SYMPTOM PATTERNS AND THEIR ASSOCIATION WITH INFLUENCING

FACTORS IN ADULTS WITH LONG COVID

- A SECONDARY ANALYSIS

by

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Presented to the Faculty of the Honors College of

The University of Texas at Arlington in Partial Fulfillment

of the Requirements

for the Degree of

HONORS BACHELOR OF SCIENCE IN NURSING

THE UNIVERSITY OF TEXAS AT ARLINGTON

May 2023

ACKNOWLEDGMENTS

ABSTRACT

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The University of Texas at Arlington, 2023

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Currently available information on the risk factors, manifestation, treatments, and long-term effects of the long COVID is inconclusive, requiring further research to identify timely interventions that may help treat long COVID patients, reduce symptom burden and restore functional abilities. This research aims to analyze symptom patterns and their association with influencing factors in adults with long COVID by examining intercorrelations among symptoms, identifying influencing factors of symptoms, and examining the associations of symptoms with disability and quality of life over time in long COVID patients. The Theory of Unpleasant Symptoms developed by Lenz et al. (1997) is applied as the conceptual framework to guide the proposed research. The study's goal is to contribute to identifying treatment options and means of prevention for further disability from long COVID and developing evidence-based practice guidelines for

symptom management in long COVID patients. This study was a descriptive secondary analysis using data collected from an ongoing longitudinal study consisting of 19 subjects with long COVID. The present study found that participants have been experiencing persistent COVID-related symptoms for months. Among five symptoms, participants reported "quite a bit of" fatigue, moderate amount of dyspnea with daily activities, and "somewhat level" of pain interference/intensity. In addition, participants reported that they had at least one cause of cognitive discomfort such as difficulties with concentrating, headache, or brain fogginess. The majority of participants were female, were overweight or obese based on BMI (kg/m2) >25.0 and had high number of COVID-19 symptoms at the time of COVID-19 diagnosis. In addition, some of them had common co-existing conditions of Connective Tissue Disorders or Chronic Pulmonary Obstructive Disorders. Moreover, compared to the general United States population, they had poorer quality of life composed of physical and mental health components. Thus, there is a need for further research replicating these results in a larger sample and examining the interventions to improve quality of life by reducing symptom burden and improving physical and emotional function.

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CHAPTER 1

INTRODUCTION

1.1 Introduction of Long COVID

There have been 102,998,014 cases of COVID-19 in the United States with a total of 1, 113, 254 deaths resulting from COVID-19.94 (CDC, 2022). Of the people who have been diagnosed with COVID-19, up to 30% develop post-acute sequelae of COVID-19, the interchangeable term for long COVID (CDC). This population experiences persistent, debilitating, variable, and inter-related symptoms for weeks or months. The common symptoms in adults with long COVID are dyspnea (shortness of breath), fatigue, pain, chest tightness, and "brain fog." The number and severity of symptoms perceived by these individuals, or "symptom burden," contributes to limitations in physical and psychosocial function, altogether limiting the ability to perform activities of daily living and thereby reducing quality of life (Amdal et al., 2021; Ladds et al., 2020; Lopez et al., 2021; Torres-Castro et al., 2021). Thus, symptom burden from long COVID may result in significant and multi-faceted personal and societal challenges.

However, it is unknown how symptom patterns in adults with long COVID affect their long-term health. There is a pressing need to comprehensively examine symptom patterns including the associations with other outcomes (i.e., limitations on physical and psychosocial function and quality of life) as well as the effects of demographic factors (age, gender, education, comorbidities) and severity of COVID-19 (number of COVID-19

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symptoms at the time of COVID-19 diagnosis) on persistent COVID-19-related symptoms. In addition, current guidance for accurate diagnosis and treatment for clinicians and researchers is lacking. Given the continued report of COVID-19 cases and the long-lasting health impacts, knowledge about how symptoms occur together and affect each other and what factors influence symptoms is essential for more effective and efficient assessment of symptoms for developing therapeutic and clinical interventions in adults with Long COVID.

<u>1.2 Statement of Purpose and Research Question</u>

This study is designed to gain a better understanding of the persisting symptoms in adults with long COVID. This research aims to analyze symptom patterns in adults with Long Covid, how influencing factors composed of physiological and situational factors impact symptom patterns and how persistent symptom patterns impact the patient's quality of life. Therefore, for the proposed study, the research questions are:

1. What are the characteristics of symptom patterns in adults with Long COVID?

2. Are symptoms patterns related to influencing factors in adults with Long COVID?

3. How does the persistence of long COVID symptoms impact the subject's quality of life?

CHAPTER 2

LITERATURE REVIEW

2.1 Defining Long Covid

Long COVID describes a range of persistent symptoms following the COVID-19 infection. There is currently no widely accepted definition for the condition. Many studies use terms such as post-acute Covid-19 syndrome, post-acute Covid or post Covid to refer to persisting symptoms of COVID. The working definition of COVID developed by the Department of Health and Human Services (HHS) is:

Long COVID is broadly defined as signs, symptoms, and conditions that continue or develop after initial COVID-19 or SARS-CoV-2 infection. The signs, symptoms, and conditions are present four weeks or more after the initial phase of infection; may be multisystemic; and may present with a relapsing– remitting pattern and progression or worsening over time, with the possibility of severe and life-threatening events even months or years after infection. Long COVID is not one condition. It represents many potentially overlapping entities, likely with different biological causes and different sets of risk factors and outcomes. (para. 3)

2.2 Long Covid: Prevalence and Statistics

According to the Centers for Disease Control and Prevention (CDC) (2022), over 3,500 Americans have died from long COVID (CDC, 2022). As of April 2022, approximately 3.8% of all COVID-19 deaths involved long Covid (CDC, 2022). Men accounted for 51.5% of long COVID deaths while women accounted 48.5% (CDC, 2022).

Additionally, about 14% percent of all adults in the United States have experienced long COVID at some point (CDC, 2023).

<div align="center">2.3 Consequences of Long COVID</div>

2.3.1 Potential Etiology of Long COVID

The etiologies of long COVID remain unclear because of its complexity. Multiple persistent symptoms may be related to impairment in multiple physiologic systems resulting from virus-specific pathophysiologic changes and inflammatory damage, immobility and physical deconditioning, and/or mental distress in response to acute infection (Tenforde et al., 2020) The first pulmonary sequalae are fibrotic changes in the lungs and restrictive pulmonary illness that are possibly responsible for dyspnea and chest tightness (Nalbandian et al., 2021; Torre-Castro et al., 2021). Individuals with long COVID have reported similar symptoms (fatigue, myalgia, dyspnea, tachycardia, reduced exercise tolerance, anxiety, "brain fog") to the symptomatology of cardiovascular autonomic dysfunction.

