Use of Remote Patient Monitoring (RPM) Platform for COVID-19 Patients

SIGNIFICANCE

COVID-19 pandemic and significant background information

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) continues to impact the world with its exponential growth and fatalities related to coronavirus disease (COVID-19). (1) We have seen a global spread of the virus with the current number of reported cases exceeding 2,000,000. (2) While there have been other viral outbreaks in the past years (MERS, SARS, H1N1), SARS-CoV-2 has profoundly penetrated and impacted the world. (3) Our healthcare systems have been stretched to their limits, especially in designated "hotspots," such as all boroughs of New York City. It is clear that given the current outbreak of COVID-19 and previous viral contagions, a comprehensive system is necessary for patient care during a pandemic. The need for risk stratification of infected patients with longitudinal monitoring is pivotal for the current as well as future pandemic response strategies. We believe that emerging technologies incorporating remote patient monitoring (RPM) will play a key role in current and future systems-level solutions that can rapidly and accurately identify patients who require escalation of care and potentially reduce the need for inpatient admission and hospital length of stay.

The clinical presentation of COVID-19 patients varies widely from asymptomatic or mild illness to a more severe and life-threatening condition. According to published literature, most COVID-19 patients present with mild to moderate symptoms, approximately 14%-20% of patients develop severe symptoms that require hospitalization, and 5% of these patients require critical care services. (4-8) One of the most troubling features of COVID-19 is the unexpected and rapid deterioration of some infected patients. An estimated 10% of COVID-19 patients can develop life-threatening conditions such as acute respiratory distress syndrome (ARDS), the treatment of which requires aggressive intervention. (9) As observed in other diseases, a delay in identifying clinical deterioration can result in belated therapeutic interventions, thereby increasing morbidity and mortality. (2,10,11).The clinical variability of symptoms and progression of disease makes triaging and disposition of COVID-19 patients extremely challenging.

Similar to SARS, MERS, and H1N1, respiratory failure plays a central role in COVID-19 morbidity and mortality.(12,13) The pathological data of SARS-CoV-2 is associated with patchy inflammatory cellular infiltration of the lung tissue. (14) Even though there are several reasons for death in COVID-19 patients, respiratory involvement manifested as severe cough, and shortness of breath are two early warning signs associated with adverse events. (15) It is important to note that while respiratory involvement is an important issue for the spread and overall morbidity of these patients, there are also systemic responses and deterioration of other organs. (15,16). Therefore, a comprehensive remote patient monitoring (RPM) system must incorporate a number of physiologic parameters in order to rapidly and reliably identify patients in clinical distress requiring escalation of care.

As this is a novel pandemic, there are limited resources available for accurate identification of patients at high risk for respiratory failure and other adverse events. Studies have demonstrated that delays in the identification of clinical deterioration resulting in late therapeutic interventions are associated with increased mortality and morbidity. (17) Strategies for identifying patients at highest risk and mobilizing early interventions have the potential to improve outcomes. Patients presenting to the hospital late in their clinical course are challenging to manage and often require rescue interventions such as mechanical ventilation or extracorporeal membrane oxygenation (ECMO). Moreover, early identification and subsequent intervention could mitigate disease progression, deterioration, and the need for more advanced therapies.

Lack of these predictive measures forces our healthcare system to adopt a "one-size-fits-all" model, which is inefficient, prohibitively expensive, and clinically ineffective in too many patients. As in the case of COVID-19, lack of a valid risk stratification tool and the possibility of the rapid deterioration of symptoms warrant continuous monitoring of non-hospitalized patients during their symptomatic phase. (18) The use of RPM could be instrumental in understanding and developing an algorithm for escalation of care and therapeutic interventions in our patient population. Moreover, during the medical surge, resource utilization is one of the pivotal strategies that must be considered in epidemic and pandemic preparedness. Appropriate resource utilization is essential to provide quality care to every patient and to mitigate the adverse outcomes associated with pandemics. The 4 "S' s," staff, stuff, space, and systems are the critical factors in pandemic preparedness and resource utilization.

COVID-19 in the minority population

It is readily apparent that our minority and lower socioeconomic populations are significantly more vulnerable in this pandemic. COVID-19 has been shown to have higher mortality rates among the African-American and Hispanic populations. (19) The Bronx represents one of the most diverse populations in the country and has been profoundly affected by COVID-19. An ability to monitor patients in an out-patient setting with wearable technology has the potential to address some of the historical obstacles to timely healthcare access for our patient population. The use of continuous monitoring would allow us to understand the progression of SARS-CoV-2 in our community while providing a mechanism for intervention. Whereas our patients may be less likely to seek medical attention, the use of RPM allows the medical facility to maintain a level of monitoring and provide a safety net in the event of clinical deterioration.

