CITY OF HOPE NATIONAL MEDICAL CENTER
1500 E. DUARTE ROAD
DUARTE, CA 91010

DEPARTMENT OF Surgery

TITLE: Perioperative Telemonitoring to Optimize Cancer Care and Outcomes

CITY OF HOPE PROTOCOL NUMBER: 20717 PROTOCOL DATED: 05/24/2023

DATE(S)/ OF AMENDMENT(S)/REVISION(S):

COH Initial Approval	Protocol dated 03/24/21	Packet 00
COH Amendment 01	Protocol dated 09/15/21	Packet 01
COH Amendment 02	Protocol dated 12/15/21	Packet 02
COH Amendment 03	Protocol dated 12/15/21(tp)	Packet 03
COH Amendment 04	Protocol dated 12/15/21 (tp)	Packet 04
COH Amendment 05	Protocol dated 12/15/21 (tp)	Packet 05
COH Amendment 06	Protocol dated 12/15/21 (tp)	Packet 06
COH Amendment 07	Protocol dated 12/15/21 (tp)	Packet 07
COH Amendment 08	Protocol dated 05/24/23	Packet 08
COH Amendment 09	Protocol dated 05/24/23 (tp)	Packet 09
COH Amendment at Continuation	Protocol dated 05/24/23 (tp)	Packet 10

SPONSOR/IND NUMBER: NR019866-01
DISEASE SITE: GI
STAGE (if applicable): NA
MODALITY: Intervention
PHASE/TYPE: Pilot/Feasibility
ClinicalTrials.gov identifier: NCT04986566

PRINCIPAL INVESTIGATORS: Laleh Melstrom, MD

COLLABORATING INVESTIGATORS: Virginia Sun, PhD, RN, Darrell Fan, Kristen Limbach, MD, Marta Jankowska, PhD, Calvin Tribby, Sarah Alismail, PhD

PARTICIPATING CLINICIANS: Loretta Erhunmwunsee MD, Jae Kim MD, Dan Raz MD, Andreas Kaiser MD, Lily Lai MD, Kurt Melstrom MD, Gagandeep Singh MD, , Yanghee Woo MD, Yuman Fong MD

STUDY STATISTICIANS:	Joycelynne Palmer, PhD, Timmy Okunowo, MS, Yan Wang, MS
NON-PHYSICIAN CONSENTERS:	Fernanda Perez, BS, Evelyn Leyva, BSN, RN, Randy Lee, MHA, , Jacqueline Carranza, BS, , Elizabeth Bustamante, BS, Rosemary Prieto, RN, BSN, Patricia Esslin, PhD, APRN-CNS, CNE, Maricela Haj, RN, Maria Pakhdikian, M.A.

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Protocol Synopsis

Protocol Title:
Perioperative Telemonitoring to Optimize Cancer Care and Outcomes
Brief Protocol Title for the Lay Public (if applicable):
NA
Study Phase:
Pilot/Feasibility
Participating Sites:
Duarte Campus
Rationale for this Study:
The most common and successful component of cancer treatment is surgery. However, patients experience abrupt declines in functional capacity after major surgical procedures. In addition to postoperative functional decline, patients experience an increase in symptoms, such as pain, fatigue, and distress.[1-3] Postoperatively, these symptoms contribute to a dramatic decline in quality of life (QOL).[4-6] Recovery from these challenges is compounded by healthcare systems-related trends, including pressures to reduce readmissions and length of stay. As a result, the majority of postoperative care and recovery takes place at home. Unfortunately, while at home physical function can decline severely before the surgical team is notified. This means that about one third of patients will become symptomatic from a complication and may require hospital readmission.[2, 7-9] A promising approach to early identification of post-discharge complications is through remote, real-time perioperative telemonitoring of patient-generated health data (PGHD) and electronic patient-reported outcomes (ePROs). In our preliminary studies, telemonitoring was feasible and acceptable in the perioperative setting.[10] We found that patient-generated daily steps data was associated with the risk for postoperative complications.[10] However, the current perioperative care model is largely reactive and does not address the need for monitoring and supporting postoperative recovery. Therefore, remote and scalable telemonitoring approaches are urgently needed to improve perioperative cancer care in a healthcare system that demands early discharge and reduced hospital readmissions.
Objectives:
1. Feasibility Retention and acceptability of the intervention through statistics of participation, intervention, completion (retention) rates and qualitative data from exit interviews. 2. Surgical outcomes (post operative complications), healthcare utilization (postoperative complications, readmissions), PROs (symptoms, QOL) and functional recovery (pedometer) will be examined by treatment arm

Study Design:
Pilot RCT (1:1 randomization)
Endpoints:
Primary: severity (grade) of postoperative complications from discharge to day 30 post discharge.
Sample Size:
160 patients (80 per arm)
Estimated Duration of the Study
30 months
Summary of Subject Eligibility Criteria:
Study eligibility criteria include: • Cancer patients scheduled to undergo major abdominal surgery for GI malignancies. GI procedures include esophagectomy, gastrectomy, colectomy, abdominoperineal resection/low anterior resection, hepatectomy, pancreatectomy (distal or pancreaticoduodenectomy), and cytoreductive surgery for peritoneal carcinomatosis. We will include patients scheduled for an ostomy (colostomy or diverting ileostomy), • Age 18 years or older, • Ability to read and understand English or Spanish.
Investigational Product Dosage and Administration:
NA
Clinical Observations and Tests to be Performed:
NA
Statistical Considerations:
We will need 128 patients (64 per arm) to detect an effect size of 0.5 in the primary outcomes as described in Aim 2 (postoperative complications, lower readmission rates, improved symptoms, QOL, and functional recovery) between the two groups, with a two-sided 0.05 significance level using a two-sample t-test and at least 80% power. We will enroll a total of 160 (80 per arm to account for an expectation of 20% attrition. Thus, we will have sufficient power for all primary outcomes, including our primary endpoint of postoperative complications.
Sponsor/Licensee:
NINR
Case Report Forms
NA

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Abbreviations

Abbreviation	Meaning
AE	Adverse Event
CFR	Code of Federal Regulations
COH	City of Hope
CTCAE	Common Terminology Criteria for Adverse Events
DSMC	Data Safety Monitoring Committee
ECOG	Eastern Cooperative Oncology Group
ERAS	Enhanced Recovery After Surgery
FDA	Food and Drug Administration
GCP	Good Clinical Practice
ICF	Informed Consent Form
IRB	Institutional Review Board
KPS	Karnofsky Performance State
LOS	Length of Stay
MDASI	MD Anderson Symptom Inventory
MIPS	Merit-Based Incentive Payment System
NCI	National Cancer Institute
PGHD	Patient-Generated Health Data
PI	Principal Investigator
PMT	Protocol Monitoring Team
PRO	Patient Reported Outcomes
QOL	Quality of Life
SAE	Serious Adverse Event

1.0 Goals and Objectives (Scientific Aims)

The most common and successful component of cancer treatment is surgery. However, patients experience abrupt declines in functional capacity after major surgical procedures. In addition to postoperative functional decline, patients experience an increase in symptoms, such as pain, fatigue, and distress.[1-3] Postoperatively, these symptoms contribute to a dramatic decline in quality of life (QOL).[4-6] Recovery from these challenges is compounded by healthcare systems-related trends, including pressures to reduce readmissions and length of stay. As a result, the majority of postoperative care and recovery takes place at home. Unfortunately, while at home physical function can decline severely before the surgical team is notified. This means that about one third of patients will become symptomatic from a complication and may require hospital readmission.[2, 7-9]

A promising approach to early identification of post-discharge complications is through remote, real-time perioperative telemonitoring of patient-generated health data (PGHD) and electronic patient-reported outcomes (ePROs). In our preliminary studies, telemonitoring was feasible and acceptable in the perioperative setting.[10] We found that patient-generated daily steps data was associated with the risk for postoperative complications.[10] However, the current perioperative care model is largely reactive and does not address the need for monitoring and supporting postoperative recovery. Therefore, remote and scalable telemonitoring approaches are urgently needed to improve perioperative cancer care in a healthcare system that demands early discharge and reduced hospital readmissions.

