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

DEPARTMENT OF Population Sciences – Division of Nursing Research and Education

TITLE: Comparative Effectiveness Trial of Perioperative Telemonitoring for Functional Recovery and Symptoms

CITY OF HOPE PROTOCOL NUMBER: 20370 **PROTOCOL DATED: 09/14/2022**

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

Initial Approval	Protocol dated 07/20/20	Version 00
Amendment 1	Protocol dated 11/12/20	Packet 01
Amendment 2	Protocol dated 02/05/21	Packet 02
Amendment 3	Protocol dated 04/06/21	Packet 03
Amendment 4	Protocol dated 04/06/21 (tp)	Packet 04
Amendment 5 at Continuation	Protocol dated 04/06/21 (tp)	Packet 05
Amendment 6	Protocol dated 03/14/22	Packet 06
Amendment 7	Protocol dated 09/14/22	Packet 07
Amendment 8	Protocol dated 09/14/22 (tp)	Packet 08
Amendment 9	Protocol dated 09/14/22 (tp)	Packet 09
Amendment 10	Protocol dated 09/14/22 (tp)	Packet 10
Amendment 11	Protocol dated 09/14/22 (tp)	Packet 11
Amendment 12 at Continuation	Protocol dated 09/14/22 (tp)	Packet 12
Amendment 13	Protocol dated 09/14/22 (tp)	Packet 13
Amendment 14	Protocol dated 09/14/22 (tp)	Packet 14
Amendment 15	Protocol dated 09/14/22 (tp)	Packet 15

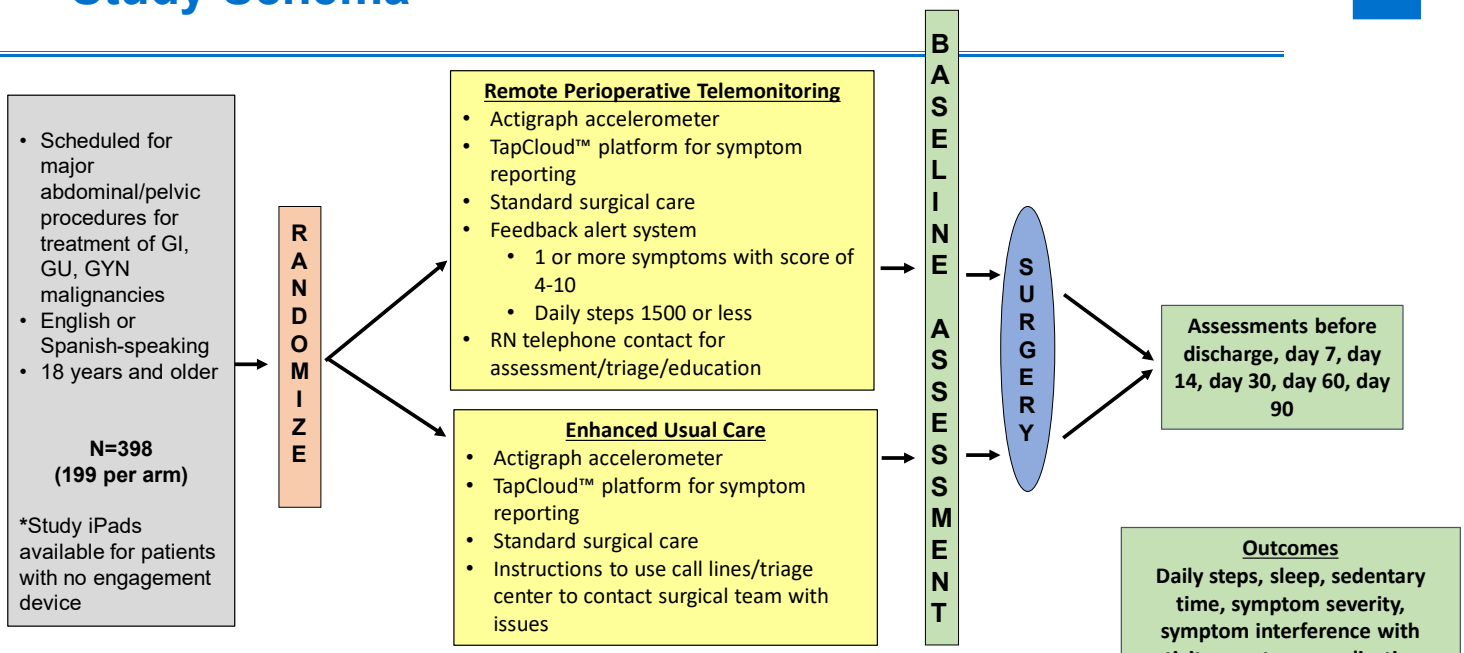
SPONSOR/IND NUMBER: Patient-Centered Outcomes Research Institute (PCORI)
DISEASE SITE: GI, GU, GYN
STAGE (if applicable): NA
MODALITY: Intervention
PHASE/TYPE: Phase III/Randomized
ClinicalTrials.gov identifier: NCT04596384

PRINCIPAL INVESTIGATORS: Virginia Sun, PhD, RN

COLLABORATING INVESTIGATORS: Yuman Fong, MD, Betty Ferrell, PhD, FAAN, Dan Raz, MD, Laleh Melstrom, MD, Thanh Dellinger, MD, Bertram Yuh, MD, Heather Player, MD**,** Hans

	Schoellhammer, MD, Marta Jankowska, PhD, Calvin Tribby, Maria Pakhdikian, MA, Jiue-An (Jay) Yang, PhD, Sarah Alismail, PhD
PARTICIPATING CLINICIANS:	Jae Kim, MD, Loretta Erhunmwunsee, MD, Lily Lai, MD, Kurt Melstrom, MD, Andreas Kaiser, MD, Stephen Sentovich, MD, Gagandeep Singh, MD, Mustafa Raoof, MD, Clayton Lau, MD, Kevin Chan, MD, Jonathan Yamzon, MD, , Roger Satterthwaite, MD, Ernest Han, MD, Lorna Rodriguez, MD, Stephen Lee, MD, , Isaac Paz, MD, Lawrence Wagman, MD, Mark Hanna, MD, Mehdi Kebria, MD, Wei-Chien Lin, MD, Aziz Ahmad, MD, Yih-Dar Nien, MD, Maria de Leon, MD, Kristina Wittig, MD, Harold Huss, DO, Adrian Kohut, MD, Bradford Kim, MD, Thinzar Lwin, MD, Ali Zhumkhawala, MD
PATIENT PARTNERS AND OTHER STAKEHOLDERS (not obtaining consent):	Linda Cota-Robles, Enrique Cota-Robles, Margaret Nolde, Scott Racusin
STUDY STATISTICIANS:	Yi Xiao, MS, Joycelynne Palmer, PhD
NON-PHYSICIAN CONSENTERS:	Fernanda Perez, BS, Evelyn Leyva, BSN, RN, Randy Lee, MHA, Jacqueline Carranza, BS, , Rosemary Prieto, BSN, RN, Elizabeth Bustamante, BS, Jennifer Tee, BSN, RN, Maricela Haj, RN, Suzanne Graf, MSN, RN, AGCNS-BC, OCN, Maria Pakhdikian, MA

Study Schema



City of Hope.

