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Tele-rehabilitation following Covid-19: a sub analysis dependant on level of respiratory intervention during hospitalisation

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2. Simpson, A. J., Green, A., Nettleton, M., Hyde, L., Shepherdson, J., Killingback, C., ... & Crooks, M. G. (2023). Group-based pulmonary telerehabilitation is feasible, safe, beneficial and well-received in patients who have been hospitalised with COVID-19. *ERJ open research*, *9*(2).
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Abstract

Introduction: Tele-rehabilitation has been shown to be effective in improving exercise capacity, quality of life, fatigue and mood in patients discharged from hospital following Covid-19 infection. It remains unknown however whether the level intervention received during hospitalisation is associated with the response to tele-rehabilitation. The aims of this research were therefore to identify the effect tele-rehabilitation in individuals that received high, low and no respiratory intervention during hospitalisation. **Methods:** Forty patients (Female; n=17, Male; n=23) discharged from two University Teaching Hospitals in the North of England following Covid-19 infection participated in a single centre, mixed methods, fast-track, randomised control trial of tele-rehabilitation. Participants completed a 6-week tele-rehabilitation programme, with exercise sessions occurring twice a week and weekly education events and peer support. **Data analysis and outcome measures:** Participants were split by the level of intervention they received during hospitalisation, which were high respiratory intervention (Ventilation, Continuous Positive Airway Pathway), low respiratory intervention (High Flow Nasal Oxygen, Oxygen) and no respiratory intervention. The primary outcome measures were exercise capacity (1 minute sit-to-stand), Quality of life, [EuroQol -Visual Analogue Scale (EQ-VAS)], Fatigue [Functional Assessment of Chronic Illness Therapy - Fatigue (FACIT-F)] and mood [Hospital Anxiety and Depression Scale (HADS)].

Results: Improvements in exercise capacity, respiratory symptoms, and quality-of-life were seen. Sit-to-stand scores improved from 19 (14-24) at baseline to 26 (23-28) following telerehabilitation ($p<0.01$). The change was numerically bigger in the high respiratory intervention group (15 at baseline to 24 post intervention, ($p<0.01$)) compared to the low intervention group (21 at baseline to 24 post-intervention ($p<0.01$)). MRC Dyspnoea scores improved from 3.5 (3-4) at baseline to 3 (3-4) following in the high intervention group

($p<0.05$) and 2 (2-4) at baseline to 2 (1.5-3.5) ppst-intervention in the low intervention group ($p<0.05$). Anxiety scores however no improvement the high intervention group ($P>0.05$), however improved in the low respiratory intervention group from 11 (4.75-13.75) at baseline to 7 (6-11) post-rehabilitation ($p<0.05$).

Conclusion: Our results show that tele-rehabilitation is a successful method of providing rehabilitation in patients regardless of the level of intervention during hospitalisation. However, data indicates the need for more psychological support in individuals that received intensive hospital treatment, which should be considered during the development of long-covid treatment strategies.

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1.0 Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), otherwise known as Covid-19, is one of the fastest spreading viruses, with numbers continuing to rise; Global cases have reached over 591 million, and deaths approximately 6 million (World Health Organisation, 2022). Despite often presenting as mild symptoms, due to the high-levels of transmission, Covid-19 has resulted in mass hospitalisation, with around 14% of individuals developing severe disease, often requiring intensive care treatment (Maves et al., 2020).

Tele-rehabilitation has previously been identified as an effective form of rehabilitation (Frederix, Vanhees, Dendale & Goetschalckx, 2015), which includes assessment, monitoring, intervention, supervision and education from healthcare professionals. Our research team has conducted a single centre, mixed-methods, fast-track (wait-list), randomised controlled trial of telerehabilitation for patients who have been hospitalised with Covid-19 (Hyde et al., 2022). Here we have shown, for the first time, that group-based pulmonary telerehabilitation is feasible, safe, beneficial, and well-received in patients that have been hospitalised with Covid-19 (Simpson et al., 2023). What remains unknown, however, is whether the level of respiratory support provided during hospitalisation is associated with the response to tele-rehabilitation. This information could help personalise the rehabilitation pathway.

2.0 Literature Review

2.1 Introduction

The SARS-CoV-2 (Covid-19) pandemic has been the most widespread worldwide outbreak of disease since the Spanish Flu (Influenza A/H1N1) pandemic of 1918-1920, which records estimate to have caused around 500 million infections (CDC, 2019), and up to 50 million deaths (Trilla, A., Trilla, G. and Daer, C., 2008). SARS-CoV-1, more commonly known as severe acute respiratory syndrome (SARS), resulted in a previous coronavirus outbreak in 2003, which presented as fever and dry cough, with many developing pneumonia 2 to 7 days after first symptom onset (WHO, 2019). Unlike Covid-19, SARS-CoV-1 only spread to 4 countries from its origin of China, with 8098 infections, and 774 deaths being reported between 16 November 2002 – 19 May 2004 (NHS, 2019). SARS-CoV-1 was the first severe and readily transmissible new disease to emerge in the 21st century and showed a clear capacity to spread along the routes of international air travel (WHO, 2019)

The Covid-19 pandemic originated in the Hubei province of China, and within one month had spread to multiple nations, including Nepal, France, Australia, Malaysia and the United States of America (WHO, 2020). Mass hospitalisations subsequently occurred worldwide, with the UK averaging 15,609 new Covid hospitalisations each week, within the first 5 weeks of the first wave of the pandemic (Covid-19 Data Explorer, 2021). Roughly 14% of all Covid-19 cases develop severe disease, which often requires intensive care treatment with respiratory support (Li, Liu, Zhang, Xu, Dai, Tang, Su & Cao, 2020). A further 5% develop critical disease with respiratory failure, septic shock and/or multiple organ dysfunction/failure (Li, Liu, Zhang, Xu, Dai, Tang, Su & Cao, 2020). It is also estimated that 17% of hospitalisations require high dependence or intensive care input (Zaim, Chong, Sankaranarayanan & Harky, 2020). These hospitalisations gradually decreased over the months of May to August 2020, with a further spike in admissions during the second wave

from December 2020 to February 2021.

Despite declining rates of Covid-19 hospitalisations, many patients are still relying on hospital and NHS services after their Covid-19 infections (typically a 2-week period) and are, suffering with lasting symptoms such as continued severe fatigue, chest tightness, pins and needles, and an inability to recall i.e., 'brain fog' (Asadi-Pooya et al., 2022). This has been characterised and named as 'Long Covid'.

2.2 Methods of respiratory intervention

During the Covid-19 pandemic, many hospitalised patients required different levels of respiratory support. For many Covid-19 patients admitted to intensive and critical care units across the pandemic, there was a development of acute respiratory distress syndrome (ARDS). Acute respiratory distress syndrome is a life-threatening illness, where the respiratory system cannot provide a suitable oxygen supply to vital organs, often triggering multiorgan failure. ARDS is usually caused by a complication of a pre-existing health condition, which during the pandemic was often Covid-19. A study conducted by Gibson, Qin & Puah (2020) into the clinical features and differences from typical pre-Covid-19 ARDS found that ARDS develops in 42% of patients presenting with Covid-19 pneumonia, and 61-81% of those requiring intensive care. Treatment for patients developing ARDS usually consists of mechanical ventilation, prone positioning and extracorporeal membrane oxygenation. For those patients that did not develop ARDS or require very high levels of mechanical ventilation, other methods of respiratory assistance were provided. This included continuous positive airway pressure (CPAP), high flow nasal oxygen and oxygen. Some patients however required no respiratory intervention and recovered spontaneously.

2.2.1 Mechanical Ventilation

Mechanical ventilation uses invasive methods to provide support for those struggling or unable to breathe independently. This includes the patient having a tube inserted into the airway (intubation) and being attached to a mechanical ventilator to help oxygen move in and out of the respiratory system. Generally, intubated ventilated patients are lightly sedated, however ARDS patients in ICU with Covid-19, who have had a tracheostomy have been seen to need heavier sedation, allowing for a longer period for their lungs to heal (MacMillan, 2020). In some cases, Covid-19 causes fluid and mucus to build up in the lungs, or causes severe damage to alveoli and tissue, preventing the lung tissue being oxygenated. Many patients develop ventilator-induced respiratory muscle weakness. While ventilators enable Covid-19 patients to breathe, they also decrease the load placed on the respiratory muscles. Alongside mechanical ventilation, steroids and medicines to help maintain ventilation have resulted in respiratory muscle weakness and subsequent physical deconditioning (Martin et al., 2005).

2.2.2 Continuous Positive Airway Pressure (CPAP)

Continuous positive airway pressure (CPAP) is a machine that increases air pressure in the throat, ensuring the throat cavity and airway passage do not collapse during respiration. This generally comes in the form of a mask. CPAP is most used to treat sleep apnoea, however, has other uses, such as neonatal intensive care to help premature babies breathe.

CPAP was adopted during the pandemic to treat Covid-19 patients that were suffering from ARDS to establish an open-air passage when patients' lungs became swollen or collapsed. CPAP was utilised in patients deemed not likely to benefit from invasive respiratory assistance, such as mechanical ventilation (Bradley et al., 2021). Ashish et al., (2021) identified that CPAP was found to be significantly associated with lower risk of death in patients with hospital stay equal to, or below 7 days. This study also identified that the use of

CPAP within the first days of hospitalisation (before intubation or tracheostomy) save between 10% to 20% of patients with severe ARDS.

2.2.3 High Flow Nasal Oxygen (HFNO)

HFNO has also been an adopted method of treating Covid-19 patients. HFNO provides heated and humidified oxygen via nasal cannula at a flow rate of 15L/min. Like CPAP, HFNO has many clinical applications such as the treatment of acute hypoxemic respiratory failure, post-surgical respiratory failure and for acute heart failure and/or pulmonary oedema (Ko et al., 2020). During the pandemic, high flow nasal oxygen was used to treat patients not needing intense breathing assistance, but still those with moderate ARDS. Studies have shown that the use of HFNO has helped patients with Covid-19-infection to avoid escalation to ICU care and receive better outcomes than ordinary oxygen treatment (Lyons & Callaghan, 2020). Similarly, a study conducted by Mellado-Artigas et al. (2021), found that the use of high-flow nasal oxygen upon ICU admission in patients with Covid-19 related acute hypoxemic respiratory failure led to an increase in ventilator-free days and a reduction in ICU length of stay by 8 days.

Some individuals who were hospitalised with respiratory symptoms however do not require any of the above treatments and are aided through medication and breathing techniques. Whilst various methods of hospital care exist, little is known about the outcomes of such care on post-hospitalisation function and symptoms. Further, whether hospital intervention is associated with patients' response to rehabilitation remains unknown.

2.3 Long Covid

Long Covid, defined as ‘signs and symptoms that develop during or following an infection consistent with Covid-19 which continue for more than 12 weeks and are not explained by an alternative diagnosis’ (NICE, 2020). Long-Covid was difficult to ascribe with official terminology, due to symptoms being diverse and effecting multiorgan systems (Baig, 2020). Long Covid affects around 10% of 18–49-year-olds who become unwell with Covid-19, rising to 22% of people aged over 70 (Sudre et al., 2020). A research team in Rome discovered that 87% of patients discharged from one hospital after recovering from Covid-19 still experienced at least one symptom after 60 days of virus onset (Carfì, Bernabei & Landi., 2020). Thirty two percent of these patients reported having 2 symptoms, and 55% reported having 3 or more symptoms (Carfì, Bernabei & Landi., 2020). The most common symptoms being fatigue (53%), dyspnoea (43%), joint pain (27%), and chest pain (22%), with 44.1% of patients subsequently reporting a much-worsened quality of life (Carfì, Bernabei & Landi., 2020).