An integrative review was conducted by Pierce et al. 2022 to evaluate the post-COVID-19 syndrome from a biological perspective. The definition of post-COVID-19 syndrome according to (Pierce et al., 2022) is, "persistent symptoms and/or complications lasting beyond 4 weeks" (para. 1). The definition of post-COVID-19 by Greenhalgh et al. (2020) is explained by (Pierce et al., 2022) as "an extended illness for more than 3 weeks after the acute onset of symptoms" (para. 20). While the definition of chronic COVID-19 according to (Pierce et al., 2022) is, "persistent symptoms extending beyond 12 weeks after the onset of symptoms." (para. 20). Other terms used to describe persistent symptoms of COVID-19 include post-COVID-19 syndrome, long COVID-19, and post-COVID-19

condition (Pierce et al., 2022). This research discovered that the four pathophysiological categories involved in long COVID include virus-specific pathophysiological variations, oxidative stress, immunologic abnormalities, and inflammatory damage (Pierce et al., 2022). The article further discusses how COVID-19 has high morbidity and mortality rates due to severe damage of multiple organs (Pierce et al., 2022). Many of the symptoms experienced by individuals with post-COVID-19 syndrome are due to damage to the respiratory, cardiovascular, neurological, gastrointestinal, and other systems (Pierce et al., 2022). While many make it through the acute phase of the illness, COVID-19 can significantly impact their quality of life due to persistent symptoms including dyspnea, fatigue, cognitive impairment, and chest pain (Pierce et al., 2022). Since many individuals are unable return to their usual state of health after contracting COVID-19, it is important to understand the pathophysiology of long COVID -19. This study helps shed some light on what systems may be involved in the post-covid syndrome.

A retrospective cohort study by Sudre et al. (2021) utilized the COVID symptoms Study app to discover that early symptoms patterns may be used to predict a diagnosis of long COVID. In this study, short COVID and long COVID were distinguished at seven days. The study found that long COVID was more likely with increasing age, body mass index and female sex. Experiencing five or more symptoms during the acute phase of the infection is also associated with developing long COVID. By identifying the early indicators of long COVID, we can help prevent progression in COVID-19 patients. The most commonly reported symptoms were fatigue (97.7%) and Intermittent headaches (91.2%) (Sudre et al., 2021).

2.3.2 Symptom Burden in Long COVID

A retrospective cross-sectional study conducted by David et al. (2021), used an online survey to trace symptoms in patients with suspected and confirmed diagnosis of COVID-19 (Davis et al., 2021). Long Covid is defined as, "a collection of symptoms that develop during or following a confirmed or suspected case of COVID-19, and which continue for more than 28 days." (para. 7). The majority of the respondents took longer than 35 weeks to recover. The symptoms that were most frequently present amongst the respondents include fatigue, malaise, and cognitive dysfunction. According to the study, many of the respondents had not recovered by seven months and were unable to return to previous levels of work due to debilitating symptoms (Davis et al., 2021). The results from the study suggest that long Covid symptoms affect multiple organ systems and include a wide range of neurologic symptoms. Memory and cognitive dysfunction were experienced by over 88% of the respondents and had a significant impact on daily life. The study also identified many symptoms which are not commonly associated with long COVID such as seizures, suicidality, vision loss and facial paralysis. This research provides valuable insight into how symptom burden can cause significant change in quality of life of patients with long Covid (Davis et al., 2021).

A systemic review and meta-analysis conducted by Lopez et al. (2021) assessed the long-term health effects of COVID-19. The results of the study estimated that 80% of the patients with COVID-19 develop one or more long-term symptoms (Lopez et al., 2021). The study assessed symptoms in neurological, respiratory, gastrointestinal, cardiac, endocrine, dermatological, hepatic, and renal systems. A total of 55 long-term effects associated with COVID-19 were identified. Most common among these symptoms were fatigue (58%), headache (44%), attention disorder (27%), hair loss (25%) and dyspnea

(24%). The study found that COVID-19 can lead to a wide range of long-term health problems affecting multiple organ systems, including respiratory, cardiovascular, neurological, and psychological symptoms. The study also indicates that multi-disciplinary teams are crucial to developing preventive measures, rehabilitation techniques, and clinical management strategies with a patient-centered approach designed to address long COVID-19 care (Lopez et al., 2021).

Long COVID symptoms are varied and present throughout the body. Davis et al. (2021) reported that, among 3,762 respondents, fatigue (77.7%), post-exertional malaise (72.2%), and cognitive impairment (55.4%) were the most common symptoms. Lambert et al. (2021) verified that among 5,163 COVID-19 survivors who experienced symptoms for more than 21 days, more than 50% of them reported fatigue, headache, shortness of breath, and difficulty concentrating.

Other studies also reported fatigue (79.0%), headache (55.3%), shortness of breath (55.3%), difficulty concentrating (53.6%) dough (49.0%), changed sense of taste (44.9%), diarrhea (43.9%), and muscle or body aches (43.5%) (Logue et al., 2021).

Pizarro et al. (2021) conducted another systemic review of nine studies that applied a physical capacity test in COVID-19 patients, post-infection. As there is little knowledge about the impact of long COVID on patients' lives, this study aims to understand how contracting COVID-19 can affect activities of daily living (ADL) in patients experiencing persistent symptoms. According to the all the studies in the research, there was a reduction in ADL performance in COVID-19 patients past the acute phase of the infection. According to the results, functionality prior to the COVID-19 infection is an important predictor of the severity and mortality of the disease. Impairment such dyspnea, weakness,

myalgia, and pain significantly limit the patient's ability to perform ADL (Pizarro et al., 2021). The patients who had the worse results were older patients or patients with complications during their hospital stay such as mechanical ventilation, delirium or cerebral microbleed. Participation in a rehabilitation program was a significant factor in modifying the outcomes of functional capacity. However, not all patients had improvement in performance. The article also highlights the importance of assessing patients' ADL status in both the acute and post-acute phases of COVID-19 to formulate appropriate interventions. The study also explores different tools that can be used to assess ADL such as the Barthel Index, ADL score, Functional Independence Measure, Composite Functional score, Modified Rankin scale and EQ-5D-5L (Pizarro et al., 2021).

2.3.3 Risk/ Influencing Factors of Long COVID

There are several predictors of Long COVID. Women are more likely to suffer from Long COVID. and experience fatigue. Risk for Long COVID increases with age, body mass index, and comorbidities, such as hypertension or diabetes (Lavie et al.2019). In spite of a lack of association between the severity of the acute COVID-19 infection and Long COVID (Novak et al., 2022), experiencing more than five symptoms during the first week of COVID illness is positively associated with Long COVID (Malkova et al., 2021). Black individuals carry higher Long COVID burden due to the increased presence of comorbidities (e.g., obesity, cardiovascular disease, and diabetes) and inadequate healthcare access (Malkova et al., 2021).

