Faculty of Medical Sciences
Department of Paraclinical Services Public Health and Primary Care Unit

DM Family Medicine
The University of the West Indies St. Augustine

RESEARCH MANUSCRIPT

Patient-reported outcome measures, one-year after COVID-19: A Cohort Study in South Trinidad, 2020-2021

NAME OF STUDENT: Kavita Dharamraj

CLASS OF 2022

LECTURER: Dr. Shastri Motilal

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DECLARATION OF STUDY:

Full name: KAVITA DHARAMRAJ

Email address: kavita.dharamraj@my.uwi.edu ; kavita.dharamraj@gmail.com

Student number:

Course Code: *MEDC 6650*

Module code: MEDC 6650

Declaration by student

I understand what plagiarism is. This assignment is my own work, and all sources of information have been acknowledged. I have taken care to cite/reference all sources as required.

Signed by the student: Kavita Dharamraj Date: 12h December 2022

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LIST OF ACRONYMS

BMI	Body Mass Index
COPD	Chronic Obstructive Pulmonary Disease
Couva MMF	Couva Medical and Multi-Training Facility
COVID-19	Coronavirus disease 2019
CI	Confidence Interval
CKD	Chronic Kidney Disease
CVA	Cerebrovascular accident
CVD	Cardiovascular disease
ED	Emergency Department
EQ-5D-5L	EuroQol 5 Dimension 5 Level
EQ-VAS	EuroQol Visual Analog Scale
GAD-2	Generalized Anxiety Disorder-2
HCW	Health care worker
HDU	High dependency unit
HRQoL	Health-related quality of life
HTN	Hypertension
ICU	Intensive Care Unit
IHD	Ischaemic Heart Disease
IQR	Inter-quartile range
mMRC	Modified Medical Research Council
MOH	Ministry of Health
OR	Odds ratio

PCC	Post-COVID condition
PHC	Primary Health Care
PHQ-2	Patient Health Questionnaire-2
PHQ-4	Patient Health Questionnaire-4
PTSD	Post-traumatic stress disorder
Q-Q	Quantile-quantile
RHA	Regional Health Authority
RT-PCR	Reverse transcription polymerase chain reaction
SARI	Severe acute respiratory infection
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
SD	Standard Deviation
SFGH	San-Fernando General Hospital
SFTH	San-Fernando Teaching Hospital
SWRHA	South-West Regional Health Authority
T2D	Type 2 Diabetes Mellitus
TPHL	Trinidad Public Health Laboratory
T&T	Trinidad and Tobago
UWI	University of the West Indies
WHO	World Health Organization

ABSTRACT

Background: The long-term health consequences of COVID-19 remains unclear. This study aimed to describe the patient-reported long-term health effects one-year post-acute COVID-19 infection, and predictors, according to illness severity.

Methods: In this retrospective cohort study a sample of 324 participants, ≥ 18 years, who were symptomatic with laboratory confirmed COVID-19 infection between March 2020 and May 2021, who resided in South-West Trinidad and gave informed consent were included. Participants were followed up after 12-months post-acute COVID-19 infection and were interviewed for persistent symptoms. Primary outcomes measured included fatigue or muscle weakness, anxiety or depression, degree of dyspnoea, and health-related quality of life (HRQoL). Multivariable adjusted linear and logistic regression models estimated the ORs and 95% CIs for associations between disease severity and long-term health consequences.

Results: A total of 324/431 eligible participants were enrolled, response rate 75.2%, after 107 were excluded. The median (IQR) age was 41.0 (34-52) years, with 51.23% men and 33.02% with co-morbidities. One year later, 60% reported ≥1 persistent symptom: dyspnoea (52.16%), fatigue (42.59%), muscle weakness (31.48%); PHQ-4: anxiety/depression (13.58%). Overall, in the unadjusted analysis, participants with moderate/severe illness, had a significantly increased risk of developing fatigue or muscle weakness ($p=0.043$); anxiety/depression ($p<0.001$); breathlessness ($p<0.001$) and reduced HRQoL ($p<0.001$). When adjusted for age, gender and co-morbidities, their risk of developing fatigue or muscle weakness, anxiety/depression, breathlessness was nullified, except for HRQoL. Overall, the mean (SD) health index value score was 0.931 (0.13), comparable to the national norms of 0.95; for those with moderate/severe illness, mean (SD), 0.894 (0.16), with a statistically significant decrease compared to mild illness

($p<0.001$).

Conclusions: One-year post-acute COVID-19 infection, a significant proportion of survivors have persistent symptoms. The health index value for those with moderate/severe illness was below the population norms. Interventions should be prioritized for their long-term recovery.

Keywords: Post-acute COVID-19 syndrome, Post COVID-19, Long COVID

INTRODUCTION

COVID-19 was first detected in Wuhan, China in December 2019, and has been an ongoing global threat [1–3]. As of March 30, 2022, the global pandemic of COVID-19 has led to more than 481 million confirmed cases with over 6.13 million deaths [4]. In Trinidad and Tobago (T&T), since March 12, 2020, there has been, over 182 thousand confirmed cases, 174 thousand "recovered" cases and 4100 deaths [5].

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection ranges from being asymptomatic to severe or fatal [2,6–9]. The pathogenesis, clinical, epidemiological characteristics, and complications for acute COVID-19 have been well documented [1–3]. Most persons recover after 2 to 6 weeks [7,10]. However, it has been observed that in an increasing number of patients, recovering from COVID-19, a wide constellation of symptoms may persist for weeks or months [11–14].

Known by diverse names, in September 2020, in a 'WHO-led Delphi' process, the final consensus definition for adults: "post-COVID-19 condition occurs in individuals with a history of probable or confirmed SARS-CoV-2 infection, usually 3 months from the onset, with symptoms that last for at least 2 months and cannot be explained by an alternative diagnosis. Common symptoms include, but are not limited to, fatigue, shortness of breath, and cognitive

dysfunction, and generally have an impact on everyday functioning. Symptoms might be new onset following initial recovery from an acute COVID-19 episode or persist from the initial illness. Symptoms might also fluctuate or relapse over time [15]".

There has been notable impact on the physical, cognitive, mental and social health status of patients, regardless of illness severity [14,16–18].

Published studies have focussed on previously hospitalized patients with severe COVID-19 illness, reporting symptoms up to 6-months after [11,19,20]. However, there is paucity of data regarding one-year health consequences post COVID-19 infection [12,13,19,21]. Through this study, the long-term burden of COVID-19 may be better understood in Trinidad and Tobago (T&T).

RESEARCH QUESTIONS

Primary Research Question:

- What is the HRQoL, symptomology and mood disorders in persons, one-year after being diagnosed with COVID-19 in South Trinidad, 2020-2021?

Secondary Research Question:

- Is there a difference in the following outcomes, one-year post-acute COVID-19 infection, based on severity of initial COVID-19 infection, socio-demographics and other baseline factors:
  - ✓ HRQoL
  - ✓ Symptoms
  - ✓ Anxiety/Depression
  - ✓ Degree of breathlessness

AIMS AND OBJECTIVES:

Aim: To describe the patient-reported long-term health consequences, one-year after being diagnosed with COVID-19, and predictors, according to illness severity in South Trinidad, 2020-2021.

Objectives:

- To determine the difference in HRQoL, symptoms, anxiety/depression, degree of breathlessness experienced one-year after being diagnosed with COVID-19 according to severity of illness.
- To determine the predictors/factors associated with these main outcomes.

LITERATURE SEARCH STRATEGY AND REVIEW

Several databases were searched – PubMed, Medline and Scopus, up to March 2021. The search terms used were "(**COVID-19** OR **Coronavirus disease 2019** OR **2019-nCoV** OR **SARS-Cov-2** OR **post-acute COVID-19 syndrome** OR **post-COVID-19** OR **post-acute sequelae of COVID-19** OR **long COVID)** AND (**one-year health consequences** OR **12-month health consequences** OR **long-term health consequences** OR **long-term sequelae**)." Early in the pandemic related studies were found and critiqued [11,20,22] (Appendix 4). Post-covid symptoms, such as, chronic fatigue, anxiety and depression were frequently reported, up to 6 months or earlier after hospital discharge. There was a paucity of data regarding one-year long-term health consequences.

As the pandemic progressed, one-year post COVID-19 studies were published and relevant findings were compared to ours in the discussion [8,12,13,21,23,24]. Most studies looked at hospital

discharged patients, and a wide variation was seen in the prevalence of post-covid conditions globally.

METHODOLOGY:

Study Design: This was a retrospective cohort (analytical) study.

Research Setting: At the onset of the pandemic in T&T, as part of the national response to contain the spread of COVID-19, community epidemiological surveillance has been ongoing through the communities of counties Victoria, St. Patrick and Caroni South, at the South-West Regional Health Authority (SWRHA). The geographical distribution of COVID-19 surveillance sites is shown in figure 1 and the processes at the research setting are shown in figure 2, according to the recommended protocol by the MOH, T&T.

Study population: All 324 symptomatic laboratory confirmed patients who had COVID-19 for a minimum period of one year prior, at the time of data collection, and met the inclusion criteria. (Appendix 5).

Inclusion Criteria: Symptomatic laboratory confirmed COVID-19 adult patients ≥ 18 years, who resided in the communities of Counties Victoria, St. Patrick and Caroni South, SWRHA, during the study period (baseline: 12-03-20 to 31-05-21; one-year follow-up: 26-07-21 to 31-05-22) and gave informed consent.

Exclusion Criteria: Non-laboratory confirmed COVID-19 adults; asymptomatic laboratory confirmed COVID-19 cases; persons who were re-infected with COVID-19 at follow-up; pregnant

women with acute COVID-19 infection; pregnant women at follow-up; children and adolescents < 18 years; non-residents of county Victoria, St. Patrick or Caroni; non-English speaking; those with a history of pre-existing conditions that may affect outcomes of interest (for eg. cardiorespiratory conditions that cause shortness of breath, thyroid and autoimmune diseases that may cause fatigue); persons with diminished autonomy who were incapable of providing informed consent; persons who died before one year follow-up; those who did not consent to participate and those who could not be contacted.

Sampling methods: Consecutive convenient sampling was used. If a person ended up in the study and could not be contacted or did not consent, the next person on the list was chosen. Participants were selected based on the specific problem under investigation, not because of any social bias, ease of availability or diminished autonomy.

Measures were taken to reduce sources of bias:

Non-response bias - The data collection tool was pre-tested to identify possible sources of bias in the length or content of questionnaire and minimize the non-response rate.

Recall bias –To recall some of the baseline information, persons may have difficulty recalling the information. The interviewer prompted their memory in this regard.

Sample size: A sample of 324 participants was recruited, based on a 30% prevalence for mild disease [19] and a 55% prevalence for moderate/severe disease[25], using a type 1 margin of error, 0.05, at the 95% confidence interval, with a power of 80% (Appendix 6).

Data Collection Tool:

The 'COVID-19 Data Collection tool' consisted of seven (7) sections (Appendix 2).

The first section was designed to collect baseline data is a community-based surveillance tool tailored to a local setting after review of the WHO COVID-19 data capture instruments. All variables were defined (Appendix 3). This information was collected at the time of the patient's nasopharyngeal swab. One year after baseline data was collected, data on health-related outcomes was collected using the following questionnaires:

- "Symptom Questionnaire: Participants were asked to report on persistent, newly occurring or worsening symptoms before COVID-19 [(11)]."
- "Modified Medical Research Council (mMRC) dyspnoea scale: This is a five-category scale, which characterizes the level of dyspnoea with physical activity. Higher scores correspond with increased dyspnoea[(26)]. It quantifies the disability associated with breathlessness, by identifying if breathlessness occurs when it should not."
- "HRQoL: The EQ-5D-5L is a validated questionnaire to evaluate patient quality of life by assessing the following five factors: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each factor is divided into five levels that range from none to extreme problems[(27)]."
- "EuroQol Visual Analog Scale (EQ-VAS): This is a patient's assessment of subjective assessment of generic health ranging from 0 to 100, with higher scores representing better subjective health experience[(27)]."
- "Patient Health Questionnaire-2 (PHQ-2): A depression screening and severity measure [(28)]."
- "Generalized Anxiety Disorder Questionnaire-2 (GAD-2): A brief screening test for detecting generalized anxiety disorder [(29)]."

- "Patient Health Questionnaire-4 (PHQ-4): The four-item patient health screening questionnaire for detecting depression and anxiety[30]."

Data collection methods:

The study was approved by the University of the West Indies (UWI) (Approval 1) and the SWRHA (Approval 2). Permission was granted from the Medical Director, Primary Health Care (PHC) (Approval 3) to access the SWRHA COVID-19 surveillance data from March 12, 2020, to May 31, 2021. This secondary data source was compiled by physicians and nurses who worked on the surveillance team. The first section was completed.

The instruments were pre-tested on 20 participants. One-year post-acute infection, data on health-related outcomes was collected using the questionnaires, outlined in Appendix 2. Informed consent was obtained from the participant (Appendix 1). Virtual interviews (zoom video conferencing and telephone) were conducted due to safety concerns in the COVID-19 pandemic. Permission to use the ED-5D-5L questionnaire and the EQ-VAS was granted from the EuroQol Research Foundation (Approval 4). Instructions were given to the participant to indicate how good or bad his/her health was on the scale. Primary outcomes measured included fatigue or muscle weakness, anxiety or depression, degree of breathlessness (mMRC score), and health-related quality of life (health index value). Those who had persistent symptoms were offered referral to the long-COVID clinic at the San-Fernando Teaching hospital.

Statistical Analysis:

Baseline characteristics and one-year health consequences of symptomatic laboratory-confirmed COVID-19 participants were shown: normally distributed continuous variables were expressed as means (SDs) and non-normally distributed as medians (IQRs), and absolute values (N), with percentages (%) for categorical variables. Tests for normality of continuous data were done looking at skewness and kurtosis, the Shapiro-Wilk test and the quantile-quantile (Q-Q) plots. Participants were categorised into two groups according to their illness severity at acute infection. Comparisons of baseline characteristics, symptoms, degree of breathless and HRQoL, anxiety and depression were done between mild and moderate/severe groups. For this study, cut-points for positive screens for: anxiety/depression, PHQ-4 score ≥6 [30]; depression, PHQ-2 score ≥3 [28] and anxiety, GAD-2 ≥3 [29] were used. For parametric data, the student's t test and for non-parametric data the Mann-Whitney U test and Wilcoxon rank-sum test was used. A χ^2 test or, if the cells had expected frequencies of < 10, the Fisher's exact test was used to compare categorical variables.

Multivariable adjusted logistic regression models were used to estimate the odds ratios (ORs) and 95% CI for association between illness severity and categorical outcomes (fatigue or muscle weakness, degree of breathlessness, anxiety/depression), stratified by ICU admission. For association between illness severity and continuous outcomes (health index value), multivariable adjusted linear regression models were used to estimate β estimates and 95% CIs. Adjustments were made for the effects of the predictor variables including age, gender, co-morbidities, previous history of anxiety/depression and PHQ-4 score, using regression models. A two-sided p-value ≤ 0.05 was considered statistically significant. There was no missing data. Statistical analysis was done using Stata Version 16 and Microsoft Excel 2019.

RESULTS:

Baseline socio-demographics

The response rate was 75.2% (Figure 3). Selected characteristics of symptomatic persons who tested positive for COVID-19 (n=324), from South Trinidad, and met the inclusion criteria, stratified by illness severity, are summarized in Table 1. In this study, 50.0% of participants, 162, experienced mild illness while 50.0% experienced moderate/severe illness. For the purposes of this study, patients who met the hospital admission criteria stated in Appendix 7 were considered moderately/severely ill while those who did not were considered mildly ill.

The median (IQR) age of the population was 41.0 (34-52) years, range 18 to 79 years. Persons with moderate/severe illness were slightly older, median (IQR), 42.0 (36 -52), than those with mild illness, median (IQR), 41.0 (31-52). More men, 51.23% (166), than women, 48.77%, were included in this study. More men, 58.02% (94) had mild illness, while more women, 55.56% (90) had moderate/severe illness, p=0.014. Patients were selected from three (3) counties in South Trinidad: Victoria, 33.95% (110), St. Patrick, 33.33% (108) and Caroni South, 32.72% (106). Eleven percent (18) of participants with moderate/severe illness were health care workers (HCWs). Age (p=0.15), geographical location (p=0.098) and being a HCW (p=0.070) had no statistically significant association with illness severity.

Clinical characteristics

Approximately, one third of the study participants, 33.02% (107) had co-morbidities. Approximately 40.0% of patients with moderate/severe illness had co-morbidities, and 73.46% of patients with mild illness had no co-morbidities. Patients with co-morbidities were more likely to experience moderate/severe illness as compared to non-comorbid patients (p=0.013).