Similarly, Davis et al. (2021) identified that 96% of patients across 56 countries reported having long-Covid symptoms beyond 90 days of Covid symptom onset and/or a positive Covid test result. The most frequent symptoms reported after 6 months were fatigue, post-exertional malaise, and cognitive dysfunction (Davis et al., 2021). More than 85% of individuals experienced set back with exercise, physical or mental activity, and stress as the main triggers. Forty-five percent of people reported requiring a reduced work schedule compared to pre-illness and 22% were not working at the time of survey due to their health conditions (Davis et al., 2021). Sudre et al., (2020) reported that patients experiencing over 5 symptoms during the first week of illness was associated with developing long-Covid, with 1 in 20 potentially developing the condition.

2.4 Rehabilitation Therapy

Rehabilitation is formally defined as ‘a set of interventions designed to optimise functioning and reduce disability in individuals with health conditions in interaction with their environment’ (World Health Organisation, 2023). Rehabilitation aims to restore an individual’s health or way of living through therapy and training programmes, and can be implemented following health issues, addiction, and imprisonment. There are seven main forms of rehabilitation, and these are Cognitive Rehabilitation, Pharmacological Rehabilitation, Occupational Therapy, Physical Rehabilitation, Recreational Therapy, Speech and Language Therapy and Vocational Therapy.

Within a healthcare setting, the National Health Service defines rehabilitation as ‘the restoration, to the maximum degree possible, of an individual’s function and/or role, both mentally and physically, within their family and social networks and within the workplace where appropriate’ (NHS- N.I.Q, 2014). Rehabilitation services include a wide range of professionals, including physiotherapists, occupational therapists, consultants, doctors, nurses, and counsellors, who work as part of multi-disciplinary teams in acute and community care (NHS- N.I.Q, 2014). Rehabilitation offered by the NHS for specific patient conditions include stroke rehabilitation, major trauma rehabilitation, musculoskeletal rehabilitation, pain rehabilitation, neurological rehabilitation, and pulmonary rehabilitation. These rehabilitation services are offered in different formats, being ward based, group based, and individual therapy.

2.55 Pulmonary Rehabilitation

One of the main treatments recognised by leading professionals in the recovery of hospitalised Covid patients experiencing long-Covid is pulmonary rehabilitation (PR). Pulmonary rehabilitation is defined as 'comprehensive intervention based on a thorough patient assessment followed by patient-tailored therapies that include, but are not limited to, exercise training, education, and behaviour change, designed to improve the physical and psychological condition of people with chronic respiratory disease and to promote the long-term adherence to health-enhancing behaviours' (Rochester et al., 2015), and is typically delivered to groups of 8-16 people in multiple healthcare settings by teams comprising of nurses, occupational therapists, health care assistants, physiotherapists.

Pulmonary rehabilitation combines multidisciplinary teams to improve physical and social functioning of patients with chronic respiratory issues (Hill, 2006). As a multidisciplinary service, pulmonary rehabilitation aims to control and alleviate symptoms of respiratory damage, with the overall aim to improve patients' quality of life. Typically, pulmonary rehabilitation consists of physical exercise training, education sessions, dietary advice, and psychological and emotional support over a six-week period, usually with two sessions a week (Bolton et al., 2013).

Pulmonary rehabilitation is beneficial to those suffering with respiratory diseases such as chronic obstructive pulmonary disease (COPD), pulmonary fibrosis and bronchiectasis. A study conducted by Scott, Baltzan, Fox, & Wolkove (2010) identified that 62% of their participants with COPD had a successful response in physical activity levels to pulmonary rehabilitation treatment. Schroff et al. (2017) identified that pulmonary rehabilitation improved physical function, health perception, physical role, emotional role, social function,

mental health, pain, vitality, and depression independent of baseline measurers in patients with COPD, with these benefits being independent of baseline exercise capacity, dyspnoea and lung function. A study conducted by Gloeckl, Schneeberger, Jarosch, & Kenn, (2018) identified similarly beneficial results, with patients showing statistically significant and clinically relevant improvement in physical performance, with pulmonary rehabilitation significantly lowering the rate of readmission to hospital, whilst also improving physical performance ability and quality of life

Positive effects of pulmonary rehabilitation have been seen across various respiratory diseases. Florian et al,. (2013) found that six-minute walk distance and reported quality of life was significantly greater after pulmonary rehabilitation in patients with pulmonary fibrosis, pulmonary emphysema, and other advanced lung disease waiting for lung transplants. Trevor et al., (2015) found that patients with asthma who completed PR had improvement in physical function and emotional well-being, with observations of increased six-minute walk distance, decreased body mass index and depression rating scores. Similarly, Zampogna (2020) reported pulmonary rehabilitation significantly improved six-minute walk distance, Borg dyspnoea and muscle fatigue in patients with asthma. Zampogna (2020) also noted that oxygen saturation significantly improved in severe asthma patients with bronchiectasis and/or obstructive sleep apnoea syndrome.

Since the Covid-19 outbreak, pulmonary rehabilitation has become common in the treatment of post-Covid patients and long-Covid sufferers. A study conducted by Zampogna et al. (2021) identified high prevalence of muscle weakness and physical performance impairment in those hospitalised with Covid-19 and conducted a pulmonary rehabilitation programme, assessing Short Physical Performance Battery (SPPB), Barthel Index (BI), and six-minute

walking distance. It was concluded that pulmonary rehabilitation is feasible and effective in patients recovering from Covid-19, with results showing improvements in Short Physical Performance Battery and Barthel Index, as well as in other assessed outcome measures such as six-minute walking distance.

Similarly, Al Chikhanie et al. (2021) identified that pulmonary rehabilitation induced greater 6-minute walking distance improvement in Covid-19 patients than in other respiratory failure patients post-discharge from intensive care. Further, the earlier pulmonary rehabilitation was performed post-intensive care unit, the more likely patients were to show more improved results. However, despite this, there were still significant physical and psychosocial impairments which remained post-pulmonary rehabilitation treatment.

A prospective cohort study conducted by Gloeckl et al., (2021) which specifically searched for the benefits of pulmonary rehabilitation to treat Covid-19 also identified that pulmonary rehabilitation improved 6- minute walking distance scores and forced vital capacity scores in two subgroups: i) patients with mild-moderate Covid-19, and ii) patients diagnosed with severe-critical Covid-19.

2.5 Tele-rehabilitation

Social distancing measures have been implemented in many countries across the world to manage the spread of Covid-19, thus health services have adapted to continue providing services for patients, via online platforms. A systematic review conducted by Monaghesh & Hajizadeh (2020), identified the role of telehealth during the Covid-19 pandemic. Monaghesh

& Hajizadeh (2020) concluded that for healthcare providers and patients who are self-isolating, telehealth is appropriate in minimising the risk of Covid-19 transmission. This solution therefore had the ability to prevent any direct physical contact, provide continuous care, and reduce potential morbidity and mortality of Covid-19. Similarly, Monaghesh & Hajizadeh (2020) concluded that the 'calls for expended use of telehealth as an innovative solution clearly highlight unmet needs in the world healthcare system.' A further study conducted by Li, J. A et al., (2021) investigated the superiority of tele-rehabilitation for Covid-19 (TERECO) patients over no rehabilitation. These results showed that a telerehabilitation programme was superior to no rehabilitation, with results indicating improvements in 6-minute walking distances, lower limb strength and physical quality of life.

As investigative research into the effects of pulmonary rehabilitation for Covid-19 and Long Covid continue, it has been observed that in most of this research, the rehabilitation programmes and studies do not provide all aspects of pulmonary rehabilitation. Specifically, no telerehabilitation studies have maintained a group-based exercise programme, which is possible via an online video conferencing platform. This therefore leaves a large gap in understanding the role of a full telerehabilitation programme on the treatment of Covid-19 and long-Covid, and whether telerehabilitation is a feasible and successful form of treatment for those suffering with prolonged effects and symptoms of Covid-19

Our research team conducted a single centre, fast-track (waitlist), randomised mixed-methods, feasibility trial of tele-rehabilitation for patients that have been hospitalised with Covid-19 and has shown group-based pulmonary telerehabilitation is feasible, safe, beneficial and well-received in patients that have been hospitalised with Covid-19 (Simpson et al, in

press). However, it remains unclear as to whether the level of respiratory support received during hospitalisation is associated with the recovery seen with telerehabilitation.

2.6 Aims

The aim of this research is to address the uncertainties relating to the effectiveness of a tele-rehabilitation programme in individuals that receive high, low and no respiratory intervention during their hospitalisation with Covid-19. This research explored changes in exercise capacity, respiratory symptoms, quality of life, fatigue and mood. A subgroup analysis of our research (Hyde et al., 2022, Simpson et al in press), will be conducted across patients who required high, low and no respiratory intervention whilst hospitalised with Covid-19.

3.0 Methodology

3.1 Research Governance and Ethical Approval

An NHS Research Ethics Committee approval was obtained (reference number; 20/IEC08/0017) and the trail registered with clinicaltrials.gov (reference; 285205). The University of Hull research ethics team granted ethical clearance. The protocol for the full trial is published (Hyde et al., 2022) and details provided below.

3.1.2 Research Misconduct Avoidance

To ensure research misconduct was prevented during this research, each member of the team completed good clinical practice training, provided by the National Institute for Health Research. Good Clinical Practice (GCP) is the international standard to which all clinical research is conducted. GCP training is a requirement for Health and Social Care Research which has been developed by the Health Research Authority for researchers conducting clinical trials of investigational medicinal products (CTimp). This also applies to the conduct of non CTimp studies. This training assures patients and the public that the rights and wellbeing of individuals taking part in studies are protected. This also ensures data gathered from the research is consistent.

3.2 Participants

Forty participants (Male:23, Female:17) aged 30 to 90 under the care of Hull University Teaching Hospitals NHS Trust were recruited for this study. Participants were hospitalised with Covid-19 within the last 6 months and suffered ongoing persistent breathlessness and/or functional limitations compared with pre-Covid-19 illness at the time of recruitment (long-Covid). Participants were identified 4 to 6 weeks after hospital discharge. Patients were also considered if they presented with persistent breathlessness (MRC ≥2) and/or functional limitation compared with pre-Covid-19 hospitalisation. Full inclusion and exclusion criteria are presented in Table 1.

To answer the research question, participants were grouped into three categories; high respiratory intervention (which included individuals placed on mechanical ventilation. CPAP and HFNO), low respiratory intervention (which included individuals on Oxygen treatment) and no respiratory intervention.

