard/knowing their limits		Need to get Emily's nodes for this as I don't have it
Return to work	Returning on reduced /different hours	*"I only work part-time, thank God. I only work 16 hours a week, so I use to do 3 in a row, I used to do Tuesday, Wednesday, Thursday. Now I do Tuesday, Wednesday Friday – I can't do the three together, because I'm just too tired" – 9*	Interesting to look at this in more detail and link to the quant findings. Again there was variation between people returning to work, returning to work on different/reduced hours, doing different types of work and not returning at all. Nobody was fully back to work with no issues.
	Changing the type of work that they do	*"I stepped away from the ward before Christmas, to*	

		kind of settle down and just kind of build up a little bit more strength, then I started to look after the COVID ward. I struggled with that more physically than I did the last time. Like I am able to work but it's definitely different" – 11 *"I still had office work and I still had – but everything was on zoom calls and teams calls-* *Because I was sick for more than 12 days I'm supposed to report that to the licensing authorities* *and eh you know once I got my license back I kind of had more to do* *I tried to get back flying and what not. It was kind of the various steps in a formal way sort of directed me back into getting back to fitness or being fit again.* *I've only done like since November- I've done 4 flights" – 6*	
	Not returned to work	*"Well I'm still out of work, I'm hoping to go back to work in the next few weeks, I'm going to go back part-time." When asked how long they were off work for* *"Ehm since April so will be 10 months or 11 months" – 5* *"I've been out of work, yeah I've been on extended- well on COVID leave since last April, since I went out in April. So ideally I'm looking, I'm focusing on, would like to go back if at all possible, but that*	

		may not be until the summer anyway" – 7	
	Returned to work as normal	*"I had two weeks off, 14 days isolated, and after the two weeks I was perfectly alright, the first day I resumed duty and I was – nothing, no problem at all" – 10*	
Investigations	Link with satisfaction of investigations they have had done		As mentioned above, while some patients were satisfied with the follow-up investigations they got, and even though they had persistent symptoms, they got some sort of consolation from their normal investigations. Others felt they required more invesigations and they rationalised that with wanting to know how having COVID affected their hearts or lungs, again suggesting fear of the unknown long-term effects of COVID.
	Lack of correlation with results of investigations and how they are feeling	*"My breathing, he done a breathing test on me, nobody rang me back and said your breathing was fine, or we found this or we didn't find this or ehm, how do you feel about it? Like I was saying to you I know I have a problem. You know, or to find out why my breathing was like this. I've asked all of these questions and got no follow-up on it you know. And that's the biggest thing that I found. No follow-up on any of this"*	On the flip-side some patients expressed confusion and nearly frustration that their investigations were normal yet they were experiencing persistent symptoms.

		"And even though I got my breathing test and they said it's fine!? There is something underlying that's there" – 4 *"ehm I think the way COVID is showing up now , because your x-ray is okay or as you say you medically look okay even though you still have symptoms ehm there was kind of no – I felt like I was lost to follow-up" – 5*	
	The desire for more investigations	*"Yeah, the only other thing I would say is that I would love to get another scan on my lungs, just to see how they are coming on because I remember seeing the last one, eh, there was still some damage on the lungs. I'd love to see whether they're clearing, or what's happening with them really, that's the only other thing that concerns me you know" – 12* *"Well I would like a lot more tests done on me. I'd like to get ECGs, it's so long since I have ECGs, you know the other one?* *I'd like to get an xray of my lungs as well" – 18*	
Recommendations for recovery going forward	More follow-up	*"Well I do think that, I do think physio should be very much involved, respiratory physio , I did find it very, very good but I ya know" – 5* *"I felt that the COVID section of the hospital should have done it" – 1 (when speaking about investigating whether people infected with COVID had immunity)*	The main suggestion for what could have helped more with their recovery was more follow-up – this is something that is well-recognised with the development of post-acute and long covid clinics nationally.

		"ou have been brilliant but what I would say is maybe, and I know hopefully everything is sort of calming down now at this point, but I don't know – maybe some sort of a patient advocate or something would be a good thing" – 17 *"a little bit more follow-up would have been better" – 3* *"if you left the hospital with one of those machines, or something to track your activity levels, maybe that wouldn't be a bad idea. Ehm as part of the packing up out of hospital routine. I felt that really helped,ehm it really helped me anyway, so" – 6*	