Protocol Synopsis

Protocol Title:
Comparative Effectiveness Trial of Perioperative Telemonitoring for Functional Recovery and Symptoms
Brief Protocol Title for the Lay Public (if applicable):
NA
Study Phase:
Phase III Interventional
Participating Sites:
COH Duarte, COH South Pasadena, COH Antelope Valley, and COH Upland.
Rationale for this Study:
Patients experience a decrease in functional capacity following their surgery with an increase in symptoms, resulting in a dramatic decline in their quality of life (QOL). In addition to these challenges, patient's postoperative care and recovery primarily takes place in home settings due to increasing pressures to reduce readmissions and earlier postoperative discharge by the health care systems. As a result, physical function can decline severely and symptoms can progress before the surgical team is notified.
Objectives:
The primary purpose of this study is to test the efficacy of remote perioperative telemonitoring for functional recovery and postoperative complications in 438 GI, GU, GYN cancer surgery patients (398 patients for main trial, 40 for focus groups), comparing remote perioperative telemonitoring and surgeon care only patients.
Study Design:
This is a prospective, randomized, mixed methods, comparative effectiveness trial (1:1 randomization) of perioperative telemonitoring in cancer surgery (GI, GU, GYN). We plan to enroll 438 subjects (398 patients for the main trial, 40 for focus groups) over an approximate 40 months. This study will utilize the TapCloud™ application to conduct study procedures. Patients enrolled in the study will use the TapCloud™ application to capture subjective ePROs (symptoms). Patients will also be given an Actigraph GT9X Link, a research-grade accelerometer, to capture and report functional activity data (daily steps and sedentary time) throughout the duration of the study to the TapCloud™ application. The remote perioperative telemonitoring program consists of a real-time, alert/feedback system that will trigger alerts into the TapCloud™ application when pre-determined thresholds are exceeded. Clinical RNs will respond by initiating contact using the TapCloud™ application's secure messaging system, or telephone calls if unsuccessful, to assess, triage, manage, and resolve the issue.
Endpoints:
Primary:

Higher daily steps, lower postop complications Secondary: Sleep, sedentary time, symptom severity, symptom interference, readmissions
Sample Size:
438 Patients (398 patients for the main trial, 40 for focus groups)
Estimated Duration of the Study
40 months
Summary of Subject Eligibility Criteria:
Study eligibility criteria include: • Cancer patients scheduled to undergo major abdominal surgery for GI, GU, or GYN malignancies or presumed GI, GU, or GYN malignancies (as determined by surgeons); • Ability to read and understand English or Spanish, and • Age 18 years or older
Investigational Product Dosage and Administration:
NA
Clinical Observations and Tests to be Performed:
Diagnosis, tumor stage, neoadjuvant treatments, Charlson-Deyo co-morbidity index, time to adjuvant treatment, pre-op Zubrod/ECOG performance score, name of 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, preop objective functional measures (6-Minute Walking Test, Timed Up and Go, Short Physical Performance Battery.
Statistical Considerations:
Aim 1 - The Aim's primary endpoint will be the percent change from preoperative baseline in daily step count during the first 2 weeks post-discharge from hospital (measured on Discharge Day, Day +7, and Day +14). To recognize that these data may be missing not at random (ie, due to adverse event, distress, or withdrawal of consent), the effect of study intervention on primary endpoint will be modeled jointly with early withdrawal from data collection of that endpoint. Within the joint model, the sub-model for the primary endpoint will use generalized linear mixed modeling (with treatment and covariates as fixed factors, patient ID as random factor), while the other sub-model will analyze time to early withdrawal (Aim 3's primary endpoint) using proportional hazards regression. Similar joint modeling will be carried out for Aim 1's secondary endpoints (change from baseline in sedentary time, general symptoms, disease-specific symptoms). **Aim 2 -** The Aim's primary endpoint will be maximum Comprehensive Complications Index (CCI) during the 30 days post-discharge. Maximum CCI will be categorized as above vs below 15, and logistic regression will be used to evaluate the effect of study intervention. The Aim's secondary endpoint, time to hospital readmission through 90 days, will be subjected to survival analysis, handling any early withdrawal from study as a competing endpoint.

Aim 3 - Treatment will be evaluated for association with this Aim's primary endpoint, time to early withdrawal, using proportional hazards regression. This analysis will be generated as a sub-model of the joint modeling for Aim 1. **Aim 4 -** Qualitative data from open-ended exit surveys and focus groups will be analyzed using the conventional content analysis approach.[73] For focus groups, participants can choose to attend by telephone, videoconferencing, or in-person. This approach is used to describe a phenomenon where existing theory or research literature is limited. Data 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 to derive codes, and sorted into themes based on links and relationship. Dr. Sun and Dr. Ferrell will conduct a final validation review of the codes/themes to ensure consistency and clarity across all qualitative data. Data discordantly coded will be discussed for refinement and consensus purposes with the SAC.
Sponsor/Licensee:
Patient-Centered Outcomes Research Institute
Case Report Forms
Not Applicable

Table of Contents

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 effective treatment for cancer is surgery. By definition, surgical procedures are invasive; patients experience an abrupt decline in functional capacity after surgery. In addition to postoperative functional declines, 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] Postoperative recovery challenges are compounded by healthcare systems-related trends, including pressures to reduce readmissions and earlier postoperative discharge. As a result, the majority of postoperative care and recovery takes place at home. After hospital discharge, physical function can decline severely and symptoms can progress before the surgical team is notified.

A promising approach to early identification of post-discharge complications is through remote, real-time perioperative telemonitoring of functional activity and patient-reported outcomes (PROs). The approach can identify patients at risk for post-discharge complications, treat symptoms/complications in a real-time fashion, and prevent readmissions. The overall purpose of this study is to conduct a multi-site, comparative effectiveness, randomized controlled trial of perioperative telemonitoring for functional recovery in 438English and Spanish-speaking cancer patients (398 for the main trial, 40 for the focus groups) scheduled to undergo major abdominal surgery (GI, GU, GYN). The program will be implemented at three geographically diverse sites in the Greater Los Angeles area, including one serving a low resource, socioeconomically-disadvantaged population. Accordingly, we propose the following specific aims:

Aim 1: Compare the impact of remote perioperative telemonitoring care versus surgeon only perioperative care on clinically significant changes in functional recovery (accelerometer daily step count) and related secondary patient-centered outcomes (sleep, sedentary time, symptom severity, symptom interference with daily activities).
Hypothesis: Remote perioperative telemonitoring improves functional recovery after major abdominal surgery.

Aim 2: Compare the impact of remote perioperative telemonitoring care versus surgeon only perioperative care on postoperative complications (Comprehensive Complications Index – CCI) and related secondary surgical outcomes (hospital readmission).
Hypothesis: Remote perioperative telemonitoring reduces postoperative complications in the 30 days after major abdominal cancer surgery.

Aim 3: Compare early withdrawal (dropout or loss of accelerometer device) between the comparators.
Hypothesis: Remote perioperative telemonitoring does not excessively burden patients and families.

Aim 4: Explore perioperative telemonitoring care-related experiences (acceptability, technology usability, uptake/integration) among patients, families, and surgeons/nurses through qualitative focus groups and open-ended exit surveys.

Research Question: What are the various stakeholder's perspectives on remote perioperative telemonitoring care?

2.0 Background

2.1 Introduction/Rationale for Development

Surgical Oncology is Increasingly Focused on Quality, Value, and Patient-Centeredness. Surgeons and cancer centers are increasingly asked to provide evidence of the quality and value of their care. Historically, surgical outcomes are measured by disease- and systems-related parameters, such as length of hospital stay, morbidity, readmission rates, and mortality.[16, 17] While important, these measures do not accurately reflect the surgical care experience from a patient's perspective. Patient-centered outcomes are increasingly being used in routine cancer care as quality and value indicators.[17-19] However, these outcomes are not adequately understood and routinely integrated into surgical oncology.