Table 1 *Inclusion and Exclusion Criteria*

Inclusion Criteria	**Exclusion Criteria**

• Males and females aged 18 years
• Suspected or confirmed Covid-19 requiring hospitalisation within 6 months of study recruitment. Requirement for either: non-invasive respiratory support [CPAP, HFNO, NIV], or invasive mechanical ventilation will be recorded but is not necessary for enrolment in the trial.
• >4weeks since hospital discharge/ first positive Covid-19 swab (whichever is later) at time of screening
• MRC dyspnoea grade 2 or more
• Perceived limitation of activities compared with pre-Covid-19 hospitalisation (patient or investigators perception)
• Internet connection and access to a device that supports video calling
	• Unwilling or unable to consent or complete study measures
	• Significant comorbid physical or mental illness considered by the investigator to:
	  • prevent engagement in modified exercise
	  • impair the participant's ability to follow instructions
	  • place the participant at undue risk during exercise training
	  • adversely affect the recovery or rehabilitation trajectory
	• Current involvement in other interventional clinical trials relating to Covid-19 (e.g., clinical trial of an investigation medicinal product)

CPAP, Continuous Pulmonary Airways Pressure; HFNO, High Flow Nasal- oxygen; NIV, Non-invasive Ventilation; MRC, Medical Research Council Dyspnoea Scale

3.3 Experimental Design

A single centre, fast-track (waitlist), randomised, controlled, feasibility trial was conducted. Participants were randomly allocated to one of two groups, using a commercial web-based randomisation system (Sealed Envelope Ltd, London, UK). Patients randomised to the 'fast-track' group received intervention 14 ± 7 days after randomisation, and patients randomised to the 'wait-list' group received the intervention 56 ± 7 days after randomisation (Table 1.). The results of the fast-track group and the wait-list group can be found in the Group-based pulmonary telerehabilitation is feasible, safe, beneficial and well-received in patients who have been hospitalised with COVID-19 paper (Simpson et al., 2023). The structure of this programme is shown below in table 2 and study flow chart in figure 1.

Table 1 *Structure of Tele-rehabilitation Programme*

	Eligibility / baseline	Fast Track Start-of-treatment	Fast Track End-of-treatment	Wait List Start-of-treatment	Wait List End-of-treatment
Day	**0**	**14 ± 7**	**56 ± 7**	**56 ± 7**	**98 ± 7**
Procedure					
Inclusion/exclusion criteria	x				
Informed Consent	x				
Medical History	x				
Medication History	x				
COVID-19 History	x				
Adverse Event Monitoring		x	x	x	x
Questionnaires:	x	x	x	x	x
1. MRC					
2. Breathlessness NRS					
3. Cough NRS					
4. EQ-5D-5L					
5. EQ-VAS,					
6. FACIT-F					
7. HADS					
8. Adverse Events					
One-minute sit-to-stand test	x	x	x	x	x
Assessment of intervention adherence			x		x
Health Care Utilisation	x	x	x	x	x

Cough NRS, Numerical Rating Score; MRC, Medical Research Council Dyspnoea Score; EQ-5D-5L, EuroQol-5 Dimension- 5 Level; EQ-VAS, EuroQol Visual Analogue Scale; FACIT-F, Functional Assessment of Chronic Illness Therapy – Fatigue; HADS, Hospital Anxiety and Depression Scale.

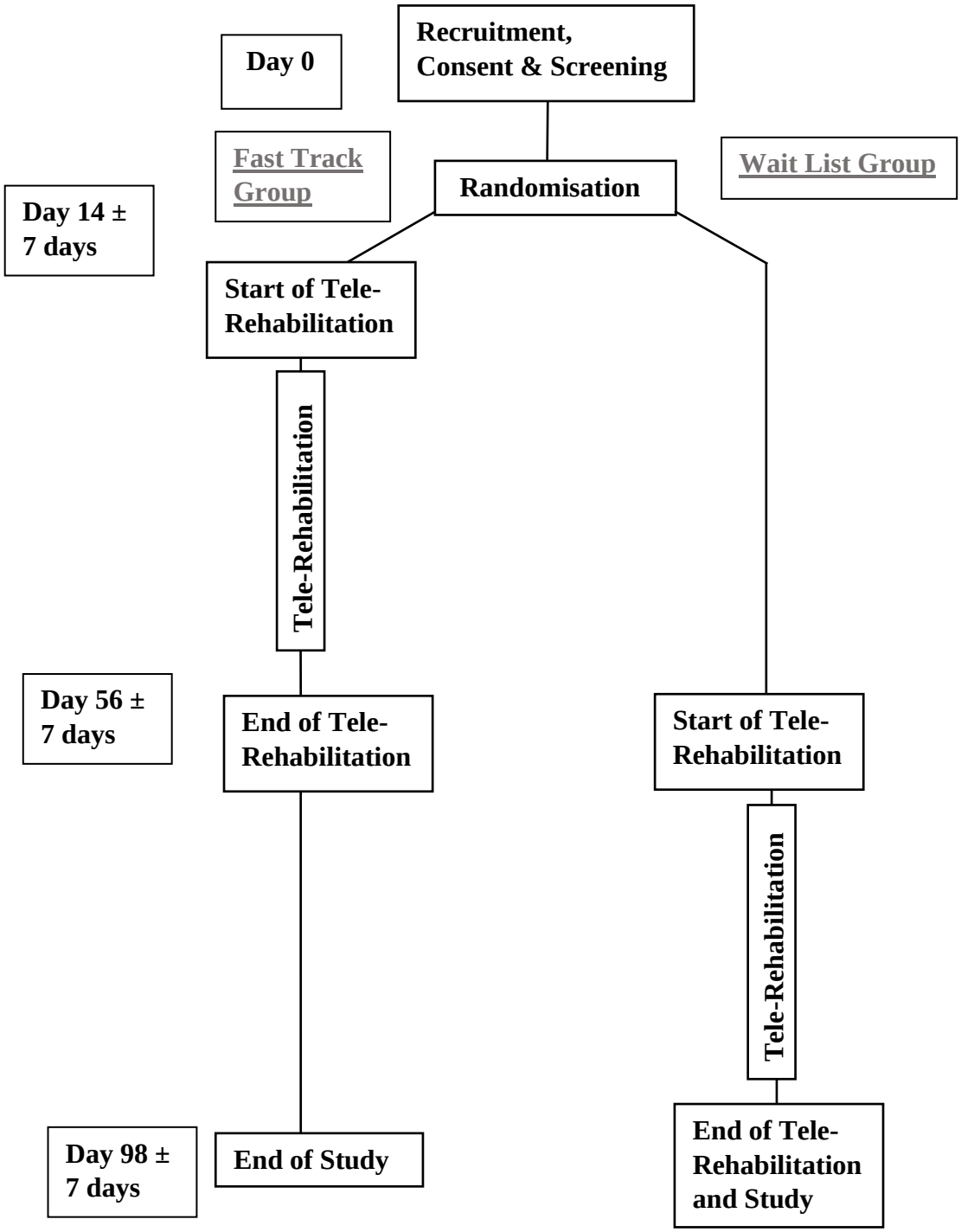

Figure 1 *Study flow chart of the tele-rehabilitation programme: left side of the diagram illustrates the time frame for the fast-track group, and the right illustrates the time frame for the wait-list group*

3.4 Baseline Assessments

Baseline assessments were recorded prior to randomisation and starting the 6-week telerehabilitation programme. Baseline measurements included medical history and review of prescribed medicines, Covid-19 history, confirmation of eligibility, and the one-minute sit to stand test. Multiple questionnaires were also completed, and these included the medical research council dyspnoea scale, Numerical rating scale to assess breathlessness, visual analogue scale to assess cough, the modified FACIT-F scale to assess fatigue, the EQ-5D-5L and EQ visual analogue scale to measure quality of life, and the hospital anxiety and depression scale to assess mood. These assessments were completed at baseline assessment, start of treatment, and at the end of treatment. Only baseline and the end of treatment measurements were considered in this research.

3.5 Clinical Outcomes

Clinical outcomes were observed through questionnaires asked at each of the time points (eligibility/baseline assessment and at the end of intervention) of the programme.

3.5.1 Respiratory Symptoms

Respiratory symptoms were measured using; the Medical Research Council Dyspnoea Scale (MRC) (Singh, Nolan and Bolton., 2022) and a Numerical Rating Scale (NRS) / Visual Analogue Scale (VAS) (scored 0-10 where 0 = no breathlessness and 10 = worst possible breathlessness) (Wysham et al., 2015).

3.5.2 Fatigue

Fatigue was measured using the Functional Assessment of Cancer Therapy: Fatigue (vFACT-F Scale (Version 4) (Al-Shair et al., 2012), Visual analogue scale (VAS) (Wysham et al., 2015). Symptoms measured using these scales assessed aspects of breathlessness, participants cough and rates of participant's fatigue.

3.5.3 Quality of Life

Quality of life was measured by the EQ-5D-5L and the EQ visual analogue scale (EQ VAS) (Herdman et al., 2011) The EQ-5D-5L measured 5 aspects of health (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) using 5 rating levels (no problem, slight problem, moderate problems, severe problems and extreme problems).

Mood was assessed using the hospital anxiety and depression scale (HADS) (Zigmond and Snaith., 1983). The EQ-5D-5L also provided an insight to the participant's mood as anxiety and depression domains were also measured.

3.5.4 Exercise Capacity

Exercise capacity was measured using the one-minute sit-to-stand test (STST) (Crook et al., 2017). Participants undertook this assessment in their own homes while observed over via an audio or video link. The sit to stand test requires no specialist equipment (other than a chair) and therefore could be undertaken by participants in their own homes.

3.6 Tele-Rehabilitation Programme

Participants completed a six-week tele-rehabilitation programme that consisted of two exercise sessions per week, which were guided and taught by a multidisciplinary team. The multidisciplinary team included a Sport Science research master's student, physiotherapists, respiratory physiologists, guided by consultants, and doctors. Prior to each exercise session, a virtual consultation was conducted over the phone, to confirm eligibility, accessibility, and safety to exercise with remote supervision. Participants took part in a 45-60-minute exercise session, which included a warmup and a cool down. The exercise sessions featured exercises which followed the general exercise principles; Frequency, Intensity, Time, Type, Volume and Progression (FITT-VP) (Pescatello, L. S., Riebe, D., & Thompson, P. D, 2014). These exercises primarily focussed on functional movement patterns, an area which has significantly deteriorated in many Covid-19 patients. Each patient also received an individual exercise programme to complete at home having been assessed for the ability to safely exercise at home without any assistance or supervision. Programmes focussed on each participant's individual exercise capacity, tolerance and goals. Over the 6 weeks, exercise intensities and repetitions and sets of exercises were increased. Exercises were also able to be regressed if participants found them too difficult, making sure individual needs were considered.

Each week, participants were invited to join an educational session. These sessions would last around 30 minutes, and covered six topics: managing breathlessness, benefits of exercise, nutrition, returning to work, fatigue management and a question-and-answer session with a specialist rehabilitation consultant. Participants were also given the opportunity to ask the session leaders questions, and were able to provide feedback about the sessions, e.g., what they liked/didn't like, what could be improved. Participants were also encouraged to talk to one another after the session.

3.7 Safety monitoring

The Adverse Events (AE) reporting period for this trial began at screening and ended at the participant's final study visit. An adverse event is defined as an untoward medical occurrence in a participant, that does not have a causal relationship with a trial intervention (Coomarasamy et al., 2016). In this instance, an adverse event would be an injurious fall or cardiorespiratory arrest during exercising, which would be directly attributed to the exercise intervention. Each trial participant was questioned about adverse events at each visit. The physiotherapist or reporter recorded all directly observed AEs and all serious adverse events (SAEs) spontaneously reported by the trial participant. A pre-existing condition (i.e., a disorder present before the AE reporting period started and noted on the pre-study medical notes), was not reported as an AE unless the condition worsened, or episodes increased in frequency during the AE-reporting period.

3.8 Statistical Analysis

Data were tested for normality using Shapiro-Wilk tests. Tables showing baseline and post-rehabilitation data for each of the groups are presented using descriptive statistics. Medians (Q1-Q3) are reported for ordinal and non-parametric data, mean (SD) for continuous data and parametric data and raw count (%) for nominal data. Differences between the low respiratory intervention and high respiratory intervention at baseline and post intervention were analysed using independent samples t-tests and Mann Whitney U-test as appropriate. Differences within groups, baseline to post intervention were analysed using paired samples t-test and Wilcoxon signed rank test. Analysis was supported with JASP (Version 0.14.1.0) and Prism and statistical significance set at $P<0.05$.. Inferential statistics for the no intervention group were not conducted due to low sample size (n=3).

