# Assessing Adherence to Home Telemedicine in Individuals with COPD

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# Protocol COPD-MM-01

**Assessing Adherence to Home Telemedicine in Individuals with COPD**

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Ms. McDaniel-Harper is a senior research coordinator at the UNC Obstructive Lung Diseases Clinical and Translational Research Center, directly supervised by Dr. Drummond. She is a certified clinical research coordinator with experience in conducting clinical trials in COPD. Her skills include participant recruitment, obtaining informed consent, regulatory oversight, and study visit conduct. For this study, she will oversee the day-to-day operations as well as ensure approval and maintenance of compliance with the IRB. She will be responsible for assisting in the recruitment, training and evaluation of research staff and will provide oversight and on-going quality control of data collection procedures.

**Study Site:** UNC Hospitals Pulmonary Specialty Clinic
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**Date and Version of Protocol:** May 24 2020
Version 2.0
Revisions: Remove all in-person visits and procedures; Redefine spirometry criteria; Revise statistical analysis plan

# 1 Protocol Synopsis

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|---|---|
| **Protocol title** | Assessing Adherence to Home Telemedicine in Individuals with COPD |
| **Study code** | COPD-MM-01 |
| **Investigators** | M. Bradley Drummond, MD MHS |
| **Indication** | Chronic Obstructive Lung Disease (COPD) |
| **Population** | COPD patients with history of increased exacerbation risk |
| **Primary Objectives** | Determine if patients with COPD with an increased risk of exacerbation will use an in-home telemonitoring system, including a home spirometer. |
| **Secondary Objectives** | • Determine if use of an in-home telemonitoring system, including a home spirometer, will reduce 30-day readmissions due to COPD.<br>• Determine if use of an in-home telemonitoring system will improve the Quality of Life scores. |
| **Study design** | This is a prospective, open label trial evaluating home telemonitoring for patients with COPD and history of increased exacerbation risk. The purpose of this study is to determine whether automated home monitoring of medication compliance and biometric parameters (FEV1, FVC, PIFR, IC, pulse oximetry, and symptoms) is acceptable to patients, can improve adherence, and may improve clinical outcomes and reduce avoidable 30-day readmissions. Slow spirometry will be performed Sundays, Mondays, Wednesdays, Fridays and Saturdays. Forced spirometry will be performed Tuesdays and Thursdays. |
| **Number of Sites** | Single Site: UNC Hospitals Pulmonary Specialty Clinic |
| **Planned sample size** | Twelve (12) patients |
| **Total study duration** | The study should be completed within nine (9) months. |
| **Subject Participation Duration** | Each patient will be enrolled for three (3) months following enrollment in the study. |
| **Study Technology** | A home telehealthcare tablet platform (GoHome) that will collect:<br>• Multiple spirometry tests each week including both forced and slow spirometry measurements<br>• Pulse Oximetry<br>• QoL Questionnaire responses<br>The platform will:<br>• Remind patients to take their medications<br>• Remind patients to perform measurements<br>• Send patients helpful information |

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| | • Execute a UNC clinic established COPD Action Plan<br>The backend of the platform is a remote server (MTI CarePortal) that collects the data, send out alerts to the Principal Investigator and can track and trend the data for them. It also sends out the medication and measurement reminders. |
| **Concomitant Medications** | • Patients can remain on all prescribed medications<br>• Medications can be changed during the study when clinically indicated by study PI or patient provider |
| **Primary Endpoint** | • Adherence to all measurement collection<br>• Quality of Life scores |
| **Secondary Endpoint** | • Patient satisfaction with monitoring system<br>• Thirty (30) day exacerbation |
| **Exploratory Endpoints** | • Thirty (30) day exacerbation stratified by FEV1<br>• Adherence to subcomponent measurements<br>• Quality of home forced spirometry measures<br>• Variability in slow spirometry and correlation of change in slow spirometry values with COPD exacerbation<br>• Quality of life scores at each visit<br>• Total number of clinical interventions by type (what the medical staff does in response to the telemonitoring)<br>• Peak inspiratory flow measurements<br>• Adherence to taking prescribed medications |
| **Patient Selection Criteria** | Inclusion Criteria:<br>• Male or Female patients<br>• 40 to 80 years of age<br>• English speaking<br>• Spirometry confirmed COPD (post-BD FEV1/FVC<0.70) and post-BD FEV1% predicted <80% at screening visit. (Target 50% of recruitment with post-BD FEV1<50% predicted (severe obstruction). Spirometry must have been collected within 24 months prior to screening.<br>• Increased COPD exacerbation risk defined as either of the following in the prior 12 months:<br>▪ One hospitalization for COPD exacerbation<br>▪ Two outpatient COPD exacerbations requiring treatment with steroids and/or antibiotics<br>• Signed informed consent<br>Exclusion Criteria:<br>• Unable to perform spirometry on their own following training.<br>• Planned discharge to a nursing home or other extended care facility<br>• Co-morbid conditions likely to result in non-preventable |