Cancer Surgery is Complex, and Post-Operative Functional Impairments and Symptom Burden Are Common. More than 45 million Americans undergo surgery each year.[20] Greater than 60% of cancer patients undergo surgical interventions[21], and surgical interventions account for the most cures after a cancer diagnosis.[22] Patients who undergo cancer surgery experience functional deficits and symptoms that negatively affect their recovery activities.[23] Post-op functional impairments are common, including inability to perform activities of daily living.[24] Postoperative physical function is predictive of complications such as thromboembolism, pneumonia, and sarcopenia, resulting in prolonged hospital stays and readmissions.[2, 25-30] Fatigue and pain are common, occurs in 80% of patients, and persists one year after surgery.[22, 31] Other common symptoms include sleep disturbance, anxiety, depression, and loss of appetite.[1, 24]

Monitoring Postoperative Recovery from Cancer Surgery is Challenging after Discharge. Due to changes in healthcare and advances in surgical techniques, surgeons are asked to discharge patients earlier after surgery. Operations that were previously associated with 10-20 day hospital stays are now outpatient or short-stay procedures. Postoperative complications that traditionally arise in the hospital are also developing in the community and at home. The current delivery model for post-discharge care is largely inefficient and not proactive.[32] Home health nurses are often dispatched for unresolved acute problems. Patients may contact the hospital when acute problems arise, but are often unaware of when to contact their surgeons (RQ-3). This often requires hours or days to resolve, and is burdensome for patients, families, and the healthcare system. Delays in communicating critical conditions may escalate problems beyond outpatient care. In critical situations, emergency room visits within the same healthcare system or at a different institution occur, resulting in inefficient and fragmented care.

The burden of postoperative hospital readmissions after major cancer surgery is high.[33-35] Depending on the tumor site, 90-day readmission rates for major cancer surgery range from 23-43%.[36] Published data suggest that 30- and 90-day readmission rates are 30% and 43% for cystectomy, and 22% and 35% for esophagectomy and pancreatectomy.[36, 37] Hospital readmissions are burdensome, and result in higher 1-year mortality rates, and delays in timing and eligibility for adjuvant therapies.[33] Predictors of readmissions are similar across different tumor sites, and include functional impairments, comorbid conditions, and postoperative complications.[36, 38]

There are Critical Knowledge Gaps on the Impact of Patient-Centered Outcomes in Cancer Surgery. The impact of routine symptom monitoring is predominantly tested in chemotherapy settings.[39,40] These findings suggest a positive effect on patient-provider communication[41-44], detection of unrecognized problems[40, 44-47], guiding clinical care[46, 48-50], health outcomes[50-54], and survival.[9] Few studies are conducted in surgical oncology, and few

included assessments/support before surgery.[29] Current evidence suggest that functional activity is correlated with surgical outcomes. Higher Fitbit step counts in elderly patients after cardiac surgery was correlated with early recovery, shorter hospital stay, and more discharge to home.[27] Other recent studies include real-time location systems to promote early mobilization after abdominal surgery[55], Fitbit step counts during inpatient recovery from metastatic cancer surgery (predictive of risk for 30 and 60 day readmission)[56], feasibility and validity of accelerometer-based physical activity data for postoperative recovery[57], and mobile application and web-based PROs after major GI and gynecologic surgery.[8, 11]

Although these data are promising, critical knowledge gaps exist. First, the empirical evidence in combining subjective and objective real-time health-related data is lacking.[32, 58] Current ongoing trials, including those funded through PCORI, are designed to focus primarily on post-operative symptoms. Second, current and prior studies did not assess outcomes at baseline (before surgery). This is important because evidence suggests that preoperative functional activity and PROs can predict the trajectory of functional and symptom recovery after surgery.[1]

Despite the documented evidence and commercial availability of patient digital engagement platforms, the question remains whether telemonitoring is equally as beneficial or more beneficial for patients and families as standard surgeon only care. Both comparators have demonstrated benefits. It is possible that telemonitoring could provide more proactive, real-time quality surgical care earlier in the treatment course, however, clinical trials have not yet compared telemonitoring surgical care with surgeon only care. In addition, despite the evidence on the benefits of telehealth in oncology care, there is a lack of consensus on how best to integrate this into surgical care. Both comparators in this study are available to patients now; however, there is a need to compare both models and generate a stronger evidence base for patient-centered surgical care to inform clinical practice and policies

2.2 Overview of Proposed Study

This is a prospective, randomized, mixed methods, comparative effectiveness trial (1:1 randomization) of perioperative telemonitoring in cancer surgery (GI, GU, GYN). 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

The remote perioperative care model is based on evidence from our previous work and several other telemonitoring interventions, including Basch and colleagues' electronic symptom assessment trial[9], and Peterson and colleagues' CYCORE trial lon mobile and sensor technology in head and neck cancer.[69] Our previous research in major abdominal cancer surgery shows that the median number of steps before surgery was 6,562; this number decreased to 483 during hospitalization, and increased to only 2,483 in the first 2 weeks post-discharge (**Figure 1**). We observed a correlation between daily steps and risk for postoperative complications as measured by the Comprehensive Complications Index (CCI) (**Figure 2**). The median number of steps at

day 7 was 1,689 (19% of steps at baseline). This strongly correlated with CCI score (r=-0.64, p<0.05), where patients with fewer daily steps were at higher risk for postop complications. Adherence rate for wearing the pedometer device was 88%. Individual symptom scores for pain, fatigue, sleep, and appetite had the highest severity during week 1 post-discharge.

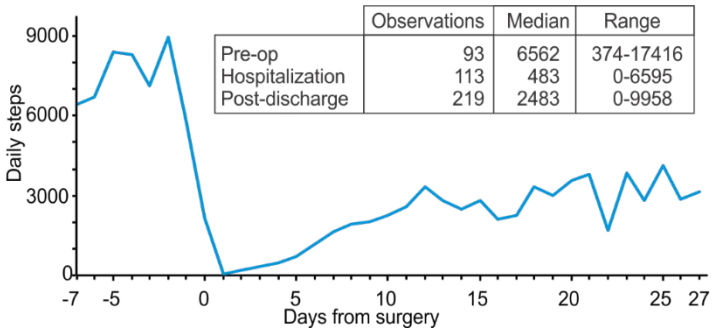


Figure 1. Median daily steps measured before surgery (pre-op), during hospitalization, and recovery (post-discharge)

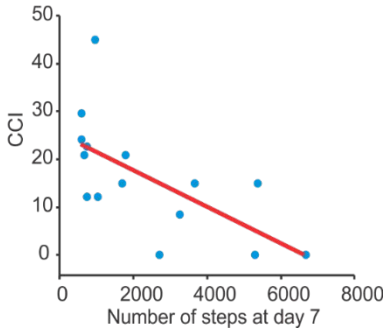


Figure 2. Association between CCI and daily steps at post-op day 7

Of the 160 monitoring encounters, 34% generated an alert. Most of the alerts were generated during the first week post-discharge. 72% of the telephone encounters triggered by an alert were for symptom management. The most commonly reported issue during the encounters was for pain. For acceptability, patients reported that the telemonitoring program was easy to use. Patients reported no difficulty in answering PROs, and the majority found that the length of time was just right for completing ePROs (95%) and using the pedometer (70%). About 25% of patients thought that the length of time for pedometer monitoring was too short (up to 2-4 weeks after discharge), and desired to use the program longer.[15]

3.0 Patient Eligibility

3.1 Inclusion Criteria

The study sample will consist of 398 patients (199 per group) across the enrollment sites. We will also enroll about 40 patients for 4 focus groups; this will yield a final total of 438 participants overall. This sample size takes into account an anticipated 20% attrition. The attrition rate is based on our pilot and previous studies in GI and thoracic surgery. We expect to have complete evaluable data on 332 patients (166 per group) at 30 days post-discharge; the 332 evaluable patients will provide sufficient power for the primary endpoints. Patient eligibility criteria include: 1) cancer patients scheduled to undergo major abdominal surgery for GI, GU, or GYN malignancies or presumed GI, GU, or GYN malignancies (as determined by surgeons); 2) age 18 years and older, and 3) ability to read and understand English or Spanish.

Several approaches will be undertaken to maximize ethnic minority recruitment and retention. These include: 1) using bilingual (English and Spanish) team members; and 2) weekly team meetings to assess ethnic minority accrual status at all four participating sites. In addition, we will leverage expertise from City of Hope's Center of Community Alliance for Research & Education (CCARE) and Division of Health Equities to develop 1) appropriate standard operating procedures (SOPs) on ethnic minority recruitment, and 2) appropriate recruitment materials (IRB approved brochures, flyers).