Hypertension (HTN) was the most co-morbidity (22.53%) seen among symptomatic persons with COVID-19, followed by type 2 diabetes mellitus (T2D) (16.36%). Persons with T2D (p=0.05) and ischemic heart disease (IHD) (p=0.024) were more likely to have moderate/severe illness than those who did not have those conditions.

Most study participants, 85.19% (276) were non-smokers, while 7.72% (25) participants were current smokers, and 7.10% (23) were ex-smokers. There was no statistically significant association between smoking status and degree of illness experienced (p=0.556).

In terms of signs and symptoms at acute COVID-19 infection, 79.94% (259) reported subjective or measured fever, 74.07% (240) had cough, 68.52% (222) had ageusia, 67.59% (219) had body pains, 62.35% (202) had anosmia, 45.68% (148) had dyspnoea. Persons with moderate/severe illness were more likely to have fever, cough, sore throat, shortness of breath, myalgia, arthralgia, anosmia or ageusia, compared to the mild cases (all p=values ≤0.05). Our surveillance teams were able to epidemiologically link 56.0% (181) of the cases: 1.85% had a travel history and 54.94% had a contact history with a positive COVID-19 case. These cases were more likely to experience moderate/severe illness (p=0.005).

Of note in the early phase of the pandemic, for the first four months, from March 12th to July 20th, 2020, state quarantine was mandatory, once COVID-19 positive, regardless of the degree of illness. In this study, 9.57% of participants were under mandatory state quarantine during this time. From phase 2, July 21st, 2020, the indication for hospitalization was for only those who met the admission criteria (Appendix 7) [(31)]. Approximately 23.0% (74) of participants were hospitalized. There were 268 (82.72%) persons in home quarantine; with equal proportions, 82.72% (134) having both mild illness and moderate/severe illness.

For those who were admitted to hospital, the median (IQR) length of hospital stay was 14 (7-21) days, and ranged from 2 to 90 days. Illness severity was not associated with length of hospital stay (p=0.225). Four percent of participants (14), were admitted to ICU; 4.63% (15) to HDU; 3.40% (11) were ventilated and 14.81% (48) were oxygenated.

The median (IQR) length of ICU stay was 6.5 (4-7) days and ranged from 2 to 21 days. The median (IQR) length of HDU stay of 7 (4-14) days and ranged from 1 to 30 days.

In this study, 'fully vaccinated' meant that they had received at least two (2) doses of Sinopharm/Astra Zeneca and/or Pfizer or one (1) dose of Johnson and Johnson. At follow-up, 236 (72.84%) participants admitted to being fully vaccinated, while 88 (27.16%) were not. The most common vaccine taken was Sinopharm -136 (41.98%) participants, followed by Astra Zeneca - 46 (14.20%), then Pfizer - 39 (12.04%); and Johnson and Johnson -15 (4.63%).

Symptoms, HRQoL at 12-month follow-up

Table 2 shows the lingering post-COVID-19 symptoms, and HRQoL at a minimum follow-up time period of 12 months stratified by severity of illness.

The median (IQR) time period from baseline to follow-up was 12 (12-13) months. Sixty percent (195) of the participants had at least one of the following post-COVID-19 symptoms outlined in table 2. Most COVID-19 survivors were troubled by fatigue 42.59% (138); muscle weakness 31.48% (102); sleep difficulties 22.84% (74); hair loss 17.28% (56); joint pains 13.58% (44) and appetite disturbance 13.27% (43). Persons who experienced moderate/severe illness were 3.5 times more likely to have at least one long-COVID symptom, as compared to those who had milder illness, (OR 3.51, 95% CI 2.19 – 5.61). Persons with moderate/severe illness were five-

times more likely to develop muscle weakness, (OR 4.96, 95% CI 2.93 – 8.40); four-times more likely to experience fatigue, (OR 4.40, 95% CI 2.74 – 7.07).

The mMRC scored were group into categories 0 and ≥ 1. A score of 0 indicated that the participant "only gets breathless with strenuous exercise," and a score ≥ 1 indicates that at minimum the participant "gets short of breath when hurrying on level ground or walking up a slight hill"(32). In the group with mild illness, 62.35% (101) scored 0 and among those with moderate/severe illness, 66.67% (108) scored ≥ 1. The risk of an mMRC score ≥ 1, was 3.3 times increased in participants with moderate/severe illness compared to those with mild illness, (OR 3.31, 95% CI 2.1 – 5.22).

From the EQ-5D-5L instrument, the health index value was derived for each participant. The mean (SD) score was 0.931 (0.13). Those with milder illness reported a slightly higher score, mean (SD) 0.967 (0.07) as compared to those with moderate/severe illness, mean (SD), 0.894 (0.16). For persons who experienced moderate/severe illness, an 8.65 unit decrease in their health index value was noted.

The mean (SD) EQ-VAS score was 79.06 (15.74). Those with mild illness reported a slightly higher score, mean (SD) 84.04 (12.58) compared to those with moderate/severe illness, mean (SD), 74.22 (17.03). For each person who experienced moderate/severe illness there was a 0.04 unit decrease in their quality of life. Using the cut-points for the screening tools[28–30] stated above for positive screens: 13.58% had anxiety/depression; 13.89% had depression and 16.98% had anxiety. Statistically significant differences were seen for anxiety/depression among those with moderate/severe illness compared to mild illness ($p<0.001$).

EQ-5D-5L responses from study cohort

In figure 4, 40.0% of respondents reported symptoms of anxiety/depression, 30%, pain/discomfort, 22.0% had problems performing their usual activities, such as work, study, housework, family or leisure activities, 11.0% had problems with mobility and 4.0% had problems with self-care.

Predictors of selected outcome measures

Table 3a-d shows multivariate regression models for the four primary outcomes. Table 3a shows a multivariate logistic regression of difference in fatigue or muscle weakness by illness severity stratified by ICU admission. Among all study participants, in the unadjusted analysis, those with moderate/severe illness had a 1.58 significantly increased risk of developing fatigue or muscle weakness (OR =1.58, 95% CI: 1.01 to 2.47; p=0.043). In model 1, when adjusted for age, gender and co-morbidities, there was no significant risk of developing fatigue or muscle weakness among all participants who had moderate/severe illness (OR = 1.40, 95% CI: 0.814 to 2.40; p=0.224). Similar trends were noted in the non-ICU group, when adjusted for age, gender, co-morbidities.

Table 3b shows the multivariate logistic regression of difference in anxiety or depression by illness severity stratified by ICU admission. In the crude model, among all participants, those with moderate/severe illness were 5.5 times more likely to experience anxiety/depression 12 months, post COVID-19 infection, compared to the mild cases (OR=5.50, 95% CI: 2.47 to 12.26; p<0.001**)**. In model 1, when adjusted for age, gender and co-morbidities, there was no significant risk of experiencing anxiety/depression among all participants who had moderate/ severe illness (OR = 0.75, 95% CI: -0.06 to 1.51; p=0.052), as well as those in the non-ICU

group. When adjusted for a previous history of anxiety or depression, the risk of having anxiety/depression among all participants, one-year post COVID-19 infection was 1.2 times higher among moderately/severely ill participants (OR 1.20, 95% CI: 0.24 to 2.17; p=0.015). Illness severity predicting anxiety or depression was dependent on prior mental health history.

Table 3c shows the multivariate logistic regression of difference in degree of breathlessness (mMRC score) by illness severity stratified by ICU admission. In the unadjusted model, among all participants, those with moderate/severe illness were 3.31 times more likely to experience breathlessness 12 months post COVID-19 infection (OR = 3.31, 95% CI: 2.10 to 5.22; p<0.001). In model 1, when adjusted for age, gender and co-morbidities, there was no significant risk of experiencing breathlessness among all participants who had moderate/severe illness (OR = 1.58, 95% CI: 0.90 to 2.78; p=0.110).

Table 3d shows the multivariate linear regression of change in HRQoL (Health Index Value) by illness severity stratified by ICU admission. In the unadjusted analysis, among all study participants, those with moderate/severe illness had a 0.071 decrease in health index value compared to those with mild illness (β =-0.071, 95% CI -0.097 to -0.044; p<0.001). When adjusted for age, gender and co-morbidities, model 1, (β =-0.044, 95% CI: -0.076 to -0.01; p=0.006), and age, gender, co-morbidities and PHQ-4 score (β =-0.026, 95% CI: -0.030 to -0.022, p<0.001), statistically significant differences were noted, among all participants as well as the non-ICU group.

DISCUSSION:

Illness Severity at baseline:

Illness severity criteria: In our study, 50% reported mild illness and 50% reported moderate/severe illness, based on the MOH, T&T criteria (Appendix 7) [31]. Illness severity criteria was sparse in the literature as most studies followed cohorts of hospitalized patients. Yang et al, in accordance with the "COVID-19 Prevention and Control Plan (Sixth Edition)," characterized patients by the severity of COVID-19 into: mild 86.8%, severe 3.5%, or critical 9.7% [3]. Garrigues et al reported on 80.0% ward versus 20.0% ICU patients [20]; Lombardo et al reported on 37.6% non-hospitalized versus 62.4% hospitalized patients [23]; Huang et al reported on 24.9% of patients did not require supplemental oxygen versus 67.7% required supplemental oxygen; 7.3% required ventilation [21]; and Maestre-Muñiz et al looked at 41.9% discharged from the emergency room versus 58.1% patients admitted to the hospital[13].

Socio-demographics: No association between age and illness severity was found. This was consistent with previous published studies [1–3]. In our study more women had moderate/severe illness. Most studies found gender independent of illness severity [1–3]. However, Maestre-Muñiz et al [13], also found that women were more likely to experience moderate/severe illness.

Co-morbidities: Hypertension (HTN), was the most common co-morbidity seen followed by T2D, consistent with national prevalences [33,34]. We found that persons with co-morbidities, particularly T2D and IHD were more likely to experience moderate/severe illness. Findings were consistent in studies published by Maestre-Muñiz et al [13] and Lombardo et al [23].

Signs/Symptoms at acute COVID-19 infection: In South Trinidad, at acute COVID-19 infection, among those moderately/severely ill, commonly reported signs/symptoms were subjective or

measured fever, cough, myalgia, ageusia, anosmia, dyspnoea and arthralgia; similar to published literature [1–3,8,12,19]. They were more significantly reported compared to mild illness. Chemosensory dysfunction has been consistently reported during acute COVID-19 infection[8,12,13,19]. Huang et al [1] and Yang et al [3] found dyspnoea more significantly reported among those moderately/severely ill.

Management: Early efforts to contain the outbreak included mandatory state quarantine. COVID-19 positive imported cases: returning and repatriated nationals, their primary contacts and HCWs who interacted with COVID-19 positive patients [36]. This unique situation allowed us to observe the clinical course of persons with asymptomatic, mild, moderate and severe SARS-CoV-2 infection. As cases increased from July 21st 2020, due to community spread, the MOH, T&T instituted a hospital admission criteria [31], attempting to support the moderately/severely ill patients. Triage was done similarly to other countries in order to prevent the collapse of the health-care system[2]. It was crucial for physicians to be able to triage patients according to illness severity. The severely ill patients had to be sent to Couva MMF and SFGH with dedicated ICUs; however, some opted to quarantine at home, due to the fear and lack of faith of the hospital setting and belief in traditional herbal medicines. After ICU, patients were managed at step-down facilities, and discharged once stable.

Treatment: Mildly ill patients were home quarantined, advised on symptomatic treatment and monitored by the surveillance team. Moderately/severely ill patients were given the required supportive therapy (anticoagulants, corticosteroids, anti-inflammatory drugs, oxygenation and ventilation) [10].

Outcomes one-year later:

Symptomology: Our study findings showed that 60% were troubled by at least one lingering symptom: 46% among the mildly ill and 75% among those with moderate/severe illness. A wide variation is seen in the prevalence of post-covid conditions (PCC) globally. In China, Huang et al., reports that the proportion of hospital discharged patients with at least one PCC decreased from 68% at 6 months to 49% at 12 months [(21)]. After one year, in Italy, Comelli et al., reports the prevalence of at least one PCC, 91.7% among hospital discharged patients [(12)]; Lombardo et al., 81%, regardless of the illness severity in the acute phase (23) ; in Moscow, Pazukhina et al., 34%, after hospital discharge (24). In mild-to-moderate cases, Boscolo-Rizzo et al., reports a one-year, PCC prevalence of 53% [(8)]; Maestre-Muñiz et al., reports 49.5% in milder cases, 66.8% hospital discharged cases [(13)].

In our study, after one year, the most commonly reported symptoms were: dyspnoea, fatigue, muscle weakness, sleep difficulties, hair loss, regardless of the illness severity in the acute phase. In comparison to international studies, some of our findings were similar, one-year post COVID-19. In China, Huang et al., most commonly reports dyspnoea, fatigue, sleep difficulties, joint pain, hair loss, among hospital discharged patients [(21)]. In Italy, Lombardo et al., found "fatigue and weakness, muscle and joint pain, sleep disorders, respiratory disorders, neurological and cognitive impairments" prevalent regardless of the illness severity in the acute phase (23). In a recent meta-analysis done by Malik et al. [(14)], fatigue, dyspnoea, anosmia, cough, sleep disturbances, arthralgia were common persistent symptoms, consistent with reported literature.

HRQoL: In our study, overall, the health index value (0.931) was comparable to national norms (37), but lower for persons with moderate/severe illness (0.894). The overall EQ-VAS score was 79.06%, lower than that for T&T, 83.6% and even lower for persons with moderate/severe illness

74.09%. For post-acute COVID-19, in a pooled prevalence of poor quality of life, EQ-VAS was 59% (95% CI: 42%–75%) [14]. At 110 days post hospitalization, Garrigues et al reported EQ-VAS 70.3%, EQ-VAS index, 0.86 [20], and 6-months post hospitalization, Huang et al [11] reported EQ-VAS, 80.0% (70.0%-90.0%).

EQ-5D-5L responses and Mental Health Outcomes: Most of our participants were able to fully recover. However, a significant proportion had problems affecting HRQoL, which could have a negative economic impact [19]. When our findings were compared to a meta-analysis, done by Malik et al., using the EQ-5D-5L instrument, lower prevalences of mobility, 11% vs, 36%; self-care, 4% vs. 8%; usual activities, 22% vs. 30% and pain/discomfort, 30% vs. 42% were found, but a higher prevalence of anxiety/depression symptoms, 40% vs. 38% [14]. Using the same instrument, Huang et al., found that, the proportion of hospital discharged patients with anxiety symptoms increased from 23% at 6 months to 26% at 12 months [21].

In our study, at 12-month follow-up, 14.0% of respondents screened positive for either anxiety or depression. No similar studies were found for comparison of anxiety/depression using the PHQ-4, PHQ-2 and GAD-2 questionnaires among COVID-19 survivors, one-year later. Possible reasons for anxiety/depression may include: fear of death, loss of loved ones, isolation, loss of employment and incomplete recovery of physical health [21]. Strengthening of a health care policy that supports service for the emotional needs of HCWs is needed. For some participants, being ill with COVID-19 made them focus more on their self-care, spirituality, exercise and muscle strengthening.

Key Predictors

Age, gender, and co-morbidities were confounders of the predicted primary outcomes, except for HRQoL. Illness severity predicting anxiety/depression was dependent on prior mental health history. HRQoL was worse in those with moderate/severe COVID-19 compared to mild disease, one year later even after adjustment for demographics and PHQ-4 score. It is possible that factors other than age, gender, co-morbidities and PHQ-4 score were responsible for the participants' decreased quality of life, such as socio-economic challenges.

The long-term sequelae after acute COVID-19 needs to be studied so that an evidence-based multidisciplinary team approach could be developed to care for these patients [(16)]. Care should include: optimization for underlying co-morbidities, physiotherapy, occupational therapy and psychological support [(17)]. In South Trinidad, at 12-month follow-up, patients with persistent symptoms were referred to post COVID clinic at the SFTH. Our multi-disciplinary team consists of an internist, cardiologist and a psychiatrist. Further evaluation, rehabilitation and appropriate care are offered to these patients.

Strengths:

To our knowledge, this study is the first of its kind to be conducted in the Caribbean; its large sample size (n=324), with sufficient power to show associations between comparison groups; randomized cohort selection and long follow-up duration provides a good foundation for future related studies. The questionnaire, allowed the investigation of many areas of the participant's health status. Standardized pre-tested data collection instruments were used. The response rate was good, providing a good estimation of the proportion of COVID-19 patients who presented to

a health facility. The study was a community-based, and included patients in home quarantine as well as those hospitalized.