Utilization of wearable patches for remotely monitoring COVID-19 patients

Wearable technologies are continuing to impact healthcare decision making. Fitbits, smartwatches, and wearable patches have become everyday devices capable of collecting physiological data such as heart rate, blood pressure, body temperature, and blood oxygen saturation. (20) The utilization and success of wearable technologies have been demonstrated in various medical conditions, such as cancer, respiratory diseases, heart disorders management, and diabetic care management. (21-23)In a recently published study, researchers demonstrated the utilization of wearables to track the resting heart rate and sleep pattern to predict the incidence of influenza-like illness. (24) The improvements in wearable technologies provide opportunities for clinicians to deliver patient-centered care and engage patients in shared decision-making. In addition, detailed, longitudinal physiologic data could provide more insight into the development of advanced analytical tools for a better understanding of disease development and progression, early detection, and intervention. Data-driven clinical decisions, coupled with advanced analytical methods such as artificial intelligence (AI), have the potential to revolutionize how healthcare is delivered and improve the outcomes. The steady stream of information provided by these wearable devices can be utilized for monitoring real-time disease progression and providing individualized care.

Newly emerging and re-emergence of known and unknown pathogens have created unpredictable threats to global public health. In the recent period, infectious diseases such as mumps, measles, Ebola, and SARS have created unprecedented challenges for healthcare systems. Effective measures to limit the contagion include disease surveillance, hygiene measures, self-isolation, social distancing, travel restrictions, quarantine, and case isolation. Of all the above-described actions, case isolation (self-isolation) and contact precautions are the most proven method in reducing the contagion and the full spread of the diseases. One of the potential ways to safely implement self-isolation without impeding care is to develop protocols to monitor isolated patients remotely.

Hypothesis

The central hypothesis motivating this study is that remote patient monitoring (RPM) of infectious disease patients can efficiently facilitate self-isolation. Additionally, RPM can assist in more rapid identification of patients at risk, facilitate detection of patient deterioration, and enable early interventions, all of which play a vital role in resource utilization and outcomes.

Specific Aims

Aim-I **To develop and test a clinical care pathway that can be utilized in similar epidemic conditions in the future**. To study this aim, we will be using the COVID-19 medical surge as a condition to evaluate the framework of delivering care through remote patient monitoring. The success of this care delivery model will be evaluated on ease of model implementation, patient satisfaction, clinical outcomes, and the utilization of shared decision making.

Aim-II **To evaluate remote patient monitoring for appropriate resource utilization in epidemic and pandemic conditions**. To evaluate this aim, we plan to compare the emergency department (ED) visits and inpatient admission of patients with and without wearable remote patient monitoring devices. Additionally, we will compare the number of patients that required critical interventions (mechanical ventilation and ECMO) during the hospital stay.

Aim III **To evaluate the utilization of wearable technology for upfront predictions of patients that would require inpatient admissions.** To evaluate this aim, patients who are diagnosed with COVID-19 and are undergoing self-quarantine will be closely monitored using a wearable device, and shared-clinical decisions will be made based on the monitored data and patient diary. The comparison group will be patients undergoing routine standard of care at the hospital. ED visits, inpatient hospital admissions, and patient satisfaction will be the outcome measures compared between the two groups.

Aim IV **To evaluate the association between early identification of critical, abnormal vital signs and the prevention of serious adverse events.** To evaluate this aim, patients in the monitored group and non-monitored group will be compared for ED visits, inpatient admissions, length of hospital stay, and serious adverse events.

Objectives

The primary purpose of the study is to compare the number of inpatient admissions between the monitored and non-monitored patients.
The secondary endpoints are to compare the number of ED visits, length of stay, patient satisfaction, the incidence of mechanical ventilation, ECMO, and serious adverse events (events requiring extended hospital stay).