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| | readmissions (e.g., terminal malignancy, cirrhosis or end-stage liver disease, chronic wound infections, etc.)<br>• Uncontrolled or untreated medical conditions that would predispose the patient to recurrent COPD exacerbations (i.e., bronchiectasis)<br>• Patient refusal to or inability to comply with monitoring requirements, for any reason including but not limited to dementia, a history of dementia, or other significant mental impairment<br>• Patients enrolled in any other clinical trials or therapeutic studies of drugs, devices, or biologics |
| **Safety Monitoring** | As this study is deemed low risk, oversight for this feasibility study will be conducted by the PI (Dr. Drummond). The PI will monitor data to ensure the safety of participants. |
| **Sample Size Justification** | This is a technical evaluation intended to determine if telehealth monitoring can be integrated into the home monitoring of patients with COPD and determine both the acceptance and value of its use. The sample size is not powered or intended to establish statistically significant differences from historic experience. |
| **Statistical Analysis** | The sample size of this technical evaluation is not powered or nor intended to establish statistically significant differences. The adherence and utilization of the platform, as defined by the physiologic and QoL measurements, will be helpful in establishing guidance for future efficacy trials. Nevertheless, descriptive characteristics of the patients prior to, during, and at the end of the study will be tabulated.<br><br>The study is based on two primary endpoints, adherence to home device measurement collection and baseline to Week 12 change in Total Score of COPD Assessment Test (CAT). Home device measurement adherence is described as percentage of participants achieving >50% completion of all planned device measurements (spirometry, pulse oximetry and questionnaires) over three months. Change in CAT score is defined as percentage of participants achieving ≥2 point decrease in CAT from baseline to three months. Additional secondary and exploratory outcomes are also identified in the full protocol.<br><br>The primary outcome will be reported as proportion with 95% confidence intervals. Other outcomes will be described with proportion and 95% confidence interval, rate, or descriptive summary measures as defined in the full protocol. All tests with p value < 0.05 will be interpreted nominally as statistically significant. In addition, the results will be used to identify technological deficiencies and provide data to inform the power requirements for future studies. |

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# 3 List of Abbreviations

| Abbreviation | Definition |
|---|---|
| AE | Adverse events |
| ATS/ERS | American Thoracic Society/European Respiratory Society |
| CMS | Centers for Medicaid and Medicare |
| COPD | Chronic Obstructive Pulmonary Disease |
| CRF | Case report form |
| DPI | Dry Powder Inhaler |
| FDA | US Food and Drug Administration |
| FEV1 | Forced Expired Volume in 1 Second |
| FEV1/FVC | Forced Expired Volume in 1 Second/ Forced Vital Capacity |
| FVC | Forced Vital Capacity |
| GCP | Good Clinical Practice |
| HCT | Hematopoietic Cell Transplant |
| HIPAA | Health Insurance Portability and Accountability Act |
| HRRP | Hospital Readmissions Reduction Program |
| IC | Inspiratory Capacity |
| ICF | Informed Consent Form |
| IRB | Institutional Review Board |
| MD | Medical Physician |
| MDM | Mobile Data Management |
| PHI | Personal Health Information |
| PI | Principal Investigator |
| PIFR | Peak Inspiratory Flow Rate |
| QoL | Quality of Life |
| RPM | Remote Patient Monitoring |
| SAE | Serious adverse event |
| SPC | Statistical Process Control |
| SSL | Secure Sockets Layer |
| SVC | Slow Vital Capacity |
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# 4. Introduction

## *4.1. Background*

The Hospital Readmissions Reduction Program (HRRP), mandated by the Affordable Care Act/Social Security Act, results in reduced Centers for Medicaid and Medicare (CMS) payments to hospitals with excess readmissions.[1] The HRRP targets six conditions that contribute heavily to unplanned readmissions: heart attack, heart failure, pneumonia, Chronic Obstructive Pulmonary Disease (COPD), hip/knee replacement, and coronary artery bypass graft surgeries. It is the expectation of CMS that hospitals cut readmissions through process improvement, specifically by improving transitions of care and improving quality of care. One reported mechanism of improving patient care is the use of remote patient monitoring (RPM), which utilizes technology to connect patients and healthcare providers. Remote patient monitoring can improve patient compliance with maintenance medications and provide targeted intervention/follow-up through symptom monitoring for the six target conditions.

However, for a home RPM program to work, patients need to accept and utilize the technology. In a previous study using the same technology in patients with post-hematopoietic cell transplant (HCT), Sheshadri demonstrated the feasibility of implementing a home spirometry program in HCT recipients who survive to day 100 using the same MTI platform as proposed in this study.[2] Study participants were able to achieve technical proficiency with home spirometry without substantial coaching. Agreement with clinic-based spirometry was acceptable, spirometric data were reproducible over time, and day-to-day variation in measurements was small. Furthermore, they achieved high rates of adherence to the study protocol, with the majority of participants completing the study. They concluded that implementation of a home spirometry program may be a cost-effective way to monitor for early pulmonary impairment in HCT recipients. The COPD patient population may be an older group of patients with potentially more comorbidities and therefore it is important to understand if this technology can fit in as a component of the management of patients with COPD.