The **primary objective** of this proposal is to conduct a pilot randomized trial of a remote, perioperative telemonitoring intervention to improve patient-centered outcomes, surgical outcomes, and healthcare resource use in English and Spanish-speaking patients scheduled to undergo major abdominal gastrointestinal (GI) cancer surgery. The intervention includes: 1) objective, device monitoring of physiologic parameters (temperature, blood pressure, heart rate, pulse oximetry, weight); 2) objective, wristband pedometer monitoring of functional activity (daily steps taken); 3) ePROs (symptoms, QOL); and 4) a real-time, alert/feedback system. Telemonitoring will begin before surgery, during hospitalization, and end at 30 days post-discharge. The feedback system is triggered by deviations from predetermined clinical thresholds, and results in telehealth nursing assessment, triage, and management. Our **central hypothesis** is that remote telemonitoring of PGHD and ePROs are feasible and acceptable to patients, and will enhance surgical outcomes, reduce undesirable healthcare utilization, and improve PROs compared to the enhanced usual care condition. We will test our central hypothesis and accomplish our overall objective by pursuing the following **specific aims**:

Specific Aim 1: Assess the feasibility, retention, and acceptability of the remote perioperative telemonitoring intervention as measured by the percentage of patients who a) agree to participate; b) complete ≥70% of the telemonitoring; and c) report satisfaction with the intervention through structured exit interviews.

Specific Aim 2: Determine the preliminary efficacy of the remote perioperative telemonitoring intervention on surgical outcomes, healthcare utilization, PROs, and functional recovery.

Hypothesis 2.1: Patients randomized to the telemonitoring arm will experience reduced severity (grade) of postoperative complications, lower readmission rates, and improved symptoms, QOL, and daily steps.

This research builds on informative preliminary evidence from our team.[10, 11] The proposal addresses a key strategic plan of the National Institute of Nursing Research (NINR) to "explore a wide range of technologies that can be used to support real-time clinical decisions to improve health."[12] It is a response to the 2013 Institute of Medicine call for high-quality, patient-centered cancer care.[13] It addresses two key priorities of the American College of Surgeons (ACS): 1) the critical role of patients as integral members of the surgical team, and 2) that the active involvement of patients in care can decrease complications through early identification of risks.[14]

This application is significant because we are addressing a "critical challenge" to quality perioperative care in the current healthcare environment that calls for the development and testing of novel approaches to early and safe hospital discharge. Our **long-term goal** is an R01 submission to conduct a Phase III trial of the proposed intervention to establish efficacy. We will use the findings from this R21 to further refine and develop the Phase III trial design, infrastructure, and implementation strategy. This includes identifying the effect size needed for calculating sample size, and procedures for intervention implementation, data collection, and data analysis.

2.0 Background

2.1 Introduction/Rationale for Development

Surgeons and cancer centers are increasingly asked to provide evidence of the quality and value of their care. Historically, medical outcomes, including surgical outcomes, are measured by disease- and systems-related parameters, such as length of hospital stay, morbidity, readmission rates, and mortality.[2,3] While important, these measures do not accurately reflect the surgical care experience from a patient's perspective. Patient-generated health data (PGHD) and patient-centered outcomes, including patient-reported outcomes (PROs), are increasingly being used in routine cancer care as quality and value indicators.[3-5] However, these outcomes are not adequately understood and routinely integrated in surgical oncology.

More than 45 million Americans undergo surgery each year, with expenditures exceeding $500 billion (40% of national healthcare spending).[6] Expenditures for cancer care, including surgery, were $127 billion in 2013; this cost is projected to increase to $158 billion in 2020.[7] More than 60% of cancer patients undergo surgical interventions[8], and surgery is often used as either the sole treatment modality or in combination with radiation and/or chemotherapy. Surgical interventions account for the most cures after a cancer diagnosis.[9]

Due to changes in the healthcare system and advances in surgical techniques, surgeons are asked to discharge patients earlier and earlier after surgery. Operations that were previously associated with 10-20 day hospital stays are now either outpatient procedures or short-stay procedures. Given increasing incentives that mandate shorter hospital stays, postoperative complications that traditionally arise in the hospital are also developing, potentially unnoticed, in the community and at home.

In recent years, surgical care is increasingly focused on using enhanced recovery after surgery (ERAS) pathways to improve surgical outcomes.[10] ERAS pathways are created to include standard, prescribed tasks in the perioperative care setting to shorten length of hospital stay (LOS) and contain cost.[11] A typical ERAS pathway includes the following tasks: 1) pre-op food and fluid intake; 2) analgesics/pain management; 3) hypothermia precautions; 4) DVT and antibiotic prophylaxis; 5) parameters for postoperative labs; 6) bowel care; and 7) early

ambulation. A critical gap in ERAS pathways is the lack of remote recovery monitoring capabilities after discharge. Perioperative care provided through ERAS pathways should also include remote monitoring and real-time interventions after hospital discharge and until full post-surgical recovery.

The current delivery model for post-discharge care and monitoring is largely inefficient, not proactive, and not cost-effective.[12] Visiting home health nurses are often dispatched for patients with unresolved acute problems (i.e. surgical wound infections, rehabilitation needs). Patients may contact the hospital when acute problems arise. This often requires hours or days to resolve, and is burdensome for patients, families, as well as the healthcare system. In critical situations, visits to the emergency room or paramedics care are accessed, either within the same healthcare system or at a different institution; these are costly and inefficient. Delays in communicating critical conditions may escalate problems beyond outpatient care. These emergency problems may also result in patients being cared for outside of the index medical system and increase cost.