<u>2.4 Symptom Management in Long COVID Patients</u>

A narrative review of literature on existing knowledge of post-acute COVID-19 was conducted by Greenhalgh et al. in 2020. This review provides an overview of the

symptoms and management of Long COVID (Greenhalgh et al., 2020). According to Greenhalgh et al. (2020), post-acute COVID-19 is described as, "extending beyond three weeks from the onset of first symptoms and chronic covid-19 as extending beyond 12 weeks." (para. 2). According to the review, around 10% of patients who have tested positive for COVID-19 experience symptoms beyond the first 3 weeks. The authors describe the various symptoms of post-acute COVID-19, including fatigue, breathlessness, cognitive impairment, and mental health problems. The research strongly recommends a patient-centered approach to management that includes symptom monitoring, individualized care plans, and multidisciplinary support. Medical management for patients with long COVID includes symptom management, controlling long term conditions, treating complications, and empathetic care. The study highlights the importance of communication between patients and healthcare providers and recommends the use of tools such as patient diaries and symptom trackers to facilitate this communication. Although not needed for most patients, specialist referrals such as respiratory, cardiology and neurology can be made to help with symptom management (Greenhalght et al., 2020).

An article by Nquyen- Hoang, published in the British Journal of Nursing, discusses the potential benefits of nutrition therapy in managing the symptoms of patients with long COVID. The definition of long COVID used by the article is the clinical definition released by the World Health Organization (WHO) which is when, "symptoms are continuing for 3 months and beyond." The author explores how dietary and lifestyle factors can prolong symptoms and impact the ability to return to full health (Nguyen, 2021).

The Royal College of General Practitioners conducted a survey consisting of approximately 1,500 individuals who experienced a loss of smell and taste during the onset

of COVID-19. According to the survey findings, more than half the patients reported impaired smell and taste 3 months post COVID. The participants' symptoms and recovery were monitored for an average of 200 days since the onset of COVID-19 infection (Nguyen, 2021).

The results of the study show that two thirds of the participants continued to experience symptoms at the 200-day follow-up point (Nguyen, 2021). Weight loss and malnutrition also appeared to be common trends amongst the patients in the study. The article notes that smell and taste disorders can potentially trigger the process of malnutrition and inflammation. The author suggests that nutrition therapy, which involves dietary change and incorporating nutrients to manage health conditions, may help alleviate some of the symptoms of Long COVID. It then goes on to explain that a plant-based diet can help lower inflammatory effects and improve symptoms such as fatigue, insomnia, and musculoskeletal pain. While dietary supplements are not to be considered as substitutes for an adequate diet, they can offer additional benefits for individuals whose diet is insufficient in essential nutrients. Supplementing with nutrients such as Vitamin D, Vitamin C, Zinc, Magnesium, and probiotics can help support overall health. The nursing implication that can be derived from this article is to assess the nutritional status of individuals with long COVID and develop individualized nutrition plans based on their symptoms and needs. Nurses can help identify nutritional deficiencies and develop a nutrition plan that helps address these issues with the help of dieticians. Nurses also play a significant role in educating individuals with long COVID about the importance of maintaining a balanced diet and staying hydrated to support their recovery (Nguyen, 2021).

<div align="center">2.5 Conceptual Framework: The Theory of Unpleasant Symptoms</div>

The Theory of Unpleasant Symptoms was used as the conceptual framework for the proposed study. The theory is used to understand multidimensional symptoms by assessing influencing factors and symptoms. Performance is an outcome resulted from a reciprocal effect of the physiological, psychological, and situational factors. The theorist addressed that a single symptom may co-occur with other symptoms which is explaining the situation of what adults with long COVID have been suffering from multiple persistent COVID-related symptoms (Lenz et al., 1997).

The Theory of Unpleasant Symptoms consists of three major factors which include the symptoms experienced by the patient, the factors influencing the symptoms and the consequences of those symptoms. The symptoms themselves are measured in terms of intensity, duration, level of distress and quality and the consequences of the symptoms are referred to as performance. Physiological, psychological, and situational factors interact with one another and influence symptoms. The measures of symptoms also interact with one another and influence performance (Lenz et al., 1997).

Figure 1 shows the conceptual framework to guide the proposed study. Researchers of patients with cancer, end-stage renal disease or chronic heart failure have shown the applicability of this conceptual framework to address the importance of nursing interventions targeted on identified intercorrelated symptoms to optimize symptom management and improve the outcomes (Lenz et al., 1997).
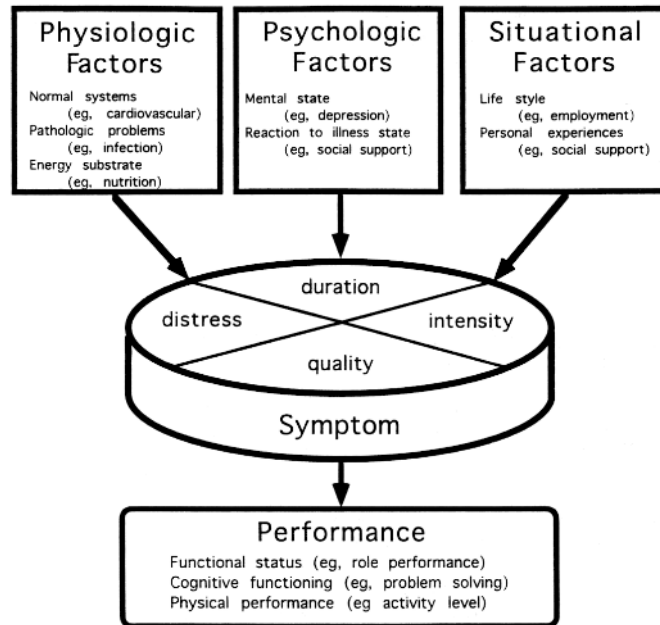
Figure 2.1: The Theory of Unpleasant Symptoms

Overall, the theory of unpleasant symptoms is a particularly useful theoretical framework for understanding and addressing the complex and varied symptoms experienced by patients with chronic illnesses such as long COVID (Lenz et al., 1997). Thus, the purpose of this study was to describe five common persistent symptoms, as opposed to concentrating on a single symptom, and their potential multiplicative relationships on quality of life after controlling influencing factors on symptom patterns in adults with long COVID.