## *4.2. Study Design*

This is a prospective, open label trial evaluating home telemonitoring for patients with COPD and a history of increased exacerbation risk. The purpose of this study is to determine whether automated home monitoring of medication compliance and biometric parameters (FEV1, FVC, PIFR, IC, pulse oximetry, and symptoms) is acceptable to patients, can improve adherence, and may improve clinical outcomes and reduce exacerbations and avoidable 30-day readmissions. Slow spirometry will be performed Sundays, Mondays, Wednesdays, Fridays and Saturdays. Forced spirometry will be performed Tuesdays and Thursdays.

# 5. Study Endpoints

## *5.1. The specific Primary Endpoints of this study are:*

- Adherence to measurement collection
- Quality of Life scores

## *5.2. The specific Secondary Endpoints of this study are:*

- Variability in slow spirometry and correlation of change in slow spirometry values with COPD exacerbation
- Patient satisfaction with the monitoring system
- Thirty (30) day exacerbations
- Total number of clinical interventions by type (what the medical staff does in response to the telemonitoring)
- Ability for early identification of loss of DPI effectiveness
- Adherence to taking prescribed medications

# 6. Selection of Study Population

Eligible participants include those being managed for COPD by the UNC Hospitals Pulmonary Specialty Clinic in Chapel Hill, NC and who have been identified to be at a higher risk of exacerbation of their COPD. We plan to enroll twelve (12) patients for three (3) months of monitoring each. The study will be at a single center and anticipated to be completed within nine (9) months.

## *6.1. Inclusion Criteria:*

- Male or Female patients
- 40 to 80 years of age
- English
- Spirometry confirmed COPD (post-BD FEV1/FVC<0.70) and post-BD FEV1% predicted <80% at screening visit. (Target 50% of recruitment with post-BD FEV1<50% predicted (severe obstruction). Spirometry must have been collected within 24 months prior to screening.
- Increased COPD exacerbation risk defined as either of the following in the prior 12 months:
  - One hospitalization for COPD exacerbation
  - Two outpatient COPD exacerbations requiring treatment with steroids and/or antibiotics
- Signed informed consent

## *6.2. Exclusion Criteria:*

- Unable to perform spirometry on their own following training.
- Co-morbid conditions likely to result in non-preventable readmissions (e.g., terminal malignancy, cirrhosis or end-stage liver disease, chronic wound infections, etc.)

- Uncontrolled or untreated medical conditions that would predispose the patient to recurrent COPD exacerbations (e.g., bronchiectasis)
- Patient refusal to or inability to comply with monitoring requirements, for any reason including but not limited to dementia, a history of dementia, or other significant mental impairment
- Patients enrolled in any other clinical trials or therapeutic studies of drugs, devices, or biologics

# 7. Study Procedures:

## *7.1. Patient Identification and Informed Consent*

COPD patients under care at, or referred to the UNC Hospitals Pulmonary Specialty Clinic, who meet the basic entry criteria will be identified by the PI or site clinical personnel. Once a patient is identified as meeting all study criteria, they will be called on the telephone by the investigator/study staff and the study will be thoroughly explained. Verbal informed consent, following UNC Guidelines for verbal consents, will be obtained after the participant has had a chance to have the consent fully explained, have all questions answered, demonstrates an understanding of the study purpose (through verbal discussion with consenter) and has agreed to participate in the study. Verbal consent to HIPAA requirements will also be documented.

## *7.2. Study Home Equipment*

All measurement devices placed in the patient's home are FDA cleared for their intended use. These include a home spirometer (GoSpiro®, Monitored Therapeutics, Dublin, OH) and a finger pulse oximeter (3230 Pulse Oximeter, Nonin Medical, Plymouth, MN). Both of these devices are Bluetooth capable, requiring no wires for connection to the GoHome™ Personal Health Monitor data collection platform.

The GoHome is built on a Samsung tablet working with the Android operating system. It is an auto-start system requiring no patient tablet knowledge to operate the system. Its "home" page is a clock and calendar with a five-day weather forecast which is always kept on. At appropriate times, it will receive and display messages and reminders for the patient. It has a Bluetooth radio for connecting to the spirometer and pulse oximeter. The GoHome will also be used for collecting the Quality of Life questionnaires and for providing educational information for the patient.

Communication with the MTI CarePortal cloud server from the GoHome is through either Wi-Fi or its built-in cellular radio. Patients will not be able to access the internet for personal use on these devices, they will only be able to transfer data for the purposes of this study.

Eligible patients will be sent a participation kit containing the GoHome, GoSpiro and pulse oximeter following their completion of the informed consent and HIPAA authorization. A virtual (phone or video) appointment will be made with the patient by the study staff to train the patient at home how to operate the technology and confirm eligibility. Additional videos on the GoHome will provide additional instructions on use of the GoHome and GoSpiro.

## *7.3.Study Data Platform*

Data collected from patients' homes will be stored on the MTI CarePortal (See Section 10), a cloud server hosted in Dublin, Ohio. This portal will monitor all data received or expected to be received and will send alerts via text and/or e-mail to the investigative team based on pre-defined thresholds. These alerts will be sent for missed spirometry sessions as well as for spirometry which falls below alert thresholds. It will also send alerts based on oxygen saturation alarm thresholds as well as missed medications or measurements or changes in their CAT score.