The past 50 years have seen an explosion in biomedical knowledge, dramatic innovations in surgical procedures, and management of complex medical conditions, with ever more exciting clinical capabilities on the horizon. Yet, the American healthcare system is falling short on key components of quality, outcomes, and cost.[13] The overarching imperatives for healthcare include the need to develop ways to manage its ever-increasing complexity, and curb ever-escalating costs. Opportunities now exist to address these problems; these include 1) computational power that is affordable and widely available; 2) connectivity that allows information to be accessed in real-time virtually anywhere; 3) human and organizational capabilities that improve the reliability and efficiency of care processes; 4) the recognition that effective care must be delivered in a patient-centric fashion; and 5) the recognition that, regardless of incentive structures, penalties, and payment reforms, nothing about the experiences and outcomes/value of care will improve until progress is made to revolutionize the care delivery system.[7,13,14]

Improving outcomes after cancer surgery relies on symptom management, complication avoidance, and readmission prevention.[15] Modern-day wearable and digital patient engagement technology has the potential to transform the current surgical care paradigm.[16-18] It allows individuals to track and store measurable health parameters. This phenomenon allows surgeons to access patient-centered data that can help with care decisions in a timely fashion. In the clinical setting, wearable technology can assist surgeons with evaluating physical function to guide and monitor perioperative care.[12] The technology has the following advantages compared to current care delivery models: 1) they are highly scalable; 2) they do not depend on a patient's cognition, language, or health status; 3) they serve as an efficient and unobtrusive method for monitoring postoperative recovery; 4) they complement and augment ERAS care pathways; and 5) they are deployable in various geographic locations and communities. Importantly, it has the potential to identify patients who are in need of interventions to optimize recovery and outcomes.[19-21]

From a policy and reimbursement perspective, there are major reimbursement avenues for remote patient monitoring in 2018 and beyond. In 2017, the following telehealth-related milestones were reached: 1) 48 states, including California and the District of Columbia, provided reimbursement for live video consults in their Medicaid fee-for-service programs; 2) 21 Medicaid programs reimbursed for remote patient monitoring; and 3) 36 states (including California) and the District of Columbia had laws governing coverage by private payers of telehealth services. Furthermore, beginning in 2018, CMS will support providers who leverage

remote monitoring tools, such as wearables and smart devices at home, and use patient-generated health data in care coordination and management. Providers will soon be able to receive reimbursement separately for time spent on collection and interpretation of health data that is generated by a patient remotely, digitally stored, and transmitted to the provider. The changes would enable providers utilizing "non-face-to-face chronic care management using remote monitoring and or telehealth technology" to receive Advance Care Information (ACI) program points for activities like collecting, monitoring and reviewing patient physiological data and prescribing patient education. ACI is one of the four performance categories under the Merit-Based Incentive Payment System (MIPS).

Our partnership with an existing home health monitoring and digital patient engagement infrastructure (mTelehealth™ and Aetonix) leverages a "real world" platform, which will enhance the successful implementation of this study and enhance future adoption into clinical surgical oncology practice. Our study design moves away from traditional clinic-based care paradigms to telehealth patient engagement. The challenges of the US healthcare system demand an innovative, transformed approach to perioperative and post-discharge care.[13]

2.2 Overview of Proposed Study

This is a pilot RCT (1:1 randomization) of a remote perioperative telemonitoring intervention in major abdominal cancer surgery. We will focus on GI malignancies, because the surgical procedures, extent of resection, and expected surgical outcomes are similar. In Aim 1, we will assess the feasibility, retention, and acceptability of the intervention through statistics of participation, intervention completion (retention) rates, and qualitative data from exit interviews. In Aim 2, surgical outcomes (post-operative complications), healthcare utilization (postoperative complications, hospital readmissions), PROs (symptoms, QOL), and functional recovery (pedometer steps) will be examined by treatment arm. Our primary endpoint is severity (grade) of postoperative complications from discharge to day 30 post-discharge. This study will be conducted in compliance with the protocol, Good Clinical Practice (GCP) and the applicable regulatory requirements.

2.3 Preclinical Studies

Not Applicable

2.4 Human Studies

This proposal builds on over 15 years of research in patient-centered outcomes in gastrointestinal (GI) cancer populations. Our interdisciplinary team includes expertise in surgical oncology (Melstrom - PI), technology-driven intervention methodology (Sun), and perioperative outcomes (Melstrom, Sun). The investigators have designed and tested rigorous telehealth intervention trials. Study team roles and responsibilities are described in **Section 3.5** of the PHS Human Subjects and Clinical Trials Information form.

Preliminary Studies - We assessed the feasibility and acceptability of perioperative telemonitoring of functional activity, PGHD and ePROs (N=20).[10] Patients were given a wristband pedometer (Vivofit 2) to monitor daily steps and completed ePROs (MD Anderson Symptom Inventory - MDASI and EQ-5D-5L). Daily steps and ePROs were monitored 3-7 days prior to surgery, during hospitalization, and up to two weeks after discharge. A real-time alert/feedback system was initiated when an encounter fell beyond the

following predetermined thresholds: 1) symptom score of 4/10 or higher (high severity); 2) QOL score of 2/5 or higher (indicates problem). Nurses contacted the patient for further assessment, triage and management.

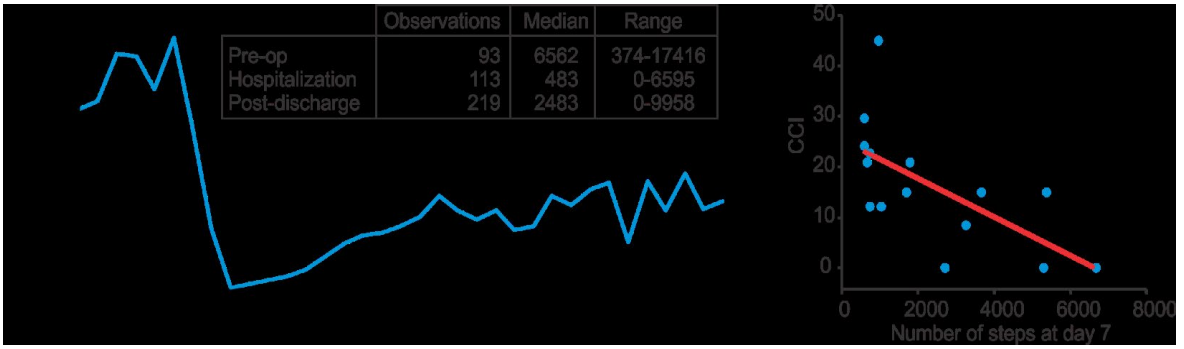


Figure 1 depicts the number of daily steps from before surgery to 2 weeks post –discharge. Exploratory analysis (**Figure 2**) revealed a correlation between the number of daily steps and risk for postoperative complications (as measured by the comprehensive complications index – CCI) ($r=-0.64$, $p<0.05$). Patients with fewer daily steps were at higher risk for complications (higher CCI score). Telemonitoring was feasible; 88% of patients wore the pedometer device during hospitalization (median = 6 days), and 83% after discharge (median=15 days); 65% completed all symptom assessments, and 75% completed all QOL assessments. Average time to complete MDASI and EQ-5D-5L were 7 and 4 minutes respectively. Pain, fatigue, sleep and appetite had the highest symptom severity at day 5 post discharge. Correspondingly, QOL scores worsened at discharge and day 5 post–discharge. Of the total 160 PRO monitoring encounters, 54 (34%) generated an email alert during the first week post-discharge. The majority of alerts were encounters (72%) related to symptom management, with pain being the most commonly reported symptom issues during encounters. Overall, patients were highly satisfied with telemonitoring.

3.0 Patient Eligibility

3.1 Inclusion Criteria

Study eligibility criteria include:

- Cancer patients scheduled to undergo major abdominal surgery for GI malignancies. GI procedures include esophagectomy, gastrectomy, colectomy, abdominoperineal resection/low anterior resection, hepatectomy, pancreatectomy (distal or pancreaticoduodenectomy), and cytoreductive surgery for peritoneal carcinomatosis. We will include patients scheduled for an ostomy (colostomy or diverting ileostomy),
- Age 18 years or older,
- Ability to read and understand English or Spanish.

3.1.1 Disease Status

We are targeting patients across all stages of disease.