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 trial is based on the NIH's age criteria, which defines an adult as individuals 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 or electronic 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. Efforts will be made to extend the accrual to a representative population.

4.0 Screening and Registration Procedures

4.1 Screening Procedures

All eligible patients who meet study inclusion criteria will be identified through the Department of Surgery and all solid tumor surgery outpatient clinics at all participating sites. 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. Research staff will also attend key clinics and meetings (ambulatory clinics, tumor boards) on a weekly basis to identify eligible participants. 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.

. The 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. Research Nurses and CRAs will be bilingual (English and Spanish), to ensure that informed consent is conducted in a linguistically-appropriate fashion. If necessary (i.e. if potentials have left the clinic), a telephone/verbal informed consent will be obtained first in order to begin study in a timely manner. Signed informed consent will then be obtained for this study when participants are at COH, or emailed or mailed to them, or other elect and returned to COH when signed, or completed via other electronic applications (i.e. DocuSign). Documentation of informed consent will be maintained in the subject's research chart and electronic health records.
We will obtain the following information from the EHR to track characteristics of patients who are screened as eligible but declined participation. Age, gender, race/ethnicity data will be obtained from the EHR on patients that declined participation. No other PHIs will be collected for patients who declined participation. In addition, if declined patients are willing, reasons for decline will be obtained verbally.
We will track and report ethnic minority retention weekly during standing research team meetings and reports. Reports will be generated weekly to show data on ethnic minority retention. Efforts will be made to improve retention if retention is low and/or problematic.

4.3 Registration Requirements/Process

The Research Nurses and CRAs will establish eligibility and consent before contacting the registrar at the time of enrollment. The registrar will enter the patient on a pre-established randomization log, and report the assignment to the Research Nurses and CRAs, who will then communicate the assignments to the participants in both study arms. Participants will complete baseline assessment following informed consent.

4.4 Randomization and/or Dose Level Assignment

Each patient will be randomly assigned to either the remote perioperative telemonitoring or surgeon only perioperative care arm, using a stratified and blocked randomization. Strata will be defined by diagnosis (GI, GU, GYN) and surgical technique (minimally-invasive versus open). Variable block sizes will be used to maintain approximate balance and pre-assignment masking.

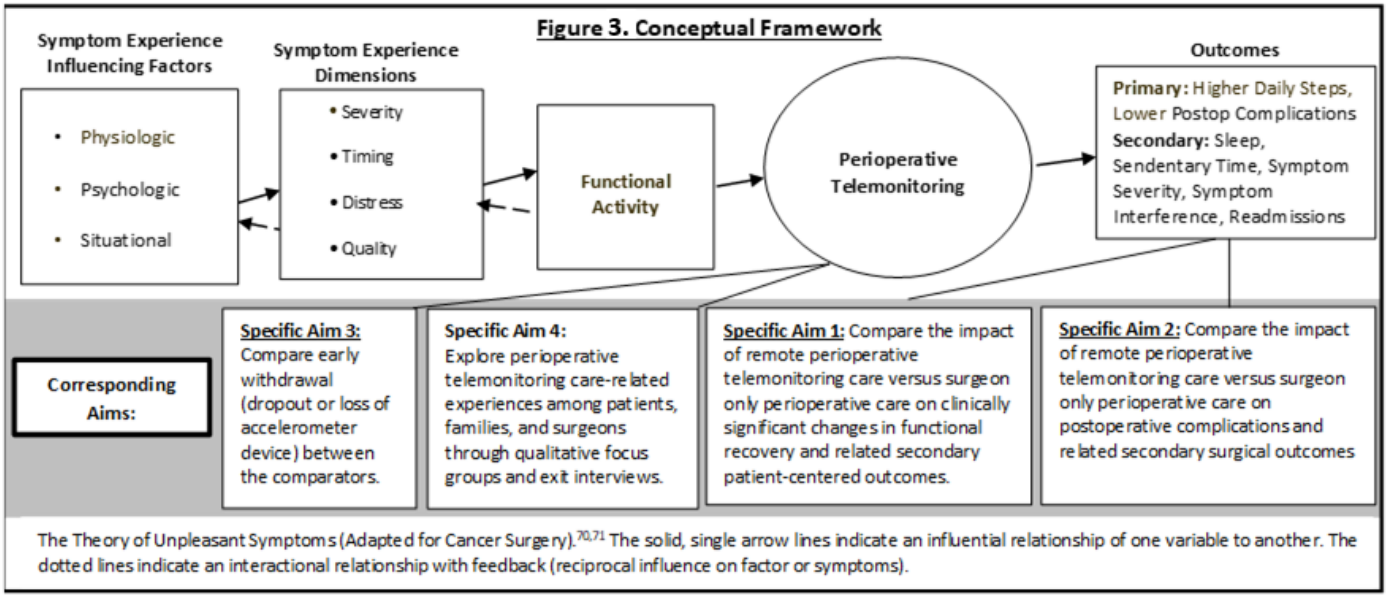
5.0 Treatment Program

5.1 Program Overview – Conceptual Framework

The study design is based on Lenz and Pugh's Theory of Unpleasant Symptoms[67, 68], adapted for cancer surgery. The theory has three major components: 1) the symptom experience, 2) factors that influence the symptom experience, and 3) consequences of the symptom experience. Although symptoms can occur alone, cancer patients often experience multiple symptoms that

interact with each other. Important dimensions to the symptom experience include intensity, timing, level of distress, and quality.

As depicted in **Figure 3**, physiologic, psychologic, and situational factors can influence the patient's symptom experience. Physiologic factors include sociodemographic, disease, and surgical characteristics. Psychologic factors include a patient's emotional reaction to the illness and treatment. Situational factors include aspects of the social and physical environment (i.e. access to care) that may affect the symptom experience. These factors interact with each other to influence the symptom experience.



The Theory of Unpleasant Symptoms (Adapted for Cancer Surgery).[70,71] The solid, single arrow lines indicate an influential relationship of one variable to another. The dotted lines indicate an interactional relationship with feedback (reciprocal influence on factor or symptoms).

The consequence of the symptom experience is functional activity. Functional activity has a reciprocal relationship to the symptom experience and influencing factors. Symptoms may have a direct, inverse relationship with the number of daily steps. For example, postoperative pain may limit a patient's ability to walk. Depression/anxiety may limit a patient's willingness to walk.

The proposed **comparators** include the following: Remote Perioperative Telemonitoring Care[7-15], which will include: 1) objective assessment of functional activity using Actigraph GT9X Link accelerometer with comprehensive assessment of functional capacity to guide prehabilitation needs; 2) subjective ePROs (TapCloud™ digital engagement platform); 3) real-time, RN-driven alert/feedback system based on pre-determined outcome thresholds (daily steps of ≤ 1500; 1+ symptoms rated moderate to severe intensity) and triggered based on patient input; and 4) standard post-surgical care. When thresholds are met, RNs will proactively initiate patient contact via TapCloud™ secure messaging followed by telephone calls to asses, triage, and manage. Telemonitoring begins before surgery, and continues after discharge. Surgeon Only Perioperative Care involves routine care by the surgeon/surgical team of functional declines/symptoms. Patients/families will meet with the surgeon at least once before surgery, have pre-anesthesia assessment for pre-op final evaluation, be managed daily during postop inpatient acute care, have first postop visit 1-4 weeks after discharge, with follow-up as needed thereafter. Patient contacts after discharge are primarily reactive through standard procedures,

including: 1) contacting the surgeon if symptoms become severe and physical function worsens; and 2) use of the hospital call line to report problems.