The platform will also:

- Remind patients to take their medications
- Remind patients to perform measurements
- Send patients helpful information
- Execute a UNC clinic established COPD Action Plan

## *7.4.Study Procedure*

Patients will be enrolled in the study for up to fifteen (15) weeks, including twelve (12) weeks for active monitoring. The study timeline for all procedures is defined in the Section 17 table. All patients enrolled in the study, following the collection of a verbal informed consent, will have a medical history recorded by phone. Upon confirmation of basic eligibility, patients will be sent a telemonitoring system consisting of the GoSpiro®, a pulse oximeter and a GoHome tablet. A member of the Clinic research staff will schedule a (virtual (phone or video) appointment with the patient for when the system has arrived. They will train each patient on how to use the devices and will instruct the patient how and when to record measurements. Pulse oximetry (SpO2 and HR), as well as slow and forced spirometry with the GoSpiro will be collected during this training call. These instructions will also be provided on patient information material (See Appendices A and B). Patients should exhibit proficiency with the devices and demonstrate understanding of the measurement schedule prior to ending the call.

The study nurse will contact the patient the following day by phone to confirm that the patient is able to set up the GoHome and use the devices for measurements. In the event the participant is not able to provide and transmit satisfactory data collection after one week (due to technical or training reasons) they will be removed from study and replaced with another participant toward the total recruitment goal. The study nurse will call the patient every four (4) weeks to collect information on any changes to inhaled medication, steroids or antibiotics and assist the patient with any operational questions. Between phone calls, Clinic research staff or device manufacturer's support personnel will be available to assist the patient should questions or technical issues arise. The study nurse will conduct a final phone visit to collect close out data prior to the participant returning the devices (see Section 17).

Physiologic data from the patients will be transmitted automatically following each measurement and will be available on the CarePortal within a few minutes of its collection. Physiologic data (spirometry and oxygen saturation) will be collected every day. Medication reminders, COPD Action Plan communications, etc. will be sent every day if scheduled. In addition to monitoring parameters, health

teaching tips as part of the COPD Action Plan will also be incorporated into the GoHome software to educate and motivate patients regarding self-care. A Quality of Life questionnaire (COPD Assessment Test) will also be collected every 4 weeks from the patients through the GoHome tablet.

At the end of study (after completion of final phone visit), the patients will return the equipment to UNC via a pre-paid FedEx air bill that has been included with the original shipment. A member of the Clinic research study team will have a final call with the patient to check on the patient's respiratory status and have them complete a usability questionnaire by phone.

# 8. Quality Control Measures

Quality control of the lung function measurements will include automatic ATS/ERS intra-measurement grading of the forced flow-volume loops and slow spirometry to ensure interpretable and actionable home spirometry.[5] MTI will assist with determining the number of missed spirometry sessions with seven times per week testing, and determining any technical issues in transmission of data from the spirometer to the MTI CarePortal.

The GoSpiro home spirometer meets the 2019 ATS/ERS criteria for accuracy and reproducibility.[5] Baseline pulmonary function will be defined as the mean FEV1 over the first two weeks of the study (six measurements). If older data is available for the patient, that data may be included in establishing historic values for analysis. Variability of pulmonary function for alerts to Clinic staff will include a decrease by one personalized z-score using pulmonary function measurements for an individual patient and calculated over the length of the study as well as using historic data if available.

Alerts from acute declines in pulmonary function will be defined as any decrement in either FEV1, FVC or IC >10%. Oxygen saturation readings below 88% will trigger an alert. For patients being managed with DPI delivered inhaled drugs, monitoring of peak inspiratory flow for detection of inadequate flows to aerosolize and deliver the powder, will also generate alerts. The MTI CarePortal will provide daily reports to the Clinic research staff of patient trending towards alert levels, as well as patients with low adherence to medications or measurements.

# 9. Assessments

## *9.1. Timing of Assessments*

See Section 17

## *9.2. Clinical Assessments and Interventions*

### *9.2.1. Patient Characteristics and Medical History*

Demographic information (age, gender, race) will be captured at Screening. Relevant medical history, prescription drugs, including history of smoking, other pertinent history and information regarding underlying diseases will be recorded at Screening.

### *9.2.2. Vital Signs*

Heart rate, respiration rate, and oxygen saturation measurements will be performed and recorded after resting for 5 minutes during the training call and at the week 13 final phone visit.

### *9.2.3. Spirometry*

Patients will be performing slow spirometry measurements five (5) times per week on Sundays, Mondays, Wednesdays, Fridays and Saturdays. They will be performing forced spirometry measurements on Tuesdays and Thursdays. Measurements will be performed in the morning at least 15 minutes following them taking their inhaled medications. The reliability and repeatability of effort dependent tests or tests that require patients to follow specific steps, depend on patients understanding how to perform the test.