3.1.2 Age Criteria, Performance Status and Life Expectancy

Age criterion for this study is based on the NIH's age criteria, which defines an adult as individuals aged 18 years and over. There are no restrictions related to performance status or life expectancy.

3.1.3 Child Bearing Potential

Not applicable.

3.1.4 Protocol-Specific Criteria

Not applicable.

3.1.5 Informed Consent/Assent

All subjects must have the ability to understand and the willingness to sign a written informed consent.

3.1.6 Prior Therapy

Not applicable.

3.2 Exclusion Criteria

3.2.1 Study-Specific Exclusions

Not applicable.

3.2.2 Non-Compliance

Subjects, who in the opinion of the investigator, may not be able to comply with the safety monitoring requirements of the study.

3.3 Inclusion of Women and Minorities

The study is open to anyone regardless of gender or ethnicity.

4.0 Screening and Registration Procedures

4.1 Screening Procedures

All eligible patients who meet study inclusion criteria will be identified through the Division of Thoracic Surgery, Division of Surgical Oncology, Division of Urologic Oncology, and the Division of Gynecologic Oncology outpatient clinics. Clinical Research Nurses and CRAs will work with surgeons to identify eligible patients. Surgeons will notify the research staff, and staff will contact eligible patients to explain the study purpose, answer any questions, and ascertain interest in participation. If the patient agrees to participate, informed consent will be obtained in person or via mail, electronic mail, or other electronic applications (i.e. DocuSign) to obtain

electronic signatures from each patient per standard practice. Clinical Research Nurses and CRAs will be responsible for obtaining informed consent and study implementation.

4.2 Informed Consent

The investigational nature and objectives of the trial, the procedures and treatments involved and their attendant risks and discomforts, and potential alternative therapies will be carefully explained to the subject and a signed informed consent will be obtained in person or via mail, electronic mail, or other electronic applications (i.e. DocuSign) to obtain electronic signatures from each patient per standard practice. Documentation of informed consent will be maintained in the subject's research chart and electronic health records.

4.3 Registration Requirements/Process

Not applicable.

4.4 Randomization and/or Dose Level Assignment

Each patient will be randomly assigned to either the remote perioperative telemonitoring or enhanced usual care arm. The assignments will be placed in sealed envelopes and opened sequentially. The PI, co-Is, participating clinicians and study CRN will be blinded to randomization assignment until envelopes are opened. The study CRN will share randomization assignement information with consented participants.

5.0 Treatment Program

5.1 Program Overview

The perioperative telemonitoring intervention includes four key components. The first component involves objective assessment of functional activity. Patients will receive a Vivofit 4 to wear for daily steps monitoring. Vivofit 4 is a commercially-available wristband pedometer (Garmin Company). It functions as a watch, but also can track activity level such as the number of steps taken. Vívofit 4 stores this data in the device. The device follows activity progress 24/7 and can stay on for more than a year without a battery change. It is waterproof and can be worn in the shower and while swimming.

The second component involves subjective, electronic assessment of PROs (symptoms, QOL). We will deploy the Aetonix A Touch Away™ digital engagement platform to remotely capture PROs in real-time. The A Touch Away™ platform is a HIPAA compliant, multi-faceted patient engagement system that remotely connects and conveys critical health information between patients and clinicians. The Aetonix application has been utilized in several clinical settings including monitoring patients with chronic obstructive pulmonary disease and congestive heart failure. Patients will use the application on a smart device (phone, tablet), home computer, or study tablet to complete ePROs and share with the surgical team.

The third component involves objective, remote assessment of physiologic patient generated health data (PGHD). Physiologic parameters of interest include pulse oximetry, temperature, blood pressure, heart rate, and weight assessed from the patient's home. Patients will be given a package that contains the following FDA-cleared devices: Nonin 3230 Bluetooth Smart Pulse Oximeters, FORA IR20 Ear Thermometer, A&D Medical Blood Pressure Monitor, and A&D Medical Weight Scale.

The fourth and final component involves a real-time, alert/feedback system based on pre-determined outcome/clinical thresholds. All PGHD and ePRO data captured via the devices and patient engagement application will be streamed in real-time to a dashboard accessible from any device for the surgical team to monitor. The dashboard provides a graphic visualization over time of all patients and their data to identify outcome trends, including onset, worsening/improving measures, and sporadic vs. consistent measures.
Figure 3 provides a graphic depiction of the perioperative telemonitoring care design.

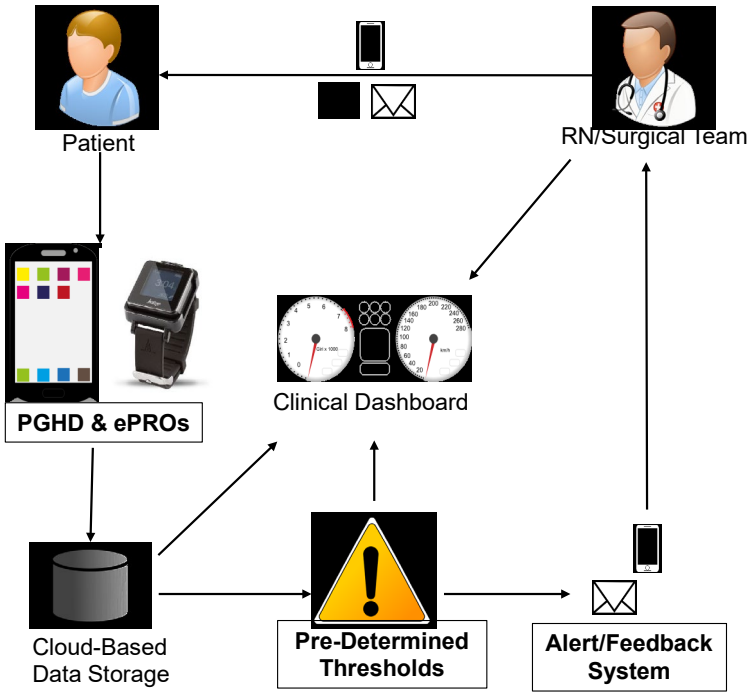
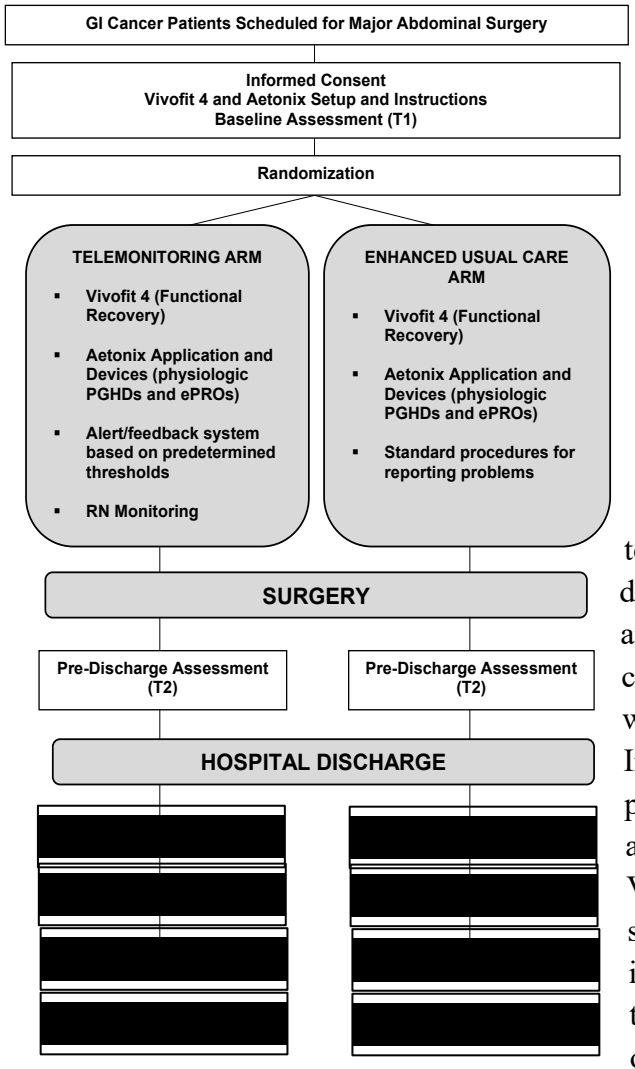