Limitations:

One limitation of the retrospective cohort design is the lack of data at baseline for certain symptoms measured at 12-month follow-up. Also, comparisons could not be made with those who were not infected with COVID-19 as validation of absent COVID-19 in matched controls was beyond the scope of this study. Even though the tools were aimed to be very comprehensive, some symptoms may not have been captured. Establishing a structured, validated questionnaire encompassing the full clinical spectrum of long COVID would enhance the replicability of clinical studies [8]. It was assumed that the laboratory confirmed COVID-19 cases are true positives, and that persons were not re-infected with COVID-19 after the first time. Questionnaires were limited to patient-reported outcomes, via virtual interviews. With, face-to-face consultations, objective measurements such as BMI, could have been done which may have influenced their health outcomes. This study results may not be generalizable to all COVID-19 positive cases in T&T as there were equal proportions of mild and moderate/severe cases. It is possible that mild cases were under-reported, as more moderate/severe cases may have presented to health facilities and therefore captured by the surveillance teams.

CONCLUSION:

Significant proportions of COVID-19 survivors have post-COVID symptoms after one year. The health index value of all participants, was below the population norms, and even lower among those with moderate/severe illness. Interventions should be prioritized for those with the highest

burden of persistent symptoms to aid their recovery. Further longitudinal observational national studies and clinical trials are needed to better understand the long-term burden of COVID-19 in T&T.

RECOMMENDATIONS:

In T&T, it is hoped that long-term surveillance programs and more long-COVID clinics would aid long haulers. An integrated approach of multidisciplinary teams with medical, psychological and rehabilitation services, with appropriate follow-up should be available for patients [38,39]. Further studies can be done to evaluate whether these interventions are beneficial.

Public health and social policies need to be implemented, to aid survivors who had severe disease, eg. disability grants, flexible working hours. Trials of biologics for those with severe long-COVID symptoms could be done, similar to the PHOSP-COVID study in the UK [39].

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APPENDICES:

APPENDIX 1

PARTICIPANT INFORMATION SHEET AND INFORMED CONSENT FORM FOR PARTICIPATION IN RESEARCH PROJECT

Study Title: One year health consequences of persons infected with COVID-19 cases in South Trinidad, 2020-2021: a cohort study.

Invitation to Participate and Description of Project: You are invited to participate in a research study. This study is designed to assess the long-term health consequences of persons infected with COVID-19 cases in South Trinidad. Through studying the lingering symptoms, we hope to achieve better patient outcomes. In order to decide whether or not you wish to be a part of this research study you should know enough about its risks and benefits to make an informed decision. Laboratory confirmed COVID-19 cases who are residents of County Victoria, St. Patrick, Caroni South, SWRHA during the period March 12 2020 to October 31 2020, and give informed consent will be included in this study.

Description of the procedures: If you agree to participate in this study, we will be asking you a few brief questions about some of the long-term health consequences that may be related to you testing positive for COVID-19.

Risks and Inconveniences: There are no anticipated risks or inconveniences.

Benefits: More research into the lingering symptoms of COVID-19, may contribute to better health outcomes for patients.

Confidentiality and Privacy: Confidentiality will be ensured by assigning a study identification number to each patient. The data will be entered electronically on a Microsoft Excel database and will be password protected by the investigators. All data will be kept securely through the

office of the Medical Director Primary Health Care, SWRHA and stored securely for a period of five (5) years. Data would only be accessed by the investigators, who are physicians assigned to work on the SWRHA COVID-19 Surveillance team. Only aggregated data will be presented in any publicly disseminated materials. No personal identifying information on health conditions would be linked back to you.

Voluntary Participation and Withdrawal: You are free to choose not to take part in this study. Your health care will not be affected if you do not agree to participate. You are free to stop and withdraw from this study at any time during its course and your health care would not be impacted.

Questions: We have used some technical terms in this form. Please feel free to ask about anything you do not understand and to consider this research and the consent form carefully – as long as you feel is necessary – before you make a decision.

Authorization and Permission: I have read (or someone has read to me) this form and have decided to participate in the project described above. Its general purposes, the particulars of my involvement and possible risks and inconveniences have been explained to my satisfaction.

By signing this form, I give permission to the researchers to use information about me for the purposes described in this form. By not giving permission, I understand that I will not participate in this research. If you have any further questions about the study or wish to withdraw, please contact Dr. Kavita Dharamraj at 1-868-730-3418.

Name of Subject: _____

Signature: _____ Date: _____

Signature of Person Obtaining Consent: _____ Date: _____

APPENDIX 2:

ONE-YEAR CONSEQUENCES OF PERSONS INFECTED WITH COVID-19 IN SOUTH TRINIDAD 2020-2021: A COHORT STUDY

COVID-19 Data Collection Tool

SECTION 1: BASELINE DATA

Demographics

Study ID#: _____ Date: DD/MM/YYYY

Date of Birth: DD/MM/YYYY Age: _____ (years) Gender: □ Male □ Female

County: □ Victoria □ St. Patrick □ Caroni South

Street Address: _____ Town: _____

Tel. No.: _____ Occupation: _____

Organization: _____ □ NA

Health Care Worker: □ Yes □ No

Source of Referral: □ MOH □ PHC □ ED □ Contact Tracing

Co-morbidities: □ None □ Asthma □ COPD □ Diabetes- type 2 □ Hypertension

□ Ischaemic Heart Disease □ Immunodeficiency □ Malignancy

□ Cerebrovascular Disease □ Chronic Kidney Disease □ Other _____

Smoking: □ Current smoker □ Ex-smoker □ Non-smoker **Pregnant:** □ Yes □ No □ NA

Signs/Symptoms: □ Fever □ Cough □ Runny Nose □ Sore Throat □ Shortness of Breath

□ Body pains (Myalgia) □ Arthralgia □ Ageusia (loss of taste) □ Anosmia (loss of smell)

□ Other _____

Date of Onset of Symptoms: DD/MM/YYYY □ Not Applicable

Number of days with symptoms: _____

Developed SARI symptoms: □ Yes □ No

Travel History: □ Yes □ No

Contact History: Contact: □ Yes □ No Primary Contact: □ Yes □ No

Secondary Contact: □ Yes □ No Tertiary Contact: □ Yes □ No

Epidemiologically Linked: □ Yes □ No

Quarantine: □ Yes □ No

Home Quarantine: □ Yes □ No State Quarantine: □ Yes □ No

Swabbed: □ Yes □ No

Location of Swab procedure: _____ □ NA

Swab Date: DD/MM/YYYY □ Not Applicable

Swab Results: □ Positive □ Negative □ Pending □ Rejected □Not swabbed

Date Results Received: DD/MM/YYYY

Referral: Referred to SFGH: □ Yes □ No

Referred to Caura/Couva: □ Yes □ No

Home quarantined requiring transfer to facility: □ Yes □ No

Hospitalized: □ Yes □ No Length of hospital stay (days): _____ □ NA

Admitted to HDU: □ Yes □ No Length of HDU stay (days): _____ □ NA

Admitted to ICU: □ Yes □ No Length of ICU stay (days): _____ □ NA

Ventilated: □ Yes □ No

Mild Illness: □ Yes □ No **Moderate/Severe Illness:** □ Yes □ No

Vaccinated: □ Yes □ No Type of vaccine: _____ □ NA

Date of first dose: DD/MM/YYYY □ NA Date of second dose: DD/MM/YYYY □ NA

Outcome: □ Ongoing □ Warded □ Discharged □ Died □ County /RHA Transfer □ Unaccounted

ONE-YEAR FOLLOW-UP:

Time period, baseline to follow-up: _____ months

SECTION 2: Symptom Questionnaire:

12. Do you have any obvious discomfort since you were discharged from hospital?

If yes, please specify _____

2. How would you comment your current health status?

□ Same as prior to COVID-19

□ Often feel fatigue, and easier to get tired after activity now than prior to COVID-19

□ Better health condition than prior to COVID-19

3. Have you experienced any of the following pain symptoms that appeared post COVID-19 and are persistent?

□ No □ Headache □ Myalgia □ Chest pain □ Joint pain (if yes, please fill in the table below)

□ Any other if yes, please specify _____

Joints	Hand	Foot	Wrist	Ankle	Jaw	Elbow	Shoulder	Neck	Hip	Knee
Tenderness										
Swollen										
Numerical pain scale (0-10)										

12 → 10

No pain — Intolerable pain

4. Do you have any of the following symptoms that are newly onset post COVID-19 and persistent?

□ No □ Sore throat □ Difficult to swallow

5. Do you have any of the following symptoms that are newly onset post COVID-19 and

persistent?

□ No □Low grade fever (37.3-38.0°C) □ Palpitations □ Dizziness □ Nasal congestion □ Skin rash

6. Are you more prone to suffer from the following symptoms after discharge?

□ No □ Diarrhea □ Nausea □ Vomiting

7. How do you feel about your sense of smell compared with the status prior to COVID-19?

□ Same as before □ Worse than before □ Better than before □ Total loss

8. How do you feel about your sense of taste compared with the status prior to COVID-19?

□ Same as before □ Worse than before □ Better than before □ Total loss

9. How do you feel about your appetite compared with the status prior to COVID-19?

□ Same as before □ Worse than before □ Better than before

10. What do you think about your sleeping compared with the status prior to COVID-19?

□ Same as before □ Worse than before □ Better than before

11. How do you feel about your muscle strength compared with the status prior to COVID-19?

□ Same as before □ Worse than before □ Better than before

10. Have you experience hair loss now compared with the status prior to COVID-19?

□ No hair loss before or after COVID-19 □ Hair loss is same as before

□ Lose more hair than before □ Lose less hair than before

Reference: Huang C, Huang L, Wang Y, Li X, Ren L, Gu X, Kang L, Guo L, Liu M, Zhou X, Luo J. 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study. The Lancet. 2021[(11)].

SECTION 3: Modified Medical Research Council (mMRC) dyspnea scale

Grade	Description of Breathlessness
0	I only get breathless with strenuous exercise
1	I get short of breath when hurrying on level ground or walking up a slight hill
2	On level ground, I walk slower than people of the same age because of breathlessness, or have to stop for breath when walking at my own pace
3	I stop for breath after walking about 100 yards or after a few minutes on level ground
4	I am too breathless to leave the house or I am breathless when dressing

mMRC score: □ 0 □ ≥ 1

Reference: Fletcher CM, Elmes PC, Fairbairn MB, et al. The significance of respiratory symptoms and the diagnosis of chronic bronchitis in a working population. British Medical Journal 1959; 2:257 [(32)].

SECTION 4a: Health-related Quality of life

EQ-5D-5L descriptive system

Under each heading, please tick the ONE box that best describes your health TODAY

Mobility:

□ I have no problems in walking about

□ I have slight problems in walking about

□ I have moderate problems in walking about

□ I have severe problems with walking around

□ I am unable to walk around

Self-Care:

□ I have no problems washing or dressing myself

□ I have slight problems washing or dressing myself

□ I have moderate problems washing or dressing myself

□ I have severe problems washing or dressing myself

□ I am unable to wash or dress myself

Usual activities (e.g. work, study, housework, family or leisure activities):

□ I have no problems doing my usual activities

□ I have slight problems doing my usual activities

□ I have moderate problems doing my usual activities

□ I have severe problems doing my usual activities

□ I am unable to do my usual activities

Pain/Discomfort:

□ I have no pain or discomfort

□ I have slight pain or discomfort

□ I have moderate pain or discomfort

□ I have severe pain or discomfort

□ I have extreme pain or discomfort

Anxiety/Depression:

□ I am not anxious or depressed

□ I am slightly anxious or depressed

□ I am moderately anxious or depressed

□ I am severely anxious or depressed

□ I am extremely anxious or depressed

Reference: Feng et al. Health and Quality of Life Outcomes (2015) 13:171[27].

SECTION 4b: EUROQoL VISUAL ANALOG SCALE:

Reference: Feng et al. Health and Quality of Life Outcomes (2015) 13:171[27].

We would like to know how good or bad your health is TODAY.

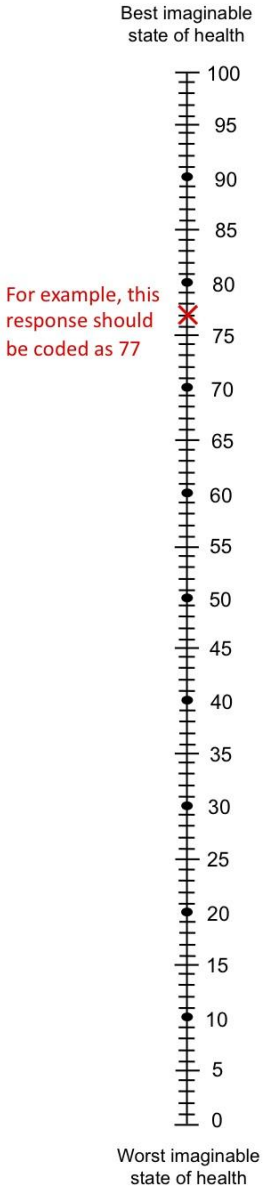
This scale is numbered from 0 to 100.

100 means the best health you can imagine.
0 means the worst health you can imagine.

Mark an X on the scale to indicate how your health is TODAY.

Now, please write the number you marked on the scale in the box below.

YOUR HEALTH TODAY = **77**



SECTION 5: PATIENT HEALTH QUESTIONNAIRE-2 (PHQ-2)

The PHQ-2 inquires about the frequency of depressed mood and anhedonia over the past two weeks. The PHQ-2 includes the first two items of the PHQ-9.

- The purpose of the PHQ-2 is to screen for depression in a "first-step" approach.
- Patients who screen positive should be further evaluated with the PHQ-9 to determine whether they meet criteria for a depressive disorder.

Over the last two (2) weeks, how often have you been bothered by any of the following problems?

PHQ-2	**Not at all**	**Several days**	**More than half the days**	**Nearly every day**
1.Little interest or pleasure in doing things	0	1	2	3
2.Feeling down, depressed or hopeless	0	1	2	3

PHQ-2 score obtained by adding score for each question (total points).

Interpretation:

- A PHQ-2 score ranges from 0-6. The authors identified a score of 3 as the optimal cut-point when using the PHQ-2 to screen for depression.
- If the score is 3 or greater, major depressive disorder is likely.
- Patients who screen positive should be further evaluated with the PHQ-9 other diagnostic instruments, or direct interview to determine whether they meet criteria for a depressive disorder.

Reference: Kroenke K, Spitzer RL, Williams JB. The Patient Health Questionnaire-2: Validity of a Two-Item Depression Screener. Medical Care. 2003; 41:1284-92[(28)].

SECTION 6: GENERALIZED ANXIETY DISORDER QUESTIONNAIRE-2-item (GAD-2)

The Generalized Anxiety Disorder 2-item (GAD-2) is a very brief and easy to perform initial screening tool for generalized anxiety disorder.

Over the last two (2) weeks, how often have you been bothered by any of the following problems?

GAD-7	Not at all	Several days	More than half the days	Nearly every day
1.Feeling nervous, anxious or on edge	0	1	2	3
2.Not being able to stop or control worrying	0	1	2	3

GAD-2 score obtained by adding score for each question (total points)

Interpretation: A score of 3 points is the preferred cut-off for identifying possible cases and in which further diagnostic evaluation for generalized anxiety disorder is warranted. Using a cut-off of 3 the GAD-2 has a sensitivity of 86% and specificity of 83% for diagnosis generalized anxiety disorder.

Reference: Kroenke K, Spitzer RL, Williams JB, Monahan PO, Löwe B. Anxiety disorders in primary care: prevalence, impairment, comorbidity, and detection. Ann Intern Med. 2007;146:317-25[29].

SECTION 7: PATIENT HEALTH QUESTIONNAIRE-4 (PHQ-4)

Over the last two (2) weeks, how often have you been bothered by any of the following problems?

	Not at all	Several days	More than half the days	Nearly every day
1. Feeling nervous, anxious or on edge	0	1	2	3
2. Not being able to stop or control worrying	0	1	2	3
3. Feeling down, depressed or hopeless	0	1	2	3
4. Little interest or pleasure in doing things	0	1	2	3

Total score is determined by adding together the scores of each of the 4 items.

Interpretation:

- Scores are rated as normal (0-2), mild (3-5), moderate (6-8) and severe (9-12).
- Total score ≥ 3 for first 2 questions suggest anxiety.
- Total score ≥ 3 for last 2 questions suggest depression.

Reference: Kroenke K, Spitzer RL, Williams JB, Lowe B. An ultra-brief screening scale for anxiety and depression: the PHQ-4. Psychosomatics. 2009; 50 (6): 613-21. From Principles of Neuropathic Pain Assessment and Management, November 2011 [30].