2.6 Significance of Research

COVID-19 is one of the most concerning global health challenges of modern times. About 30% percent of people who contract COVID-19 are diagnosed with long COVID (CDC). However, currently available information on the risk factors, manifestation, treatments, and long-term effects of the long COVID is inconsistent requiring further research to develop an evidence-based practice guideline for long COVID management. A

substantial percentage of patients with a COVID-19 diagnosis continue to suffer from worsening function and symptom burden long after the acute phase of the infection. Further research is necessary to identify timely interventions that may help treat long covid patients, reduce symptom burden and restore functional abilities. Dr. Seo's research aims to gain a better understanding of long COVID symptoms patterns and can contribute to studies seeking to understand the progression of the disease process and identifying treatment options and means of prevention.

CHAPTER 3

METHODOLOGY

3.1 Study Design

This study will be a secondary analysis using Dr. Seo's data collected from an actively ongoing study entitled, "Evaluating Persistent Symptoms and Associations with Disability and Quality of Life in Post-CVID-19 Adult Survivors". Currently, Dr. Seo conducts a study examining intercorrelations among five symptoms: fatigue, dyspnea, chest tightness, muscular/joints pain, or cognitive discomfort [e.g., cognitive fogginess]) The study is designed to identify influencing factors of symptoms as well as examine the associations of symptoms with disability and quality of life over time at baseline, and between two and six months later, in COVID-19 adult survivors.

3.2 Sample and Setting

Subjects were recruited at the COVID recovery clinic at the Department of Physical Medicine and Rehabilitation University of Texas at Southwestern (UTSW) Medical Center and data was collected at the University of Texas at Arlington (UTA) Science and Engineering Innovation and Research (SEIR) lab.

In Dr. Seo's study, inclusion criteria are: (1) have a diagnosis of COVID-19 confirmed by a primary provider (MD or NP); (2) aged 19 years or older; (3) have one of seven COVID-19 symptoms (fatigue, dyspnea, chest tightness, myalgia, cognitive impairment, depression/anxiety, sleep disturbance) ≥ 4 weeks after the onset of COVID-19 regardless of hospitalization or non-hospitalization; (4) be cognitively intact [score <

Ten on Short Orientation-Memory-Concentration test] (Katzman et al., 1983); and (5) have a telephone with internet accessibility.

Exclusion criteria are: (1) have severe neurological/skeletal conditions or suffer severe pain interfering with the 6-minute walk test; (2) have moderate to severe COPD indicated by forced expiratory volume in 1s (FEV1) $\geq$ 50% or restrictive lung disease limiting DB practice; (3) have a medical history of uncontrolled diabetes mellitus, a myocardial infarction (MI), or coronary artery bypass surgery within the last three months, chronic renal failure, or uncontrolled arrhythmia; and (4) on 24-hour supplemental oxygen.

For the present study, a convenient sample of 19 adults who met the inclusion and exclusion criteria was used for the secondary analysis.

3.3 Measurements

Symptom burden was measured by frequency, intensity, and distress of five common symptoms. First, for measuring fatigue and pain (i.e., myalgia), subscales of the Patient-Reported Outcomes Measurement Information System (PROMIS)-29 v2.0 were used. In the PROMIS-29 Profile v2.0, all items were measured over the past 7 days on a 5-point Likert scale, except for pain intensity which was rated from 0 to10, with 0= no pain and 10= worst imaginable pain. In the validation study, all but one of the PROMIS-29 subscales had reliability of >0.95; the exception was fatigue with a reliability estimate of 0.76.68-70 PROMIS scores was summed and then converted to standardized T scores (Cella et al., 2010; Cella et al., 2019). For the present study analysis, the average of the raw scores were used. Increased symptom severity was reflected by higher scores for fatigue, pain interference, and pain intensity.

Second, for measuring dyspnea, there were two tools: 1) A 10-point Likert scale with 18 activities including basic activities of daily living, instrumental activities of daily living, and other activities related to physical function. Subjects was asked to rate intensity of dyspnea on a scale of "0=no shortness of breath" to "10=unable to complete an activity due to shortness of breath." It has good internal consistency (Cronbach's α ranged from .86 to .96) in adults with heart failure (Seo et al., 2016); and 2) The Borg scale, from 6–20, to rate perceived exertion and dyspnea before, during, and immediately after the 6-minute walk test (Guyatt et al., 1985). Third, for measuring chest-tightness, Dr. Seo developed three items to measure frequency, severity, and intensity of chest tightness. Fourth, for measuring cognitive discomfort, Dr. Seo also developed three items (i.e., difficulties attention, memory loss, and brain fog) with frequency (all the time to never), severity (0 to 10 scale), and distress (0 to 10 scale).

According to the Theory of Unpleasant Symptoms, performance is broken down into functional status, cognitive functioning, and physical performance. For measure of performance according to Lentz et al. 1997's Theory of Unpleasant Symptoms, quality of life (QOL) was measured using the SF-12 Health Survey version 2 (SF-12v2) developed by Ware and colleagues (Ware et al., 1996). SF-12 items are physical restrictions, physical functioning, bodily pain, general health, vitality, social functioning, role limitations due to emotional issues, and mental health. For data analysis, the physical component and the mental component summary was calculated following published guidelines (Ware et al., 2002) The higher score, the better QOL. Reliability and validity in various conditions are well documented (Galenkamp et al., 2018)

For measuring influencing/risk factors related to long COVID, demographic data and clinical variables were collected. Subjects were asked to answer demographic data (age, sex, education, ethnicity), time since COVID diagnosis and current medications. The body mass index was calculated after measuring body weight and height at the UTA laboratory visit. Charlson's Co-morbidity Index was used to measure the number and severity of co-morbid conditions (Charlson et al., 1987).

3.4 Procedures

According to Dr. Seo's protocol, after UTA IRB approval, participants were referred from the UTSW Medical Center after their first visit to the COVID recover clinic when they were eligible for the study confirmed by co-investigator and his staff. Baseline data was collected at the UTA SIER research lab. Follow-up data was also collected between two months and six months at the UTA SIER research lab. The participants stayed at the research lab for one and half hours for data collection which includes direct measurements and completing the self-reported questionnaires. For the current study, UTA IRB was waived because this was the secondary study, and no identification information was provided (refer to Appendix A for the attached letter from the UTA IRB office). For the current study, the data collated at the baseline was used for the data analysis.

3.5 Data Analysis

Statistical Package for Social Science (SPSS /- PC+) version 25 was used to manage and analyze the data. Frequency distributions, means, and standard deviation was be computed for all variables. Alpha of .05 was used to assess significance of testing the research questions. For examining the relationships between symptom patterns and influencing factors, correlation with the Pearson correlation coefficient was used.