The GoHome comes with Avatar-Assisted-Technology to coach the patient through each measurement. The Avatar follows ATS/ERS recommendations for instructions and coaching. At the end of each measurement, the Avatar reviews the results and instructs the patient how to correct maneuver errors. All of this takes place without human intervention. Experience to date indicates that use of the Avatar-Assisted-Technology results in data collection as good as from hospital PFT laboratories and better than from physician offices.[3]

Spirometry will be performed in accordance with the 2019 ATS/ERS recommendations for intra-measurement performance. To increase adherence to performing spirometry measurements, a Statistical Process Control approach will be used as recommended for COPD patients.[4] This approach will be used for both FVC and SVC testing.

### *9.2.4. Oxygen Saturation*

Oxygen saturation will be measured by pulse oximetry at all clinic visits and daily while the patient is monitored at home. Oxygen saturation will be measured prior to the measurement of spirometry.

### *9.2.5. Quality of Life (QoL) Surveys*

The COPD Assessment Tool (CAT), a validated survey, consisting of 8 questions, each on 0-5 Likert scale, will be used to assess the patient's health and quality of life. Patients will be asked to fill it out at enrollment and again at the end of weeks of 4, 8 and 12.

### *9.2.6. Medication Adherence*

Automatic reminders will be sent to patients on their GoHome to take medications. Patients will self-report in response to the reminders whether or not they took their medications. The medication tracking function of the MTI CarePortal will provide report cards to patients (and optionally copied to healthcare providers) as to their adherence, on each Monday for the previous week. These reminders can also be issued "on demand" by the healthcare providers monitoring the patients directly from the MTI CarePortal.

### *9.2.7. Measurement Adherence*

Automatic reminders will be sent to patients on their GoHome to perform measurements. The measurement tracking function of the CarePortal will generate alerts to healthcare providers as to their adherence, based on programmed alarm settings.

### *9.2.8. Incidence of Clinical Interventions*

Clinic personnel will maintain records of any changes in clinical care, additional clinic visits or hospitalizations during the monitoring period. These will be used to determine the effectiveness of the monitoring in either identifying the need for a clinical intervention or preventing the need for one.

### *9.2.9. COPD Action Plan*

The MTI CarePortal architecture includes the MTI CareBook that provides the ability to implement a specific patient-centric COPD Action Plan with appropriate cultural and literacy considerations. The CareBook enables the Action Plan through the use of two primary functions, CareText® and CareTips.

CareText® generate engagement with patients using its ability for simple bi-directional messaging using questions with pre-formatted responses, requiring only a single key response to answer the question. These CareTexts can be sent in several different formats including Yes/No, emoticons, multiple choice, or a slide bar scale. The questions as well as the responses are stored and are viewable on the MTI CarePortal. CareTexts can be automatically sent out as part of a CareBook, maintaining engagement and collecting simple feedback from patients.

CareTips are a shorthand approach to educate the patients about their disease, how to improve their quality of life, and to have them execute small concepts that the caregivers want them to do. These can be something as simple as a health tip to a streaming video on any subject matter.

An interactive COPD Action Plan, built around the MTI CareBook will be used to engage patients during the study. The contents of the Action Plan are in the Appendices.

### *9.2.10. Usability Questionnaire*

At the End-of-Study phone call, the patient will be given a brief Usability Questionnaire to collect their opinions on use of the GoSpiro and GoHome, both for usability and perceived value to them and the management of their health. The Usability Questionnaire is in the Appendices.

## 10. Data Collection and Confidentiality Procedures

The data collection tablets placed in patients' homes are based on the Android operating system. They are locked down with a Samsung Knox Mobile Device Management (MDM) control system that prevents anyone from making changes to the programs or applications. Although the tablets connect with the MTI CarePortal via the internet (either Wi-Fi or cellular), patients have no access to the internet outside of the applications running on the tablet.

For each patient, a randomized numeric token is sent to the data collection device in their home. All data collected from proprietary data collection devices such as the GoHome Personal Health Monitor or the GoClinic Android tablet are then returned to the server with the token. When received, the server reidentifies the data based on the token number and locates the data in the appropriate patient file. No personal health information (PHI) is ever transferred between a remote location and the MTI CarePortal. The access to the data storage system on the MTI CarePortal is limited to web browsers (SSL Secured), direct messaging and electronic data transfer facilitated with a data token.

The MTI CarePortal cloud server, where the data is stored, is hosted by Expedient Inc. with the main server located in, Dublin, OH. Operating mirrored drives, data is backed up in Pittsburgh, PA. The system contains a disaster recovery center in Carmel, IN. Expedient is a global data management company that complies with HIPAA, HITRUST and GDPR requirements for data security.

Settable authorization levels limit users to a) inquiry (read only) capabilities, b) inquiry with also the ability to set alarm limits, establish reminders, care plans and the like, and c) full access for editing and updating capabilities depending on the level of authorization. Users have no access to the underlying code running the user facing application or the MTI CarePortal infrastructure.

### *10.1. Access to Records*

The records are available for direct inspection, verification, and copying, as required by applicable laws and regulations, by officials of the regulatory health authorities (FDA and others). The investigator shall comply with applicable privacy and security laws for use and disclosure of information related to the research set forth in this protocol.