APPENDIX 3

INSTRUCTIONS/VARIABLE DICTIONARY

Demographics	
Study ID Number	Study identification number in consecutive number of enrolment of study (e.g., 1, 2, 3, 4….)
Date	Date the interview was conducted in the format (DD/MM/YYYY)
Date of Birth	Participant's Date of Birth in the format (DD/MM/YYYY)
Age	Participant's current age in years
Gender	Participant identified as either: "*Male*" or "*Female*"
County	Tick to indicate whether participant is from "*Victoria", "St. Patrick"* or *"Caroni South"*
Street Address	State *"Street Address"* where participant lives
Town	State *"Town"* where participant lives
Telephone Number	Participant's Telephone Contact Number
Occupation	Enter participant's occupation.
Organization	Enter organizations which participant works. Tick *"NA"* if *"Not Applicable."*
Health Care Worker	Tick to indicate if participant is a health care worker: "*Yes" or* "*No"*
Source of Referral	Tick to indicate if participant was referred from "*Ministry of Health (MOH)", "Primary Health Care (PHC)," Emergency Department (ED)", "Contact Tracing."*

Co-Morbidities	Tick to indicate if participant says he/she has been diagnosed with "*Asthma*", *"Chronic Obstructive Pulmonary Disease (COPD)"*, *"Type 2 Diabetes Mellitus (T2D)", "Hypertension (HTN)", "Ischaemic Heart Disease (IHD)", "Immunodeficiency", "Malignancy", "Cerebrovascular accident", "Chronic Kidney Disease (CKD),* and/or *"Other".* For *"Other",* please specify.
Smoking status	Tick to indicate if participant says he/she is a "*Current smoker*", if he/she smoked at least one (1) cigarette in the past 12 months, an *"Ex-smoker"*, if he/she stopped smoking cigarettes past 12 months, or a *"Non-smoker,"* if he/she never smoked a cigarette in his/her lifetime.
Pregnant	Tick to indicate if participant is pregnant: "*Yes" or* "*No."* Tick *"NA"* if *"Not Applicable."*
Signs/Symptoms	Tick to indicate if participant complains of "*Fever*", "*Cough"*, *"Runny nose", "Sore Throat", "Shortness of breath", "Body pains (Myalgia)"*, *"Arthralgia", "Ageusia (loss of taste)", "Anosmia (loss of smell)"* and/or *"Other".* For *"Other",* please specify.
Date of Onset of Symptoms	Date participant reported his/her first symptom in the format (DD/MM/YYYY). Tick *"NA"* if *"Not Applicable."*
Number of days with symptoms	On the date of interview, according to the patient, number of days that the participant experienced symptoms.
Developed SARI symptoms	Tick to indicate if the developed SARI symptoms during monitoring: "*Yes" or* "*No"*
<u>Travel History</u>	
Travel History	Tick to indicate if participant had a recent history of travel within the past fourteen (14) days: "*Yes" or* "*No"*
<u>Contact History</u>	

Contact	Tick to indicate if participant is a contact of a known COVID-19 positive patient: "*Yes" or* "*No."*
Primary Contact	Tick to indicate if participant is a primary contact of a known COVID-19 positive patient: "*Yes" or* "*No."*
Secondary Contact	Tick to indicate if participant is a secondary contact of a known COVID-19 positive patient: "*Yes" or* "*No."*
Tertiary Contact	Tick to indicate if participant is a tertiary contact of a known COVID-19 positive patient: "*Yes" or* "*No."*
Epidemiologically Linked	
Epidemiologically Linked	Tick to indicate if the case is epidemiologically linked: "*Yes" or* "*No,"* that is, if the participant had a travel history to an area with community transmission and exposure to a primary, secondary or tertiary contact at any time within the 14 days prior to onset of symptoms.
Quarantine	
Quarantine	Tick to indicate if the participant was placed under quarantine: "*Yes" or* "*No."*
Home Quarantine	Tick to indicate if the participant was placed under home quarantine: "*Yes" or* "*No."*
State Quarantine	Tick to indicate if the participant was placed under state quarantine: "*Yes" or* "*No."*
Swabbed	
Swabbed	Tick to indicate if participant had a nasopharyngeal swab for Covid-19: "*Yes" or* "*No."* If *"Yes*", state the location of the swab procedure: _____ If *"No",* tick *"Not applicable (NA)"*

Swab Date	Date participant had a nasopharyngeal swab for COVID-19 in the format (DD/MM/YYYY). Tick *"NA"* if *"Not Applicable."*
Swab Results	Tick to indicate if swab results was "*Positive*", "*Negative", "Pending", "Rejected", "Not swabbed."* If applicable, indicate the date results received in the format (DD/MM/YYYY)
Referral	
Referred to SFGH	Tick to indicate if participant was referred to SFGH: "*Yes" or* "*No."*
Referred to Caura/Couva	Tick to indicate if participant was referred to Caura/Couva: "*Yes" or* "*No."*
Home quarantined requiring transfer to a facility	Tick to indicate if participant was home quarantined requiring transfer to a facility: "*Yes" or* "*No."*
Hospitalized	Tick to indicate if participant was hospitalized: "*Yes" or* "*No."* If *"Yes"* indicate the length of hospital stay in days. Tick *"NA"* if *"Not Applicable."*
Admitted to ICU	Tick to indicate if participant was admitted to ICU "*Yes" or* "*No."* If *"Yes"* indicate the length of ICU stay in days. Tick *"NA"* if *"Not Applicable."*
Admitted to HDU	Tick to indicate if participant was admitted to HDU: "*Yes" or* "*No."* If *"Yes"* indicate the length of HDU stay in days. Tick *"NA"* if *"Not Applicable."*
Ventilated	Tick to indicate if participant was ventilated: "*Yes" or* "*No."*
Severity of Illness	
Mild Illness	Tick to indicate if the participant exhibited one or more of the following symptoms for a 'symptomatic case' and did not meet the admission criteria for COVID-19 Home Quarantined Patients (Appendix 4): "*Yes" or* "*No."*

Moderate/Severe Illness	Tick to indicate if participant met the admission criteria for COVID Home Quarantined Patients (Appendix 4), or if he/she presented with severe acute respiratory illness (SARI): acute respiratory infection with history of fever or measured fever of ≥ 38 C°; and cough; with onset within the last 10 days at the time of presentation and were admitted to hospital: "*Yes" or* "*No."*
Vaccinated	Tick to indicate if participant is currently vaccinated: "*Yes" or* "*No."*
Type of vaccine	Enter type of vaccine participant received. Tick *"NA"* if *"Not Applicable."*
Date of first dose	Date participant had first vaccination dose in the format (DD/MM/YYYY). Tick *"NA"* if *"Not Applicable."*
Date of second dose	Date participant had second vaccination dose in the format (DD/MM/YYYY). Tick *"NA"* if *"Not Applicable."*
Outcome	
Outcome	Tick to indicate the participant's outcome: "*Ongoing",* "*Warded", "Discharged," "Died," "County/RHA Transfer" Unaccounted."*

APPENDIX 4

CRITICAL APPRAISAL OF LITERATURE

Similar studies were found and critiqued.

Article 1:

Huang C, Huang L, Wang Y, Li X, Ren L, Gu X, et al. 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study. Lancet [Internet]. 2021;397(10270):220–32[(11)].

Purpose/Problem Statement: This study looks at the long-term health effects of patients infected with COVID-19 who were discharged from hospital and examines associated risk factors, particularly the disease severity.

Study type: Prospective longitudinal

Findings: Six months after onset of symptoms, most patients had at least one symptom, particularly chronic fatigue, anxiety, depression or muscle weakness. The seropositivity and titres of the neutralizing antibodies were significantly lower than at acute phase.

Overall Quality:

Strengths: This study has a large cohort (n=1733) with a long duration of follow-up, and looked at the consequences of patients discharged from hospital. Some of the study findings were consistent with data from previous SARS long term follow-up studies. It is a good foundation for future related studies.

Limitations: Baseline data for pulmonary function and six-minute walking distance were missing. There was a fairly low proportion of patients with chronic pulmonary and heart disease in this cohort. This may have resulted in underestimation, as it was self-reported by patients. Secondly, for new onset of symptoms, post-COVID-19, the data was not stratified further to

determine if the symptoms were persistent following COVID-19, worsened after COVID-19 recovery, or occurred post-discharged. Thirdly, patients with mild COVID-19 symptoms who stayed in Fangcang shelter hospitals were not enrolled in the study.

Further efforts are needed to compare the long-term outcomes between inpatients and outpatients. There was a limited number of participants, with SARS-CoV-2 antibody test results both at acute phase and follow-up. For future studies, a larger sample would be needed to clarify the dynamic changes of antibodies against SARS-CoV-2. Longer follow-up durations in large populations are necessary to better understand a wider spectrum of health consequences from COVID-19.

Article 2:

Garrigues E, Janvier P, Kherabi Y, Le Bot A, Hamon A, Gouze H, et al. Post-discharge persistent symptoms and health-related quality of life after hospitalization for COVID-19. J Infect. 2020;81(6):e4–6 [20].

Purpose/Problem Statement:

The main aim of the study was to assess the persistent symptoms post-discharge as well as the health-related quality of life (HRQoL) of patients hospitalized in a COVID-19 ward unit more than 100 days after their admission.

Study type: Prospective longitudinal

Findings: One hundred and twenty (120) patients after a mean (±SD) of 110.9 (±11.1) days following admission were included in this study. The most frequently reported persistent symptoms were fatigue (55%), dyspnoea (42%), loss of memory (34%), concentration and sleep

disorders (28% and 30.8%, respectively). Comparisons between ward- and ICU patients led to no statistically significant differences regarding those symptoms. In both groups, EQ-5D (mobility, self-care, pain, anxiety, depression, usual activity) was altered with a slight difference in pain in the ICU group.

Conclusion: Most patients requiring hospitalization for COVID-19 still have persistent symptoms. While there were few differences between HRQoL between ward and ICU patients, our findings must be confirmed in larger cohorts, including more severe patients.

Overall Quality

Strengths: This study looks at post-discharge persistent symptoms and health-related quality of life after hospitalization for COVID-19. It is a good foundation for future related studies.
Limitations: The small number of patients, the single-centre nature for the study and the high rate of patients who could not have been contacted, may have led to differential bias.

Article 3:

Lam MH-B. Mental Morbidities and Chronic Fatigue in Severe Acute Respiratory Syndrome Survivors. Arch Intern Med [Internet]. 2009 Dec 14;169(22):2142 [(22)].

Purpose/Problem Statement

From short-term follow-up of survivors who had severe acute respiratory syndrome (SARS), their physical conditions continuously improved in the first year, however, their mental health did not. The study looked at the long-term psychiatric morbidities and chronic fatigue among SARS survivors.

Findings

Over 40% of the respondents had active psychiatric illnesses, 40.3% reported a chronic fatigue problem, and 27.1% met the modified 1994 Centers for Disease Control and Prevention criteria for chronic fatigue syndrome. Psychiatric morbidities and chronic fatigue persisted and continued to be clinically significant among the survivors at the 4-year follow-up. Optimization of the treatment of mental health morbidities by a multidisciplinary approach with a view for long-term rehabilitation, especially targeting psychiatric and fatigue problems and functional and occupational rehabilitation would be needed.

Overall Quality

Strengths: This study is one of the largest long-term studies of the mental co-morbidities of survivors, following the SARS epidemic.

Limitations: The response rate was about 63%, however some participants did not complete all parts of the study. There were slight differences (a few months) in the duration of the follow-up study between the respondents and nonrespondents. Information on medical complications was retrieved from medical records and reports from study participants. Additional physical workup, especially on hormonal profiles, would provide more information and directions for future studies.

APPENDIX 5:

DEFINITION OF TERMS:

For the purposes of this study, the terms are defined as follows:

- Symptomatic case – A person who tested positive for COVID-19 infection and reported any of the following signs/symptoms: fever (measured ≥ 38 C° or reported), cough, runny nose (coryza), sore throat, shortness of breath (dyspnea) or body pains, joint pains, loss of taste and/or smell.
- Asymptomatic case – A person who tested positive for COVID-19 infection but did not report any of the above stated symptoms.
- Mild illness case – A person who exhibited one or more of the above stated symptoms but did not meet the admission criteria for COVID Home Quarantined Patients (Appendix 4).
- Moderate/Severe illness case - A person who met the admission criteria for COVID Home Quarantined Patients (Appendix 7). Persons who presented with severe acute respiratory illness (SARI): acute respiratory infection with history of fever or measured fever of ≥ 38 C°; and cough; with onset within the last 10 days at the time of presentation and were admitted to hospital were included in this category [(40)].
- Epidemiologically Linked: A person with a travel history to an area with community transmission and/or exposure to a primary, secondary, or tertiary contact anytime within the 14 days prior to symptom onset.
- Confirmed COVID-19 case - A person with laboratory confirmation of COVID-19 infection, based on real time RT-PCR from a nasopharyngeal swab, irrespective of clinical signs and symptoms [(40)].

APPENDIX 6:

Population Proportion – Sample Size

Sample size: The intended minimum calculated sample size is 254, using a 0.05 margin of error at the 95% confidence interval, calculated as follows:

Using a sample size calculator, the following formula for the sample size, $\boldsymbol{n}$ was used:

$\boldsymbol{n}$ = N*X / (X + N – 1), where,

$X = Z_{\alpha/2}^2 * \hat{p} * (1-\hat{p}) / \varepsilon^2$,

$Z_{\alpha/2}$ is the critical value of the normal distribution at α/2 (for a confidence level of 95%, α is 0.05 and the critical value is 1.96)

Margin of error, ε = 0.05

Population size, N = 1000

Sample proportion, $\hat{p}$ = 0.33

(32.6% of patients reported persistent symptoms including 18.9% with new or worsened symptoms)[18]

$\boldsymbol{n}$ or Sample size = 254 patients

Note that a Finite Population Correction has been applied to the sample size formula, to adjust a variance estimate when sampling without replacement [(41)]:

Comparing two proportions - Sample size:

This calculator uses the following formula for the sample size, $\boldsymbol{n}$ [(42)]:

$\boldsymbol{n} = (Z_{\alpha/2}+Z_{\beta})^2 * (p_1(1-p_1) + p_2(1-p_2)) / (p_1-p_2)^2$

$Z_{\alpha/2}$ is the critical value of the normal distribution at α/2 (for a confidence level of 95%, α is 0.05 and the critical value is 1.96)

p_1 = 55%

(55% of patients continued to experience three or more symptoms of hospitalized patients with moderate/severe disease) [16]

$p_2 = 30\%$

(30% of patients reported persistent symptoms among a high proportion with mild disease)[22]

Margin of error, $\varepsilon = 0.05$

Power of study = 80%

***n* or Sample size = 58 patients per group (116 patients in both groups)**

$Z_{\alpha/2}$ is the critical value of the Normal distribution at $\alpha/2$ (e.g. for a confidence level of 95%, α is 0.05 and the critical value is 1.96),

Z_β is the critical value of the Normal distribution at β (e.g. for a power of 80%, β is 0.2 and the critical value is 0.84) and p_1 and p_2 are the expected sample proportions of the two groups.