Remote Perioperative Design and Content - The telemonitoring care includes three key components. The first component involves objective assessment of functional activity. Before surgery, we will complete comprehensive functional activity assessment, using three objective functional measures (6 Minute Walking Test, Timed Up and Go, and the Short Physical Performance Battery). These measures, collectively, assesses functional impairments, risk for falls, and lower extremity capacity. Participant's home environment (number of stairs) will also be assessed. Participants will undergo personalized prehabilitation based on assessment findings. We have experience with perioperative physical interventions that begins before surgery.[70]

Throughout the study, we will use Actigraph GT9X Link (Actigraph Corp), a research-grade accelerometer, to capture data. The GT9X Link captures multiple activity-related data, including daily steps taken and sedentary time. It uses a solid state 3-axis accelerometer to capture and record data. The device continuously monitors activity trends; data can be stored for up to 180 days on the device. It is water-proof with a battery life of 14 days, and weighs 14 grams. The device has a programmable LCD window that can be configured to display date/time and real-time activity feedback. Actigraph is among the most widely used and extensively validated device for activity monitoring.[71]

The second component involves subjective ePROs (symptoms). We will deploy the TapCloud™ application to capture P in real-time. TapCloud™ is a HIPAA-compliant, multi-faceted digital patient engagement system that remotely connects and conveys critical health information between patients and clinicians. Patients use the application on a smart device (phone, tablet) or home computer to collect and track symptoms. TapCloud™ has been tested in oncology populations, including surgical populations. A recent quality improvement project on rural palliative care established feasibility in technology literacy with participants (N=101) who lived in rural North Carolina; more than 50% of participants were 65 years and older.[72]

All patient data captured via TapCloud™ application (PROs, Actigraph) will be streamed to a clinical dashboard that provides a consolidated view accessible from any device via an internet connection. The dashboard provides a graphic visualization over time of all patients, their accelerometer activity data, and symptoms. It is designed to facilitate outcome pattern and trends, including onset, worsening/improving measures, and sporadic vs. consistent measures.

The third component involves a real-time, alert/feedback system based on pre-determined outcome thresholds. Alerts are triggered in real-time based on patient input into the TapCloud™ application. Pre-determined thresholds include: 1) daily steps of ≤ 1500; or 2) one or more symptoms rated 4 or greater (moderate-severe intensity). When thresholds are met, trained clinical RNs will receive secure alerts via the TapCloud™ application. The clinical RNs will initiate contact with patients via secure messaging through the application as a first attempt to assess and remedy the problem. If unsuccessful, telephone calls will be used to further assess, triage, manage, and resolve the issue. **Figure 4** provides a graphic depiction of the telemonitoring care design. All participants will also receive standard surgical care.

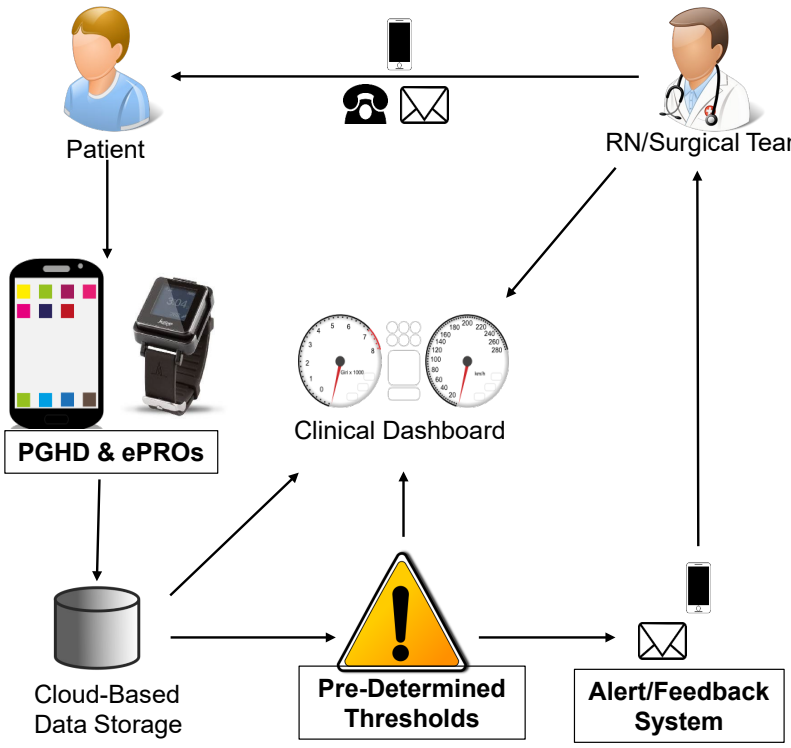


Figure 4. Perioperative Telemonitoring Care

Surgeon Only Perioperative Care - The "standard perioperative care" includes surgeon/surgical team management of functional declines/symptoms. Patients/families will meet with the surgeon at least once prior to surgery, have pre-anesthesia clinic visit for pre-op final evaluation, be managed daily during postop inpatient acute care, have first postop visit 1-4 weeks after discharge, with follow-up as needed thereafter. Patients may or may not undergo prehabilitation as this is not the current standard of care for the participating sites. Referral for functional and nutritional prehabilitation are at the discretion of the surgeon/surgical team. There are no scheduled contacts with the patient between discharge and 1-4 weeks after. Patients/families are instructed to follow the standard procedures for reporting problems between clinic visits, including: 1) contacting their surgical team if symptoms become severe and physical function worsens; and 2) use of the hospital call line to report problems.

Study Procedures

Following informed consent, a brief, 1-item health literacy screen (Screening Question for Limited Health Literacy) will be completed. Research staff will provide additional support (written instructions, telephone calls) for patients with limited health literacy. The Accrual/Evaluation RNs will engage patients in understanding the type and method of data collected, and how the data will be used to support decisions on personalized perioperative care.

The Research staff will then address technology capacity and needs. This assessment includes 1) whether the patient has an engagement device and/or WiFi connection, 2) whether the patient lives in rural communities (as defined by the US Rural-Urban Commuting Area Codes – RUCA), and 3) technology literacy (comfort in using mobile applications and

smartphone/tablet/computers/laptops). The team will assist patients with identifying a patient-owned engagement device (smartphone, tablet, computer), and assist with setup and initial testing of TapCloud™ application on selected device. If the patient does not have an engagement device, a study iPad will be loaned out to the patient along with an iPad loaner agreement. A mobile hotspot device will also be loaned out to the patient if they do not have internet access at home.The team will directly engage the patient (vs simply providing an instruction sheet) and will walk the patient through the setup in a step-by-step fashion. The patient will also be given a TapCloud™ instruction document. Setup will include downloading the application and testing the system to assure the application functions properly. Setup procedures also include a second test call to re-test the engagement device and mobile application, if needed.

All patients will be provided with Actigraph GT9X Link (Actigraph Corp), a research-grade accelerometer and instructions on using the device. The Research staff will setup the device for patients and conduct initial testing to insure successful data transmission. For patients who do not have a device and wish to participate, an iPad with TapCloud platform already downloaded and ready for use will be provided for the duration of the study. Actigraphs and study iPads 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.

We will assess technology uptake by quantifying 1) the type of digital engagement device selected for use by participants (smartphone, tablets, laptop); 2) number of participants who used a study iPad or mobile hotspot; and 3) all technological issues. This data will be documented by the team into the REDCap database, and monitored throughout the study period. The team will specifically monitor for any disproportionate technology uptake challenges by race/ethnicity and rurality.

Patients will complete patient reported outcomes and objective assessments of functional activity before surgery. Patients will then be randomized to either the remote perioperative telemonitoring care group or surgeon only perioperative care group.

Following surgery and before discharge, patients will complete patient reported outcomes. Patients will complete patient reported outcomes day 7, 14, 30, 60, and 90 post-discharge from hospital. On day 90 post-discharge, patients will participate in a brief open-ended exit surveys.