Figure 3: Study Schema



Study Procedures

Before Surgery:

The study schema is presented in Figure 3. Patients will be recruited from the surgical clinics at COH's Duarte campus only. Research staff will explain the study purpose, answer questions, and obtain informed consent. Patients will be enrolled at least 3-7 days before surgery. Following informed consent, the study CRA will assist patients with identifying a patient-owned engagement device (smartphone, tablet, computer), and assist with setup and initial testing of the Aetonix application on the device of choice. For patients who do not have an engagement device or have poor connections at home, a study Samsung tablet will be provided for the duration of the study. In our previous experience, only about 1.5% of patients had no device or inadequate internet access.48 All patients will be provided with a Vivofit 4 and instructions. The study CRA will setup the device for patients and conduct initial testing to insure successful data transmission. Patients will wear the Vivofit 4 on their non-dominant wrist. Patients in both arms will receive a package with the Aetonix physiologic PGHD home monitoring devices described previously. The study CRA will provide instructions (both verbal and in writing) on device use. All patients will be instructed to complete baseline assessment (T1) of PGHD and ePROs while at home.

Following completion of baseline assessment, participants will be randomly assigned to either the telemonitoring or enhanced usual care arm, using stratified and blocked randomization. Strata will be defined by diagnosis (upper GI, colorectal, hepatobiliary) and surgical technique (minimally-invasive versus open). Variable block sizes will be used to maintain approximate balance and pre-assignment masking. A pre-established randomization log will be created by the project biostatistician. The study staff will communicate group assignments to the patients.

For patients assigned to the telemonitoring arm, the alert/feedback system, monitored by the CRN, will be initiated for each patient. The system will be triggered on the occurrence of predetermined threshold events for physiologic PGHDs and ePROs, as described previously. Patients assigned to the enhanced usual care arm will use the Aetonix application to report

physiologic PGHD and ePROs, but will be informed via electronic messages that their data will be used for research purposes only and would not be monitored. They will be instructed to follow the standard institutional procedure for reporting concerns and issues. This includes 1) contacting their surgical team if symptoms become severe and physical function worsens between clinic visits; and 2) use of the hospital call line to report problems between visits.

After Surgery and Before Hospital Discharge: After surgery, research staff will ensure that patients resume wearing the Vivofit 4 as soon as possible and no later than post-op day 2. Patients will complete repeat electronic PROs prior to discharge (T2). The surveys will take about 20 minutes to complete. Patients will be given instructions, prior to discharge, on when to use the home monitoring device.

After Hospital Discharge: After discharge, all patient-generated physiologic data and PRO assessments will be repeated day 2 (T2), day 7 (T3), day 14 (T4), and 30 days (T5) post-discharge. At day 30, patients randomized to the telemonitoring arm will participate in a brief exit interview. All patients will receive a $25 remuneration after completion of the day 7, 14, and 30 assessments ($75 per patient total).

All devices and loan study tablet will be returned upon study completion via postage-paid packages or in-person during a routine scheduled clinic visit. They will be cleaned with alcohol-based cleansers following standard protocols prior to re-use. Patients have the option of keeping the Vivofit 4 wristwatch or returning it to the research team. Patients will not be responsible for replacing lost study devices.

Feedback/Alert System and Thresholds: The following thresholds will be used to trigger the feedback and alert system monitored by the Research RNs.

1. Physiologic Health Parameters:
   a. Weight – decrease in 2 kg since discharge or increase of 2 kg since discharge
   b. Temperature - >38 C with heart rate >110 or systolic blood pressure <90 or >180; >38.3 C independent of other vital signs
   c. Oxygen saturation - <90% oxygen saturation - Nurses should confirm that waveform data on heart rate and oxygen saturation are adequate (i.e not artifact)
   d. Heart rate - >110 beats per minute (>120 if last heart rate at discharge was >100)
   e. Blood pressure – systolic blood pressure <90 (<85 if last systolic blood pressure at discharge was <100) or >180; diastolic blood pressure ≥ 95 (low alert) and ≥ 100 (high alert).
   f. Functional activity - daily steps of ≤ 1500.

2. Patient-Reported Outcomes:
   a. One or more symptoms rated 4 or greater (moderate-severe intensity)
   b. One or more QOL questions rated moderate, severe, or unable to accomplish

Pathway for RN Triage and Management:

1. Patients will measure their vital signs once a day after discharge at 9 AM. Patients will have the option of measuring their vitals again at 3PM if they choose to
2. If RN identifies deviations from a priori thresholds, they will:

i. Call the patient, and ask them to repeat all vital signs.
ii. Ask the patient if they are having: nausea, vomiting, fevers worsening pain, spreading redness around their incision, new or worsening drainage from their incision, chest pain, shortness of breath, difficulty breathing. Also ask if the patient is drinking at least 1.5 liters of fluid a day.

3. If vital signs on re-check are beyond threshold values but all the above patient-generated metrics are normal/negative, relay information to the on-call physician or health care provider for further determination of next course of action.
4. If vital signs on re-check are beyond threshold values and at least one of the patient-generated metrics is abnormal/positive, the patient should be evaluated within the next 24 hours. Relay information to the on-call physician or health care provider to determine exactly when/how evaluation should take place.
5. Evaluation within the next 24 hours may be:
   i. Repeat vital signs in a pre-defined period of time to be reviewed by a health care provider
   ii. Planned repeat phone conversation with the patient
   iii. Clinic visit that day or the next business day
   iv. Evaluation in the evaluation and treatment center or other urgent care/emergency department

5.2 Planned Duration of Therapy

Study participation is planned for approximately 2-3 months. The timeframe covers before surgery, postop acute care, and up to 30 days post-discharge.

5.3 Criteria for Removal from Treatment

The only criterion for disenrollment is if participants desire to discontinue with study participation.

5.4 Subject Follow-Up

Subjects will be followed for approximately 2 months.

5.5 Supportive Care, Other Concomitant Therapy, Prohibited Medications

The study Clinical Research Nurses and CRAs will review participant's responses to all outcome measures and alert the attending surgeon if participants show risk of self-harm or other serious conditions. These participants will be referred to supportive care and social work as necessary after evaluation by the attending surgeon and/or other healthcare providers. Otherwise, there are no restrictions to the use of supportive care medications, other concomitant therapy and no prohibited medications.

5.6 Additional Studies

Not applicable.

5.6.1 Laboratory Studies

Not applicable.

5.7 Definition of Dose-Limiting Toxicity (DLT)

Not applicable.

6.0 Dose Delays/Modifications for Adverse Events

Not applicable.