4.0 Results

4.1 Consort Flow Diagram

Two-hundred and eighty-eight participants were approached and offered the opportunity to be part of this trial. Of these patients, 188 either declined the offer or were not eligible as they did not fit the inclusion criteria or were unable to be contacted. A full list of explanations for lack of participation can be seen in figure 3.

The total number enrolled on this trial equalled 40, with 13 dropouts after allocation, 5 of which were in the fast-track group and 8 being in the wait list group. Twenty-seven participants therefore completed this study and their data presented below.

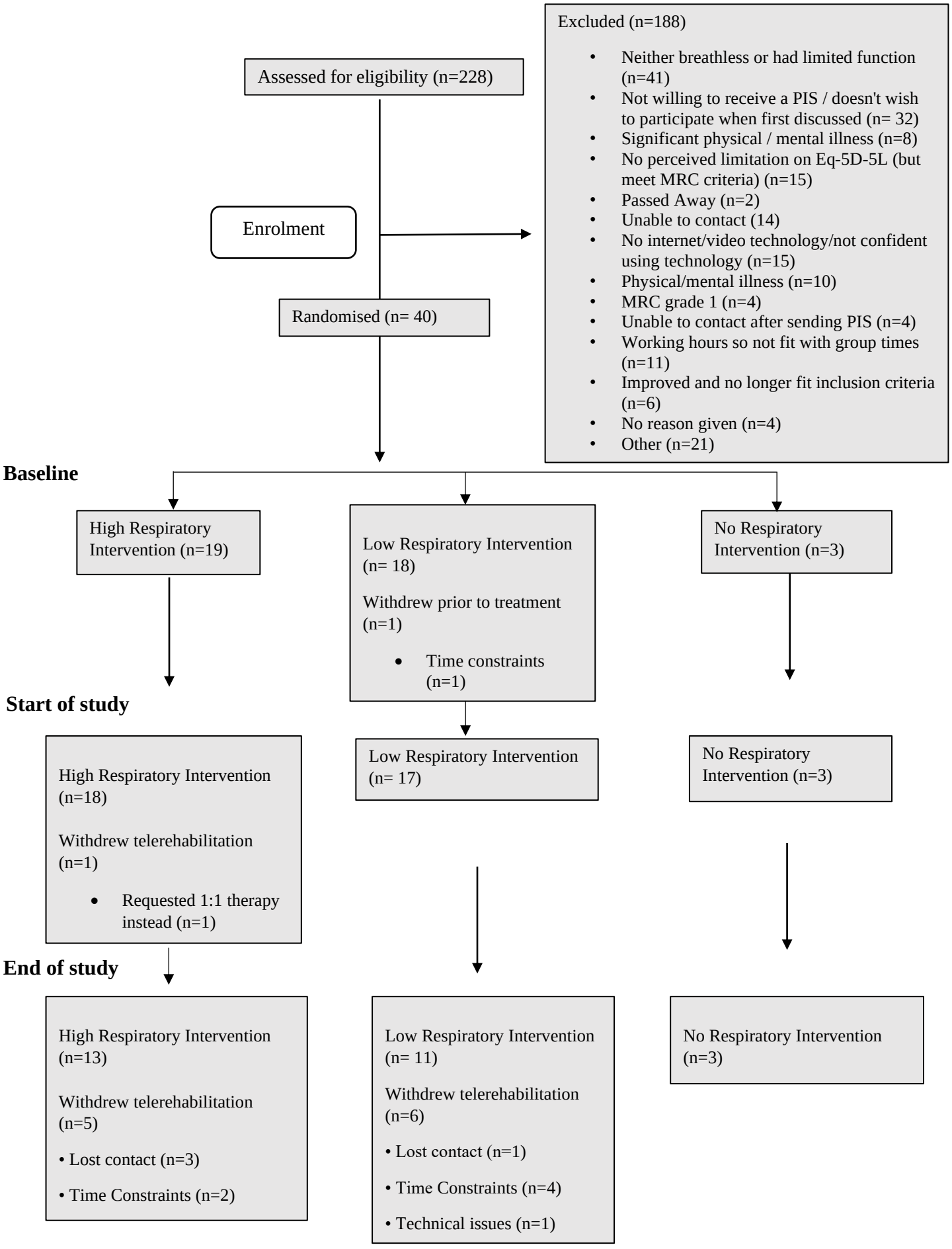

Figure 2 *A consort flow diagram showing the phases of a randomised trial.*

4.2 Patient Characteristics

Participant characteristics are presented in Table 3. There is very little difference in age and gender distribution across all three sub-groups (Table 3). By definition, the high respiratory intervention group had higher respiratory intervention during hospitalisation, with intubation and high flow nasal oxygen equally being the most needed apparatus (42%), compared to low respiratory intervention and no respiratory intervention groups, who required only standard O_2 treatment or no intervention. Patients in the high respiratory intervention group spent the longest time in hospital 14 (10-26) days, with the low respiratory intervention group staying 4 (3-6) days.

Table 2 *Patient Characteristics*

	Total (n=40) Baseline	**High Resp Intervention (n=19) Baseline**	**Low Resp Intervention (n=18) Baseline**	**No Resp Intervention (n=3) Baseline**
Age, mean (SD)	58 (12)	55 (10)	61 (14)	55 (3)
Gender, n (%)				
Male	23 (58)	12 (63)	10 (56)	1 (33)
Female	17 (43)	7 (37)	8 (44)	2 (67)
Highest Level of respiratory support, n (%)				
CPAP	3 (7.5)	3 (15)	0 (0)	0 (0)
High Flow Oxygen	8 (20)	8 (42)	0 (0)	0 (0)
Intubation/Ventilation	8 (20)	8 (42)	0 (0)	0 (0)
O_2	18 (45)	0 (0)	17 (94)	1 (33)
Nothing	3 (7.5)	0 (0)	1 (6)	2 (67)
Total days in Hospital, median (Q1-Q3)	8 (3-15)	14 (10-26)	4 (3-6)	0 (0-2)

CPAP, Continuous Positive Airway Pressure

4.3 Physical Well-being/Wellness

4.3.1 Sit-to-Stand

Improvement in one-minute sit to stand scores can be seen across the three groups (high respiratory intervention [$p<0.01$), low respiratory intervention ($p<0.01$) and no respiratory intervention], with the greatest improvement within the high respiratory intervention group (Table 4, Figure 3). Overall, 60% of participants improved their sit-to-stand scores. The high respiratory intervention group produced the lowest number of sit-to-stand repetitions at baseline ($p<0.05$), however showed the greatest increase in sit-to-stand scores from baseline to post-rehabilitation, with a median increase of sit-to-stands of 9 (Table 4). The low respiratory intervention group produced higher baseline sit-to-stand scores, however only improved sit-to-stand scores on average by 3.5 repetitions (Table 4). The no respiratory intervention group produced the highest one-minute sit-to-stand repetitions at both baseline (31) and post intervention (39), with scores increasing by a median of 8 repetitions (Table 4). The minimal clinically significant difference for thirty-second sit-to-stand is ≥ 3 (Schneeberger et al., 2018) so it can be assumed that all groups met this minimal clinically important difference.

Table 3 *Participant Results*

	Total	High Respiratory Intervention		Low Respiratory Intervention		No Respiratory Intervention	
Baseline (n=40)		Baseline (n=19)	Post-Rehab (n=15)	Baseline (n=18)	Post-Rehab (n=14)	Baseline (n=3)	Post- Rehab (n=3)
Cough NRS	2 (1-5)	2 (1-5.5)	3 (1-5)	2 (1-5.5)	1 (0-3.5)	1 (0-1.5)	0 (0-0.5)
MRC	3.5 (3-4)	4 (3-4)	3 (3-4) ×	2 (1.5-3.5)	2 (2-4) ×	2 (2-2.5)	1 (1-1.5)
One Minute Sit-to-stand	20 (14-24)	15 (12-20)*	24 (19.5-26.5)××	21 (15-25)	24.5 (24-28) ××	31 (27.5-39.5)	39 (34.5-52)
EQ-5D-5L							
Mobility	3 (2-4)	3 (2-4)×	3 (2-3.5)	3 (2-3)	2 (2-3)	2 (1.5-2.5)	1 (1-1)
Self-care	2 (1-3)	2 (1-3)	2 (1-2.5)	2 (1.25-3)	1 (1-1.75)	1 (1-1)	1 (1-1)
ADLs	3 (2-3)	3 (2-4)	3 (2-3.5)	2 (2-3)	2 (2-3)	2 (2-2)	1 (1-1.5)
Pain	2 (1-3)	3 (1.5-3.5)	2 (2-3)	2 (1.25-2.75)	1.5 (1-2.75)	1 (1-1.5)	1 (1-1.5)
Anxiety	2 (1-3)	2 (1-3)	2 (1-3)	2 (2-2.75)	2 (1-3)	2 (1.5-2)	2 (2-2)
EQ -VAS	56 (20)	56 (18)	66 (19)	54 (21)	61 (18)	76 (15)	87 (7)
FACIT-F							
General	11 (5-13)	10 (4.5-12.5)	10 (7.5-16) ×	11 (8-13)	11 (10-14)	12 (9-16)	17 (16-18.5)
Function	3 (2-4)	3 (1.5-4)	2 (1.5-4)	2 (2-4)	3 (2.25-4)	4 (3-5.5)	7 (5.5-7.5)
Psychosocial	3 (2-5)	4 (1-5)	4 (1.5-7.5)	2.5 (2-4)	3 (2-5)	4 (3-6)	7 (5.5-7.5)
Overall	17 (9-20)	17 (8.5-19.5)	15 (10.5-20)	16 (11-20)	18 (16.25-19.75)	20 (15-27.5)	32 (27.5-33.5)
HADS							
Anxiety	8 (4-13)	7 (5-11)	6 (3-10)	11 (4.75-13.75)×	7 (6-11)	5 (4.5-7.5)	1 (0.5-2.5)
Depression	8 (5-10)	8 (5-10.5)	6 (3-11)	8.5 (6-10)	9 (6-10)	4 (3-5.5)	2 (2-5)
HADS							
Borderline	4 (10)	1 (5)	0 (0)	2 (11)	5 (28)	1 (33)	1(33)
Case	31 (78)	15 (79)	9 (47)	14 (78)	9 (50)	2 (67)	0 (0)
Normal	5 (13)	3 (16)	6 (32)	2 (11)	0 (0)	0 (0)	2 (67)
Missing			4 (21)		4 (22)		0 (0)

Data represented as Median (Q1-Q3), Mean (SD), or N (%) as appropriate. Cough NRS, Numerical Rating Score; MRC, Medical Research Council Dyspnoea Score; EQ-5D-5L, EuroQol-5 Dimension- 5 Level; EQ-VAS, EuroQol Visual Analogue Scale; FACIT-F, Functional Assessment of Chronic Illness Therapy – Fatigue; HADS, Hospital Anxiety and Depression Scale. * Indicates the difference from low respiratory intervention and high respiratory intervention. × : $p<0.05$, ××: $p<0.01$, ×××: $p<0.001$.