CHAPTER 4

RESULTS

4.1 Sample Characteristics

This analysis included a convenient sample of 19 adults (17 female and 3 males; mean age: 47.68 ±10.87 years) who were diagnosed with COVID-19 by their primary care physician.

Table 4.1: Sample Characteristics

Sex	
Female	17 (89.5)
Marital Status	
Married	17 (89.5)
Ethnicity	
Hispanic	4 (21.1)
Race	
White	18 (94.7)
Education	
≥ College	14 (73.7)
Insurance	
Insured	17 (89.5)
Loneliness	

≥ Sometimes	10 (52.6)
Working Status	
No work after COVID Diagnosis	6 (31.6)

The following table showed the persistence COVID-19 symptoms, scales used to measure those symptoms, ranges for each scale, and the mean (M) and standard deviation (SD) for each symptom.

Table 4.2: Persistent COVID-19 Symptoms

Symptom	Scale	Ranges	M ± SD
Fatigue	Likert	1-5	3.86 ± 1.14
Shortness of Breath	Visual Analogue Scale	0-10	4.31 ± 2.83
Pain	Likert	1-5	3.06 ± 1.32
Chest Tightness	Likert	0-2.66	1.80 ± 1.22
Cognitive Discomfort	Likert	0-1	0.84 ± 0.32
Quality of Life	Likert	Norm (50)	
Physical Health Component			28.80 ± 8.13
Mental Health Component			44.84 ± 11.44

According to the results, 14 (73.68) felt quite a bit or more tired in the past 7 days.
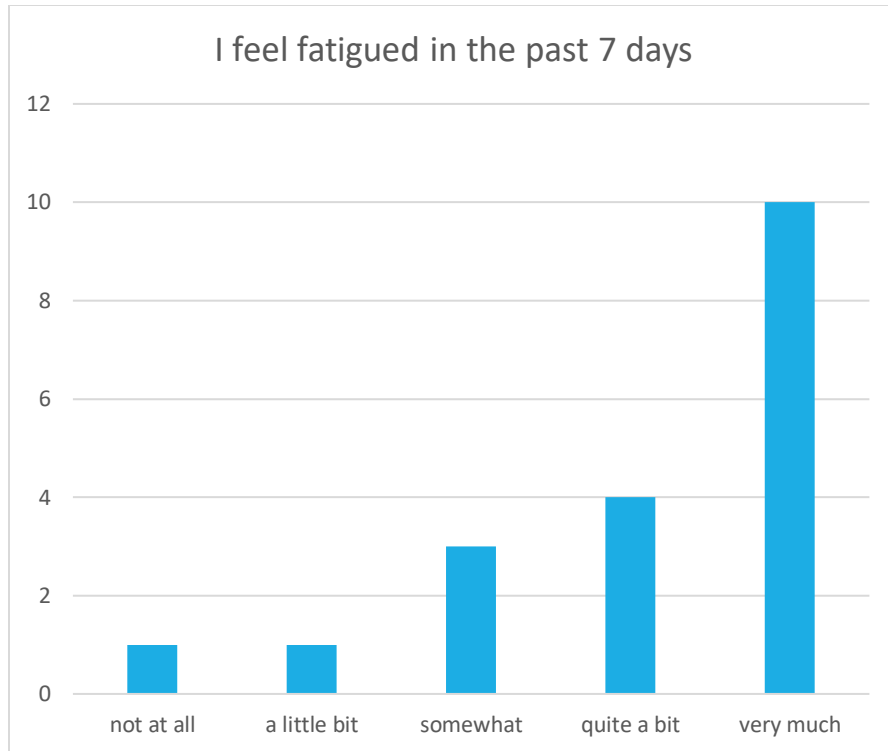
Figure 4.1: I feel fatigued in the past 7 days

The findings of the study showed that 12 (63.18) had quite a bit or more trouble

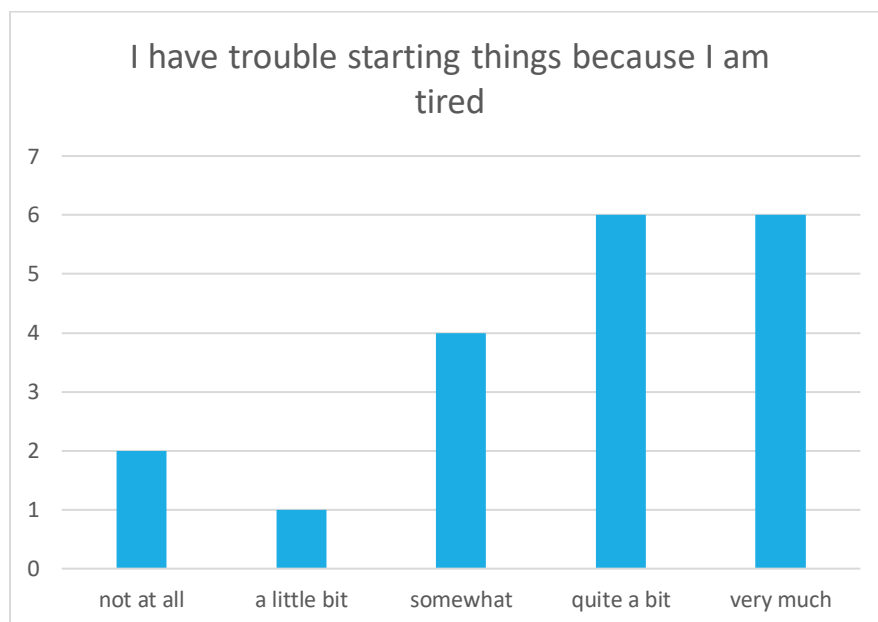starting things because they were tired.