Methods

In this prospective observational study, we are planning to recruit COVID-19 positive patients visiting emergency rooms (ER) associated with Montefiore Medical Center

Inclusion Criteria

- Diagnosis of COVID-19 (first-time COVID-19 diagnosis)
- Able to read and understand English

- Able to navigate and fulfill tasks on an electronic tablet
- 21 years and older
- Patients that do not require an inpatient admission as per the treating physician
- Patients who are insured through Medicare
- Patients who are staying in the same household for at least 15 days
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Exclusion Criteria

- Have never used a mobile phone or tablet in the past
- Patients with an implanted pacemaker
- Patients with a diagnosis of hyperhidrosis
- Acute allergic reactions to the patches
- Confirmed diagnosis of psychiatric illness or anxiety disorder
- All private insurance patients

Recruitment Strategy

Every day around 4 pm, the research team will generate a list of patients who were tested COVID-19 positive and are discharged from ER without requiring inpatient admission. This list will include all the COVID-19 positive patients from all the emergency departments associated with Montefiore Medical Center. The potential patient list will be generated on every alternate day; for example, the list will be generated on (Monday, Wednesday, and Friday). We are only planning to enroll 5-6 patients on a single day. Alternate day enrollment will potentially allow us to have a balance in the number of patients in the intervention and the control group. Also, it helps us to streamline the study logistics. After screening for inclusion and exclusion criteria, the research team will identify potential patients eligible for the study.

The research team will call the patients in the evening and explain the purpose of the study and will obtain oral consent. Before calling the patient, the research team will review the EPIC notes to make sure their COVID results are shared and discussed with the patients. Oral consents will serve as a method of patients giving consent for engaging in the study discussion. The paper consents will be delivered to the patients with the study materials (tablet, sensors SPO2, and blood pressure cuff). After reading the consents, patients have the opportunity to decline participation in the study and return the study materials. Once patients sign the consent, patients will have two options to return the signed copy. Either they can take a picture of the signature page and email or text it to the research team, or at the end of the study, they can return the signed consents along with the tablet. We will keep a registry of the consenting process, which includes date and time, and the name of the personnel involved in the consenting process. For patients who email the signature, the investigator portion will be signed and dated on the day of receiving the email. For patients who are returning the signed consent with the tablet package, the investigator portion will be signed and dated on the day of receiving the tablet.

Delivery and Return of the Study Materials

The following day morning, the research staff will drop off the monitoring packages at the patient's preferable drop-off locations. The research team will call the patients to confirm the receiving of the study materials. Once the packet is delivered, the study team will share the details of the patients with ImagineMic, the external company which will be monitoring the patients. Once the patient completes

the 14 days of participation, the patient is required to return the study materials to the study team. The research team will make the necessary arrangements for the return of the study materials.

External Monitoring

ImagineMic will be monitoring the patients for CDC recommended 14 days. (25) ImagineMIC has extensive monitoring experience and is providing services in different capacities and capabilities. (25) ImagineMic uses a secure, HIPPA compliant platform for monitoring the patients. Additionally, round the clock, licensed healthcare professionals continuously monitor these data from a monitoring intervention center. Detailed monitoring plans are explained in the submitted brochure (Appendix-1).

Monitoring will be prematurely terminated if the patient requires inpatient hospitalization; in all other cases, monitoring will be continued for fourteen days. During the monitoring period, patients will have the opportunity to call and speak to the medical professional at the Monitoring Intervention Center and also can call 911 in case of a severe emergency. Additionally, submitted is the guidelines put together by IMagineMic regarding the treatment and transfer of COVID-19 patients from home to the emergency (Appendix-2)

The patients will be remotely monitored for their vital signs such as blood pressure, heart rate, SPO_2, skin temperature, respiratory rate, two lead ECG, and accelerometer.
All the collected physiologic data will be transmitted to a central monitoring station where it will be evaluated continuously by licensed healthcare workers (MD, RN, and NP) who will provide real-time support to the patients. Also, the research team will obtain all the data points for future analytic purposes. Additionally, the research team will conduct a 30 day follow up phone call to catch information needed in case subjects end up visiting an outside institution.

Control Group
In this study control group will be patients those patients who are COVID positive and discharged from the ER and are not contacted by the study team during the same study period. In order to avoid chronological bias, it is essential to have controls from the same period as in the intervention group. The standard of care, the presentation, and the outcome of the disease are very much different in the surge phase of the COVID when compared to post surge months. Hence it is crucial to avoid chronological bias when comparing intervention and control groups. Additionally, in terms of evaluating the efficacy of the intervention, using patients from the surge period as a control group could potentially impact the conclusion of the study.

Regarding the care given to the control patients, Montefiore Emergency Department has a standard of operating protocols for patients discharged from the emergency room. All the usual standard of care available for the patients discharged from the emergency room will be provided to the patients, including telephone consultations. The study team will not interfere or dictate the care provided to the control patients.