APPENDIX 7:

ADMISSION CRITERIA FOR COVID HOME QUARANTINED PATIENTS
30-Aug-20

Patients with No Co-morbid diseases	
Increasing SOB	Any combination of 3 of these symptoms triggers Covid Hospital Admission **Note**: SpO2 ≤ 94% HR ≥ 110bpm By itself triggers admission
Increasing Fatigue	
Confusion	
Chills	
Persistant Fever	

Patients with Co-morbid diseases		
Co-morbidiries		**Worsening Symptoms**
Immune. Compromised (on steroids, chemo etc)	Any 1 of these Co-rmobidities + any 2 worsening symptoms Refer to Covid Hospital	Increasing SOB** (Class 3 -4)
End Stage Renal Failure		CNS*
Chronic Pulmonary Dis.		Increasing Fatigue
CCF/ other Cardiovas. Dis.	Any 2 of these Co-morbidities + any 3 worsening symptoms Refer to Covid Hospital	Chills
Cancer		Persistant Fever
Diabetes		Chest Pain/Discomfort
Hypertension		
Note: SpO2 ≤ 94% HR ≥ 110bpm By itself triggers admission		

* CNS- Take note of Headaches, dizziness, impaired consciousness, uncoordinated movements, somnolence. (22% of patients who died experienced a disorder of consciousness)
BMJ 2020;368:m109

**New York Heart Association Classification Dyspnea	
CLASS 1	No limitation during normal activity
CLASS 2	Slight limitation during normal activity
CLASS 3	Symptomatic with normal activities without symptoms at rest
CLASS 4	Unable to undertake physical activity without symptoms . Symptoms present at rest

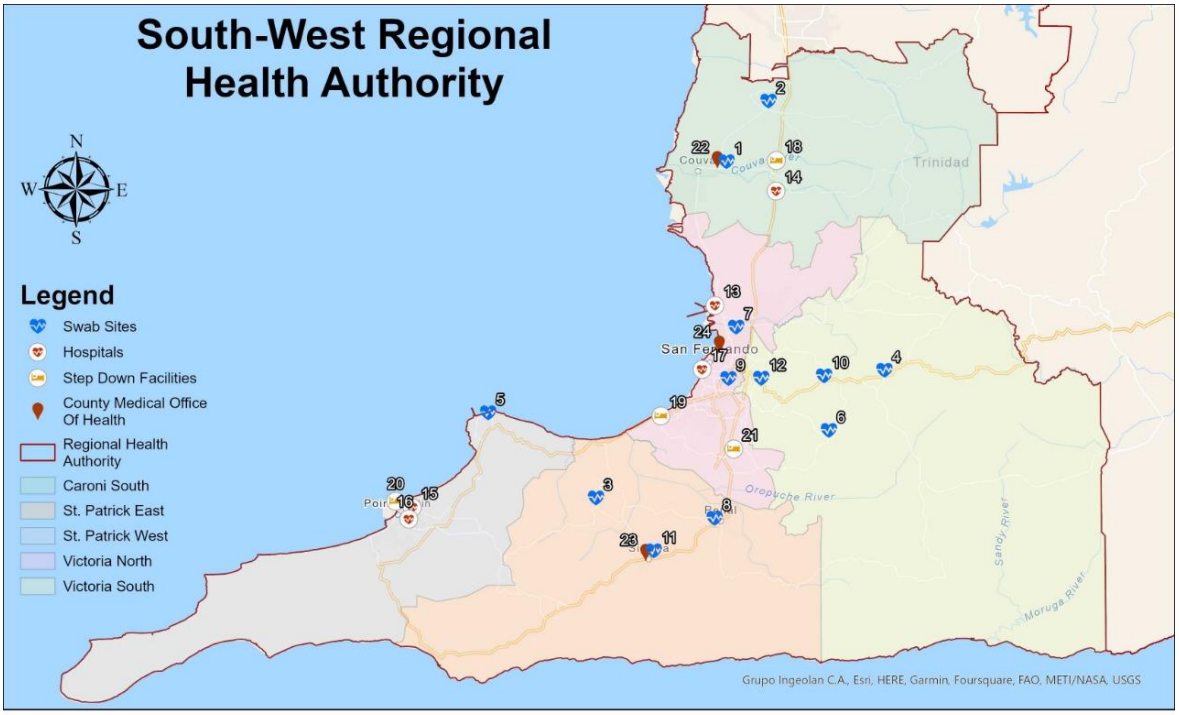
Note: Respiratory distress Class 3 or 4 is sufficient in the absence if any other symptom, is sufficient to trigger admission to Hospital

Version 1.0

Reference: Ministry of Health, Trinidad and Tobago, 2021 [31]

APPENDIX 8: TABLES AND FIGURES

Figure 1: Geographical distribution of COVID-19 surveillance sites, South Trinidad



1	Couva District Health Facility	9	Pleasantville Health Centre	17	San Fernando General Hospital
2	Freeport Health Centre	10	Princes Town District Health Facility	18	Home of Football
3	Fyzabad Health Centre	11	Siparia District Health Facility	19	Paria Suites Hotel
4	Indian Walk Health Centre	12	Ste. Madeleine Health Centre	20	Point Fortin Heritage Site
5	La Brea Health Centre	13	Augustus Long Hospital	21	Debe Quarantine Facility
6	Lengua Health Centre	14	Couva Medical and Multi-Training Facility	22	CMOH Caroni South
7	Marabella Health Centre	15	Point Fortin Area Hospital	23	CMOH St Patrick
8	Penal Health Centre	16	Point Fortin Health Centre	24	CMOH Victoria

Produced by: GIS Unit,
Epidemiology Division,
Ministry of Health.
22nd July, 2022

Kilometers
0 2.5 5 10 15 20

Figure 2: Processes at Research Setting

COVID-19 Testing:

Nasopharngeal swabs done at the viral pathways at:

- **Local Health Centres**
- **District Health Facilities**
- **ED SFGH**
- **RNA extracted and tested by real-time RT-PCR at TPHL and SFGH**

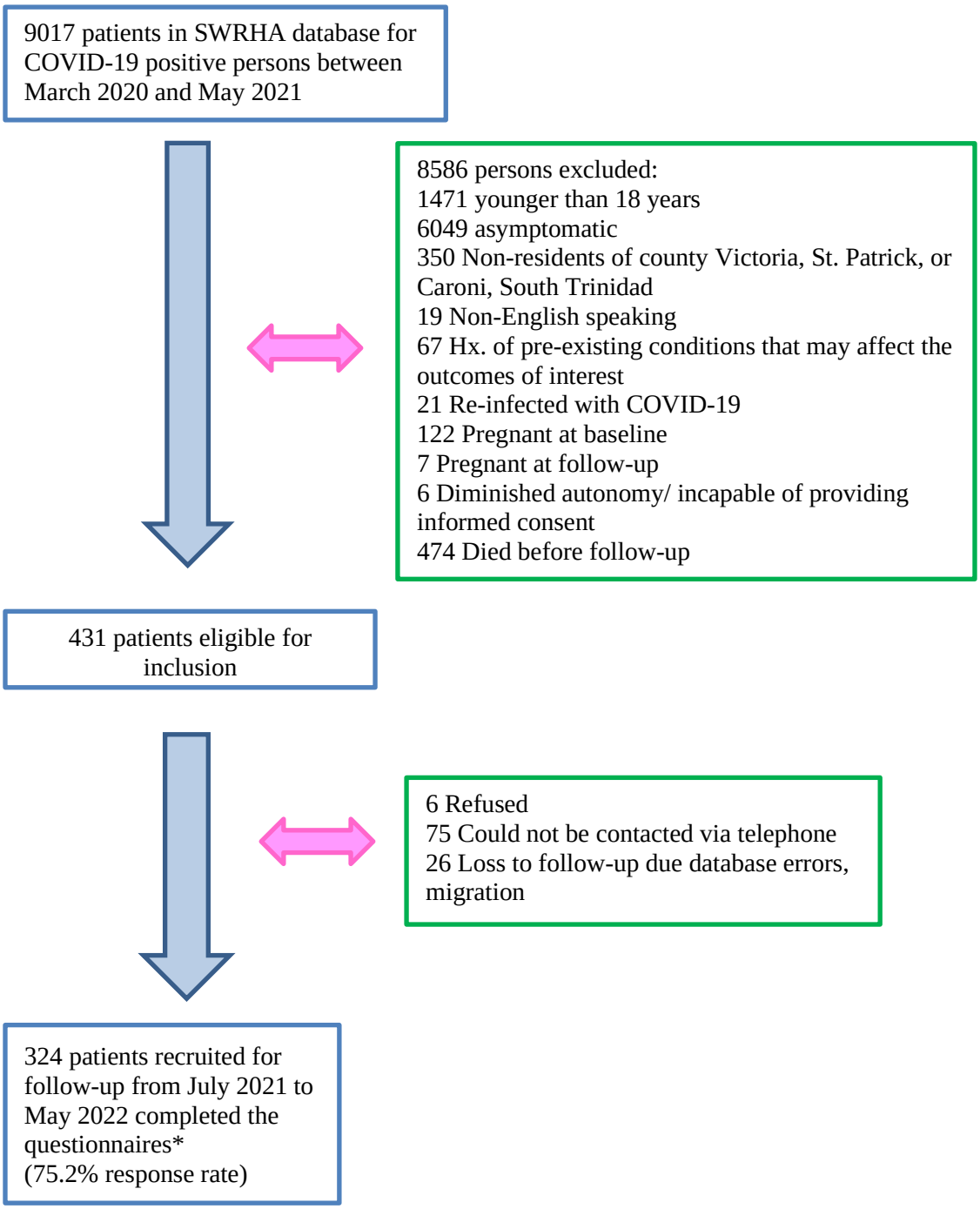
INCIDENT COMMAND CENTRES, SWRHA
Community Epidemiological Surveillance at CMOH offices:

- **Contact Tracing**
- **Identification**
- **Quarantine**
- **Monitoring of clinically confirmed and suspected cases**
- **Done by trained physicians via telephone working in the SWRHA COVID-19 Surveillance Team.**

Patients with SARI are held at:

- **The Augustus Long Hospital and/or transferred to**
- **The Couva Hospital and Multi-training facility**
- **The Caura Hospital**
- **Patients who improve are sent to a step-down transition facility**
- **Mild symptoms – home quarantine**

Figure 3: Flow chart of the recruitment of the study participants



*A series of questionnaires included a patient-reported symptom questionnaire, the modified Medical Research Council dyspnoea scale, the EQ-5D-5L questionnaire, the EuroQol Visual Analog scale, the Patient Health Questionnaire (PHQ-2) and the Generalized Anxiety Disorder Questionnaire (GAD-2).

TABLE 1: Baseline characteristics of symptomatic COVID-19 cases, South Trinidad

	Total	**Mild**	**Moderate/Severe**	**p-value**
Demographics	**N (%)** 324 (100%)	**N (%)** 162 (50%)	**N (%)** 162 (50%)	
Age, mean (SD)	42.84 (12.52) 95% CI (41.47 – 44.20)	41.83 (12.70) 95% CI (39.86-43.80)	43.84 (12.29) 95% CI (41.9-45.75)	p=0.150
Age, median (IQR)	41.0 (34-52)	41.0 (31-52)	42.0 (36-52)	
Gender				
• Male	166 (51.23%)	94 (58.02%)	72 (44.44%)	**p=0.014**
• Female	158 (48.77%)	68 (41.98%)	90 (55.56%)	
Geographical Location				
County				
• Victoria	110 (33.95%)	64 (39.51%)	46 (28.40%)	p=0.098
• St. Patrick	108 (33.33%)	51 (31.48%)	57 (35.19%)	
• Caroni South	106 (32.72%)	47 (29.01%)	59 (36.42%)	
Health Care Worker				
• Yes	27 (8.33%)	9 (5.56%)	18 (11.11%)	p=0.070
• No	297 (91.67%)	153 (94.44%)	144 (88.89%)	
No co-morbidities	217 (66.98%)	119 (73.46%)	98 (60.49%)	**p=0.013**
Co-morbidities	107 (33.02%)	43 (26.54%)	64 (39.51%)	
• Asthma	15 (4.63%)	6 (3.70%)	9 (5.56%)	p=0.428
• Type 2 Diabetes Mellitus	53 (16.36%)	20 (12.35%)	33 (20.37%)	**p=0.050**
• Hypertension	73 (22.53%)	30 (18.52%)	43 (26.54%)	p=0.084
• Ischemic Heart Disease	5 (1.54%)	0 (0.0%)	5 (3.09%)	**p=0.024**
• Cerebrovascular Disease	2 (0.62%)	0 (0.0%)	2 (1.23%)	p=0.156
• Chronic Kidney Disease	1 (0.31%)	0 (0.0%)	1 (0.62%)	p=0.317
Smoking status				
• Non-smoker	276 (85.19%)	135 (83.33%)	141 (87.04%)	p=0.556
• Current smoker	25 (7.72%)	15 (9.26%)	10 (6.17%)	
• Ex-smoker	23 (7.10%)	12 (7.41%)	11 (6.79%)	
Signs and Symptoms				
• Fever	259 (79.94%)	115 (70.99%)	144 (88.89%)	**p<0.001**
• Cough	240 (74.07%)	110 (67.90%)	130 (80.25%)	**p=0.011**
• Ageusia (loss of taste)	222 (68.52%)	94 (58.02%)	128 (79.01%)	**p<0.001**
• Body Pains (Myalgia)	219 (67.59%)	82 (50.62%)	137 (84.57%)	**p<0.001**
• Anosmia (loss of smell)	202 (62.35%)	87 (53.70%)	115 (70.99%)	**p=0.001**

• Sore Throat	151 (46.60%)	60 (37.04%)	91 (56.17%)	**p=0.001**
• Arthralgia	151 (46.60%)	46 (28.40%)	105 (64.81%)	**p<0.001**
• Shortness of Breath	148 (45.68%)	43 (26.54%)	105 (64.81%)	**p<0.001**
• Runny Nose	119 (36.73%)	53 (32.72%)	66 (40.74%)	p=0.134
Travel History				
• Yes	6 (1.85%)	4 (2.47%)	2 (1.23%)	p=0.410
• No	318 (98.15%)	158 (97.53%)	160 (98.77%)	
Contact History				
• Contact	178 (54.94%)	101 (62.35%)	77 (47.53%)	**p=0.007**
• Not a contact	146 (45.06%)	61 (37.65%)	85 (52.47%)	
Primary Contact				
• Yes	177 (54.63%)	100 (61.73%)	77 (47.53%)	**p=0.010**
• No	147 (45.37%)	62 (38.27%)	85 (52.47%)	
Epidemiologically Linked				
• Yes	181 (55.86%)	103 (63.58%)	78 (48.15%)	**p=0.005**
• No	143 (44.14%)	59 (36.42%)	84 (51.85%)	
Home Quarantined				
• Yes	268 (82.72%)	134 (82.72%)	134 (82.72%)	p=1.000
• No	56 (17.28%)	28 (17.28%)	28 (17.28%)	
State Quarantined – Hospitalized				
• Yes – Early phase	31 (9.57%)	26 (16.05%)	5 (3.09%)	**p<0.001**
• Yes	74 (22.84%)	11 (6.79%)	63 (38.89%)	
• No	219 (67.59%)	125 (77.16%)	94 (58.02%)	
Both state and home quarantined				
• Yes	49 (15.12%)	9 (5.56%)	40 (24.69%)	**p<0.001**
• No	275 (84.88%)	153 (94.44%)	122 (75.31%)	
Admitted to ICU				
• Yes	14 (4.32%)	0 (0.0%)	14 (8.64%)	**p<0.001**
• No	310 (95.68%)	162 (100.0%)	148 (91.36%)	
Admitted to HDU				
• Yes	15 (4.63%)	2 (1.23%)	13 (8.02%)	**p=0.004**
• No	309 (95.37%)	160 (98.77%)	149 (91.98%)	
Admitted to both ICU and HDU				
• Yes	9 (2.78%)	0 (0.0%)	9 (5.56%)	**p=0.002**

• No	315 (97.22%)	162 (100.0%)	153 (94.44%)	
Ventilated				
• Yes	11 (3.40%)	1 (0.62%)	10 (6.17%)	**p=0.006**
• No	313 (96.60%)	161 (99.38%)	152 (93.83%)	
Oxygen				
• Yes	48 (14.81%)	6 (3.70%)	42 (25.93%)	**p<0.001**
• No	276 (85.19%)	156 (96.30%)	120 (74.07%)	
Fully vaccinated				
• Yes	236 (72.84%)	124 (76.54%)	112 (69.14%)	p=0.134
• No	88 (27.16%)	38 (23.46%)	50 (30.86%)	
Type of vaccine				
• Sinopharm	136 (41.98%)	69 (42.59%)	67 (41.36%)	p=0.323
• Astra Zeneca	46 (14.20%)	28 (17.28%)	18 (11.11%)	
• Pfizer	39 (12.04%)	18 (11.11%)	21 (12.96%)	
• JJ	15 (4.63%)	9 (5.56%)	6 (3.70%)	
• NA	88 (27.16%)	38 (23.46%)	50 (30.86%)	
	N= 105	N=37	N=68	
Length of hospital stay (days) mean, (SD)	16.51 (13.24) 95% CI (13.95 – 19.08)	14.38 (9.78) 95% CI (11.11-17.64)	17.68 (14.73) 95% CI (14.11-21.24)	p=0.225
Length of hospital stay (days) median, (IQR)	14 (7-21)	14 (7-21)	14 (7-24)	
	N=14	N=0	N=14	
Length of ICU stay (days) mean, (SD)	8.07 (6.74) 95% CI (4.18 – 11.96)	0 (0.0)	8.07 (6.74) 95% CI (4.18 -11.96)	-
Length of ICU (days) median, (IQR)	6.5 (4-7)	0 (0.0)	6.5 (4-7)	
	N=15	N=2	N=13	
Length of HDU stay (days) mean, (SD)	9.2 (8.05) 95% CI (4.74 – 13.65)	3.5 (2.12) 95% CI (-15.56 - 22.56)	10.08 (8.30) 95% CI (5.06-15.09)	p= 0.299
Length of HDU (days) median, (IQR)	7.0 (4-14)	3.5 (2-5)	7.0 (5-14)	

Data are n/N (%) or mean (SD), unless otherwise specified.
p-values ≤ 0.05 are statistically significant.