Figure 4.2: I have trouble starting things because I am tired

13 (68.42) of the subjects reported feeling quite a bit or more run down on average.
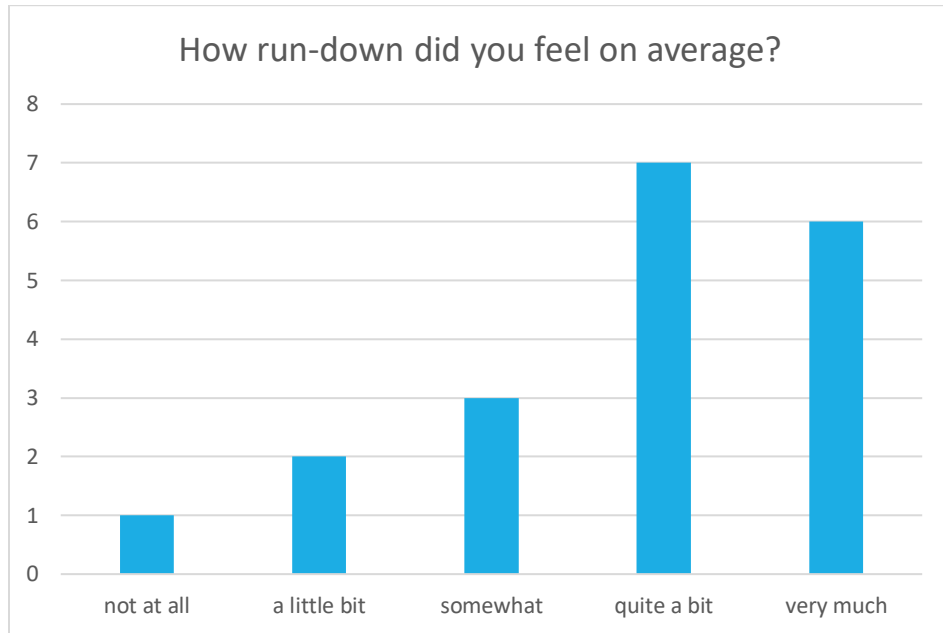
How run-down did you feel on average?

Figure 4.3: How run-down do you feel on average?

The data showed that 15 (78.95) of the subjects felt quite a bit or more fatigued on average.
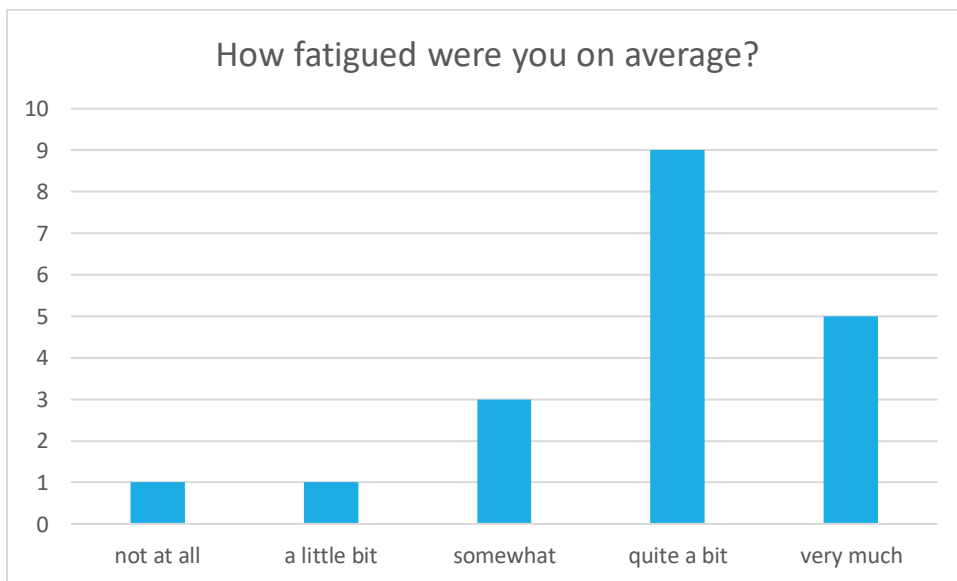
How fatigued were you on average?

Figure 4.4: How fatigued were you on average?

For the second measure of dyspnea, the perceived level of exertion rated on a level of 6 to 20 during the 6-Minute Walk Test was evaluated. Out of the patients that participated in the study, 2 (10.6) took a break during the walk test and 1 (5.3) used a cane for assistance. All 19 (100) participants completed the 6-Minute Walk Test.
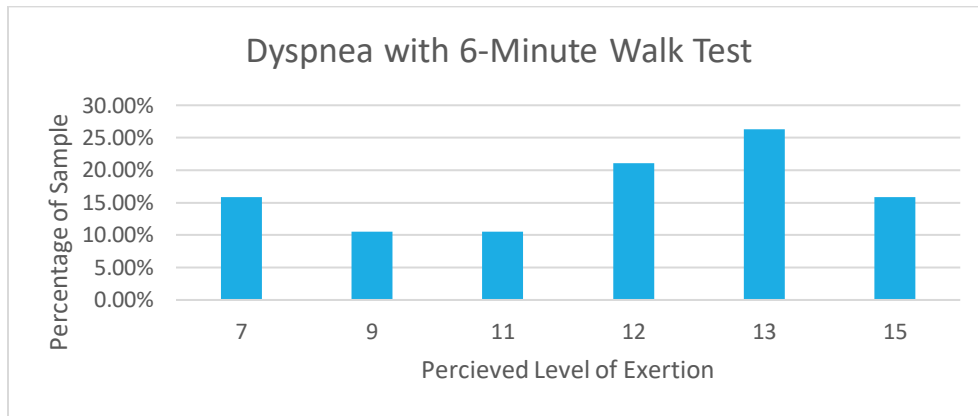
Figure 4.5: Dyspnea with 6-Minute Walk Test

4.3 Influencing Factors

4.3.1 Risk Factors

BMI was a significant influencing factor in the study as 18 (94.73) of the participants were overweight and had a BMI of greater than 25. The mean and standard deviation for BMI was 28.91 ± 4.94.
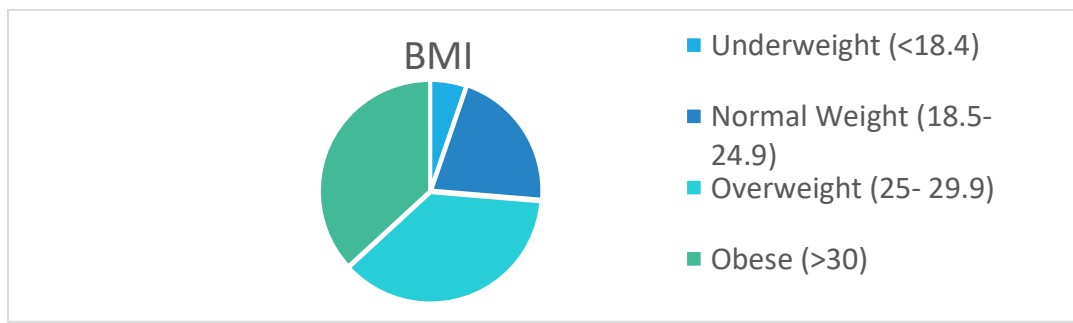
Figure 4.6: Body Mass Index

The study also analyzed comorbidities in patients with long COVID. Connective tissue disease 7 (36.4) and chronic obstructive pulmonary disease 7 (36.4) were found to

be the most common comorbidities amongst the sample. Other comorbidities amongst the participants included ulcer disease 4 (21.1), diabetes 2 (10.5), mild liver disease 1 (5.3), peripheral vascular disease 1 (5.3), and myocardial infarction 1 (5.3).