Technology
This study will be integrating two technologies; an FDA approved proprietary body patch and a digital monitoring platform. The FDA approved body patch that will be used in this study is lifesignal biosensor 1AX*, which is capable of monitoring vital signs, including blood pressure, heart rate, temperature, respiratory rate. (26) These patches are also capable of generating electrocardiogram (ECG) and function

as an accelerometer. Additionally, an FDA approved pulse oximeter, and blood pressure monitor will be used to measure the peripheral oxygen saturation and blood pressure, respectively

The digital monitoring platform ImagineMic will be utilized for continuous digital monitoring of the physiologic measurements. (27) The vital signs generated through the biosensor patch will be continuously supervised at the Monitoring Intervention Center (MIC) by licensed healthcare professionals. These data points are monitored 24/7and alerts will be provided to patients in case an intervention is needed. Additionally, based on the condition of the patient, the monitoring staff will facilitate ambulance support if required. The schematic representation of the study proposal is depicted in figure 1.

In addition to remote monitoring, the monitoring team will collect the data about their daily clinical symptoms, including cough, myalgia, difficulty in breathing, and any other clinically significant symptoms. Additionally, at the end of the monitoring period (14days), a personal well-being questionnaire will be administered to those patients who experience no adverse events.

Cost and Reimbursement

There will be no cost for the patient to participate in this study. The department of the anesthesiology (grant fund) and ImagineMic (company monitoring the patients) will share the cost of the wearables. The cost of the monitoring will be billed to the insurance company by ImagineMic. Patients will not be reimbursed for participating in the study.

Data Collection and Storage

All the study data will be collected on a paper case report form (CRF), which will be entered into the computer database. All the data points will be collected and managed using RedCap electronic data capture tools. All the electronic files will be saved in a password-protected computer in the research office. Additionally, de-identified continuous monitoring data will be shared with the Montefiore Center for Health and Data Innovation team for additional analysis.

DSMB

The first DSMB meeting will be conducted after the completion of 50% of the enrollment. The safety of the RPM will be the only outcome discussed during the DSMB meetings. Additionally, all the adverse events associated with the RPM will be reported to the DSMB and the IRB. In the event of serious adverse events, the termination or the continuation of the study will be at the discretion of the IRB. No interim analysis will be conducted, and the efficacy of the study will not be discussed at the DSMB meetings.

Statistical Analysis

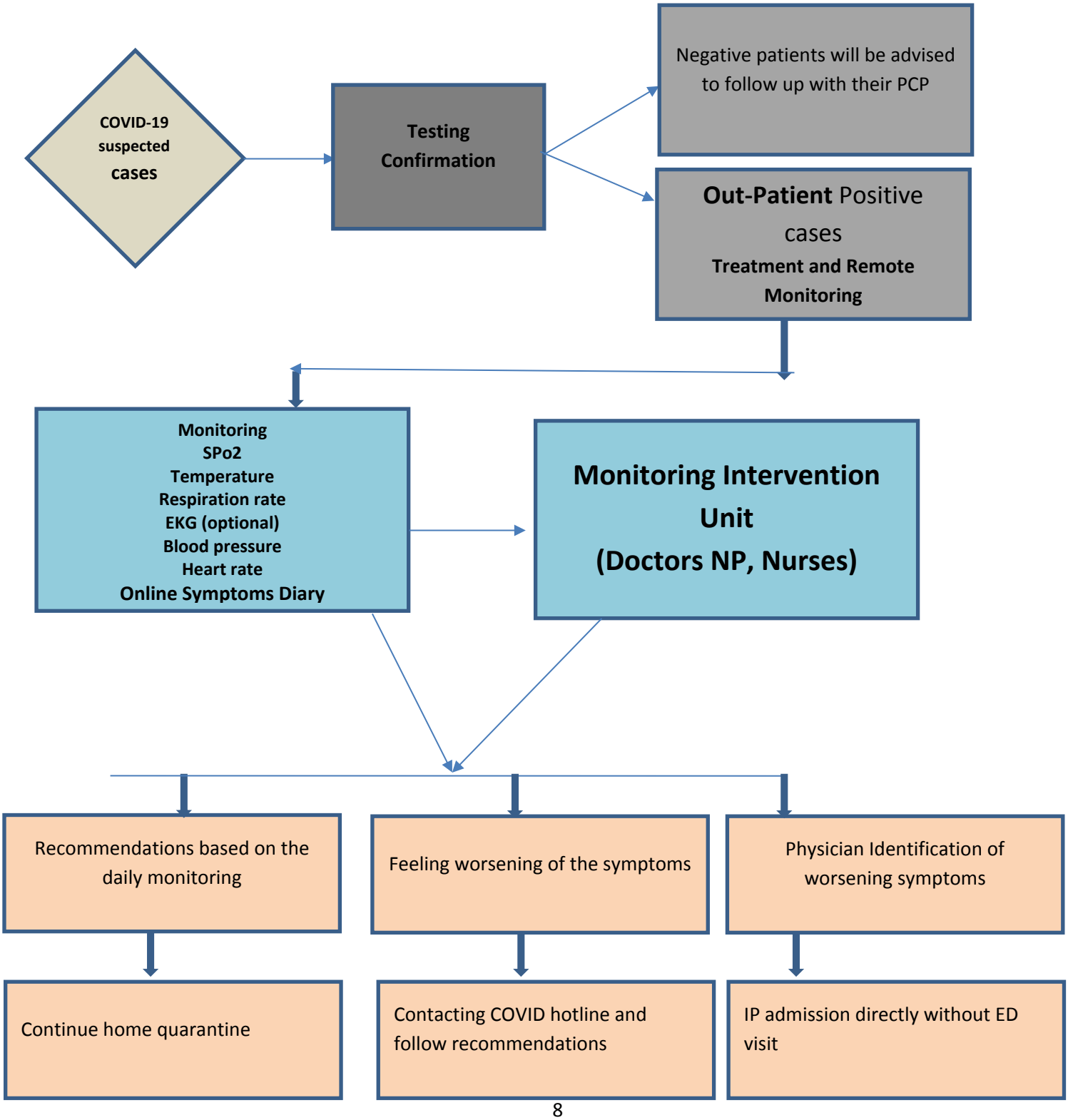
In this prospective observational study, we are evaluating the efficacy of continuous monitoring in preventing inpatient admissions. A sample size of 300 patients is targeted for enrollment; 150 in the monitoring and 150 in the non-monitoring group. The sample size calculation is based on the hypothesized reduction of 10% inpatient admission between the two groups; 15% admission in the non-monitoring group and 5% in the monitoring group, 80% statistical power, and 20% type –II error.