### *10.2. Patient Privacy*

To maintain patient confidentiality, all study reports, and communications relating to the study will identify patients by assigned subject numbers. The FDA (or other regulatory authority) or the Institutional Review Board may also request access to all study records, including source documentation, for inspection.

As applicable, in accordance with HIPAA and associated privacy regulations, a patient's authorization to use personally identifiable health information may be required from each patient before research activities begin. This authorization document shall clearly specify which parties will have access to a patient's personal health information, for what purpose, and for how long.

### *10.3. Record Retention*

The PI will maintain all study records according to GCP guidelines.

## 11. Withdrawal from Study

Patients should immediately be withdrawn from the study for any of the following reasons.

- A condition or adverse event that would prevent the patient from performing the

specified measurements in the protocol
- At the discretion of the patient
- At the discretion of the Investigator, if deemed appropriate, for any reason

If a patient is withdrawn because of an adverse event, the patient will be followed and treated by the Investigator until the abnormal parameter or symptom has resolved or stabilized. The adverse events must be followed to resolution and the follow-up evaluations should be performed when the patient has stabilized.

Any patient that is withdrawn from the study within the first two weeks due to technical or training reasons will be replaced.

If for any reason a patient does not complete the study, the reason will be entered on the CRF. All patients are free to withdraw from participation at any time, for any reason, specified or unspecified, and without prejudice. The Investigator must record the reason for the early termination.

# 12. Concomitant Medications

Patients can remain on all prescribed medications. Medications can be changed during the study when clinically indicated by the study PI or patient provider.

# 13. Statistical Considerations:

This is a technical evaluation intended to determine if remote patient monitoring can be integrated into the home monitoring of patients with COPD and determine both the acceptance and value of its use. The sample size is not powered or intended to establish statistically significant differences from historic experience. The adherence and utilization of the platform, as defined by the physiologic and QoL measurements, will be helpful in establishing guidance for future efficacy trials.

Nevertheless, descriptive characteristics of the patients prior to, during, and at the end of the study will be tabulated. Using the full analytical set (FAS), specific variables (demographics and clinical variables, baseline maintenance and rescue inhaler use, and modified Medical Research Council Score) will be summarized using descriptive measures (mean and standard deviation, min, max, median) and graphical displays (boxplots, histograms) as appropriate.

Differences between important continuous variables at two specific times will be evaluated with the two-sided paired t-test ($P<0.05$). Important categorical events such as changes in FEV1, Inspiratory Capacity, QoL, medication adherence, rehospitalization and incidence of adverse events will be evaluated by constructing 95% confidence limits in their incidence, and also with descriptive statistics. In addition, the results will be used to identify technological deficiencies and provide data to inform the power requirements for future studies.

**Primary Endpoint Definitions**

The first primary endpoint variable for this study is the change from baseline in Total Score of COPD Assessment Test (CAT). The total CAT score is calculated by summing the scores of all items and ranges from 0 to 40, higher scores indicating severe condition. The change will be calculated as the CAT score at Week 12 minus the CAT score at Enrollment. A negative change in CAT score will indicate an improvement in patient status.

The second primary endpoint variable for this study is adherence to performing scheduled measurements and responding to scheduled questionnaires. For each subject the adherence will be recorded based on the data uploaded to the CarePortal. The adherence percentage will be calculated by the difference in recorded measurements and answered questionnaires versus the scheduled measurements and questionnaires.

**Analysis of Primary Endpoints**
The primary outcomes will be reported as proportions with 95% confidence intervals, on the FAS.

**Secondary Endpoint Definitions**
The prespecified secondary endpoints for this study will include:

- Participant satisfaction survey scores at 3 months (Time frame: 3 months) defined as the percentage of participants with score of 4 or higher on individual survey domains. A satisfaction survey (investigator-developed, 15 questions, each question is graded on a scale of 1-5, 1 being not at all and 5 being extremely) will be used to measure home spirometry and table ease and usefulness.

- Rate of self-reported COPD exacerbations (Time frame: 3 months) defined as the 30-day COPD exacerbation rate, defined as the mean number of events/30 days of follow-up (using three months of follow-up data). COPD exacerbation events are defined as self-reported COPD exacerbations requiring treatment with antibiotics or steroids.

**Analysis of Secondary Endpoints**
The secondary endpoints will be reported as proportion with 95% confidence interval of participants with score of 4 or higher on individual survey domains of patient satisfaction summary score; Descriptive analysis of patient satisfaction summary scores will include mean (SD), median (IQR), range of scores.

For the COPD exacerbation analyses, the proportion of patients with COPD exacerbations and the rate of exacerbations occurring during follow-up will be reported along with 95% CI. A patient will be considered censored for exacerbations at the time of the last documented visit, the end of the study, or death (whichever occurs earlier), if they did not experience an exacerbation before.

**Exploratory Endpoints Definitions**
The study contains exploratory endpoints to examine individual components of the monitoring functions and their impact. These include:

- Rate of self-reported COPD exacerbations stratified by FEV1 and defined as the 30-day COPD exacerbation rate, defined as the mean number of self-reported COPD exacerbations

requiring treatment with antibiotics or steroids per 30 days of follow-up (averaged using 3 months of follow-up data), stratified by FEV1 (separately <50% predicted and >=50% predicted).