Figure 4.7: Comorbidities

4.3.2 COVID-19 Diagnosis and History

Results indicated that a significant portion of the sample experienced shortness of breath, myalgia and fatigue among other symptoms while infected with COVID-19.
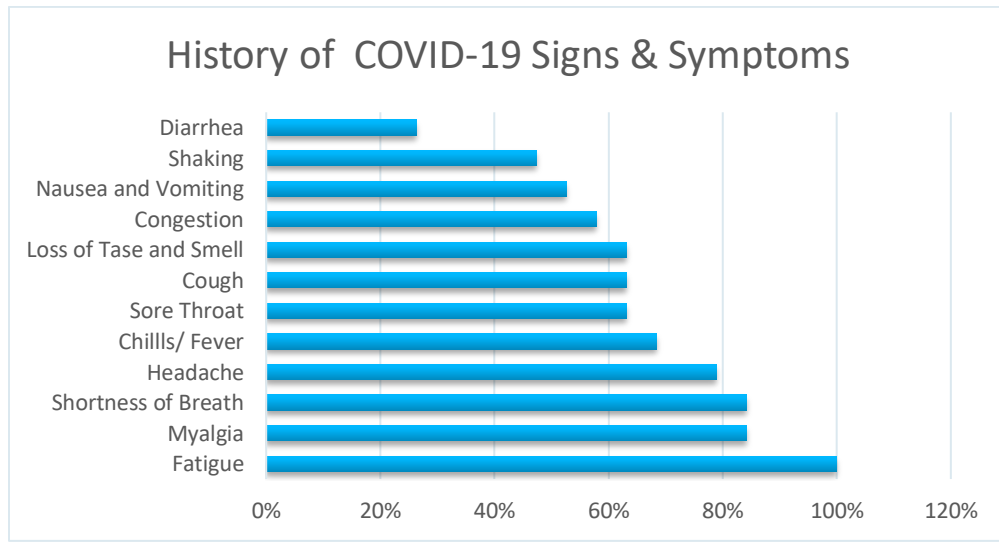
Figure 4.8: History of COVID-19 Signs & Symptoms

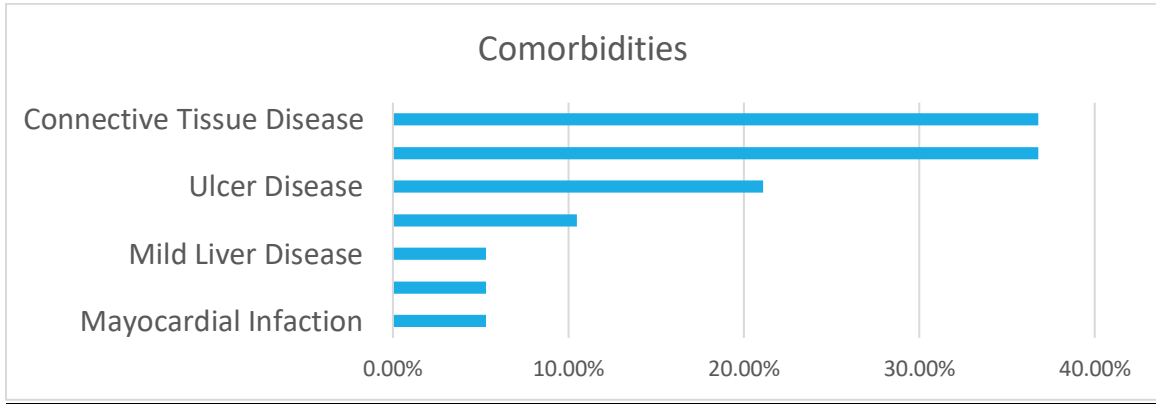The date of the initial COVID diagnosis and the date of interview was used to determine the average number of days (530 ± 280.94) the patients had persisting symptoms associated with COVID-19.

Out of the patients that participated in the study, 6 (31.5) have been diagnosed with COVID-19 more than once. 9 (47.37) of the patients received hospitalized care and 5 (26.31) were admitted to the Intensive Care Unit (ICU).
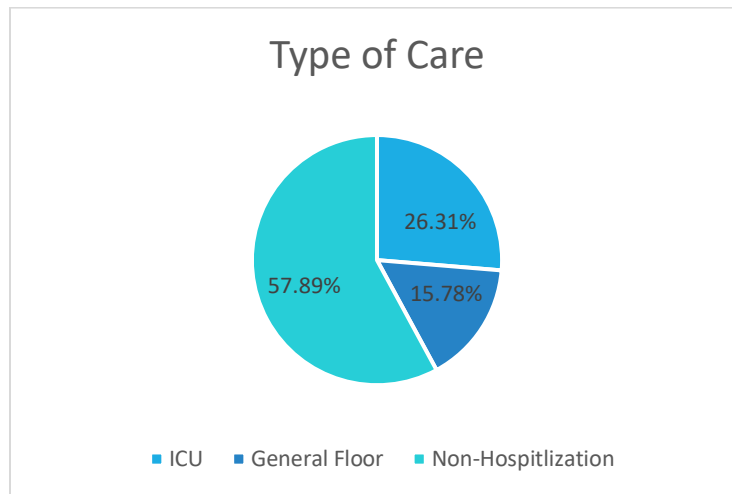
Figure 4.9: Type of Care

The data collected also showed that 17 (89.47) of the participants were diagnosed with COVID-19 during or prior to the year 2021. There was a possibility that long COVID may be associated with earlier strains of COVID-19. This information also highlighted the importance of developing options for treatment and symptoms management as many of the patients with long COVID have been suffering from persisting symptoms for multiple years.
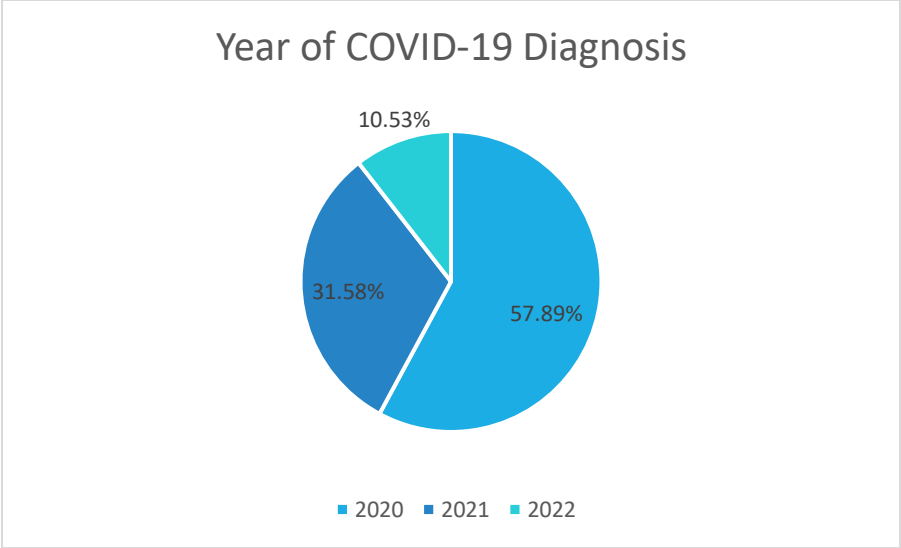
Figure 4.10: Year of COVID-19 Diagnosis

