

Virtual At Home Monitoring During A COVID-19 Infection

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2023-05-16

1 Introduction

1.1 COVID-19

The COVID-19 pandemic, caused by the highly contagious SARS-CoV-2 virus, has had widespread global consequences. Emerging in December 2019 in the city of Wuhan, Hubei Province of China, COVID-19 was declared a worldwide pandemic on March 11, 2020 by the World Health Organization (WHO). Testing centers opened across Canada as the genome was sequenced and diagnosis became increasingly available to the symptomatic. By the end of May, it had infected over 5.9 million individuals worldwide, with the infection rate doubling every 30 days (WHO Situation Report, May 31, 2020). In Canada alone, over 89,000 citizens had tested positive for the virus. Hospitals became overwhelmed; warnings by provincial health authorities in April, 2020 that intensive care units would not be able to meet demand proved true as reports of overwhelmed emergency departments, critical care beds and ICUs became part of daily reports by health authorities by May.

A December 2022 WHO study comprehensively evaluated pandemic-caused deaths, estimating 14.8 million excess deaths worldwide during 2020 and 2021. In the absence of vaccination and targeted treatments, during 2020 the most effective strategy for curbing the spread of COVID-19 included quarantine, isolation, and physical distancing measures. At the time, COVID-19 was believed to be primarily a respiratory disease with most individuals experiencing mild symptoms, while others developed complications ranging from asymptomatic hypoxia to pneumonia. The most severe cases escalated to acute respiratory distress syndrome requiring ventilation. In-clinic or in-hospital treatment was reserved only for the most critically ill. Media reports at the time document ill patients left, and sometimes dying, at home as ambulances followed directives to not transport any but the most seriously ill. More mild cases were instructed to isolate at home and self-manage their symptoms.

Gaps in healthcare services were present even before the pandemic and continue to disproportionately affect certain populations. Individuals residing in rural communities, confined environments, and Indigenous populations frequently experience suboptimal access to quality healthcare. As the pandemic prompted widespread lockdowns and service challenges due to healthcare workers succumbing to illness and hospital beds being filled by critically ill patients, access to healthcare, even in the largest urban centers, became challenged. A significant concern was the lack of comprehensive care plans for COVID-19 positive individuals exhibiting mild symptoms. Patients discharged from hospitals, after receiving treatment for COVID-19, often lacked proper follow-up assessments, highlighting a critical disconnect between hospital and community care. Healthcare providers quickly pivoted to providing virtual care, but with a lack of knowledge about COVID-19 treatment and prevention, patients were lost to a system as overwhelmed as they were. Addressing these care gaps was an urgent and essential task.

1.2 VIRTUES

The Cardiac Network of Canada (CANet) is a pan-Canadian research network, funded by the Networks of Centre of Excellence of Canada Program (NCE), with a vision of a transformed, patient-driven, sustainable

care model for all Canadians with heart rhythm disorders. In 2022, CANet broadened its mandate to provide virtual care across a range of conditions that impact cardiovascular health.

CANet has developed the Virtual Integrated Reliable Transformative User-driven E- health System (VIRTUES), a secured, cloud-based, patient-centred virtual care platform that integrates personal health records and biosensor data with output and feedback to patients, caregivers and providers. VIRTUES was initially designed to provide virtual care for patients with cardiac implantable electrical devices, atrial fibrillation, post-myocardial infarction, and other heart rhythm disorders. VIRTUES was, at the time the pandemic began, being tested through random control trials assessing its efficacy. Early results were promising. In addition to helping to facilitate diagnosis and treatment of cardiac conditions, patient feedback suggested VIRTUES was significantly reducing patient anxiety, particularly anxiety stemming from uncertainty about disease progression and often silent symptoms that could be better captured by the monitoring devices than by patient reporting alone. Patients and providers were better able to track disease progression and initiate more timely treatment.

In early 2020, as COVID-19 spread throughout the world, CANet re-purposed VIRTUES facilitate the management of COVID-19 positive patients isolating at home. COVID-19 patients allied with the Network had reported high levels of anxiety and uncertainty as they isolated. Commonly told to access care if their symptoms became “serious”, patients reported uncertainty in terms of what “serious” meant. Media reported patients going to the ER “too late” as hypoxia symptoms are difficult for a layperson to evaluate. It was theorized by CANet that the addition of VIRTUES facilitated home monitoring of O₂ saturation levels and monitoring of symptom progression could help address this care gap.

2 Methods

2.1 Study Methods

Trial design: This was a prospective, non-randomized cohort trial. A randomized control trial (RCT) design, of either patient-level or center-level, was carefully and thoughtfully considered. In consultation with the CANet Patient Advisory Council, and after soliciting over 30 citizens’ opinion, including 10 Indigenous persons, the consensus was that an RCT with patients receiving or not receiving home care was considered too drastically different and lacked equipoise.

Research objectives: The overall purpose of this research program was to assess a virtual strategy to bring quality care to COVID-19 positive patients isolating at home.

The *primary objective* was to determine patient satisfaction with a virtual care model that integrates the VIRTUES interface with daily symptom and vital sign reporting, including O₂ saturation levels, for the management of COVID-19 at home. Patient satisfaction is further differentiated based on the demographic variables of gender (between men, women, and gender diverse people) and indigenous status (indigenous and non-indigenous persons).

The *secondary objective* was to observe patient health over the course of a COVID-19 infection to determine:

1. How patient reported QoL changed over the period
2. If patient reported QoL varied significantly by Sex (M/F)

Study population: The patient population included COVID-19 positive patients who were instructed to self monitor at home.