- Home spirometry measurement collection adherence defined as the percentage of participants achieving >50% completion of spirometry measurements over three months.
- Home pulse oximetry measurement collection adherence defined as the percentage of participants achieving >50% completion of pulse oximetry over three months.
- Home questionnaire collection adherence defined as the percentage of participants achieving >50% completion of home questionnaires over three months.
- Quality of home forced spirometry measures defined as the percentage of forced home spirometry measurements that meet ATS quality standards
- Change from baseline on COPD Assessment Test (CAT) Total Score defined as the CAT scores measured at baseline, week 4, week 8 and week 12 and the median (SD) change in CAT score from baseline will be calculated at each time point.
- Inspiratory Capacity variability defined as the coefficient of variation will be calculated by dividing standard deviation of Inspiratory Capacity values by the mean of the inspiratory capacity values. Inspiratory capacity measured via slow vital capacity maneuver will be performed at home five days per week during duration of study.
- Inspiratory Capacity before, during and after COPD exacerbations defined as the overall median Inspiratory Capacity reported at three time intervals: the week before COPD exacerbation, the week of COPD exacerbation, and the week after COPD exacerbation.
- Number of clinical interventions defined as the total number of clinical interventions per participant over study duration. Clinical interventions will be categorized into one of three types (phone contact, clinic visit, referral to Emergency Department).
- Type of clinical interventions defined as the percentage of type of clinical intervention across all study participants. Clinical interventions will be categorized into one of three types (phone contact, clinic visit, referral to Emergency Department).
- Suboptimal peak inspiratory flow measurements defined as the percentage of peak inspiratory flow measurements <3.27 liter/sec obtained on forced spirometry maneuvers.
- Maintenance inhaler adherence defined as the adherence will be defined by average number of days per week (range 0-7) participant reports maintenance inhaler use.
- Change from baseline in maintenance inhaler adherence defined as the change from baseline to 3 months in maintenance inhaler adherence. Adherence will be defined by number of days per week (range 0-7) participant reports maintenance inhaler use.
- Change from baseline in rescue inhaler use defined as the change from baseline to 3 months in rescue inhaler use. Rescue inhaler use will be categorized at baseline and 3 month visit as not at all, once a week or less, 2-3 times per week, 1-2 times per day, 3 or more times per day.

**Analysis of Exploratory Endpoints**

The exploratory endpoints will be analyzed as described below. The hypothesis testing of these additional secondary efficacy endpoints is considered exploratory. All tests with p value < 0.05 will be interpreted nominally as statistically significant.

- For stratified COPD exacerbation analyses, the proportion of patients with COPD exacerbations and the rate of exacerbations occurring during follow-up will be reported along with 95% CI stratified by FEV1 severity (<50% predicted: >=50% predicted).
- Individual home assessment component adherence will be reported as proportions with 95% confidence intervals
- Quality of home forced spirometry measures will be reported as proportions with 95% confidence intervals
- Descriptive analysis of change from baseline to weeks 4, 8 and 12 on CAT Total score including mean (SD), median (IQR), range
- Descriptive analysis of Inspiratory Capacity measurements, including mean (SD), median (IQR), range, coefficient of variation
- The overall median of Inspiratory Capacity in the week before, of, and after each exacerbation will be calculated and compared using Kruskall-Wallis testing.
- The total number and distribution of type of intervention (phone contact, clinic visit, referral to Emergency Department) will be summarized in tabular format
- The proportion of suboptimal peak inspiratory flow measurements (defined as <3.27L/sec) will be reported with 95% CI. Additional exploratory analyses include distribution of peak inspiratory flow measurements along with proportions of alternative thresholds.
- Descriptive analysis of overall maintenance inhaler adherence including mean (SD), median (IQR), range, proportion and 95% CI of participants with >50% adherence
- Descriptive analysis of change from baseline to week 12 on number of days per week of maintenance inhaler adherence including mean (SD), median (IQR), range
- Tabular summary of overall rescue inhaler use (categorized into not at all, once a week or less, 2-3 times per week, 1-2 times per day, 3 or more times per day)
- Comparative analysis (chi square) of distribution of categorical responses to rescue inhaler use comparing baseline to 12 week visit
- Tabular summary of number and type of SAE

# 14. Safety Monitoring

As this study is deemed low risk, using technology frequently prescribed for use by COPD patients at home, oversight for this feasibility study will be conducted by the PI (Dr. Drummond). The PI will monitor data to ensure the safety of participants. Only treatment-related serious adverse events (SAEs) will be reported to the IRB using the Adverse Event Template Form, per institutional and national guidelines within one business day of notification of the event. Hospitalization for COPD exacerbation will be considered an SAE. SAEs will be tracked for 30 days following termination of the study.

# 15. Administrative Requirements

## *15.1. Ethical Considerations*

The study will be conducted in accordance with the ethical principles founded in the Declaration of Helsinki, and according to local applicable laws and regulations. The institutional

review board (IRB) will review all appropriate study documentation to safeguard the rights, safety, and well-being of the patients.