TABLE 2: Symptoms, health-related quality of life at follow-up according to severity of illness

	Total	Mild	Moderate/ Severe	Unadjusted OR or β (95% CI)	p-value
	N (%) 324 (100.0%)	**N (%)** 162 (50.0%)	**N (%)** 162 (50.0%)		
Time period from baseline to follow-up (months) Mean, (SD)	12.69 (1.21) 95% CI: (12.55 – 12.82)	12.68 (1.24) 95% CI: (12.49-12.87)	12.70 (1.19) 95% CI: (12.51 – 12.88)	β 0.01 (-0.17-0.19)	p=0.891
- Median (IQR)	12 (12-13)	12 (12-13)	12 (12-13)		
Symptoms					
Any one of the following symptoms:	195 (60.19)	74 (45.68)	121 (74.69)	OR 3.51 (2.19-5.61)	**p<0.001**
Fatigue	138 (42.59)	41 (25.31)	97 (59.88)	OR 4.40 (2.74-7.07)	**p<0.001**
Muscle weakness	102 (31.48)	25 (15.43)	77 (47.53)	OR 4.96 (2.93 – 8.40)	**p<0.001**
Sleep difficulties	74 (22.84)	22 (13.58)	52 (32.10)	OR 3.01 (1.72 - 5.25)	**p<0.001**
Hair loss	56 (17.28)	17 (10.49)	39 (24.07)	OR 2.70 (1.46 - 5.02)	**p=0.001**
Joint pains	44 (13.58)	11 (6.79)	33 (20.37)	OR 3.51 (1.71 – 7.23)	**p<0.001**
Appetite disturbance	43 (13.27)	6 (3.70)	37 (22.84)	OR 7.70 (3.15-18.82)	**p<0.001**
Headache	40 (12.35)	11(6.79)	29 (17.90)	OR 2.99 (1.44 – 6.22)	**p=0.002**
Taste disturbance	31 (9.57)	9 (5.56)	22 (13.58)	OR 2.67 (1.19-5.99)	**p=0.013**
Smell disturbance	28 (8.64)	7 (4.32)	21 (12.96)	OR 3.30 (1.36-7.99)	**p=0.005**
Dizziness	27 (8.33)	6 (3.70)	21 (12.96)	OR 3.87 (1.52 – 9.87)	**p=0.002**
Chest pain	23 (7.10)	2 (1.23)	21 (12.96)	OR 11.91 (2.74 - 51.71)	**p<0.001**
Palpitations	31 (9.57)	10 (6.17)	21 (12.96)	OR 2.26 (1.03 – 4.97)	**p=0.036**
Body Pains (Myalgia)	18 (5.56)	0 (0.0)	18 (11.11)	OR 1.0	NA
Nasal congestion	18 (5.56)	6 (3.70)	12 (7.41)	OR 2.08 (0.76 – 5.68)	p=0.142
Skin rash	10 (3.09)	0 (0.0)	10 (6.17)	OR 1.0	NA
Sore throat	9 (2.78)	2 (1.23)	7 (4.32)	OR 3.61 (0.74 – 17.66)	p=0.082
Nausea	9 (2.78)	3 (1.85)	6 (3.70)	OR 2.04 (0.50 – 8.29)	p=0.306
Low grade fever	8 (2.47)	1 (0.62)	7 (4.32)	OR 7.27 (0.88 – 59.78)	**p=0.023**
Difficulty to swallow	5 (1.54)	1 (0.62)	4 (2.47)	OR 4.07 (0.45 – 36.87)	p=0.162
Diarrhoea	5 (1.54)	0 (0.0)	5 (3.09)	OR 1.0	NA

mMRC score					
○ 0	155 (47.84)	101 (62.35)	54 (33.33)	OR 3.31 (2.1 – 5.22)	**p<0.001**
○ ≥1	169 (52.16)	61 (37.65)	108 (66.67)		
Health Index Value, Mean, (SD) (T&T values =0.95)	0.931 (0.13) 95% CI: (0.92 - 0.94)	0.967 (0.07) 95% CI: (0.96 - 0.98)	0.894 (0.16) 95% CI: (0.87 - 0.92)	β -8.65 (-12.19 – -5.10)	**p<0.001**
‡Quality of Life, EQ-VAS score Mean, (SD)	79.06 (15.74) 95% CI: (77.34 -80.78)	84.04 (12.58) 95% CI: (82.09-85.99)	74.09 (16.99) 95% CI: (71.45 – 76.72)	β -0.04 (-0.06 – -0.03)	**p<0.001**
	Total N (%)	**Mild N (%)**	**Moderate/ Severe, N (%)**	**Mann-Whitney U test, z-value**	**p-value**
PHQ-4 score ≥ 6	44 (13.58)	8 (4.94)	36 (22.22)	-4.534	**p<0.001**
<6	280 (86.42)	154 (95.06)	126 (77.78)		
PHQ-2 score ≥ 3	45 (13.89)	8 (4.94)	37 (22.84)	-4.651	**p<0.001**
< 3	279 (86.11)	154 (95.06)	125 (77.16)		
GAD-2 score ≥ 3	55 (16.98)	13 (8.02)	42 (25.93)	-4.285	**p<0.001**
< 3	269 (83.02)	149 (91.98)	120 (74.07)		

Data are n/N (%) or mean (SD), unless otherwise specified. OR=odds ratio. NA=not applicable. mMRC=modified British Medical Research Council. †EQ-5D-5L= EuroQol five-dimension five-level questionnaire. ‡Quality of life was assessed using the EuroQol Visual Analog Scale, ranging from 0 (worst imaginable health) to 100 (best imaginable health). p-values ≤ 0.05 are statistically significant.

Table 3a: Multivariate Logistic regression of difference in fatigue or muscle weakness by illness severity stratified by ICU admission

ICU Admission Status	Illness Severity *(Reference group: Mild illness)*	Unadjusted OR (95% CI) p-value	Adjusted OR (95% CI) p-value
			Model 1: Adjusted for Age (centered), Gender, Co-morbidities
All participants	Moderate/ Severe	1.58 (1.01 to 2.47) **p=0.043**	1.40 (0.814 to 2.40) p= 0.224
Non-ICU admission	Moderate/ Severe	1.49 (0.95 to 2.35) p= 0.083	1.42 (0.81 to 2.48) p= 0.215

CI=Confidence Interval

Table 3b: Multivariate Logistic regression of difference in anxiety or depression by illness severity stratified by ICU admission

ICU Admission Status	Illness Severity *(Reference group: Mild illness)*	Unadjusted OR (95% CI) p-value	Adjusted OR (95% CI) p-value	
			Model 1: Adjusted for Age (centered), Gender, Co-morbidities	Model 2 Adjusted for previous history of anxiety or depression
All participants	Moderate/ Severe	5.5 (2.47 to 12.26) **p<0.001**	0.75 (-0.06 to 1.51) p=0.052	1.20 (0.24 to 2.17) **p=0.015**
Non-ICU admission	Moderate/ Severe	5.31 (2.36 to 11.95) **p<0.001**	0.72 (-0.08 to 1.52) p=0.077	1.25 (0.28 to 2.22) **p=0.012**

CI=Confidence Interval

Table 3c: Multivariate Logistic regression of difference in degree of breathlessness

(mMRC score) by illness severity stratified by ICU admission

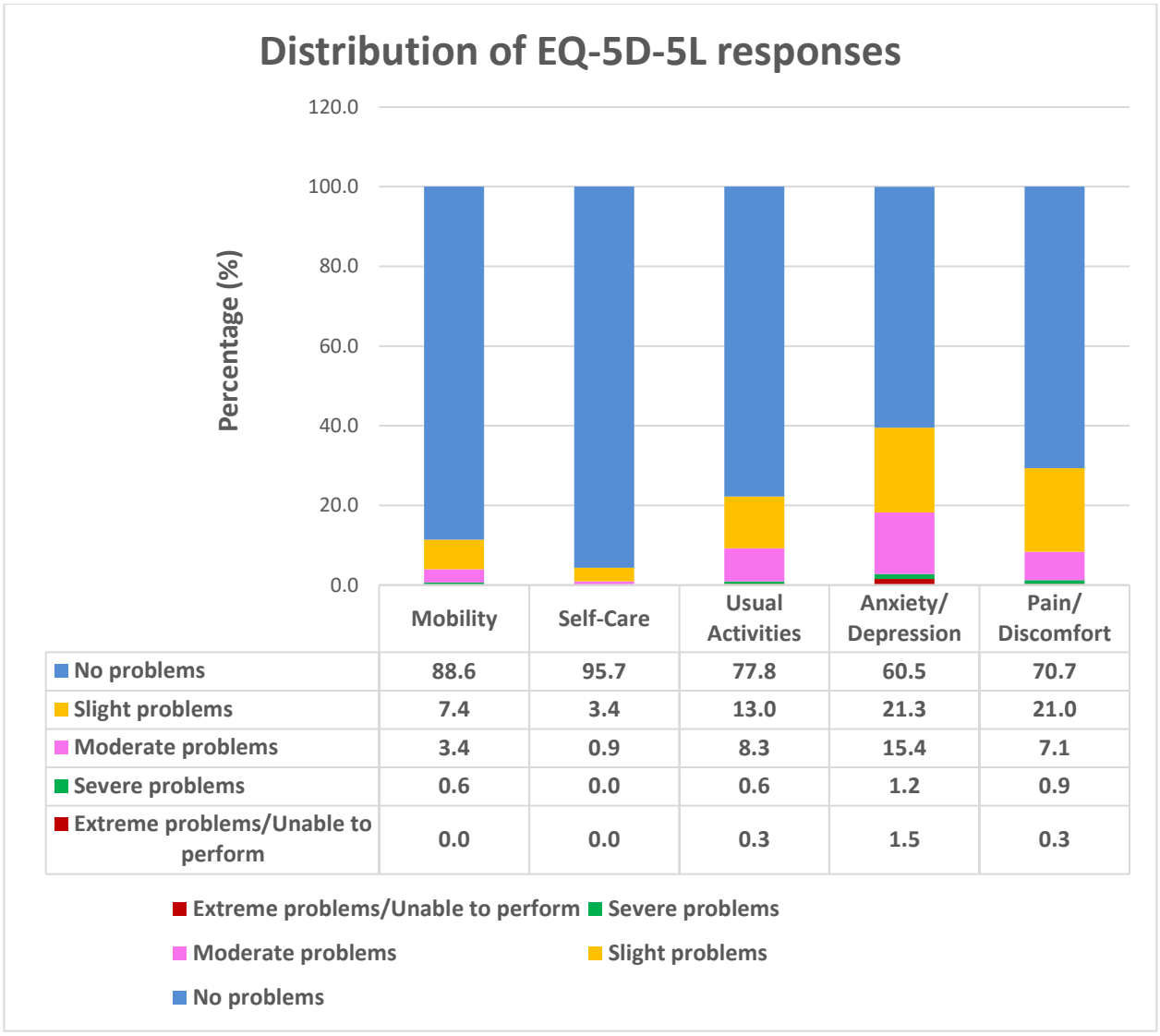
ICU Admission Status	Illness Severity *(Reference group: Mild illness)*	Unadjusted OR (95% CI) p-value	Adjusted OR (95% CI) p-value
			Model 1: Adjusted for Age (centered), Gender, Co-morbidities
All participants	Moderate/Severe	3.31 (2.10 to 5.22) **p<0.001**	1.58 (0.90 to 2.78) p=0.110
Non-ICU admission	Moderate/Severe	3.15 (1.98 to 5.01) **p<0.001**	1.43 (0.802 to 2.55) p= 0.226

CI= Confidence Interval

Table 3d: Multivariate Linear regression of change in health-related quality of life (Health Index Value) by illness severity stratified by ICU admission

ICU Admission Status	Illness Severity *(Reference group: Mild illness)*	Unadjusted β (95% CI) p-value	Adjusted β (95% CI) p-value	
			Model 1: Adjusted for Age (centered), Gender, Co-morbidities	Model 2: Adjusted for Age (centered), Gender, Co-morbidities, PHQ-4 score (centered)
All participants	Moderate/ Severe	-0.071 (-0.097 to -0.044) **p<0.001**	-0.044 (-0.076 to -0.01) **p=0.006**	-0.026 (-0.030 to -0.022) **p<0.001**
Non-ICU admission	Moderate/ Severe	-0.058 (-0.0799 to 0.036) **p<0.001**	-0.027 (-0.05 to -0.0009) **p=0.043**	-0.021 (-0.024 to -0.018) **p<0.001**

CI= Confidence Interval



	Mobility	Self-Care	Usual Activities	Anxiety/ Depression	Pain/ Discomfort
No problems	88.6	95.7	77.8	60.5	70.7
Slight problems	7.4	3.4	13.0	21.3	21.0
Moderate problems	3.4	0.9	8.3	15.4	7.1
Severe problems	0.6	0.0	0.6	1.2	0.9
Extreme problems/Unable to perform	0.0	0.0	0.3	1.5	0.3

Figure 4: Distribution of EQ-5D-5l responses in study cohort

APPENDIX 9: APPROVALS

Approval 1: Approval from the Campus Ethics Research Committee, St. Augustine

THE UNIVERSITY OF THE WEST INDIES
ST. AUGUSTINE, TRINIDAD AND TOBAGO, WEST INDIES
CAMPUS RESEARCH ETHICS COMMITTEE
TELEPHONE: (1-868) 662-2002 ext. 82755 E-mail: campusethics@sta.uwi.edu

September, 8 2021

Kavita Dharamraj,
School of Medicine, Faculty of Medical Sciences,
128 St. Croix Road, Princes Town
Email: kavita.dharamraj@gmail.com

Dear Kavita Dharamraj,

Ref: CREC-SA.1142/08/2021

Title: Health-related quality of life, symptomology and mood disorders, one-year after COVID-19 infection: A Cohort Study in South Trinidad, 2020-2021.

I am pleased to advise that your application for research on the above captioned topic has been approved on behalf of Campus Research Ethics Committee, St. Augustine.

Approval is valid for one (1) year.

Sincerely,

Professor Jerome De Lisle
Chair
Campus Research Ethics Committee

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Approval 2: Approval from the Bioethics Committee, South-West Regional Health Authority

SOUTH-WEST REGIONAL HEALTH AUTHORITY

Independence Avenue, Paradise Pasture, San Fernando, Trinidad & Tobago, West Indies.
Phones: PBX (868) 653-4259 / 9096 / 0724 / 8079, 652-6810, 657-9872
Fax: PBX ext. 2301
Email: info@swrha.co.tt Website: www.swrha.co.tt

August 20th 2021

Dr. Kavita Dharamraj
Primary Care Physician 11
South-West Regional Health Authority
Level 8, SFTH, Chancery Lane
San-Fernando.

GENERAL MANAGER
20 AUG 2021
NURSING

Ref: 1/3/40-124

Dear Dr. Dharamraj

Re: Approval to conduct Research Project

Please be advised that permission has been granted you to conduct your research project entitled: ***Request for Research "Health-related quality of life, symptomology and mood disorders, one-year after COVID-19 infection: a cohort study in south Trinidad, 2020-2021".*** It should be noted the South-West Regional Health Authority thanks you for selecting our health care facilities to conduct your research. However, it is important to note that this Region has a **confidentiality policy**.

At the completion of the research project, a **final report must** be submitted to the Ethics Committee for our records **within two (2) months**.

Also note that research findings would be reviewed by the CEO who would then determine if the research is acceptable for publication **before data collected can be published or presented in any way outside of your assignment. A copy of the final report together with approval must be submitted to the Policy Planning and Research Department, SWRHA with the request for publishing addressed to the Chief Executive Officer, SWRHA.**

Kindly note, ethics approval does not mean the researcher can proceed to collect data without approval from the Head of Department before data can be collected. Any deviation from this can result in ethics approval being withdrawn.

The Authority wishes you the very best in your future endeavours.

Yours sincerely

Your Partners in Health

K Thomas Elbourne

Mrs. Kathyann Thomas-Elbourne
GM-Nursing/Secretary –Bioethics Committee

KTE/jnb

Approval 3: Permission from the Medical Director, Primary Health Care to access the SWRHA COVID-19 surveillance database

Dr. Pedram Lalla,

Medical Director Primary Health Care,

South-West Regional Health Authority

Level 8, SFTH, Chancery Lane

San-Fernando.