7.0 Data and Safety Monitoring, Unanticipated Problems and Adverse Event Reporting

7.1 Data and Safety Monitoring

Definition of Risk Level

This is a low risk study, as defined in the City of Hope Institutional Data and Safety Monitoring Plan (DSMP), because it involves questionnaires assessing QOL and general functional status, use of pedometer, and assessment of physiologic health parameters that are routine vital signs during perioperative car. The study Principal Investigator is responsible for monitoring protocol conduct and reporting all reportable events to the City of Hope (COH) Data and Safety Monitoring Committee (DSMC) and Institutional Review Board (IRB) in accordance with the City of Hope Institutional Deviation policy, and Clinical Research Adverse Event and Unanticipated Problem policy.

All reportable events occurring at external sites will be reported to the study Principal Investigator per City of Hope institutional policies, and per their local institutional policies, as applicable.

7.2 Monitoring and Personnel Responsible for Monitoring

Monitoring and Personnel Responsible for Monitoring
The Principal Investigator (PI) is responsible for monitoring protocol conduct and reporting to the City of Hope (COH) Data and Safety Monitoring Committee (DSMC) and Institutional Review Board (IRB) as indicated in the sections below.

7.3 Reporting of Unanticipated Problems and Adverse Events

Unanticipated Problems (UP) Involving Risks to Subjects or Others
An unanticipated problem is any incident, experience or outcome that **meets all three** of the following criteria:

1. Unexpected (in terms of nature, severity, or frequency) given the following: a) the research procedures that are described in the protocol-related documents such as the IRB approved research protocol, informed consent document or Investigator Brochure (IB); and b) the characteristics of the subject population being studied; **AND**
2. Related or possibly related to participation in the research (possibly related means there is a reasonable possibility that the incident, experience, or outcomes may have been caused by the procedures involved in the research); **AND**

3. Suggests that the research places participants or others at greater risk of harm (including physical, psychological, economic, or social harm) than previously known or recognized.

Any UP that occurs during the study conduct will be reported to the DSMC and IRB in accordance with the Clinical Research Protocol Deviation policy [policy effective date: 05/14/14] using the electronic submission system, iRIS.

Deviations
A deviation is a divergence from a specific element of a protocol and that occurred without prior IRB approval. Deviations from the approved protocol should be avoided, except when necessary to eliminate an immediate hazard to a research participant. A Corrective and Preventative Action (CAPA) plan should be developed by the study staff and implemented promptly to avoid similar issues in the future. All deviations from the protocol must be documented in study source documents and promptly reported to the DSMC and IRB.

Reporting Deviations
Investigators may deviate from the protocol to eliminate immediate hazards for the protection, safety, and well-being of the study subjects without prior IRB approval. For any such deviation, the PI will notify the DSMC and IRB, within 5 calendar days of its occurrence by electronic submission of a Deviation Notice via iRIS.

Single Subject Exception (SSE) Amendment Request
Deviations from the written protocol that are not done to eliminate an immediate hazard(s) for the protection, safety and well-being of study subjects but may increase risk and/or alter the protocol integrity require prior IRB approval. The deviation is submitted as a Single Subject Exception (SSE) amendment request. An IRB approved SSE does not need to be submitted as a protocol deviation to the DSMC. The SSE should be submitted according to the IRB guidelines and Clinical Research Protocol Deviation policy [policy effective date: 11/07/11] and submitted via iRIS.

A deviation that is not an SSE (i.e., discovered after the occurrence) must be reported to the COH DSMC and IRB according to the Clinical Research Protocol Deviation policy [policy effective date: 11/07/11] and submitted via iRIS.

8.0 Information and Risks

The devices that will transmit the data will not store any data and are FDA approved. There is therefore minimal risk. The devices are the following: Physiologic parameters of interest include pulse oximetry, temperature, blood pressure, heart rate, and weight assessed from the patient's home. Patients will be given a package that contains the following FDA-cleared devices: Nonin 3230 Bluetooth Smart Pulse Oximeters, FORA IR20 Ear Thermometer, A&D Medical Blood Pressure Monitor, and A&D Medical Weight Scale.

For the steps data, patients will be wearing a Vivofit 4. Patients will sign up on the Garmin website for the Vivofit and they will agree to the terms of use as per the Garmin company. This is noted in the consent form as per advice from the cybersecurity team. Their steps data would

not be linked to any clinical data that Garmin can capture and their terms of use will be separate from the study.

9.0 Correlative/Special Studies

No correlative studies will be performed during this study.

10.0 Study Calendar

	Baseline (T1)	Before Surgery	Treatment	Before Discharge (T2)	Day 2 Post-Discharge (T3)	Day 7 Post-Discharge (T4)	Day 14 Post-Discharge (T5)	Day 30 Post-Discharge (T6)
Informed Consent	X							
Baseline Assessment	R							
DAY OF SURGERY			X					
Post-Operative Complications – Comprehensive Complications Index (CCI)[131, 132]				R	R	R	R	R
Hospital Readmissions					R	R	R	R
General Symptoms - MD Anderson Symptom Inventory (MDASI)[55, 120]	R			R	R	R	R	R
Disease-Specific Symptoms – MDASI Symptom Library	R			R	R	R	R	R
QOL – EQ-5D-5L[10,113,121-125]	R			R	R	R	R	R
Semi-Structured Exit Interview/Satisfaction Tool								R
Functional Activity (daily steps taken)[127-130]	Throughout study period							

X= Standard of care, R =Research

11.0 Endpoint Evaluation Criteria/Measurement of Effect

11.1 Response Criteria

Outcome Measures – Outcomes are assessed before surgery (baseline), before discharge, and until 30 days post-discharge (**Table 1**). Measures were selected based on reliability/validity, our preliminary studies, and brevity to minimize burden. ePROs will take about 4-7 minutes to complete. We will also obtain sociodemographic, clinical (diagnosis, tumor stage, neoadjuvant treatments, Charlson-Deyo co-morbidity index, time to adjuvant treatment), and surgical (Pre-op ECOG performance score, procedure, open or minimally invasive, ASA classification, date of surgery, post-op admission status and date, ICU days, post-operative events, discharge date, discharge status) data for all patients.

Table 1. Outcome Measures by Aims and Assessment Time Points

	Measures	Before Surgery (T1)	Pre-Discharge (T2)	Day 2 (T3)	Day 7 (T4)	Day 14 (T5)	Day 30 (T6)
SA 1 (Feasibility, Retention and Acceptability)	Participation Rate - % of eligible consented, reasons for non-participation, dropout and lost to follow-up rates, reasons for dropout, differential dropout by treatment arm.	Throughout study period					
	Telemonitoring Completion Rate – number of PGHD and ePRO assessments completed (≥70%)	Throughout study period					
	Patient Experience – Semi-Structured Exit Interview Guide						X
SA 2 (Preliminary Efficacy)	Post-Operative Complications – Comprehensive Complications Index (CCI)[131, 132]		X	X	X	X	X
	Hospital Readmissions				X	X	X
	General Symptoms - MD Anderson Symptom Inventory (MDASI)[55, 120]	X	X	X	X	X	X
	Disease-Specific Symptoms – MDASI Symptom Library	X	X	X	X	X	X
	QOL – EQ-5D-5L[10,113,121-125]	X	X	X	X	X	X
	Functional Activity (daily steps taken)[127-130]	Throughout study period					

12.0 Data Reporting/Protocol Deviations

12.1 Data Reporting

12.1.1 Confidentiality and Storage of Records

The original data collection forms will be sent to PI and stored in a locked cabinet and office in Electronic data will be stored in encrypted, password protected, secure computers that meet all HIPAA requirements. When results of this study are reported in medical journals or at meetings, identification of those taking part will not be disclosed. Electronic health records of subjects will be securely maintained in the strictest confidence, according to current legal requirements. They will be made available for review, as required by the FDA, HHS, or other authorized users such as the NCI, under the guidelines established by the Federal Privacy Act and rules for the protection of human subjects.