- Inclusion criteria:
 - Confirmed COVID-19 positive
 - Aged 18 or above

- Resident in one of 4 included health regions
- Exclusion criteria:
 - Unable or unwilling to provide informed consent
 - Currently hospitalized for any reason

Study Sites: The study included patients from 4 health regions across Ontario. These included London (n = 402), Ottawa (n = 213), Kitchener (n = 168), and the Niagara health region (n = 24). Site specific analysis was conducted on a subset of the data; the Niagara health region was removed due to sample size concerns.

Recruitment: From the inception of the study through 2021, persons who received a positive COVID- 19 test result were contacted via telephone by a public health department. All positive patients from included health regions were offered enrollment in the VIRTUES study. Patients wishing to enroll as well as patients wanting more information on VIRTUES gave consent to be contacted by CANet’s Project Coordinator who facilitated enrollment. Public health offices were not monitored for consistency in their recruitment efforts. Niagara region, for example, had very low enrollment relative to other centers.

Procedure: Participants provided recorded verbal consent as well as consent within the VIRTUES platform. Attaining written consent was not possible as physical distancing and isolation requirements prohibited face-to-face interaction.

Participants were provided a pulse oximeter for their personal use. This medical device was delivered to doorsteps in the London health region and mailed to participants outside the health district.

Participants were contacted by the research coordinator and provided instructions by telephone and in writing on how to download VIRTUES to their computers or electronic devices. They then received instructions on how to measure their oxygen saturation levels and how to enter the data and record their symptoms in the VIRTUES interface. Participants recorded their vital signs 3x daily for 21 days, completed a QoL questionnaire on days 1, 14, 28 and completed a satisfaction questionnaire on days 14 and 28. It is important to note that at the time the study was designed, the duration of a COVID-19 infection was unknown. It is now recognized that mild cases tend to resolve by 10 days. If patients missed a reporting cycle they were contacted by the research coordinator, who is an RN, to ensure wellbeing and prompt engagement.

Participants deemed to have experienced symptom progression warranting medical intervention (predetermined levels in consultation with public health authorities) were referred as needed.

2.2 Statistical Methods

Prior to analysis, the data were cleaned and prepared, including the identification and treatment of missing data. The data exhibited approximately 13% missingness, which could potentially introduce bias and affect the validity of the results. To address this concern, data was assumed missing at random (MAR) and multiple imputation (MI) was employed.

2.2.1 Missing Data

2.2.2 Comparing distributions

Likert scales were utilized to measure patient QoL and patient satisfaction over the study period. By analyzing the differences between distributions of Likert data at different time points one can better understand how these patient reported measures changed over the course of the COVID-19 infection.

T-tests are commonly utilized to compare two distributions. T-tests are a parametric method that makes assumptions about the normality of the distributions. We note that this assumption is violated by our data, making it incompatible with our analysis.

EMD: An alternative is to employ the earth mover’s distance (EMD), a measurement used to quantify the amount of work required to transform one distribution into another. The EMD is calculated by taking the

sum of the distances between the values of the two distributions, multiplied by the amount of probability mass associated with each point. This provides a measure of the difference between the two distributions. The earth mover’s distance has several advantages over other methods for analyzing Likert data: less sensitive to outliers; robust to sample size; and can capture the variability between two distributions.

Wilcoxon rank sum: Analysis of the literature also suggests the use of the Wilcoxon rank sum test, which is often described as the paired t-tests non-parametric sibling. This measure works by calculating a test statistic, based on the difference of each set of paired observations, and comparing this with a critical value.

To strengthen the trustworthiness of the results, the EMD values and Wilcoxon rank sum values will be compared.

2.2.3 Modeling

Modeling was used to better understand the factors influencing patient satisfaction with VIRTUES. CANet had undertaken a Canada-wide qualitative study during 2018-2020 to assess patient priorities related to their arrhythmia diagnosis and treatment. The findings of this study revealed that patients experience anxiety and isolation as they engage with the healthcare system and that virtual engagement with a care provider to track and manage their care would ameliorate these concerns. The COVID-19 study, however, is the first attempt to quantify patient satisfaction with VIRTUES and to assess whether it was meeting patient needs.

Generalized Linear Models (GLMs) are the most commonly employed method. The longitudinal structure of the VIRTUES data, however, renders the use of GLMs inappropriate. Longitudinal data consists of repeated measurements taken on individuals over time, often nested within hierarchical levels, such as individuals within families or patients within hospitals, which introduces correlations which are not usefully meaningful.

Controlling for correlations in the data is essential to produce unbiased estimates. Here Mixed-effects Model Repeated Measures (MMRM) and Generalized Estimating Equations (GEE) were used to model satisfaction by Quality of Life (QoL) and patient demographics while accounting for individual and site effects over time.

MMRM is a linear mixed-effects model that accounts for the within-subject correlation of repeated measurements. It models the fixed effects, such as time, and random effects, such as the patient-specific intercept and slope. MMRM is particularly useful for analyzing longitudinal data as it incorporates the correlation structure among observations and allows for flexible modeling of time effects.

GEE has roots in quasi-likelihood methods, and extends generalized linear models to accommodate correlated longitudinal data. GEE models the population average response while accounting for the within-subject correlation. It is a robust method that provides consistent parameter estimates even when the correlation structure is misspecified.

By comparing MMRM and GEE results, we gain deeper insights into patterns and relationships within the data, and reduce the risk of model misspecification.

3 Results

3.1 Q1 Satisfaction

3.2 Q2 QoL

4 Discussion

Statistical Appendix