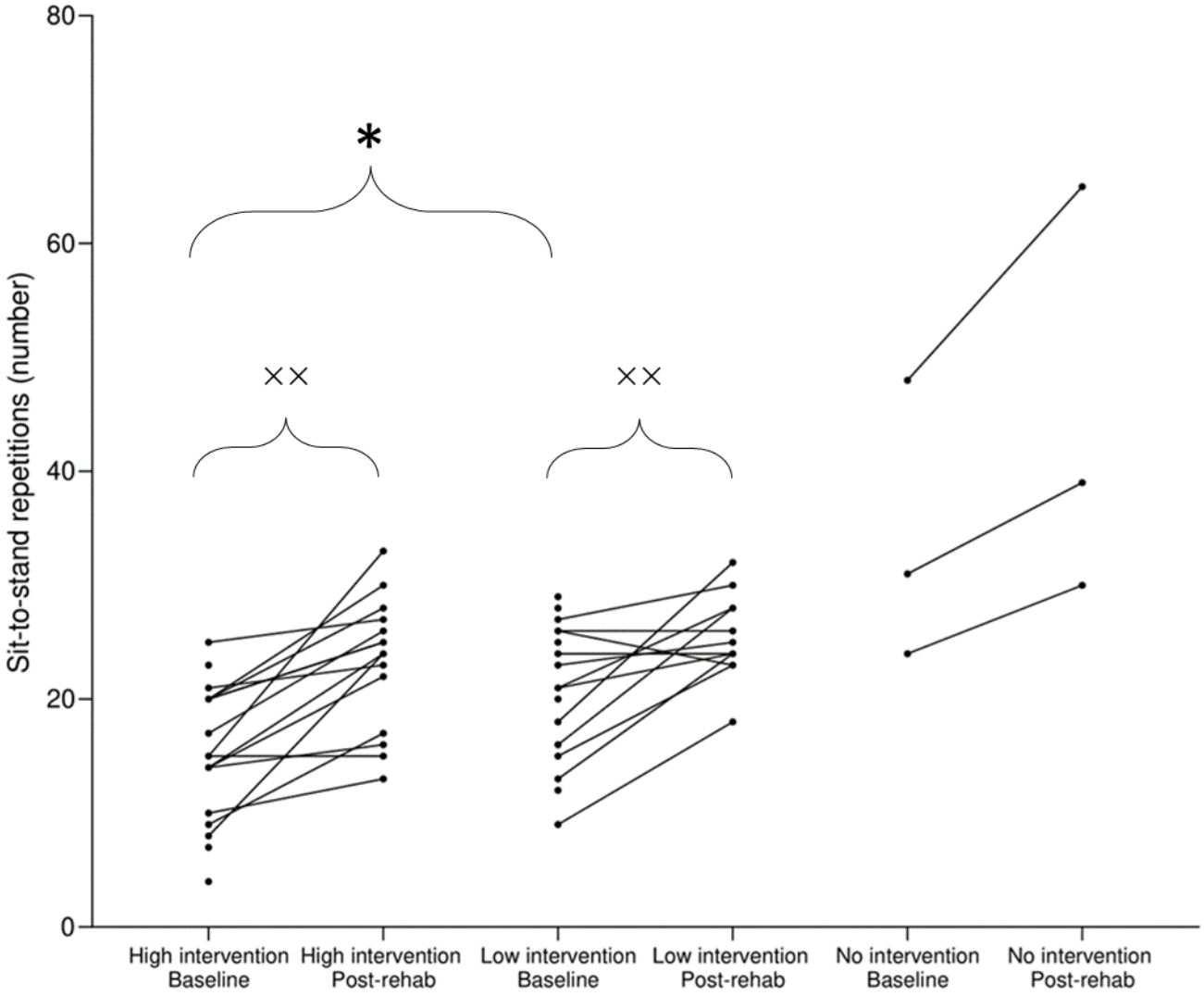

Figure 3 *Change in individual 1 minute sit-to-stand repetitions from baseline following six-weeks of telerehabilitation in patients hospitalised with Covid-19 that required either high respiratory intervention, low respiratory intervention, or no respiratory intervention.*

4.3.2 EQ Visual Analogue Scale (VAS)

EQ-VAS results indicate that all three groups had no statistical difference from pre to post-rehabilitation. Despite this, the high and low respiratory intervention groups scored lower at baseline but had a greater variance of scores compared to the no respiratory intervention group (Figure 4). The high respiratory intervention group had a median increase in score of 10 from baseline to post-rehabilitation, the low respiratory intervention group an increase of 7, and the no respiratory group an increase in average score of 11. The no respiratory intervention group also recorded high VAS scores on both baseline (76) and post-rehabilitation (81). The minimal clinically significant difference for EQ-VAS is an increase of 8 (Zanini et al., 2015) which both the high respiratory intervention group and the no respiratory intervention group achieved. The low respiratory intervention group average increase did not meet the minimal clinically importance.

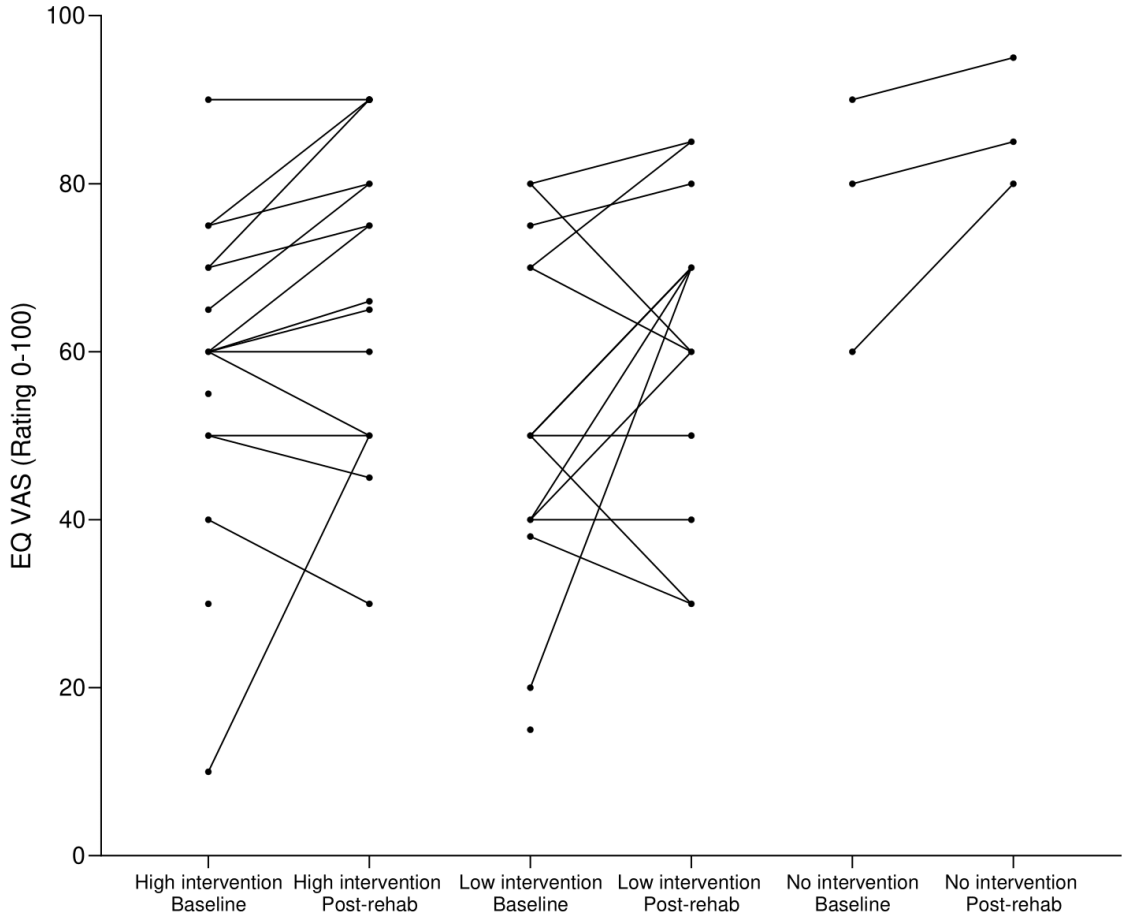

Figure 4 *Change in individual EQ VAS (rating 0-100) scores from baseline following six-weeks of telerehabilitation in patients hospitalised with Covid-19 that required either high respiratory intervention, low respiratory intervention, or no respiratory intervention.*

4.4 Respiratory Symptoms

4.4.1 MRC Dyspnoea scores

The high respiratory intervention group improved, with MRC scores decreasing over the six-week period from 4 (3-4) at baseline to 3 (3-4) post-rehabilitation, $p<0.05$ (Table 4, Figure 5). The low respiratory intervention group plateaued from baseline to post-telerehabilitation, with only a slight, albeit statistically significant, change in median and quartile scores, $p<0.05$ (Table 4). 42% of all participants (from the 3 groups) saw an improvement in scores, scoring lower MRC scores after the 6-week training programme compared to baseline results. The minimal clinically significant difference for MRC dyspnoea is a decrease in scores by 0.5 (Oliveira, Andrade & Marques.,2017). Based on this, it can be determined that both the high respiratory intervention and no respiratory intervention groups met the minimal clinically important difference after 6-weeks of training programme.

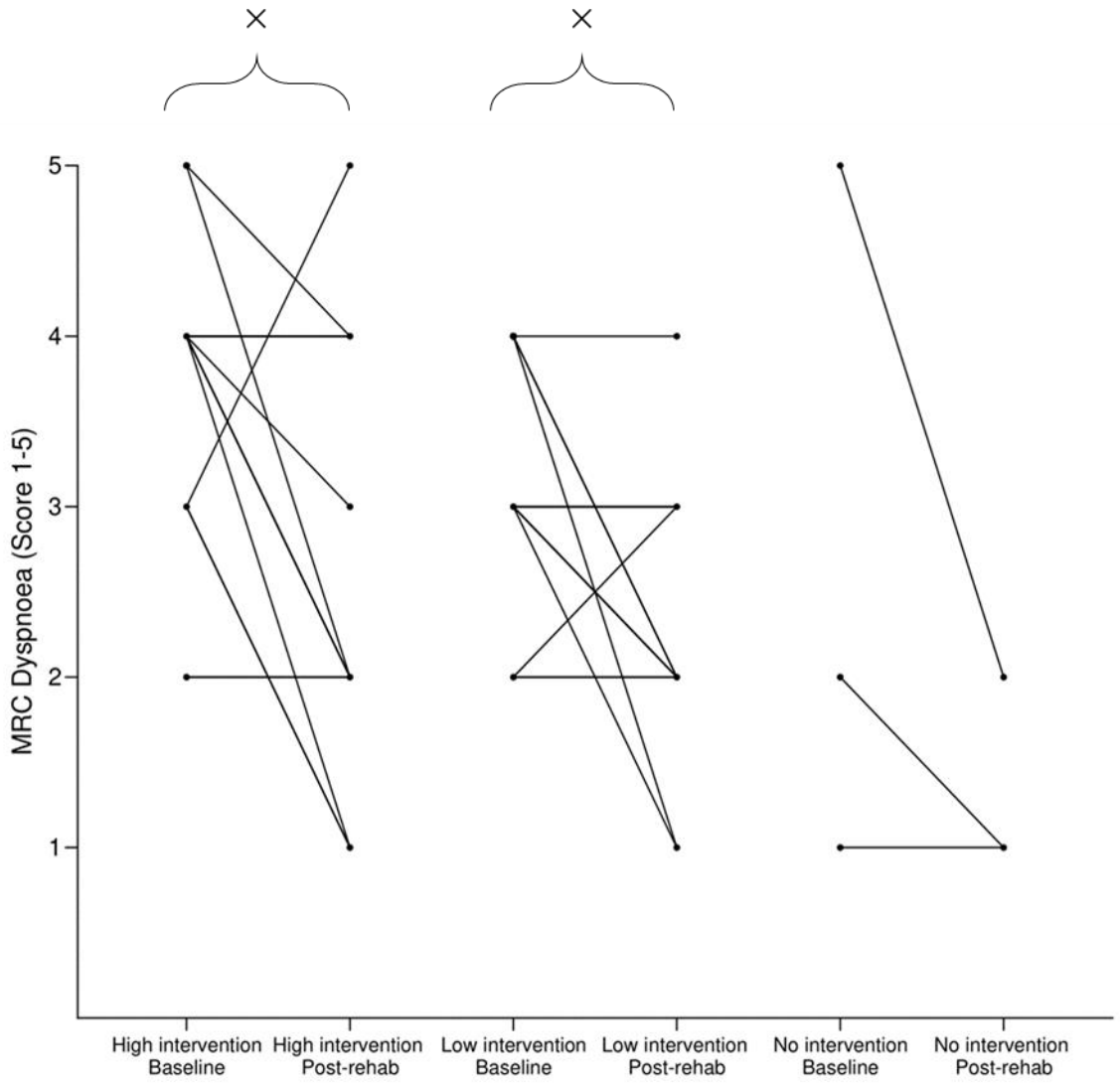

Figure 5 *Change in individual MRC dyspnoea scores from baseline following six-weeks of telerehabilitation in patients hospitalised with Covid-19 that required either high respiratory intervention, low respiratory intervention or no respiratory intervention.*