All continuous variables will be summarized using the following descriptive statistics: mean, standard deviation, median, maximum, and minimum. The frequency and percentages will be reported for all categorical variables. No interim analysis will be performed. Quantitative variables will be compared using parametric or non-parametric t-test. A Chi-square test will be used for the comparison of categorical outcomes. All significance tests will be two-tailed, and values of $P < 0.05$ will be considered statistically significant.

Risks and Benefits

Risks associated with this study are minimal. Complications from pulse oximeters and the LifeSignal Biosensor 1AX* are exceedingly rare. Complications that may occur in this study include feeling a small pinch when the monitors are placed and perhaps a small irritation to the skin. Subjects will be asked to provide personal information (PHI). All attempts will be made to keep the PHI confidential within the limits of the law. All the study documents will be kept in a locked file cabinet in the research office. Electronic files will be password protected. Informed consent will clearly state that by participating in this study, the patient's personal information will be shared with an external monitoring agency.

The potential benefits of remote monitoring are at the patient, provider, and hospital level. One of the most important benefits for the patient is that during the self-isolating, and self-quarantine period, RPM can potentially provide peace of mind and daily assurance about their condition. In addition, enrolled patients will be able to instantly connect to their provider without any additional visit to the ED or clinic. These remote interactions could play a significant role in preventing the spread of the disease. At the provider level, because of the real-time availability of patient data, providers can deliver high-quality healthcare to a higher number of patients. Also, providers could use continuous physiological data points in risk stratifying and identifying patients with evidence of clinical deterioration and the need for care escalation. At the hospital level, RPM can potentially reduce the need for inpatient hospitalization during the surge period. Additionally, RPM may allow earlier discharge of hospitalized patients, thereby generating space for new admissions. Finally, the hospital could potentially incorporate RPM as one of the key strategies of future preparedness for similar outbreaks.


COVID-19 suspected cases
Testing Confirmation
Negative patients will be advised to follow up with their PCP
Out-Patient Positive cases
Treatment and Remote Monitoring
Monitoring
SPo2
Temperature
Respiration rate
EKG (optional)
Blood pressure
Heart rate
Online Symptoms Diary
Monitoring Intervention Unit
(Doctors NP, Nurses)
Recommendations based on the daily monitoring
Feeling worsening of the symptoms
Physician Identification of worsening symptoms
Continue home quarantine
Contacting COVID hotline and follow recommendations
IP admission directly without ED visit

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