August 4, 2021

Dear Dr. Lalla,

The COVID-19 pandemic has been ongoing in Trinidad and Tobago since March 12, 2020. A lot is still unknown about how COVID-19 affects people over time. Through studying the long-term health consequences of persons infected with COVID-19 in South Trinidad, better patient outcomes may be achieved.

I wish to conduct a retrospective study on: **Health-related quality of life, symptomology and mood disorders, one-year after COVID-19 infection: A Cohort Study in South Trinidad, 2020-2021.** I am seeking permission from to obtain a list of patients who tested positive for the time period, March 2020 to November 2020 to conduct this survey.

Thanking you most sincerely in advance for your kind co-operation.

Yours respectfully,

Approved pending Ethics approval

Kavita Dharamraj

Dr. Kavita Dharamraj

Primary Care Physician 11

South-West Regional Health Authority.

Approval 4:

Approval from the EuroQol Research Foundation to use the English (UK) | EQ-5D-5L Interviewer Administration – Paper version

Registration ID TR43478

Dear Kavita Dharamraj,

Thank you for your email. You may use the **English UK** version that is available for: EQ-5D-5L Interviewer Administration - Paper

Before we can send the file, can you please review and accept the below Terms of Use?

Please be informed that the attached Terms Of Use apply to the use of the Paper version. Please confirm that you can accept the attached Terms Of Use and thereafter we will be able to send you the versions.

Please note that the following is **not allowed** according to the Terms Of Use:

- Provide the **Paper version in any other way than on paper** to be filled out with pencil, by example implement the EQ-5D Paper into an online survey, app or electronic device.
- Use of EQ-5D versions **in a new study/project without a new registration**.
- Use the requested version when the study/project is **funded by a profit-making stakeholder**.
- Use the requested version without separate permission when the intention is **to charge a fee for third party access** to the collected data in the project.
- **Distribute the versions to third parties** -other than clinical sites- without prior approval of Euroqol.
- **Modify, alter, amend** the provided EQ-5D Paper version and or EQ-5D Digital version.
- **Develop any new language** of the provided versions without permission of Euroqol.
- **Reproduce the EQ-5D** Paper or Digital module version **in a publication or on the internet** without permission.

Kind regards,

Joelle Guerin
Assistant Project Manager, VMC
EuroQol Research Foundation
A reply to e-mails can be expected within approximately 5 business days.

Dear Kavita Dharamraj,

Thank you for accepting the Terms of Use.
I have sent out the effective source file for **English (UK) | EQ-5D-5L Interviewer Administration - Paper version** via our automated system. You may need to check your spam folder.

Please let me know if you have not yet received it and I will send it manually.

Kind regards,

Joelle Guerin
Assistant Project Manager, VMC
EuroQol Research Foundation
A reply to e-mails can be expected within approximately 5 business days.

Patient-reported outcome measures, one-year after COVID-19: A Cohort Study in South Trinidad, 2020- 2021

by Kavita Dharamraj

Submission date: 30-Sep-2022 04:36PM (UTC-0400)
Submission ID: 1913292603
File name: 66915_Kavita_Dharamraj_DM_30-09-22_871893_746059979.docx (124.21K)
Word count: 4961
Character count: 28

INTRODUCTION

COVID-19 was first detected in Wuhan, China in December 2019, and has been an ongoing global threat [1–3]. As of March 30, 2022, the global pandemic of COVID-19 has led to more than 481 million confirmed cases with over 6.13 million deaths [4]. In T&T, since March 12, 2020, there has been, over 182 thousand confirmed cases, 174 thousand "recovered" cases and 4100 deaths [5].

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection ranges from being asymptomatic to severe or fatal [2,6–9]. The pathogenesis, clinical, epidemiological characteristics, and complications for acute COVID-19 have been well documented [1–3]. Most persons recover after 2 to 6 weeks [7,10]. However, it has been observed that in an increasing number of patients, recovering from COVID-19, a wide constellation of symptoms may persist for weeks or months [11–14].

Known by diverse names, in September 2020, in a 'WHO-led Delphi' process, the final consensus definition for adults: "post-COVID-19 condition occurs in individuals with a history of probable or confirmed SARS-CoV-2 infection, usually 3 months from the onset, with symptoms that last for at least 2 months and cannot be explained by an alternative diagnosis. Common symptoms include, but are not limited to, fatigue, shortness of breath, and cognitive dysfunction, and generally have an impact on everyday functioning. Symptoms might be new onset following initial recovery from an acute COVID-19 episode or persist from the initial illness. Symptoms might also fluctuate or relapse over time [15]".

There has been notable impact on the physical, cognitive, mental and social health status of patients, regardless of illness severity [14,16–18].

Published studies have focussed on previously hospitalized patients with severe COVID-19 illness, reporting symptoms up to 6-months after [11,19,20]. However, there is paucity of data

regarding one-year health consequences post COVID-19 infection [12,13,19,21]. Through this study, the long-term burden of COVID-19 may be better understood in Trinidad and Tobago (T&T).

RESEARCH QUESTIONS

Primary Research Question:

- What is the HRQoL, symptomology and mood disorders in persons, one-year after being diagnosed with COVID-19 in South Trinidad, 2020-2021?

Secondary Research Question:

- Is there a difference in the following outcomes, one-year post-acute COVID-19 infection, based on severity of initial COVID-19 infection, socio-demographics and other baseline factors:
  - ✓ HRQoL
  - ✓ Symptoms
  - ✓ Anxiety/Depression
  - ✓ Degree of breathlessness

AIMS AND OBJECTIVES:

Aim: To describe the patient-reported long-term health consequences, one-year after being diagnosed with COVID-19, and predictors, according to illness severity in South Trinidad, 2020-2021.

Objectives:

- To determine the difference in HRQoL, symptoms, anxiety/depression, degree of breathlessness experienced one-year after being diagnosed with COVID-19 according to severity of illness.
- To determine the predictors/factors associated with these main outcomes.

LITERATURE SEARCH STRATEGY AND REVIEW

Several databases were searched – PubMed, Medline and Scopus, up to March 2021. The search terms used were "(**COVID-19** OR **Coronavirus disease 2019** OR **2019-nCoV** OR **SARS-Cov-2** OR **post-acute COVID-19 syndrome** OR **post-COVID-19** OR **post-acute sequelae of COVID-19** OR **long COVID**) AND (**one-year health consequences** OR **12-month health consequences** OR **long-term health consequences** OR **long-term sequelae**)." Early in the pandemic related studies were found and critiqued [11,20,22]. (Appendix 4). As the pandemic progressed, one-year post COVID-19 studies were published and relevant findings were compared to ours in the discussion [8,12,13,21,23,24].

METHODOLOGY:

Study Design: This was a retrospective cohort (analytical) study.

Research Setting: At the onset of the pandemic in T&T, as part of the national response to contain the spread of COVID-19, community epidemiological surveillance has been ongoing through the communities of counties Victoria, St. Patrick and Caroni South, at the South-West Regional Health Authority (SWRHA). The geographical distribution of COVID-19 surveillance sites is shown in

figure 1 and the processes at the research setting are shown in figure 2, according to the recommended protocol by the MOH, T&T.

Study population: All 324 symptomatic laboratory confirmed patients who had COVID-19 for a minimum period of one year, at the time of data collection, and met the inclusion criteria. (Appendix 5).

Inclusion Criteria: Symptomatic laboratory confirmed COVID-19 adult patients ≥ 18 years, who resided in the communities of Counties Victoria, St. Patrick and Caroni South, SWRHA, during the study period (baseline: 12-03-20 to 31-05-21; one-year follow-up: 26-07-21 to 31-05-22) and gave informed consent.

Exclusion Criteria: Non-laboratory confirmed COVID-19 adults; asymptomatic laboratory confirmed COVID-19 cases; persons who were re-infected with COVID-19 at follow-up; pregnant women with acute COVID-19 infection; pregnant women at follow-up; children and adolescents < 18 years; non-residents of county Victoria, St. Patrick or Caroni; non-English speaking; asymptomatic persons; those with a history of pre-existing conditions that may affect outcomes of interest (for eg. cardiorespiratory conditions that cause shortness of breath, thyroid and autoimmune diseases that may cause fatigue); persons with diminished autonomy who were incapable of providing informed consent; persons who died before one year follow-up; those who did not consent to participate and those who could not be contacted.

Sampling methods: Random sampling was used. A random generator was used to select persons from list of eligible participants. If a person ended up in the study and could not be contacted or

did not consent, the next person on the randomized list was chosen. Participants were selected based on the specific problem under investigation, not because of any social bias, ease of availability or diminished autonomy.

Measures were taken to reduce sources of bias:

Non-response bias - The data collection tool was pre-tested to identify possible sources of bias in the length or content of questionnaire and minimize the non-response rate.

Recall bias –To recall some of the baseline information, persons may have difficulty recalling the information. The interviewer prompted their memory in this regard.

Sample size: A sample of 324 participants was recruited, based on a 30% prevalence for mild disease [19] and a 55% prevalence for moderate/severe disease[25], using a type 1 margin of error, 0.05, at the 95% confidence interval, with a power of 80% (Appendix 6).

Data Collection Tool:

The 'COVID-19 Data Collection tool' consisted of seven (7) sections (Appendix 2).

The first section was designed to collect baseline data is a community-based surveillance tool tailored to a local setting after review of the WHO COVID-19 data capture instruments. All variables were defined (Appendix 3). This information was collected at the time of the patient's nasopharyngeal swab. One year after baseline data was collected, data on health-related outcomes was collected using the following questionnaires:

- "Symptom Questionnaire: Participants were asked to report on persistent, newly occurring or worsening symptoms before COVID-19 [11]."
- "Modified Medical Research Council (mMRC) dyspnoea scale: This is a five-category scale, which characterizes the level of dyspnoea with physical activity. Higher scores correspond with increased dyspnoea[26]. It quantifies the disability associated with breathlessness, by identifying if breathlessness occurs when it should not."
- "HRQoL: The EQ-5D-5L is a validated questionnaire to evaluate patient quality of life by assessing the following five factors: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each factor is divided into five levels that range from none to extreme problems[27]."
- "EuroQol Visual Analog Scale (EQ-VAS): This is a patient's assessment of subjective assessment of generic health ranging from 0 to 100, with higher scores representing better subjective health experience[27]."
- "Patient Health Questionnaire-2 (PHQ-2): A depression screening and severity measure [28]."
- "Generalized Anxiety Disorder Questionnaire-2 (GAD-2): A brief screening test for detecting generalized anxiety disorder [29]."
- "Patient Health Questionnaire-4 (PHQ-4): The four-item patient health screening questionnaire for detecting depression and anxiety[30]."

Data collection methods:

The study was approved by the University of the West Indies (UWI) (Approval 1) and the SWRHA (Approval 2). Permission was granted from the Medical Director, Primary Health Care (PHC)

(Approval 3) to access the SWRHA COVID-19 surveillance data from March 12, 2020, to May 31, 2021. This secondary data source was compiled by physicians and nurses who worked on the surveillance team. The first section was completed.

The instruments were pre-tested on 20 participants. One-year post-acute infection, data on health-related outcomes was collected using the questionnaires, outlined in Appendix 2. Informed consent was obtained from the participant (Appendix 1). Virtual interviews (zoom video conferencing and telephone) were conducted due to safety concerns in the COVID-19 pandemic. Permission to use the ED-5D-5L questionnaire and the EQ-VAS was granted from the EuroQol Research Foundation (Approval 4). Instructions were given to the participant to indicate how good or bad his/her health was on the scale. Primary outcomes measured included fatigue or muscle weakness, anxiety or depression, degree of breathlessness (mMRC score), and health-related quality of life (health index value).

Statistical Analysis:

Baseline characteristics and one-year health consequences of symptomatic laboratory-confirmed COVID-19 participants were shown: normally distributed continuous variables were expressed as means (SDs) and non-normally distributed as medians (IQRs), and absolute values (N), with percentages (%) for categorical variables. Tests for normality of continuous data were done looking at skewness and kurtosis, the Shapiro-Wilk test and the quantile-quantile (Q-Q) plots. Participants were categorised into two groups according to their illness severity at acute infection. Comparisons of baseline characteristics, symptoms, degree of breathless and HRQoL, anxiety and depression were done between mild and moderate/severe groups. For this study, cut-points for positive screens for: anxiety/depression, PHQ-4 score ≥6 [30]; depression, PHQ-2 score ≥3 [28] and

anxiety, GAD-2 ≥3 [29] were used. For parametric data, the student's t test and for non-parametric data the Mann-Whitney U test and Wilcoxon rank-sum test was used. A χ^2 test or, if the cells had expected frequencies of < 10, the Fisher's exact test was used to compare categorical variables. Multivariable adjusted logistic regression models were used to estimate the odds ratios (ORs) and 95% CI for association between illness severity and categorical outcomes (fatigue or muscle weakness, degree of breathlessness, anxiety/depression), stratified by ICU admission. For association between illness severity and continuous outcomes (health index value), multivariable adjusted linear regression models were used to estimate β estimates and 95% CIs. Adjustments were made for the effects of the predictor variables including age, gender, co-morbidities, previous history of anxiety/depression and PHQ-4 score, using regression models. A two-sided p-value ≤ 0.05 was considered statistically significant. There was no missing data. Statistical analysis was done using Stata Version 16 and Microsoft Excel 2019.

RESULTS:

Baseline socio-demographics

The response rate was 75.2% (Figure 3). Selected characteristics of symptomatic persons who tested positive for COVID-19 (n=324), from South Trinidad, and met the inclusion criteria, stratified by illness severity, are summarized in Table 1. In this study, 50.0% of participants, 162, experienced mild illness while 50.0% experienced moderate/severe illness. For the purposes of this study, patients who met the hospital admission criteria stated in Appendix 7 were considered moderately/severely ill while those who did not were considered mildly ill.

The median (IQR) age of the population was 41.0 (34-52) years, range 18 to 79 years. Persons with moderate/severe illness were slightly older, median (IQR), 42.0 (36 -52), than those with

mild illness, median (IQR), 41.0 (31-52). More men, 51.23% (166), than women, 48.77%, were included in this study. More men, 58.02% (94) had mild illness, while more women, 55.56% (90) had moderate/severe illness, p=0.014. Patients were selected from three (3) counties in South Trinidad: Victoria, 33.95% (110), St. Patrick, 33.33% (108) and Caroni South, 32.72% (106). Health care workers (HCWs) comprised of 8.33% of study participants and more of them, 11.11% (18) experienced moderate/severe illness. Age (p=0.15), geographical location (p=0.098) and being a HCW (p=0.070) had no statistically significant association with illness severity.

Clinical characteristics

Approximately, one third of the study participants, 33.02% (107) had co-morbidities. Approximately 40.0% of patients with co-morbidities had moderate/severe illness, and 73.46% of patients with no co-morbidities had mild illness. Patients with co-morbidities were more likely to experience moderate/severe illness as compared to non-comorbid patients (p=0.013).

Hypertension (HTN) was the most co-morbidity (22.53%) seen among symptomatic persons with COVID-19, followed by type 2 diabetes mellitus (T2D) (16.36%). Persons with T2D (p=0.05) and ischemic heart disease (IHD) (p=0.024) were more likely to have moderate/severe illness than those who did not have those conditions.

Most study participants, 85.19% (276) were non-smokers, while 7.72% (25) participants were current smokers, and 7.10% (23) were ex-smokers. There was no statistically significant association between smoking status and degree of illness experienced (p=0.556).

In terms of signs and symptoms at acute COVID-19 infection, 79.94% (259) reported subjective or measured fever, 74.07% (240) had cough, 68.52% (222) had ageusia, 67.59% (219) had body pains, 62.35% (202) had anosmia, 45.68% (148) had dyspnoea. Persons with moderate/severe illness were more likely to have fever, cough, sore throat, shortness of breath, myalgia, arthralgia, anosmia or ageusia, compared to the mild cases (all p=values ≤0.05). Our surveillance teams were able to epidemiologically link 56.0% (181) of the cases: 1.85% had a travel history and 54.94% had a contact history with a positive COVID-19 case. These cases were more likely to experience moderate/severe illness (p=0.005).

Of note in the early phase of the pandemic, for the first four months, from March 12th to July 20th, 2020, state quarantine was mandatory, once COVID-19 positive, regardless of the degree of illness. In this study, 9.57% of participants were under mandatory state quarantine during this time. From phase 2, July 21st, 2020, the indication for hospitalization was for only those who met the admission criteria (Appendix 7) [31]. Approximately 23.0% (74) of participants were hospitalized. There were 268 (82.72%) persons in home quarantine; with equal proportions, 82.72% (134) having both mild illness and moderate/severe illness.