12.1.2 Subject Consent Form

At the time of registration, the original signed and dated Informed Consent form, HIPAA research authorization form, and the California Experimental Subject's Bill of Rights (for the medical record) and three copies (for the subject, the research record, and the Coordinating Center) must be available. All Institutional, NCI, Federal, and State of California requirements will be fulfilled.

12.1.3 Data Collection Forms and Submission Schedule

All data will be collected from home monitoring devices, wearable devices (pedometer), and electronic PROs. Data will be sent to the location identified in Section 12.1.1 and stored in a secure location.

EQ-5D-5L - This validated tool evaluates five QOL variables: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. One final item evaluates overall health state using a visual analogue scale with the end points labeled best to worst imaginable health state (0-100 numeric value). The EQ-5D has been widely used in clinical trials and also used in quality-adjusted survival analysis.[24-27]

MD Anderson Symptom Inventory (MDASI) - This is a brief, validated measure of 13 common cancer-related symptoms with severity of each rated on a 10-point scale. Patients also rate how much their symptoms interfered with 6 common functional domains. The MDASI has several advantages over other symptom-assessment scales in that it applies broadly across cancer types and treatments, is easy for patients to complete, and includes items related to symptom interference with daily life. Cronbach alpha reliability ranges from 0.82 to 0.94.[28,29]

Sociodemographic and health status – This tool covers social and demographic factors, including patient's age, sex, race/ethnicity, education, marital status, living situation, employment, income, religious preference, tobacco history, and symptoms. Patients will complete the tool at baseline.

Satisfaction Tool – This patient self-reported measure contains 13 questions designed to assess satisfaction with the electronic assessment. Data captured include: 1) ease of use of web-based surveys and wristband device; 2) Feedback on items in the web-based surveys that are distressing or difficult to comprehend; 3) Feedback on length of surveys and timing of administration; and 4) Suggestions for items that were not covered but should be added. It will be administered at the Day 30 post-discharge assessment. Both arms of the study will undergo this.

Surgical Outcomes: Comprehensive Complications Index (CCI) - The CCI® summarizes the entire patient postoperative experience with respect to complications (on a scale from 0 to 100), and is based on the established Clavien-Dindo classification. The CCI® was validated in a study with 1299 participants, and external validity was tested in a randomized trial evaluating pancreas, esophageal, and colon resections.[31,32]

Medical Chart Audit Form and Healthcare Resource Use - Electronic health record audits will capture: 1) 30, 60, and 90 day inpatient readmissions, 2) reasons for readmissions, and 3) ER visits. The chart audits will also capture clinical (stage of disease) and surgical characteristics. If the patient seeks emergent care outside of the primary institution, the patient's permission will be obtained to review these records.

Semi-Structured Interview Guides - The semi-structured questions for exit interviews and focus groups are designed to solicit patient and surgeon/provider's perspective on the following: 1) on-boarding and setup process; 2) use of telemonitoring application for communication; 3) use and setup process of accelerometer; 4) use of telemonitoring dashboard to guide clinical care; 5) value of monitoring PROs and functional activity; 6) likes/dislikes of the program; 7) challenges and limitations of telemonitoring; and 7) suggestions on areas for improvement.

12.1.3.1 Eligibility Checklist

The Eligibility Checklist must be completed by the Research Nurse and CRA and signed by an authorized investigator prior to registering the subject. See Section 4.3 for the registration procedure.

12.2 Protocol Deviations

12.2.1 Deviation Policy

This protocol will be conducted in accordance with COH's "Clinical Research Protocol Deviation Policy" located at http://www.coh.org/dsmc/Documents/Institutional%20Deviation%20Policy.pdf.

Deviations from the written protocol that could increase patient risk or alter protocol integrity require prior IRB approval of a single subject exception (SSE) request. In addition, if contractually obligated, the sponsor must also approve the deviation. IRB pre-approved SSE protocol modifications are considered an amendment to the protocol and not a deviation. The submission of a deviation report is not required.

Brief interruptions and delays may occasionally be required due to travel delays, airport closure, inclement weather, family responsibilities, security alerts, government holidays, etc. This can also extend to complications of disease or unrelated medical illnesses not related to disease progression. The PI has the discretion to deviate from the protocol when necessary so long as such deviation does not threaten patient safety or protocol scientific integrity. Examples include, but are not limited to: a) dose adjustments based on excessive patient weight; b) alteration in treatment schedule due to non-availability of the research participant for treatment; c) laboratory test results which are slightly outside the protocol requirements but at levels that do not affect participant safety. These instances are considered to be deviations from the protocol. A deviation report will be submitted to the DSMC/IRB within five days.

12.2.2 Reporting of Deviations

All deviations will be reported to the COH DSMC within five days. The DSMC will forward to report to the IRB following review.

12.2.3 Resolving Disputes

In situations where there is misperception or dispute regarding a protocol deviation among the persons involved in implementing the protocol, it is the responsibility of the PI to resolve the dispute and the PI may consult with the DSMC chair (or designee) to arrive at resolution.

13.0 Statistical Considerations

13.1 Study Design

13.1.1 Sample Size Calculation and Power Analysis

We will need 128 patients (64 per arm) to detect an effect size of 0.5 in the primary outcomes as described in Aim 2 (postoperative complications, lower readmission rates, improved symptoms, QOL, and functional recovery) between the two groups, with a two-sided 0.05 significance level using a two-sample t-test and at least 80% power. We will enroll a total of 160 (80 per arm to account for an expectation of 20% attrition. Thus, we will have sufficient power for all primary outcomes, including our primary endpoint of postoperative complications.

13.2 Statistical Analysis Plan

13.2.1 Managing Data

PGHD, PROs and data on actionable patient care based on alert/feedback system and CRN monitoring (i.e. educated or counseled the patient, scheduled visits) will be initially stored in a secure, HIPPA-compliant cloud-based data storage system through Aetonix. We expect a total of 20 physiologic PGHD and ePRO evaluations per participant over the approximate 2 month study duration. With a total sample of 160, this yields more than 3,200 data collection encounters overall. We expect a large number of daily steps data observations per subject because functional recovery data will be continuously recorded on a daily basis over the study duration.

Data will be transferred on a daily basis from Aetonix to a REDCap (Research Electronic Data Capture) study database housed within COH and accessible only to the research team. The study biostatistician will work closely with Aetonix to coordinate real-time data transfer, auditing, and data cleaning. In the process of data transfer and mergers, the study biostatistician and Aetonix representatives will audit the data, clean the data, apply necessary formats in SAS statistical software, and export data into the REDCap database. A query system will be developed to address data validity and integrity by early identification of data collection inconsistency, data inaccuracy or incompleteness. This will be monitored by the biostatistician on a weekly basis throughout the project. Where feasible, validation rules (e.g. logic checks, format restrictions, min/max range, etc.) will be added to ensure that the data transferred and entered is valid and accurate.