Patients will be provided a patient packet, which includes a research team contact list, patient calendar, and Activity Monitor Tracking Sheet. The patient calendar will provide key dates for patient assessments, while the Activity Monitor Tracking Sheet will track specific times when the Actigraph is not worn and patient sleeping hours. An informational brochure containing key information about this study will also be given to patient in the enrollment process.

Focus Group - In months 18-30 (Years 2-3) of the project, we will conduct 5 (4 for patients/families, 1 for surgeons/nurses) qualitative focus groups to understand the perioperative telemonitoring experiences from the patients, families, and surgeons/nurses perspectives. Focus groups are a form of focused interview[67] with the goal of examining an experience that respondents all have had and can speak about. The advantages of focus groups are 1) the group production of data and, 2) data-collection efficiency. Participants are often reassured to hear similar experiences on the part of others, and feel empowered to talk about their own ideas.[84] The patient focus groups will solicit overall perioperative care experiences, while the open-ended exit surveys will focus specifically on the perioperative telemonitoring acceptability. A total of four focus groups will be conducted with patients/families. Two will include English-speaking

patients, with one focusing on older adults (65 or older), and one on younger adults (65 or younger). Both groups will enroll a total of 6-9 participants with equal representation by cancer type (GI, GU, GYN). The two focus groups for Spanish-speaking patients will follow the same pattern. Equal representation by cancer type will be used for the one surgeon/nurse focus group.

Potential patient/family focus group participants will be drawn at random. Patients/families will be invited to participate; our consent form will have already alerted them that they may be asked to participate in a focus group study. If a patient declines participation in the focus group, families may still be approached if permitted, as the focus group questions for family caregivers will be focused on perioperative caregiving needs/caregiver support and not on the care of the patient. Surgeon focus group participants will be drawn from all surgeons/nurses who had at least one patient who participated in the study. Nurses will be drawn from those who monitored patients in the perioperative telemonitoring arm. A general rule of thumb is that focus groups work best with between 6-10 participants. However, it is frequently the case that not everybody who is invited participates[84]; therefore, we will invite 10 participants to each focus group. We anticipate about 6-9 participants for each group. For ease of participation, focus groups will be conducted via MS Teamsvideoconferencing; participants can also join by calling the telephone number for the Teams meeting. Patients/families selected to participate in the focus group will be offered $50 compensation for participation.

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. Functional activity - daily steps of ≤ 1500.

2. Patient-Reported Outcomes:
   a. One or more symptoms rated moderate-severe intensity

Pathway for RN Triage and Management

1. Patient's functional activity will be recorded throughout the study while wearing the accelerometer, and will complete patient reported outcomes before surgery, before discharge, and day 7, 14, 30, 60, and 90 post-discharge.
2. If RN identifies deviations from a priori thresholds, they will:
   i. Attempt to initiate contact with patients via secure messaging through the TapCloud™ application to assess and remedy the problem.
   ii. If unsuccessful, telephone calls will be used to further assess, triage, manage and resolve the issue.

RN Training - In order to ensure consistency and establish fidelity, study RNs will attend a 1-week training during month 2 of the project. The training goals are: (a) to provide uniform telemonitoring and engagement of participants across all sites, (b) to plan for consistent procedures for participant engagement. The training will begin with the PI and surgeon co-investigators providing an overview of the telemonitoring program via two full-day seminars. Following the seminars, mock sessions with patient/family stakeholders and surgeons will be completed by each RN. Feedback will be provided on performance, and additional training provided as needed. Training curriculum will be established for future use with other institutions.

Stakeholder Advisor Council and Stakeholder Panel - The project will be guided by a Stakeholder Advisory Council (SAC). Members will consist of the following: 3 patients, 1 family caregiver, 4 surgical oncologists, and a digital patient engagement expert. In the first 3 months of the study, all members of the SAC will meet on a weekly basis as part of the research team. The SAC will meet via videoconferencing with the PI, co-investigators, and study support staff (RNs, CRAs). In this study start-up phase, the SAC/investigators will review and refine study materials and protocols to ensure feasibility for patients, families, nurses, and surgeons. This will facilitate co-learning by establishing parameters and expectations for all roles and responsibilities. It will also allow the SAC members to immerse in the research process, and for the PI/co-investigators and research support staff to learn about patient-centeredness. During study accrual and implementation, the stakeholders will meet on a bi-weekly basis via videoconferencing; their input will be expected to inform the team of problems and possible solutions. We opted for the SAC to meet on a bi-weekly basis in order to accommodate their practical needs and availability. We believe this would not cause undue burden on our patient stakeholders and would average a 2-3 hours per month interaction as part of the research team. The SAC will have shared roles in research to identify any potential oversight, offer suggestions, and identify other concerns with study accrual and implementation. The SAC will be partners in decision-making, and will have the authority to make decisions equally with the PI and co-investigators (Reciprocal Relationships). While the PI will lead team meetings, this will be an open forum for all team members.

In addition to the core SAC, we will form a **Stakeholder Panel** of patients/families who have participated in the project. We will invite three patients/families who were participants and completed the study. The Panel will meet on a quarterly basis to provide feedback on their experience, review study implementation procedures, and provide input on implementation problems. New panel members will be recruited for each quarterly meeting. Each Stakeholder Panel member will be compensated for $100/hour.

5.2 Planned Duration of Therapy

Study participation is planned for approximately 3-4 months. The timeframe covers before surgery, postop acute care, and 90 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 3-4 months.

5.5 Supportive Care, Other Concomitant Therapy, Prohibited Medications

The 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 Risk Level 1 study, as defined in the City of Hope Institutional Data and Safety Monitoring Plan [policy effective date: 07/09/14], because it involves questionnaires assessing symptom severity and daily steps using wearable accelerometers.

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 Agent Information and Risks

Not applicable.

9.0 Correlative/Special Studies

No correlative studies will be performed during this study.

10.0 Study Calendar

Table 4. Outcome Measures by Aims and Assessment Time Points								
	Measures	**Before Surgery (T1)**	**Pre-Discharge (T2)**	**Day 7 (T3)**	**Day 14 (T4)**	**Day 30 (T5)**	**Day 60 (T6)**	**Day 90 (T7)**
Preop Functional Assessment	6 Minute Walking Time (6MWT)	X						
	Timed Up and Go (TUG)	X						
	Short Physical Performance Battery (SPPB)	X						
Aim 1	Functional Recovery (steps taken, sedentary time)	X	X	X	X	X	X	X
	General Symptoms - MD Anderson Symptom Inventory (MDASI)	X	X	X	X	X	X	X
Aim 2	Post-Operative Complications – CCI		X	X	X	X	X	X
	Hospital Readmissions			X	X	X	X	X
Aim 3	Early withdrawal (dropout, loss of device)	Throughout the Study						
Aim 4	Open-Ended Patient Exit Survey							X
	Patients/Families/Surgeon/Nurses Experience – Focus Groups	Year 2-3, Month 22-30						

11.0 Endpoint Evaluation Criteria/Measurement of Effect

11.1 Response Criteria

Not applicable.

12.0 Data Reporting/Protocol Deviations

12.1 Data Reporting

12.1.1 Confidentiality and Storage of Records

A REDCap database will be developed with support from COH's Research Informatics team for this study. All outcomes will stored electronically in the REDCap database. The database is passcode-protected, and only the PIs and research staff will have access to the REDCap database. 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

Initial verbal consenting will only be used when potential participants are not in the clinic. In these situations, the Research Nurses and CRAs will use the approved information sheet for verbal consent process. An informed consent will then be obtained either in writing in person, by mail, or electronic mail, or electronically via other electronic applications (i.e. DocuSign). Otherwise, all participants will complete written or electronic informed consent (i.e. DocuSign) informed consent prior to study participation. The study will use one written or electronic informed consent (with signature line) and one information sheet (without signature line) for patients. Documentation of initial verbal consent for study participation will be charted through progress notes and maintained in the patients' electronic medical records as required by the Institutional Review Board.