4.4.2 Cough NRS

All three groups show a decrease in NRS score from baseline to post-rehabilitation, however these did not reach statistical significance (P>0.05). A NRS change score of -2.0 and a percent change score of -33.0% are best associated with the concept of "much better" improvement (Salaffi et al., 2004). Only 23% of all the participants in this trial had a decrease in score of 2. However, table 4 indicates that overall, none of the groups met the minimal clinically significant difference score of -2. Table 4 shows that the low respiratory intervention group and the no respiratory intervention group had decreased cough NRS scores, with a median change of -1. Moreover, table 4 shows that the high respiratory intervention group's cough NRS scores in fact increase from baseline (2 (1-5.5)) to post-telerehabilitation (3 (1-5)).

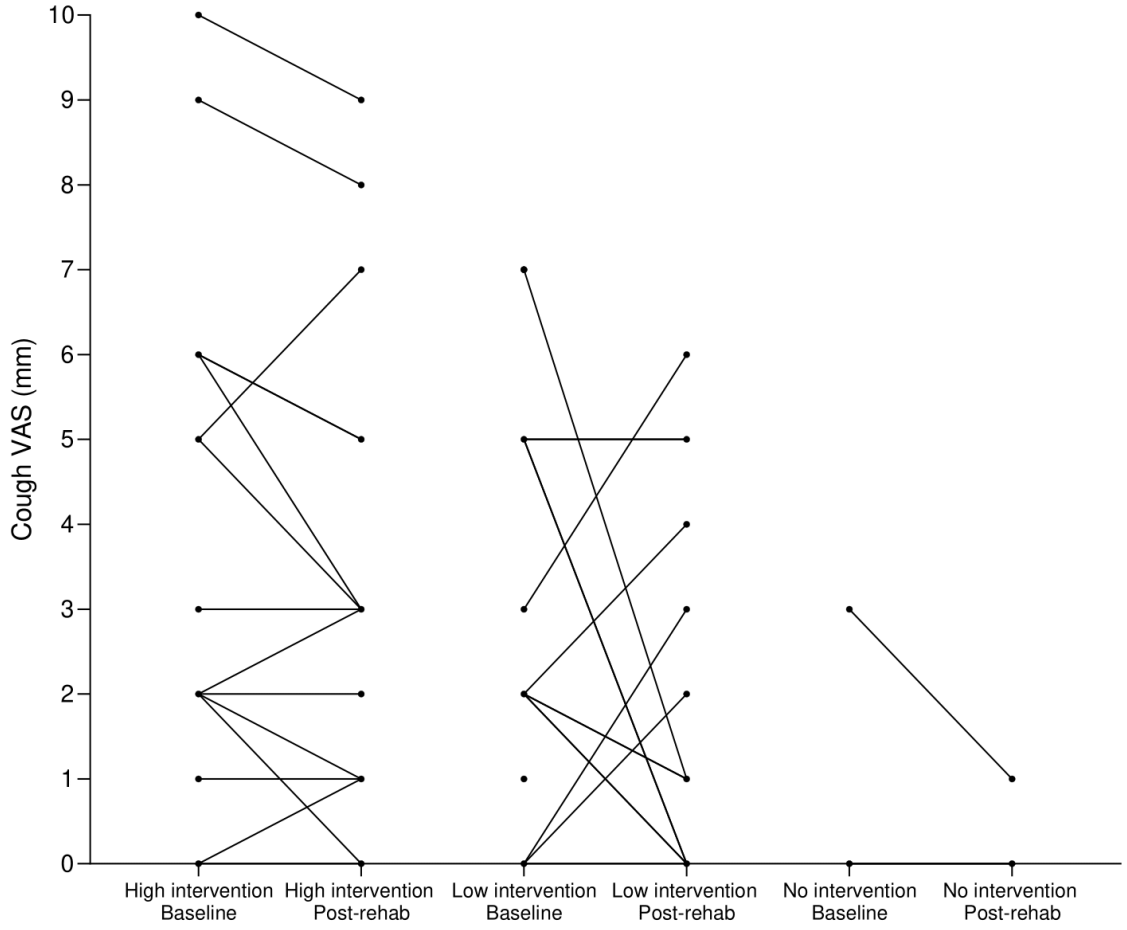

Figure 6 *Change in 1 minute sit-to-stand repetitions from baseline following six-weeks of telerehabilitation in patients hospitalised with Covid-19 that required either high respiratory intervention, low respiratory intervention or no respiratory intervention.*

4.5 Quality of Life

4.5.1. FACIT- F

FACIT-F overall score, which combines General, Functional Ability and Psychosocial health scores, with the scores ranging from 0-36. The higher the score, the better the quality of life. A paper conducted by Cella et al. (2021) states that the FACIT-F clinically significant difference is estimated to be improvement of 3-5 points (overall score). The high respiratory intervention groups median scores decreased from baseline to post-rehabilitation by 2 arbitrary units following rehabilitation. The low respiratory intervention group had an overall improvement of 2, whereas the no respiratory intervention group improved by a score of 12. It can be observed that only the no respiratory intervention group met the clinically important difference score. These changes can be clearly seen in figure 7, with the high and low respiratory intervention groups showing very similar results over the six-week period, and the no respiratory intervention group having the most significant change in results.

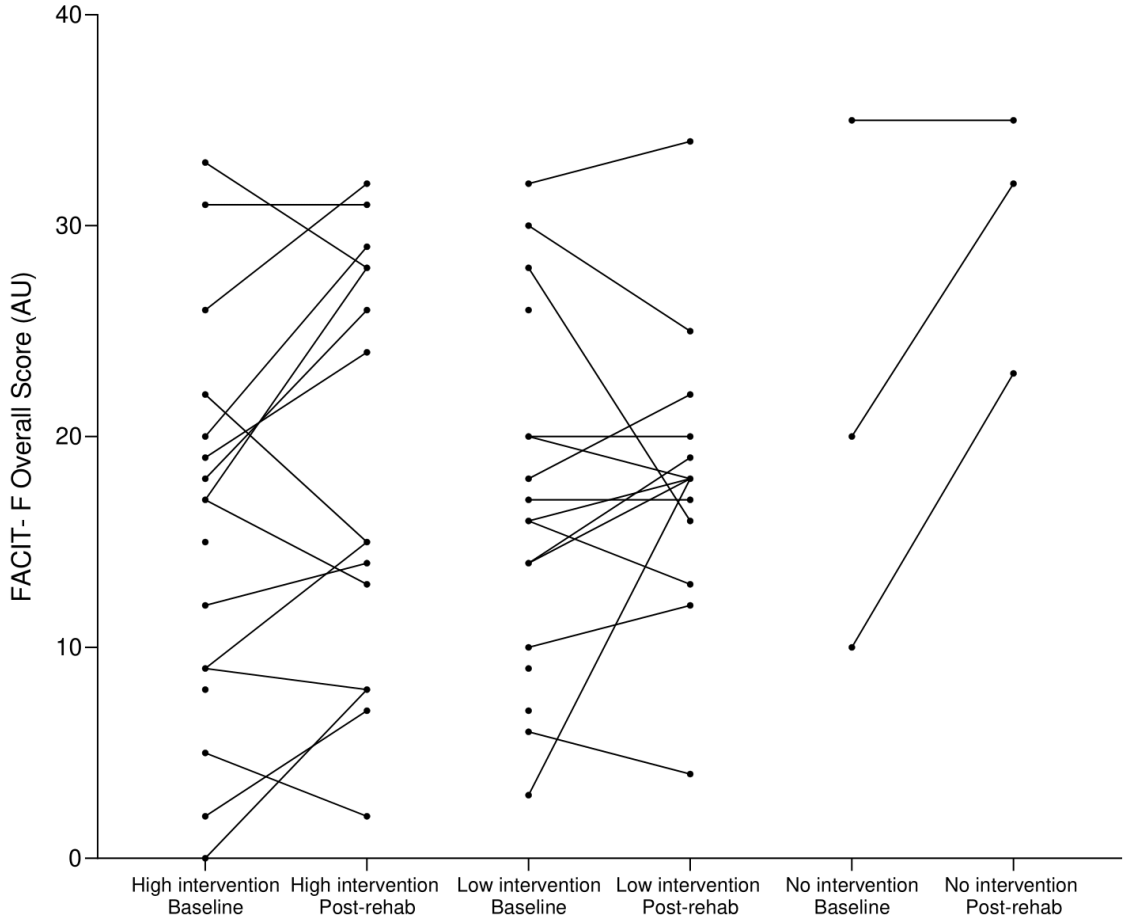

Figure 7 *Change in individual FACIT-F overall scores from baseline following six-weeks of telerehabilitation in patients hospitalised with Covid-19 that required either high respiratory intervention, low respiratory intervention or no respiratory intervention.*

4.5.2 HADS- Anxiety

HADS Anxiety scores for each group all decreased over the 6-week training period (Figure 8). A statistically significant reduction in HADS Anxiety score occurred in the low with the median anxiety rating decreasing from 11 (4.75-13.75) to 7 (6-11), ($p<0.05$). The minimal clinically significant difference for both HADS Anxiety and Depression is a decreased score of 1.7 (Lemay, Tulloch, Pipe & Reed, 2019). Based on this, the low and no respiratory intervention groups met the clinically important difference scores. The high respiratory intervention group did not achieve this clinically important difference.