In order to protect PHI data the patients will be labelled as Subject # e.g. Patient001, Patient002. Only the PI on the study and CRAs and CRN will have access to Patient Identifiers. The CRNs will have the ability to document any response to the alerts of abnormal patient generated health data as a research progress note in EPIC. The PI and the CRAs and CRNs will have access to the Aetonix app on their COH provided devices. There will be no data integration into EPIC. The devices used to transmit the patient generated health data (blood pressure, weight, temperature, pulse oximetry and heart rate) do not store any of the data and are not linked to any patient identifiers. The vivofit4 used to capture the patient steps will require that patients sign up on the Garmin website and agree to the company terms of use. These will not be linked to clinical data in any way.

13.2.1.1 Handling Missing Sessions and Data

Subjects with missing items among dependent variables will be compared with subjects having non-missing items to determine whether there is any bias underlying the missing data (i.e., whether data are

missing at random or can be accounted for by other variables). We will consider multiple imputation (MI) for estimating missing responses and covariables, which can be done using PROC MI in the SAS 9.4 system of software for analysis. The estimates obtained across (10 to 20) multiply imputed data sets can be combined using proc MIANALYZE, which provides valid standard errors for making inferences using the missing at random assumption.

13.2.1.2 Statistical Methods by Study Aims

We are proposing a two-group, randomized control design in which participants recruited into the study will be randomly assigned into the enhanced usual care (control) arm or the telemonitoring (intervention) arm. Both groups will be followed over the same time period which includes preoperative measurements and then up to 30 days post discharge. Data will be collected at five time points (T1: baseline, T2: pre-discharge, T3: 7-day post-discharge, T4: 14-day post-discharge, T5: 30-day post discharge). The primary outcomes for hypothesis testing are found in Aims 2, including postoperative complications, lower readmission rates, improved symptoms, QOL, and functional recovery. The primary endpoint is severity (grade) of postoperative complications from discharge to day 30 post-discharge. Descriptive statistics will be used to summarize all variables. For continuous variables, we will provide mean ± standard deviation (SD), median, range, and sample size. For categorical variables, we will include sample size and proportion.

Specific Aim 1: Assess the feasibility, retention, and acceptability of the remote perioperative telemonitoring intervention as measured by the percentage of patients who a) agree to participate; b) complete ≥70% of the telemonitoring; and c) report satisfaction with the intervention through structured exit interviews.

Feasibility will be assessed through: 1) the ratio of eligible participants to those enrolled and those who declines participation; 2) reasons for non-participation; 3) number of scheduled study encounters completed; 3) attrition rate between pre- and post-discharge; 4) reasons for attrition/dropout; 5) the ratio of all participants to those who completed ≥70% of the study; These data will be descriptively reported and analyzed. Qualitative data on acceptability from exit interviews will be analyzed using the conventional content analysis approach.[65] This approach is used to describe a phenomenon where existing theory or research literature is limited. Data from the audio-recorded interviews will be transcribed and analyzed using HyperRESEARCH™ qualitative software. Transcripts will be imported allowing for the development of analytic categories, data coding, and review of coded data. All data will be read repeatedly to achieve immersion and obtain a sense of the whole. Then, data will be read word by word to derive codes. Codes will then be sorted into themes based on links and relationship. Separate investigators (Dr. Melstrom and Dr. Sun) will conduct a final validation review of the codes and themes to ensure consistency and clarity across all qualitative data. Data discordantly coded will be discussed for refinement and consensus purposes.

Specific Aim 2: Determine the preliminary efficacy of the remote perioperative telemonitoring intervention on surgical outcomes, healthcare utilization, PROs, and functional recovery.

Hypothesis 2.1: Patients randomized to the telemonitoring arm will experience reduced severity (grade) of postoperative complications, lower readmission rates, and improved symptoms, QOL, and daily steps.

For Specific Aim 2, the primary endpoint is the change in Comprehensive Complications index (CCI) from discharge to day 30 post-discharge. First, change in CCI will be computed. A two-sample t-test will be conducted to determine if there is significant difference between mean CCI of the intervention arm and the control arm. Trends in CCI scores will be explored over time (T2-T5). Exploratory within subjects' correlation will be examined using Pearson correlation between adjacent time points. A random-effects model will be used to study group differences in mean over time. Other variables (e.g., age and sex) may be included in the model to adjust for possible confounding.

Similar analysis will be carried out for repeatedly measured secondary endpoints (symptom severity score, QOL). Generally speaking, we expect better scores in the intervention arm than the control arm. Healthcare resource use (e.g., hospital readmission) is a secondary endpoint. At each time point, we will estimate the ER visits/readmission rates and provide confidence intervals for each arm. Further, a binomial test for comparing two proportions will be conducted to see if there is significant difference between the readmission rates of the two arms. For simplicity, Bonferroni correction will be used both in the proportions comparisons test and the confidence intervals construction.

14.0 Human Subject Issues

14.1 Institutional Review Board

In accordance with City of Hope policies, an Institutional Review Board (IRB) that complies with the federal regulations at 45 CFR 46 and 21 CFR 50, 56 and State of California Health and Safety code, Title 17, must review and approve this protocol and the informed consent form prior to initiation of the study. All institutional, NCI, Federal, and State of California regulations must be fulfilled.

14.2 Recruitment of Subjects

Subjects will be recruited on COH's campus and through the Department of Surgery.

14.3 Advertisements

No advertisements will be used for study accrual.

14.4 Study location and Performance Sites

This study will be performed at COH.

14.5 Confidentiality

This research will be conducted in compliance with federal and state of California requirements relating to protected health information (PHI). Confidentiality is maintained by ensuring that all data collection forms contain only ID numbers rather than personal identifiers. All study files are maintained in password-protected computers or locked file cabinets (both included behind locked doors). Electronic data will be stored in encrypted, password protected, secure computers that meet all HIPAA requirements. All participant identifiers are removed from tracking spreadsheets. In addition, confidentiality is maintained in communications (emails and meetings) and only ID numbers are referenced. The PI and research team will have access to this information, but all information will be treated confidentially. No identifiers will be used in any subsequent publication of these results.

14.6 Financial Obligations and Compensation

There are no financial obligations. Participants may receive up to $75 for their participation in this study.

14.7 Informed Consent Processes

The Principal Investigator or IRB approved named designate will explain the nature, duration, purpose of the study, potential risks, alternatives and potential benefits, and all other information contained in the informed consent document. In addition, they will review the experimental subject's bill of rights and the HIPAA research authorization form. Research subjects will be informed that they may withdraw from the study at any time and for any reason without prejudice, including as applicable, their current or future care or employment at City of Hope or any relationship they have with City of Hope. Research subjects will be afforded sufficient time to consider whether or not to participate in the research.

Should sufficient doubt be raised regarding the adequacy of comprehension, further clarifications will be made and the questionnaire repeated until a satisfactory result is obtained. Prospective research subjects who cannot adequately comprehend the fundamental aspects of the research study with a reasonable amount of discussion, education and proctoring will be ineligible for enrollment. For those subjects who do comprehend the fundamental aspects of the study, consent will be obtained and documented, followed by eligibility testing. The research team will review the results of eligibility testing and determine if the subject is a candidate for study enrollment.

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