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 wearable devices (accelerometer) and electronic PROs. Data will be sent to the location identified in Section 12.1.1 and stored in a secure location.

Preoperative Functional Assessments – For prehabilitation needs (referrals to PT/OT), we will use the following: **6-Minute Walking Test (6MWT)** – This is a performance-based, 15 minute measure of functional exercise capacity.[77-79] It measures the distance that an individual is able to walk over a total of six minutes on a hard, flat surface. Patients are allowed to self-pace and rest as needed. **Timed Up & Go (TUG) -** This is a test of physical mobility. The test, measured in

seconds, is the time it takes for an individual to stand up from a standard arm-chair (approximate seat height of 46 cm), walk a distance of 3 meters (10 feet), turn, walk back to the chair, and sit down again.[80] **Short Physical Performance Battery (SPPB) -** This is a tool designed to quantify physical performance and decline over time. The test focuses primarily on lower extremity function and includes a 4 meter walk to measure gait speed, one chair stand (followed by 5 timed chair stands, if the first is successfully completed), and balance stands with the feel held in different positions for 10 seconds each. The test takes about 10 minutes to complete.[81, 82]

Health literacy screen – A brief 1-item screening will be performed following informed consent to screen for limited health literacy.

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.

General Well-Being – this will be assessed using one question: Compared to yesterday, how do you feel (worse, same, better).

MD Anderson Symptom Inventory (MDASI) - The MDASI is a validated measure of 13 common cancer-related symptoms: pain, fatigue, nausea, sleep, distress/anxiety, shortness of breath, memory, appetite, dry mouth, drowsiness, sadness, vomiting, and numbness/tingling. Each symptom's severity is rated on a 10-point scale. A score of 1-3 indicates mild intensity, and 4-10 moderate to severe intensity. Patients also rate how much their symptoms interfered with 6 common functional domains: walking, activity, working/housework, social relationships, enjoyment of life, and mood. A movement of 1.2 points is clinically meaningful. The MDASI has been validated in surgical populations; Cronbach Alpha reliability ranges from 0.82 to 0.94.[46, 83]

Functional Activity (Actigraph) – Based on published recommendations on best practice in use of accelerometry[84-87], we will initiate several parameters to ensure that the data captured is reliable. First, data will be collected in 1 second epochs and reintegrated to 60 second epochs for analysis. Non-wear time will be defined as 60 minutes of continuous 0 counts. A minimum of 4 weekdays and 1 weekend day with at least 600 minutes (10 hours) of daily wear time will be considered valid. In order to be considered a valid day, patients need to wear the accelerometer for at least 10 waking hours (600 minutes). Data capture will focus on the following: 1) number of steps taken per day and 2) sedentary time. Recommended activity counts per minute (cpm) cutpoints will be used to categorize sedentary time (<100 cpm) from light-intensity physical activity (100–1951 cpm) and moderate/vigorous intensity physical activity (≥1952 cpm).

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.[88, 89]

Readmissions - Electronic health record audits will capture: 1) 30, 60, and 90 day inpatient readmissions, 2) reasons for readmissions, and 3) ER visits. If the patient seeks emergent care outside of the primary institution, the patient's permission will be obtained to review these records.

Focus Group Guides - The semi-structured questions for focus groups are designed to solicit patient/families and surgeon/nurse perspectives on the following: 1) overall perceptions of perioperative care; 2) unmet needs during pre-and postoperative care; 3) greatest challenges before and after surgery; 4) postoperative recovery process at home; 4) use of telemonitoring application for communication (surgeon/nurses); 5) use of telemonitoring dashboard to guide clinical care (surgeon/nurses).

Exit Surveys – This survey contains several open-ended questions that participants in the perioperative telemonitoring arm will complete. The participants will provide information via written comments. The questions are designed to solicit feedback on the following: 1) on-boarding and setup process; 2) use and setup process of accelerometer; 3) value of monitoring PROs and functional activity;; 4) satisfaction with the timing of the telemonitoring (starts before surgery and continues up to 3 months after discharge from hospital); 5) satisfaction with the methods/technology used (mobile application, wristband watch) 6) most useful components of the telemonitoring for helping with postoperative recovery; 7) likes/dislikes of the program; 8) challenges and limitations of telemonitoring; and 9) suggestions on areas for improvement.

12.1.3.1 Eligibility Checklist

No eligibility checklist will be used in this study as the eligibility criteria is short.

12.1.3.2 Prior Therapy Forms and On-Study Forms

No prior therapy forms and on-study forms will be used in this study.

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

The COH Investigational Drug Service (IDS) cannot release a research agent that would cause a protocol deviation without approval by the PI. Whenever the protocol is ambiguous on a key point, the IDS should rely on the PI to clarify the issue.

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

This is a prospective, randomized, mixed methods, comparative effectiveness trial (1:1 randomization) of perioperative telemonitoring in cancer surgery (GI, GU, GYN). These cancer sites were selected because the surgical procedures, extent of resection, and expected surgical outcomes are similar. Our CER question is: What are the comparative effectiveness of remote perioperative telemonitoring care as compared to the surgeon (and surgical team) only perioperative care? This research focuses on comparing the two groups to identify which approach will most benefit cancer surgery patients.

In Aim 1, clinically significant changes in functional recovery (accelerometer daily step count) and related secondary patient-centered outcomes (sleep, sedentary time, symptoms, symptom interference with activity) will be tested over time by the comparators (remote perioperative telemonitoring care versus surgeon only perioperative care). The **primary outcome** is the clinically significant change in accelerometer daily step count over time. In Aim 2, we will test changes in postoperative complications and related secondary surgical outcomes (hospital readmissions) by the comparators. Here, the **primary outcome** is postoperative complications in the 30 days after surgery. In Aim 3, we will compare early withdrawal (dropout, loss of device) between the comparators. Finally, in Aim 4, we will qualitatively explore the perioperative telemonitoring experience from the patients, families, and surgeon's/nurse's perspective. This aim was included to explore perioperative care-related experiences (acceptability, technology usability, uptake/integration) among patients, families, and surgeons/nurses through qualitative focus groups and open-ended exit surveys. The data will be used to refine and assure model fidelity in future studies. It will also guide future integration into other healthcare system settings.

13.2 Statistical Analysis Plan

Data Management - We expect a total of 12 symptom evaluations per participant over the 3-4 month study duration. With a total sample of 332, this yields approximately 4,000 data collection encounters overall. We expect a large number of daily steps data observations per subject, as functional recovery data will be continuously recorded on a daily basis over the study duration.

Data will be transferred in real-time (within 2 minutes of participant completion) from TapCloud™ to a REDCap (Research Electronic Data Capture) study database. Daily step count will be continuously transferred to the study database in real-time. The database resides in secure COH research networks for research team access only. An assigned master's-level Statistical Research Associate (SRA) with paid effort on the project will be responsible for coordinating monthly data transfer, auditing, and data cleaning. In the process of data transfer and mergers, the study biostatistician (Dr. Behrendt), SRA, and TapCloud™ representative will audit and clean the data, apply formats in statistical software, and export data into REDCap database.

Handling Missing Data and Lost to Follow-Up - We will integrate the following strategies to prevent, detect, and remedy missing data in real time. First, participants will receive a total remuneration of $50 for providing data. Second, research staff will provide telephone/email reminders before each of the scheduled data collection timepoints to maximize adherence. Regular contact will also be provided to remind participants to wear the accelerometer. Third, research staff will provide each participant with a simple study calendar with data collection dates. Fourth, if no data is completed by participants, research staff will contact the participant in real-time to engage and assess. The Statistical Methods section below describes how data missing not at random will be handled in the analyses.

Preliminary Analysis - Descriptive statistics will be used to summarize all variables. Characteristics of participants at baseline will be reported in tabular form using appropriate descriptive statistics. Prior to hypothesis testing, the relationship between demographic variables and primary outcome variables (daily step count, postop complications) will be examined. Significant relationships/correlations will guide the addition of demographic variables to the analysis.