### *15.2. Patient Information and Informed Consent*

Explanation of the study and informed consent will be obtained by a member of the study team. Patients shall be informed that participation is voluntary and that they may withdraw from the study at any time, without prejudice to their current or future care. Once all of their questions have been answered and they have voluntarily agreed to participate in the study, each patient will be asked to give verbal consent to participate following the UNC Guidelines for verbal consent. Informed consent must be obtained from each patient before the performance of any study-related activity.

### *15.3. Investigator Compliance*

No modifications to the protocol shall be made without the approval of the IRB, except where the modification is necessary to eliminate an apparent immediate hazard to human subjects. Any departures from protocol must be fully documented in the source documentation and in a protocol deviation log.

### *15.4. ClinicalTrials.Gov Registration*

As this study meets the FDAAA 801 definition of an "Applicable Clinical Trial", it is required that the study be registered on ClinicalTrials.gov. The Principal Investigator will register and activate the study account prior to enrollment, and all results will be entered upon study completion, followings statistical analysis, per the Results Database Guidelines.

## 16. References


1. US Government, Hospital Readmissions Reduction Program, Section 3025 Affordable Care Act. 2012.
2. Sheshadri A., et al. In submission. Personal communications. 2019
3. Stenzler A. Collecting Quality Spirometry at Home. Respiratory Therapy 2018; 13:48-54
4. Stenzler A. Improving home COPD monitoring through statistical process control (SPC). Respiratory Therapy 2019; 14:44-47.
5. Graham BL, et al. Standardization of Spirometry 2019 Update. An Official American Thoracic Society and European Respiratory Society Technical Statement ATS/ERS Guidance. Am J Respir Crit Care Med. 2019; 200 (8): e70–e88

# 17. Schedule of Assessments

| **Week** | **-1 to-2** | **1** [a] | **2** [a] | **3** [a] | **4** [a] | **5** [a] | **6** [a] | **7** [a] | **8** [a] | **9** [a] | **10** [a] | **11** [a] | **12** [a] | **13** |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Description** | **Screen** | **Enroll/ Training /Monitor** | **Monitor** | **Monitor** | **Monitor** | **Monitor** | **Monitor** | **Monitor** | **Monitor** | **Monitor** | **Monitor** | **Monitor** | **Monitor** | **Final Call** |
| Subject Consent | X | | | | | | | | | | | | | |
| Demographics | X | | | | | | | | | | | | | |
| Medical History | X | | | | | | | | | | | | | |
| Height and Weight | X | | | | | | | | | | | | | |
| Vital Signs | X | X[i] | | | | | | | | | | | | X |
| Concomitant Medications[e] | X | X[i] | | | | X | | | | X | | | | X |
| Forced Spirometry | | X[c] | X[c] | X [c] | X[c] | X[c] | X[c] | X[c] | X[c] | X[c] | X[c] | X[c] | X[c] | |
| Slow Spirometry | | X[c] | X[c] | X[c] | X[c] | X[c] | X[c] | X[c] | X[c] | X[c] | X[c] | X[c] | X[c] | |
| Oxygen Saturation | | X[h] | X[h] | X[h] | X[h] | X[h] | X[h] | X[h] | X[h] | X[h] | X[h] | X[h] | X[h] | X |
| CAT Quality of Life Survey | | X | | | X | | | | X | | | | X | |
| COPD Action Plan[f] | | X | X | X | X | X | X | X | X | X | X | X | X | |
| Medication Adherence | | X | X | X | X | X | X | X | X | X | X | X | X | |
| Measurement Adherence | | X | X | X | X | X | X | X | X | X | X | X | X | |
| Nurse Call | | X[b] | | | | X[b] | | | | X[b] | | | | X |
| Adverse Events[g] | | X | | | | X | | | | X | | | | X |
| Usability Survey | | | | | | | | | | | | | | X |
| | | | | | | | | | | | | | | |

**Footnotes:**

a Medication and measurement reminders issue 7 days a week, medication report cards on Fridays

b Nurse will call first week of monitored months. Will call second day after enrollment/training to assure patient understanding.

c Measured with GoSpiro. Collected post-bronchodilator. Slow spirometry Sunday, Monday, Wednesday, Friday and Saturday. Forced Spirometry Tuesday and Thursday. At home measurements occur in the morning at least 15 minutes following them taking their inhaled medications.

e Collected by Nurse on monthly call related to changes in inhaled medications, steroids or antibiotics.

f COPD Action Plan messages vary weekly according to the plan

g Adverse events confirmed on monthly nurse call plus any reported by patient or provider.

h Oxygen saturation measured 7 days a week, preceding spirometry measurements.

i Vital signs and concomitant medications from screening can be used for enrollment visit if conducted on same day.

# 18. Appendices

Appendix A: GoHome instructions

Appendix B: Measurement Instructions.

Appendix C: MTI CareBook – COPD Action Plan

Appendix D: Usability Questionnaire

Appendix E: CAT Questionnaire