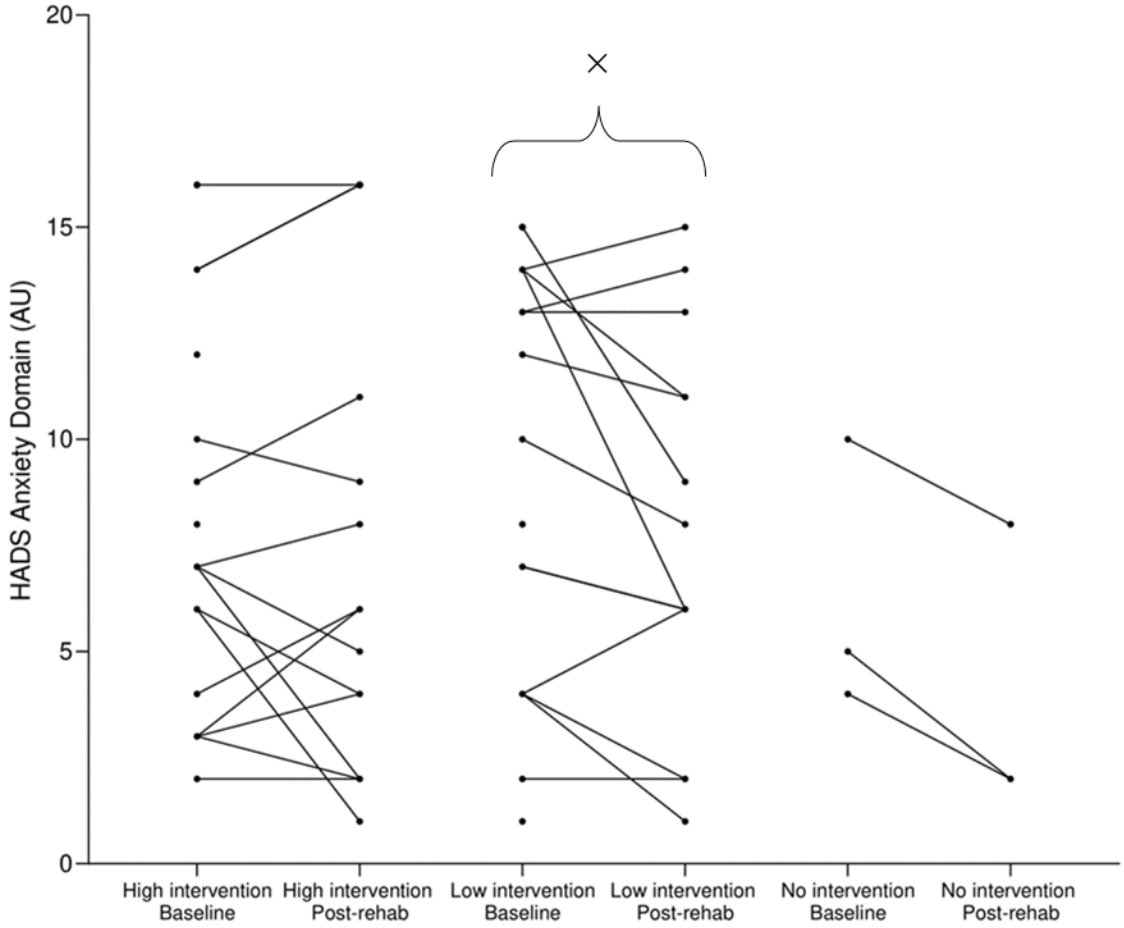

Figure 8 *Change in individual HADS Anxiety domain scores from baseline following six-weeks of telerehabilitation in patients hospitalised with Covid-19 that required either high respiratory intervention, low respiratory intervention or no respiratory intervention*

4.5.3 HADS- Depression

HADS Depression scores decreased by the clinically significant number of 1.7 in both the high respiratory intervention group (decreasing by 2) and the no respiratory intervention group (decreasing by 2) (Table 4). The low respiratory intervention group however shows an increase in median depression scores by 0.5, and therefore does not meet the clinically significance number. Multiple individuals remained to score relatively highly on the HADS Depression scale, even after the six-week rehabilitation programme. The decrease in HADS Depression scores in the high respiratory intervention group and the no respiratory intervention group can also be seen in this figure, with some 25% of participants having a reduced score of 2 from pre to post rehabilitation programme.

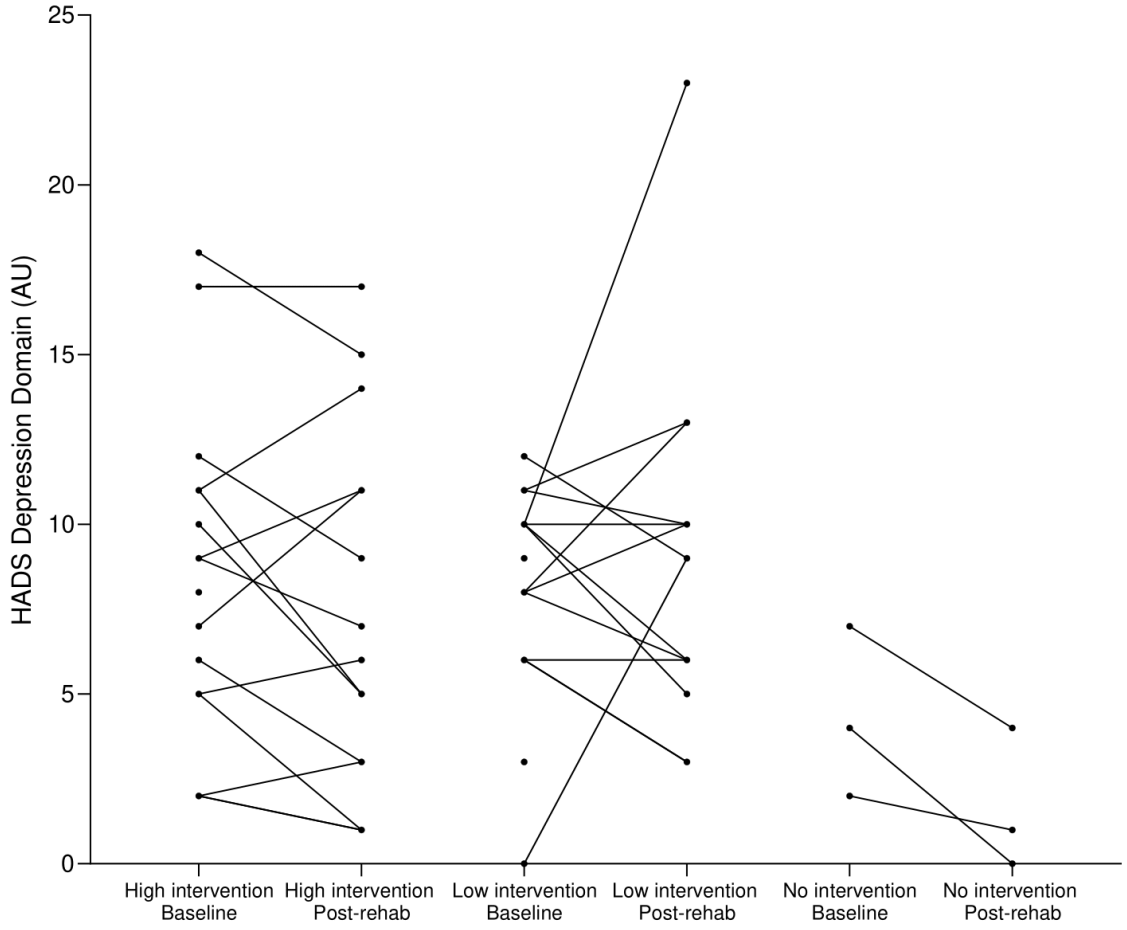

Figure 9 *Change in individual HADS depression domain scores from baseline following six-weeks of telerehabilitation in patients hospitalised with Covid-19 that required either high respiratory intervention, low respiratory intervention or no respiratory intervention.*

5.0 Discussion

The overall aim of this research was to determine the association of medical intervention during hospitalisation with Covid-19 on the outcomes of a telerehabilitation programme. Our data identified greater medical intervention during hospitalisation was associated with reduced exercise capacity, increased fatigue and worse mental health outcomes following hospital discharge. We have also shown improvements in exercise capacity, breathlessness, and respiratory symptoms, beyond the minimal clinically important differences, over the six-week telerehabilitation programme in patients receiving high, low and no respiratory input during hospitalisation. Mental health outcomes such as anxiety, however, did not improve to the same extent in individuals requiring high respiratory intervention during hospitalisation. Our data therefore support the use of telerehabilitation for the treatment of long-Covid following hospitalisation. As mental health outcomes did not change following telerehabiliation, there needs to be research to understand how mental health aspects and additional psychological support may benefit individuals who had high levels of respiratory input during hospitalisation.

Patients requiring more severe hospital intervention had a lower exercise capacity, more severe respiratory symptoms and poorer quality of life than individuals requiring less intense treatment following discharge from hospital. This is likely to be due to severity of Covid-19 infection in the first instance and, therefore, the nature of the patient's treatment whilst hospitalised with Covid-19. Further, our data show that individuals requiring high levels of respiratory intervention spent a median of 14 days in hospital, compared to 4 days in the individuals requiring less intense intervention. The deleterious effect on clinical outcomes seen in the individuals with the highest medical input likely results from more trauma and increased atrophy, following a reduction in physical activity due to longer hospitalisation, higher medical intervention and additional medication (Woods et al., 2020).

Anxiety showed little improvement following telerehabilitation in patients who required high respiratory intervention during hospitalisation. Indeed, the high respiratory intervention group started at a high level of anxiety and remained at high levels of anxiety following rehabilitation. Mechanical ventilation is known to adversely affect anxiety (Chlan, 2003)..The heightened anxiety scores at discharge and post-tele-rehabilitation programme also suggests that those with high intervention need more concentrated efforts on the mental health aspects of rehabilitation. Our data suggest that individuals suffering with long-Covid, should be provided psychological support, either as part of their rehabilitation programme or independently, and particular attention should be given to individuals who required higher respiratory care.

Figures 8, 9 and 10 show the Quality of Life of participants increased over the 6- week rehabilitation programme. Figure 8 shows FACIT-F, a combination of General, Functional Ability and Psychosocial health scores, with the high respiratory intervention groups scores barely changing. The high respiratory intervention groups median scores from baseline to post-rehabilitation decrease over the six-week period. This, along with very little changed scores in HADS Depression rating (figure 10) could again indicate those placed on high respiratory intervention methods or cared for in high intensity environments such as ICU suffered some form of trauma, which then reflected in their day to day lives after discharge.

The NRS Cough score did not improve in the high respiratory intervention group. This group included a large number of individuals who had full endotracheal intubation, who potentially suffered damage to the trachea after having been intubated and may be suffering with irritation with a cough being a resulting symptom (Ayoub et al., 1998). Patients' cough may

have also been due to greater lung inflammation in patients requiring higher levels of intervention (Low et al., 2022). This correlates with the fact that the no respiratory intervention group scored low cough NRS scores both pre- and post-rehabilitation, suggesting that they suffered no/less tracheal damage during hospitalisation interventions and less airway inflammation.

5.1 Comparison with previous literature

Like the findings of Carfì, Bernabei & Landi (2020) and Davis et al. (2021), all participants of this trial suffered with elongated Covid-19 symptoms, including fatigue, dyspnoea, a reduction of physical and mental activity, and reduced quality of life, with many suffering with a combination of symptoms. Similarly to Davis et al. (2021), our participants reported Covid symptoms beyond 90 days of covid symptom onset or a positive test result. Interventions to attenuate these symptoms are therefore required.

The telerehabilitation intervention presented here followed pulmonary rehabilitation principles advocated by Rochester et al (2015) and Hill (2006), utilising multidisciplinary teams, implementing exercise training, education and behaviour change techniques, with the aim to improve physical and social function of patients. This protocol followed the usual structure of pulmonary rehabilitation, offering two group sessions a week over a six-week period, but was delivered remotely.

A variety of telerehabilitation protocols have been utilised in patients with Covid-19 previously. Indeed, Li, J. A et al., (2021) utilised a 6-week home-based group tele-rehabilitation programme, which was able to engage participants who were physically unable to leave the house, but able to participate from their own homes. Similar to our findings, Li, J.