CHAPTER 5

DISSCUSSION

5.1 Discussion

The analysis of the study yielded numerous insights that may be beneficial in understanding the influences, risk factors, and symptoms patterns of long COVID. It was found that the most common symptoms experienced by patients during the acute phase of COVID-19 were fatigue, myalgia, and shortness of breath. According to the analysis, the patients continued to experience persisting symptoms of fatigue, shortness of breath, chest tightness and cognitive discomfort. The results from the study also showed that these symptoms had a significant impact on the patient's quality of life. Nearly 90% of the sample for the study was female, suggesting the possibility that females might be at a higher risk for being diagnosed with long COVID. The data also showed that almost 95% of the sample was overweight/obese, indicating that a BMI of greater than 25. It was also found that the most common comorbidities amongst patients with long COVID were connective tissue disease and chronic obstructive pulmonary disease.

These findings are consistent with those of the study by Lopez et al (2021) which reported fatigue (58%), dyspnea (24%) and attention disorder (27%) as among the most common symptoms. Another study by Lambert et al (2021) yielded similar results with more than 50% of the sample reporting fatigue, shortness of breath and difficulty concentrating. A similar study by Logue et al (2021) found fatigue (79.0%), shortness of breath (55.3%) and difficulty concentrating (53.6%) as common symptoms among Long

COVID patients. A study by Davis et al. 2021 also reported that the symptoms most frequently present among the respondents include fatigue and cognitive dysfunction. This study also highlighted how symptom burden caused significant change in the quality of life of patients with long COVID, which supported the present findings in our study.

The findings of the study showed that nearly 90% of the participants were diagnosed with COVID-19 during or prior to 2021, indicating that they have been suffering from persistent symptoms for years. Out of these patients, 31.5% received hospitalized care and 26.31% were admitted into the ICU. The mean measure for quality of life for physical health was 28.8 and for mental health was 44.84, both of which are below the norm (50). These findings provide insights on how persistent symptoms significantly impact the patient's quality of life over a long period of time and highlight the importance of developing options for symptoms management and treatment for patients with long COVID.

5.2 Conclusion

The data from the study shows that most of the participants continue to experience persistent COVID-19 symptoms months after acute infection leading to symptom burden and decreased quality of life. A significant portion of the sample was diagnosed with COVID-19 during or prior to the year 2021, indicating that long COVID may be associated with earlier strains of COVID-19. The analysis showed that long COVID was most common in patients with Chronic Pulmonary Disease and Connective Tissue Disease. The majority of the study participants had a BMI over 25 or greater, indicating that a BMI of greater than 25 may be a potential risk factor for long COVID.

5.3 Limitations

The subjects for the study were a convenient sample recruited at the UTSW medical center; therefore, a limitation of this study is that there may be a selection bias. The sample for the study included 19 adults, 17 (89.47) of which were female. Further studies with a larger sample size and one more representative of the general population would help add to knowledge about long COVID and develop treatment options for patients.

<u>5.4 Future Implications</u>

The goal of this study was to contribute to identifying predictors of persistent symptoms and their association with other outcomes for treatment options and means of prevention for further disability from long COVID. The findings from this study can be used in future studies to develop evidence-based practice guidelines for symptom management in long COVID patients. There is a need for further research regarding symptom management for long COVID Patients. By identifying predictors of long COVID, future treatments can be implemented to target those specific high-risk groups. Health care providers should be aware of several factors, for example, being female, adults with overweight/obese, with having comorbidities, having longer duration with persistent COVID symptoms who need interventions (e.g., rehabilitation) to promote their recovery from COVID and return to their prior health status.

APPENDIX A

UTA IRB WAIVER

November 19, 2021

Michelle Tran
Faculty Advisor: Dr. Yaewon Seo
Nursing
The University of Texas at Arlington

IRB Submission Inquiry & Project Determination of Non-HSR

Dear Michelle,

Thank you for contacting the UT Arlington Office of Research Administration; Regulatory Services regarding your use of data from Dr. Seo's heart failure study.

Upon reviewing the information that you provided, it appears this protocol would not meet the definition of, "research with human subjects" as defined by the Office for Human Research Protections (OHRP) and would therefore not be subject to review or approval by the Institutional Review Board (IRB) at UT Arlington. Per the federal regulations at 45 CFR 46:

- *Research* is defined as, "a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge."
- A *human subject* in research is defined as, "a living individual about whom an investigator conducting research: obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens."

From the description of data provided, it appears that it does not meet the definition of human subject research, as the data will not be identifiable. Dr. Seo has explained that all identifying information will be removed from the dataset that will be provided to you. 45 CFR 46.102 (e)(1) Human subject means a living individual about whom an investigator (whether professional or student) conducting research:

(ii) Obtains, uses, studies, analyzes, or generates *identifiable* private information or identifiable biospecimens.

Therefore, this project is not subject to review or approval from the UTA IRB, and you do not need to submit a protocol to our office at this time.
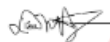
Please note that although IRB review is not required for this study, there may be other institutional requirements or agreements such as Data Use Agreements that pertain to this project. Please contact Dan Vincenzo, UT Arlington's Agreements Manager, at vincenzo@uta.edu for assistance in processing study-related legal agreements. In addition, it is your responsibility to abide by the UT Arlington Standards of Conduct and the ethical standards within your field for all projects and activities, even when IRB review is not required.

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The University of Texas at Arlington, Center for Innovation
202 E. Border Street, Ste. 201, Arlington, Texas 76010, Box#19188
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I have included the link for decision charts provided from OHRP from which this determination is made for your reference below. If the procedures that have been outlined and provided to our office change such that IRB approval might be necessary or you have any questions regarding this determination, please do not hesitate to contact us at RegulatoryServices@uta.edu .

Thank You,

Digitally signed by
Lisa Alvarez
Date: 2021.11.19
13:35:55 -06'00'

Lisa Alvarez
IRB Specialist
Office of Research Administration;
Regulatory Services

OHRP reference: http://www.hhs.gov/ohrp/policy/checklists/decisioncharts.html

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