For those who were admitted to hospital, the median (IQR) length of hospital stay was 14 (7-21) days, and ranged from 2 to 90 days. Illness severity was not associated with length of hospital stay (p=0.225). Four percent of participants (14), were admitted to ICU; 4.63% (15) to HDU; 3.40% (11) were ventilated and 14.81% (48) were oxygenated.

The median (IQR) length of ICU stay was 6.5 (4-7) days and ranged from 2 to 21 days. The median (IQR) length of HDU stay of 7 (4-14) days and ranged from 1 to 30 days.

In this study, 'fully vaccinated' meant that they had received at least two (2) doses of Sinopharm/Astra Zeneca and/or Pfizer or one (1) dose of Johnson and Johnson. At follow-up, 236 (72.84%) participants admitted to being fully vaccinated, while 88 (27.16%) were not. The most common vaccine taken was Sinopharm -136 (41.98%) participants, followed by Astra Zeneca - 46 (14.20%), then Pfizer - 39 (12.04%); and Johnson and Johnson -15 (4.63%).

Symptoms, HRQoL at 12-month follow-up

Table 2 shows the lingering post-COVID-19 symptoms, and HRQoL at a minimum follow-up time period of 12 months stratified by severity of illness.

The median (IQR) time period from baseline to follow-up was 12 (12-13) months. Sixty percent (195) of the participants had at least one of the following post-COVID-19 symptoms outlined in table 2. Most COVID-19 survivors were troubled by fatigue 42.59% (138); muscle weakness 31.48% (102); sleep difficulties 22.84% (74); hair loss 17.28% (56); joint pains 13.58% (44) and appetite disturbance 13.27% (43). Persons who experienced moderate/severe illness were 3.5 times more likely to have at least one long-COVID symptom, as compared to those who had milder illness, (OR 3.51, 95% CI 2.19 – 5.61). Persons with moderate/severe illness were five-times more likely to develop muscle weakness, (OR 4.96, 95% CI 2.93 – 8.40); four-times more likely to experience fatigue, (OR 4.40, 95% CI 2.74 – 7.07).

The mMRC scored were group into categories 0 and ≥ 1. A score of 0 indicated that the participant "only gets breathless with strenuous exercise," and a score ≥ 1 indicates that at minimum the participant "gets short of breath when hurrying on level ground or walking up a slight hill"(32). In the group with mild illness, 62.35% (101) scored 0 and among those with moderate/severe illness, 66.67% (108) scored ≥ 1. The risk of an mMRC score ≥ 1, was 3.3 times

increased in participants with moderate/severe illness compared to those with mild illness, (OR 3.31, 95% CI 2.1 – 5.22).

From the EQ-5D-5L instrument, the health index value was derived for each participant. The mean (SD) score was 0.931 (0.13). Those with milder illness reported a slightly higher score, mean (SD) 0.967 (0.07) as compared to those with moderate/severe illness, mean (SD), 0.894 (0.16). For persons who experienced moderate/severe illness, an 8.65 unit decrease in their health index value was noted.

The mean (SD) EQ-VAS score was 79.06 (15.74). Those with mild illness reported a slightly higher score, mean (SD) 84.04 (12.58) compared to those with moderate/severe illness, mean (SD), 74.22 (17.03). For each person who experienced moderate/severe illness there was a 0.04 unit decrease in their quality of life. Using the cut-points for the screening tools[28–30] stated above for positive screens: 13.58% had anxiety/depression; 13.89% had depression and 16.98% had anxiety. Statistically significant differences were seen for anxiety/depression among those with moderate/severe illness compared to mild illness ($p<0.001$).

EQ-5D-5L responses from study cohort

In figure 4, 40.0% of respondents reported symptoms of anxiety/depression, 30%, pain/discomfort, 22.0% had problems performing their usual activities, such as work, study, housework, family or leisure activities, 11.0% had problems with mobility and 4.0% had problems with self-care.

Predictors of selected outcome measures

Table 3a-d shows multivariate regression models for the four primary outcomes. Table 3a shows a multivariate logistic regression of difference in fatigue or muscle weakness by illness severity stratified by ICU admission. Among all study participants, in the unadjusted analysis, those with moderate/severe illness had a 1.58 significantly increased risk of developing fatigue or muscle weakness (OR =1.58, 95% CI: 1.01 to 2.47; p=0.043). In model 1, when adjusted for age, gender and co-morbidities, there was no significant risk of developing fatigue or muscle weakness among all participants who had moderate/severe illness (OR = 1.40, 95% CI: 0.814 to 2.40; p=0.224). Similar trends were noted in the non-ICU group, when adjusted for age, gender, co-morbidities.

Table 3b shows the multivariate logistic regression of difference in anxiety or depression by illness severity stratified by ICU admission. In the crude model, among all participants, those with moderate/severe illness were 5.5 times more likely to experience anxiety/depression 12 months, post COVID-19 infection, compared to the mild cases (OR=5.50, 95% CI: 2.47 to 12.26; p<0.001). In model 1, when adjusted for age, gender and co-morbidities, there was no significant risk of experiencing anxiety/depression among all participants who had moderate/ severe illness (OR = 0.75, 95% CI: -0.06 to 1.51; p=0.052), as well as those in the non-ICU group. When adjusted for a previous history of anxiety or depression, the risk of having anxiety/depression among all participants, one-year post COVID-19 infection was 1.2 times higher among moderately/severely ill participants (OR 1.20, 95% CI: 0.24 to 2.17; p=0.015). Illness severity predicting anxiety or depression was dependent on prior mental health history.

Table 3c shows the multivariate logistic regression of difference in degree of breathlessness (mMRC score) by illness severity stratified by ICU admission. In the unadjusted model, among

all participants, those with moderate/severe illness were 3.31 times more likely to experience breathlessness 12 months post COVID-19 infection (OR = 3.31, 95% CI: 2.10 to 5.22; p<0.001). In model 1, when adjusted for age, gender and co-morbidities, there was no significant risk of experiencing breathlessness among all participants who had moderate/severe illness (OR = 1.58, 95% CI: 0.90 to 2.78; p=0.110).

Table 3d shows the multivariate linear regression of change in HRQoL (Health Index Value) by illness severity stratified by ICU admission. In the unadjusted analysis, among all study participants, those with moderate/severe illness had a 0.071 decrease in health index value compared to those with mild illness (β =-0.071, 95% CI -0.097 to -0.044; p<0.001). When adjusted for age, gender and co-morbidities, model 1, (β =-0.044, 95% CI: -0.076 to -0.01; p=0.006), and age, gender, co-morbidities and PHQ-4 score (β =-0.026, 95% CI: -0.030 to -0.022, p<0.001), statistically significant differences were noted, among all participants as well as the non-ICU group.

DISCUSSION:

Illness Severity at baseline:

Illness severity criteria: In our study, 50% reported mild illness and 50% reported moderate/severe illness, based on the MOH, T&T criteria (Appendix 7) [31]. Illness severity criteria was sparse in the literature as most studies followed cohorts of hospitalized patients. Yang et al, in accordance with the "COVID-19 Prevention and Control Plan (Sixth Edition)," characterized patients by the severity of COVID-19 into: mild 86.8%, severe 3.5%, or critical 9.7% [3]. Garrigues et al reported on 80.0% ward versus 20.0% ICU patients [20]; Lombardo et al reported on 37.6% non-hospitalized versus 62.4% hospitalized patients [23]; Huang et al reported

on 24.9% of patients did not require supplemental oxygen versus 67.7% required supplemental oxygen; 7.3% required ventilation [21]; and Maestre-Muñiz et al looked at 41.9% discharged from the emergency room versus 58.1% patients admitted to the hospital[13].

Socio-demographics: No association between age and illness severity was found. This was consistent with previous published studies [1–3]. In our study more women had moderate/severe illness. Most studies found gender independent of illness severity [1–3]. However, Maestre-Muñiz et al [13], also found that women were more likely to experience moderate/severe illness.

Co-morbidities: Hypertension (HTN), was the most common co-morbidity seen followed by T2D, consistent with national prevalences [33,34]. We found that persons with co-morbidities, particularly T2D and IHD were more likely to experience moderate/severe illness. Findings were consistent in studies published by Maestre-Muñiz et al [13] and Lombardo et al [23].

Signs/Symptoms at acute COVID-19 infection: In South Trinidad, at acute COVID-19 infection, among those moderately/severely ill, commonly reported signs/symptoms were subjective or measured fever, cough, myalgia, ageusia, anosmia, dyspnoea and arthralgia; similar to published literature [1–3,8,12,19]. They were more significantly reported compared to mild illness. Chemosensory dysfunction has been consistently reported during acute COVID-19 infection[8,12,13,19]. Huang et al [1] and Yang et al [3] found dyspnoea more significantly reported among those moderately/severely ill.

Management: Early efforts to contain the outbreak included mandatory state quarantine. COVID-19 positive imported cases: returning and repatriated nationals, their primary contacts and HCWs who interacted with COVID-19 positive patients [36]. This unique situation allowed us to observe the clinical course of persons with asymptomatic, mild, moderate and severe SARS-CoV-2

infection. As cases increased from July 21st 2020, due to community spread, the MOH, T&T instituted a hospital admission criteria [31], attempting to support the moderately/severely ill patients. Triage was done similarly to other countries in order to prevent the collapse of the health-care system[2]. It was crucial for physicians to be able to triage patients according to illness severity. The severely ill patients had to be sent to Couva MMF and SFGH with dedicated ICUs; however, some opted to quarantine at home, due to the fear and lack of faith of the hospital setting and belief in traditional herbal medicines. After ICU, patients were managed at step-down facilities, and discharged once stable.

Treatment: Mildly ill patients were home quarantined, advised on symptomatic treatment and monitored by the surveillance team. Moderately/severely ill patients were given the required supportive therapy (anticoagulants, corticosteroids, anti-inflammatory drugs, oxygenation and ventilation) [10].

Outcomes one-year later:

Symptomology: Our study findings showed that 60% were troubled by at least one lingering symptom: 46% among the mildly ill and 75% among those with moderate/severe illness. A wide variation is seen in the prevalence of post-covid conditions (PCC) globally. In China, Huang et al., reports that the proportion of hospital discharged patients with at least one PCC decreased from 68% at 6 months to 49% at 12 months [21]. After one year, in Italy, Comelli et al., reports the prevalence of at least one PCC, 91.7% among hospital discharged patients [12]; Lombardo et al., 81%, regardless of the illness severity in the acute phase (23) ; in Moscow, Pazukhina et al., 34%, after hospital discharge (24). In mild-to-moderate cases, Boscolo-Rizzo et al., reports a

one-year, PCC prevalence of 53% [8]; Maestre-Muñiz et al., reports 49.5% in milder cases, 66.8% hospital discharged cases [13].

In our study, after one year, the most commonly reported symptoms were: dyspnoea, fatigue, muscle weakness, sleep difficulties, hair loss, regardless of the illness severity in the acute phase. In comparison to international studies, some of our findings were similar, one-year post COVID-19. In China, Huang et al., most commonly reports dyspnoea, fatigue, sleep difficulties, joint pain, hair loss, among hospital discharged patients [21]. In Italy, Lombardo et al., found "fatigue and weakness, muscle and joint pain, sleep disorders, respiratory disorders, neurological and cognitive impairments" prevalent regardless of the illness severity in the acute phase (23). In a recent meta-analysis done by Malik et al. [14], fatigue, dyspnoea, anosmia, cough, sleep disturbances, arthralgia were common persistent symptoms, consistent with reported literature.

HRQoL: In our study, overall, the health index value (0.931) was comparable to national norms (37), but lower for persons with moderate/severe illness (0.894). The overall EQ-VAS score was 79.06%, lower than that for T&T, 83.6% and even lower for persons with moderate/severe illness 74.09%. For post-acute COVID-19, in a pooled prevalence of poor quality of life, EQ-VAS was 59% (95% CI: 42%–75%) [14]. At 110 days post hospitalization, Garrigues et al reported EQ-VAS 70.3%, EQ-VAS index, 0.86 [20], and 6-months post hospitalization, Huang et al [11] reported EQ-VAS, 80.0% (70.0%-90.0%).

EQ-5D-5L responses and Mental Health Outcomes: Most of our participants were able to fully recover. However, a significant proportion had problems affecting HRQoL, which could have a negative economic impact [19]. When our findings were compared to a meta-analysis, done by Malik et al., using the EQ-5D-5L instrument, lower prevalences of mobility, 11% vs, 36%; self-care, 4% vs. 8%; usual activities, 22% vs. 30% and pain/discomfort, 30% vs. 42% were found,

but a higher prevalence of anxiety/depression symptoms, 40% vs. 38% [14]. Using the same instrument, Huang et al., found that, the proportion of hospital discharged patients with anxiety symptoms increased from 23% at 6 months to 26% at 12 months [21].

In our study, at 12-month follow-up, 14.0% of respondents screened positive for either anxiety or depression. No similar studies were found for comparison of anxiety/depression using the PHQ-4, PHQ-2 and GAD-2 questionnaires among COVID-19 survivors, one-year later. Possible reasons for anxiety/depression may include: fear of death, loss of loved ones, isolation, loss of employment and incomplete recovery of physical health [21]. Strengthening of a health care policy that supports service for the emotional needs of HCWs is needed. For some participants, being ill with COVID-19 made them focus more on their self-care, spirituality, exercise and muscle strengthening.

Key Predictors

Age, gender, and co-morbidities were confounders of the predicted primary outcomes, except for HRQoL. Illness severity predicting anxiety/depression was dependent on prior mental health history. HRQoL was worse in those with moderate/severe COVID-19 compared to mild disease, one year later even after adjustment for demographics and PHQ-4 score. It is possible that factors other than age, gender, co-morbidities and PHQ-4 score were responsible for the participants' decreased quality of life, such as socio-economic challenges.

The long-term sequelae after acute COVID-19 needs to be studied so that an evidence-based multidisciplinary team approach could be developed to care for these patients [16]. Care should

include: optimization for underlying co-morbidities, physiotherapy, occupational therapy and psychological support [17]. In South Trinidad, at 12-month follow-up, patients with persistent symptoms were referred to post COVID clinic at the SFTH. Our multi-disciplinary team consists of an internist, cardiologist and a psychiatrist. Further evaluation, rehabilitation and appropriate care are offered to these patients.

Strengths:

To our knowledge, this study is the first of its kind to be conducted in the Caribbean; its large sample size (n=324), with sufficient power to show associations between comparison groups; randomized cohort selection and long follow-up duration provides a good foundation for future related studies. The questionnaire, allowed the investigation of many areas of the participant's health status. Standardized pre-tested data collection instruments were used. The response rate was good, providing a good estimation of prevalence. The study was a community-based, and included patients in home quarantine as well as those hospitalized.

Limitations:

One limitation of the retrospective cohort design is the lack of data at baseline for certain symptoms measured at 12-month follow-up. Also, comparisons could not be made with those who were not infected with COVID-19 as validation of absent COVID-19 in matched controls was beyond the scope of this study. Even though the tools were aimed to be very comprehensive, some symptoms may not have been captured. Establishing a structured, validated questionnaire encompassing the full clinical spectrum of long COVID would enhance the replicability of clinical studies [8]. It was assumed that the laboratory confirmed COVID-19 cases are true positives, and that persons were not re-infected with COVID-19 after the first time.

Questionnaires were limited to patient-reported outcomes, via virtual interviews. With, face-to-face consultations, objective measurements such as BMI, could have been done which may have influenced their health outcomes. This study results may not be generalizable to all COVID-19 positive cases in T&T as there were equal proportions of mild and moderate/severe cases. It is possible that mild cases were under-reported, as more moderate/severe cases may have presented to health facilities and therefore captured by the surveillance teams.

CONCLUSION:

Significant proportions of COVID-19 survivors have post-COVID symptoms after one year. The health index value of all participants, was below the population norms, and even lower among those with moderate/severe illness. Interventions should be prioritized for those with the highest burden of persistent symptoms to aid their recovery. Further longitudinal observational national studies and clinical trials are needed to better understand the long-term burden of COVID-19 in T&T.

RECOMMENDATIONS:

In T&T, long-term surveillance programs and more long-COVID clinics would aid long haulers. An integrated approach of multidisciplinary teams with medical, psychological and rehabilitation services, with appropriate follow-up should be available for patients [38,39]. Public health and social policies need to be implemented, to aid survivors who had severe disease, eg. disability grants, flexible working hours. Trials of biologics for those with severe long-COVID symptoms could be done, similar to the PHOSP-COVID study in the UK [39].

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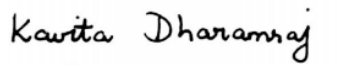

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