A et al. (2021) documented improvements in physical fitness (6-minute walking distance) and quality of life. Our protocol differed somewhat from that of Li et al., with the inclusion of social and educational components.

Zamponga et al. (2021), Al Chikhanie et al. (2021) and Gloeckl et al., (2021) used the 6-minute walk test to measure exercise capacity of post-Covid and long-Covid treatment, where this research used the one-minute sit-to stand test- an equivalent method of measuring exercise capacity (Meriem et al., 2015). It can be noted that the one-minute sit-to-stand is a substantial substitute for home-based interventions (Holland et al., 2020). Despite this difference, improvements in exercise capacity were seen in all studies. Specifically, our data aligns with Gloeckl et al.'s (2021) that identified improved exercise capacity in patients with mild-moderate Covid-19 disease, and in patients diagnosed with severe-critical Covid-19 (intubated).

The sustained increase in anxiety in the high respiratory care groups seen here has been shown previously. Al Chikhanie et al. (2021) identified that there were still significant psychosocial impairments in hospitalised Covid-19 patients following a five-week pulmonary rehabilitation programme (which included respiratory exercises, muscle strengthening and balance exercises) with depression scores (HADS-D) increasing in the low respiratory intervention group.

Our data adds to the limited research into the effects of pulmonary rehabilitation, and telerehabilitation on those infected with Covid-19, and suffering from Long Covid. This research particularly enhances research conducted by Al Chikhanie et al. (2021) and Li, J. A

et al., (2021). Indeed, we have shown benefits in additional outcome measures, in mental health and breathlessness, not previously reported.

5.2 Strengths and Limitations

This research has provided an insight into the change in physical and mental health in a cohort of patients who underwent different methods of treatment during hospitalisation with Covid-19 infection following a 6-week telerehabilitation programme. The results from this research show that a 6-week telerehabilitation programme has been beneficial in improving exercise capacity of long-Covid sufferers regardless of hospital interventions. This secondary data analysis complements the findings from our randomised, wait-list controlled trial, that was the first to show group-based pulmonary tele-rehabilitation was safe, feasible and beneficial and well-received in patients hospitalised with Covid-19. This randomised controlled trial has provided insights aimed to facilitate better patient centred care in the management of Covid-19 survivors.

The secondary analysis conducted here has allowed for more nuanced conclusions to be drawn, for example the divergence in improvements in mental health components in the high respiratory care group. The limitation however of secondary data analysis is the rather limited sample size in each group. Prospective research is therefore required to corroborate our findings on a larger scale. Further, of the 228 individuals assessed for eligibility, only 40 took part, with 13 dropouts in total. A larger sample size would provide more robust results across the three research groups. A further limitation of this study is that it is difficult to compare results to existing research, given limited research available on the effects of pulmonary/tele rehabilitation on individuals suffering with long-Covid. Further, the research using

telerehabilitation have used a variety of different protocols. A novelty of our rehabilitation programme is the use of group-based' telerehabilitation. Research conducted by Beauchamp & Eys (2014) identified that in exercise groups, increased cohesion led to better adherence rates and group performance.

Due to the relatively new disease and limited research, we recorded a large number of outcome measures, typically seen to improve following rehabilitation for COPD. Clinically significant differences for each outcome were obtained from research unrelated to Covid-19, (e.g. CVD, Paroxysmal Nocturnal Haemoglobinuria, chronic musculoskeletal pain), as such it is difficult to confirm clinically important changes in our population.

Some technological problems affecting the running of the telerehabilitation service, including internet failure, difficulties connecting to WEBEX, and sound/video issues with the participants computers, meant that a few sessions had to be cancelled. This sometimes resulted in no classes in one week, potentially hindering the rehabilitation programme, and participants progression. If this way of providing a tele-rehabilitation session is repeated by other investigators or in clinical practice, more reliable technology is required. Further, engagement could be enhanced by providing alternative class timings to facilitate engagement from individuals who have returned to work but want to be involved in a telerehabilitation classes. Classes should remain a similar size (up to 6 participants) to ensure the individual monitoring participants during the rehabilitation session can do so accurately and safely.

Digital inequalities are also worth discussing in the context of this research. Indeed, in 2019, the city of Hull was 'one of the 20% most deprived districts/unitary authorities in

England'(Public Health England, 2020) with 27.4% of the city's children living in low income families (Public Health England, 2020). As of March 2023, 21% of individuals in Hull are claiming universal credit, 7% higher than the national average in England (Data Observatory, 2023). The city of Hull also suffers with multiple health inequalities, with Public Health England finding that 'levels of excess weight in adults (aged 18+), smoking prevalence in adults (aged 18+), smoking prevalence (in routine and manual occupations) and physically active adults (aged 19+) are worse than the England average' (Public Health England, 2020). Offering telerehabilitation to these communities may not have been beneficial, as access may have been somewhat limited, with patients potentially being unable to afford computers/laptops/electronic devices and Wi-Fi to access these classes. This may have been detrimental to our study, as the highest number of hospital admissions for Covid-19 patients were in the 3 most deprived deciles in the city of Hull (Office for Health Improvement and Disparities., 2023). If a different method of rehabilitation was offered other than telerehabilitation, there may have been more uptake, and therefore a larger sample size for our study. We also acknowledge a sample bias, in that only individuals with access to appropriate technology were able to participate in the study.

A further limitation identified by this study is that there was a greater need for an interdisciplinary team rather than a multidisciplinary team. Despite the fact that nutritionists and sport and exercise scientists were asked to work alongside the multidisciplinary team of consultants, physiotherapists and nurses at Castle Hill Hospital, this study identified that there were many more complex individuals with multi-system disabilities compared to generic Long Covid symptoms, for example some of the cohort suffered from severe skin issues, amputated limbs, and neurological problems such as permanent pins and needles. This has indicated that more a bespoke interdisciplinary approach is needed to target a wider group of patients.

5.3 Interpretation and Mechanisms

Exercise capacity (sit-to-stand scores) increased in all three groups. The 6-week rehabilitation programme involved exercises which targeted specific muscle groups such as the glutes, hamstrings and quadriceps resulting in muscular hypertrophy, which could provide an explanation for 63% of the participants improving their sit-to-stand scores, as muscular strength and endurance likely improved. A research paper published by Vaidya et al. (2016) states that 'an improvement of at least three repetitions is consistent with physical benefits after pulmonary rehabilitation. Half of the participants in this study increased their sit to stand performance by 3 or more. Fifty-two percent of the high respiratory intervention group improved their sit to stand score by 3, 44% of the low respiratory group improved by 3, and 100% of the no respiratory intervention group. The results show the no respiratory intervention group scoring much higher in the one-minute sit to stand test. This may indicate that generally, the no respiratory intervention group did not suffer as much respiratory damage or muscle atrophy and were therefore starting from a higher baseline.

The individuals not requiring hospital intervention had a better quality of life score (EQ VAS) than hospitalised patients. Within the hospitalised cohorts, the high and low respiratory intervention groups displayed very varied scores throughout the 6-week programme. This indicates that those that needed any type of respiratory intervention tended to not feel as good on a day-to-day basis, be it psychologically or physically. This may have been due to the fact that those who needed respiratory intervention were cared for in high intensity situations, with some potentially suffering trauma from their admission to hospital, particularly those treated with ventilation/intubation. An example of this has been seen in Scragg, Jones, & Fauvel's (2001) research, who identified that 47% of their cohort of ICU patients reported

clinically significant anxiety and depression scores (from the HADS rating). This has further been reported by Hatch et al. (2018), who identified that 46% of patients developed anxiety and 40% developed depression following ICU discharge.

Respiratory Symptoms improved over the 6-week rehabilitation programme. Breathlessness may have reduced, as atrophied muscles such as the intercostals and diaphragm will have strengthened with endurance exercises (Powers et al., 1990) Further, breathlessness is known to be increased in unconditioned individuals (Hill & Annesley,. 2020). The six-week telerehabilitation programme aimed to gradually progress patients, allowing for the positive cycle of activity to take place. The more activity the individual does, the stronger the muscles become. This will have in turn provided more efficient oxygen delivery, enabling participants to progress in physical fitness levels. This model is based on patients with COPD, and depending on a patient's starting point, the time it takes for the cycle to occur will differ (British Lung Foundation, 2022).

A specific investigation by Tingey, Bentley & Hosey, M. M. (2020) who researched the understanding and mitigation of trauma in ICU survivors of Covid-19 highlight that individuals within the ICU setting are at a high risk of experiencing significant psychological difficulties, and patients with COVID-19 are particularly susceptible to such experiences, which can impact their recovery process. Despite this, there was overall improvement in exercise capacity/wellbeing, respiratory symptoms and quality of life for all participants, suggesting that telerehabilitation is beneficial to all in some capacity.

5.4 Clinical Interpretations and Practical Implications

The findings of this study could provide the foundations of future research into the treatment of long-Covid using telerehabilitation, or even comparing outcomes between telerehabilitation with face-to-face pulmonary rehabilitation for long Covid. Using telerehabilitation could improve patients' accessibility to pulmonary rehabilitation programmes, particularly for those who are anxious about coming into a hospital setting when coronavirus is still in circulation, or for those who, like many of the participants used in this study, at the beginning were physically unable to leave the house due to their symptoms. The findings of this research indicates that further investigation is needed to establish suitable minimally clinically significant differences for Covid and Long Covid patients, as many of the alternative clinical differences were extracted from other clinical conditions are not necessarily appropriate to this population. Further research should include a well-structured psychological provision alongside a telerehabilitation programme, specifically for patients requiring high respiratory input during hospitalisation who display higher anxiety levels post-discharge and see less improvement following telerehabilitation.

This secondary analysis was part of a randomised, wait-list, controlled trial which identified the highest number of dropouts was the wait list group. The main reasons for dropouts being time constraints of the participants as they had returned to work, and losing contact with some participants, also most likely because patients had returned to work or no longer wanted to participate in the exercise classes due to the wait time. It would be beneficial if future research reduced wait list intervention time or started sooner after recruitment and ensure that exercise programmes are at suitable times to ensure those who work during the week also have access to a rehabilitation programme.

An issue which was encountered during some rehabilitation sessions was problems with computers and technology. Several sessions had to be cancelled due to technical issues, with one individual having to drop out as their home technology was not compatible with the selected web conferencing platform (Cisco Webex). With the lifting of Covid-19 restrictions, it is likely that more 'in-person' classes will be available for long covid sufferers in the future, making this type of service more accessible for individuals. Feasibility was not an outcome measure or aim of this research, however data from this can be found in Simpson et al.,'s (2023) paper published in the European Research Journal where the feasibility outcome measures are reported and discussed in detail.

Despite these issues, the tele-rehabilitation intervention proved relatively feasible for both the fast track and wait list groups, with 67.5% of all participants completing the 6-week exercise intervention.

6.0 Conclusion

This study has shown that telerehabilitation provided significant improvements in exercise capacity, respiratory symptoms and quality-of-life measures in patients hospitalised with Covid-19, regardless of the level of respiratory intervention they required. This study has shown that physical and mental wellbeing aspects were improved, overall increasing the quality of life for the participants of this research, therefore providing support that telerehabilitation is effective for the treatment of hospitalised Covid-19 patients, with ongoing Covid symptoms. These findings add to the body of evidence that suggest that tele-rehabilitation should be offered to patients hospitalised with Covid-19 regardless of the level

of respiratory input received and additional psychological support should be considered for patients requiring more invasive respiratory intervention.

7.0 References

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