Heterogeneity of Treatment Effect - Exploratory use of interaction terms will assess whether significant effects of the study intervention differ by sex or by age (i.e., above vs below 70 years). If found to be present, any such heterogeneity of treatment effect, not having been hypothesized in advance, will be reported as a preliminary finding that awaits confirmation in future studies.

Internal/External Validity and Avoidance of Bias - To limit possible confounding of the primary results, analyses of the prespecified hypotheses will be adjusted for covariates (age, sex, physical fitness at pre-surgical baseline). To assess the representativeness of study participants, their demographic characteristics (sex, age) will be compared to those of eligible patients who are approached for consent but decline to participate in the study. Our digital engagement platform will initiate reminder systems to reduce loss to follow-up.

Statistical Methods by Study Aims - Characteristics considered as potential covariates in all analyses will be age, sex, surgical technique, residential setting, and physical fitness at preoperative baseline. Any covariate that improves the model's fit to the observed data will be retained in the final analysis.

The analyses for Aims 1-3 will be by intention to treat (ITT); the ITT population will include all subjects who have given informed consent, been randomized to intervention or control arm, and undergone the planned cancer surgery.

Aim 1 – Allowing for an anticipated 20% attrition in use of accelerometer by Day 14 across both trial arms, an initial sample size of 332 (randomized 1:1) will provide (per East 6.5 software)

80% power to detect the hypothesized 14% difference in slope due to study intervention, using a 1-sided, repeated measures-difference of slope test with alpha=0.025.

The Aim's primary endpoint will be the percent change from preoperative baseline in daily step count during the first 2 weeks post-discharge from hospital (measured on Discharge Day, Day +7, and Day +14). percent change from preoperative baseline in daily step count during the first 2 weeks post-discharge from hospital (measured on Discharge Day, Day +7, and Day +14). To recognize that these data may be missing not at random (ie, due to adverse event, distress, or withdrawal of consent), the effect of study intervention on primary endpoint will be modeled jointly with early withdrawal from data collection of that endpoint. Within the joint model, the sub-model for the primary endpoint will use generalized linear mixed modeling (with treatment and covariates as fixed factors, patient ID as random factor), while the other sub-model will analyze time to early withdrawal (Aim 3's primary endpoint) using proportional hazards regression. Similar joint modeling will be carried out for Aim 1's secondary endpoints (change from baseline in sedentary time, general symptoms, disease-specific symptoms).

Aim 2 – Because the CCI is derived from data routinely entered in the medical chart, no loss to follow-up is anticipated for this endpoint. A sample size of 332 subjects randomized 1:1 will provide (per East 6.5 software) 88% power to detect the hypothesized CCI benefit, using a 1-sided test of proportions, unpooled estimate of variance, critical p-value for efficacy=0.024, cumulative alpha=0.025.

The Aim's primary endpoint will be maximum Comprehensive Complications Index (CCI) during the 30 days post-discharge. Maximum CCI will be categorized as above vs below 15, and logistic regression will be used to evaluate the effect of study intervention. The Aim's secondary endpoint, time to hospital readmission through 90 days, will be subjected to survival analysis, handling any early withdrawal from study as a competing endpoint.

Aim 3 - The trial's sample size of n=332 will provide (per SAS software, PROC POWER for two-sample comparison of proportions) at least 80% power.

Treatment will be evaluated for association with this Aim's primary endpoint, time to early withdrawal, using proportional hazards regression. This analysis will be generated as a sub-model of the joint modeling for Aim 1.

Aim 4 - Qualitative data from exit interviews and focus groups will be analyzed using the conventional content analysis approach.[73] Written survey comments will be transferred to, and data from the audio-recorded focus groups 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 to derive codes, and sorted into themes based on links and relationship. Dr. Sun and Dr. Ferrell will conduct a final validation review of the codes/themes to ensure consistency and clarity across all qualitative data. Data discordantly coded will be discussed for refinement and consensus purposes with the SAC.

The team will use a mixed methods approach to enhance interpretation of study findings. For interpretation of study findings, the exit survey and focus group data will be used to augment quantitative data in Aims 1-3 (perioperative experience with functional recovery, symptoms,

sedentary time, postoperative complications, hospital readmissions, burden of telemonitoring). One approach to qualitative analysis is to use the quantitative outcomes of interest as themes for coding the qualitative data. Therefore, each quantitative outcome of interest will have corresponding qualitative data in the participants and stakeholder's own words. The table below illustrates the connection between quantitative and qualitative data.

Quantitative Outcomes	Connections with Qualitative Data
Functional recovery/sedentary time	Patient/family partner focus groups – overall experience with postop functional recovery/sedentary time
Sleep, symptom severity, symptom interference with daily activities	Patient/family partner focus groups – overall experience with postop symptoms
Postoperative complications (Comprehensive Complications Index – CCI) and related secondary surgical outcomes (hospital readmission).	Surgeon-nurses focus groups Patient/family partner focus groups – overall experience
Early withdrawal (dropout or loss of accelerometer device)	Telemonitoring arm open-ended exit survey

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 Duarte, South Pasadena, Antelope Valley, and Upland sites 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 three geographically diverse sites in the Greater Los Angeles area, including City of Hope at Duarte, South Pasadena, Antelope Valley, and Upland.

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

Participants will not incur any financial obligations. Participants will be compensated $25 after completion of day 60 and day 90 assessments, for a total of $50. Patients/families selected to participate in the focus group will be offered $50 compensation for participation. Each SAC member will be compensated at $25/hour for an estimated 100 hours/year (total of $2500/year). Each Stakeholder Panel member will be compensated for $100/hour.

14.7 Informed Consent Processes

The Research Nurses and CRAs will contact eligible participants and explain the study purpose, answer questions, and ascertain interest in participation. The primary approach for informed consent will be during an in-person encounter. Obtaining a signature of the consent form by the patient/caregiver may also be completed by sending the consent form by mail or electronic mail, and returned to City of Hope, or electronically via other electronic applications (i.e. DocuSign). Research team members will be bilingual (English and Spanish). We will only use telephone verbal consents in situations where patients are not returning to COH prior to surgery date. If, during, the first phone call, participants are willing to consent for enrollment, the Research Nurses and CRAs will proceed with verbal consent. The Research Nurse and CRAs will document the provision of verbal consent via progress note as required by IRB policies.

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.

15.0 References

1. Maillard J, Elia N, Haller CS, Delhumeau C and Walder B. Preoperative and early postoperative quality of life after major surgery - a prospective observational study. *Health and quality of life outcomes*. 2015;13:12.

2. Isik O, Okkabaz N, Hammel J, Remzi FH and Gorgun E. Preoperative functional health status may predict outcomes after elective colorectal surgery for malignancy. *Surg Endosc*. 2015;29:1051-6.

3. Waljee J, McGlinn EP, Sears ED and Chung KC. Patient expectations and patient-reported outcomes in surgery: a systematic review. *Surgery*. 2014;155:799-808.

4. Pompili C, Velikova G, White J, Callister M, Robson J, Dixon S, Franks K and Brunelli A. Poor preoperative patient-reported quality of life is associated with complications following pulmonary lobectomy for lung cancer. *Eur J Cardiothorac Surg*. 2017;51:526-531.

5. Jones RS and Stukenborg GJ. Patient-Reported Outcomes Measurement Information System (PROMIS) Use in Surgical Care: A Scoping Study. *Journal of the American College of Surgeons*. 2017;224:245-254 e1.

6. Cloyd JM, Tran Cao HS, Petzel MQ, Denbo JW, Parker NH, Nogueras-Gonzalez GM, Liles JS, Kim MP, Lee JE, Vauthey JN, Aloia TA, Fleming JB and Katz MH. Impact of pancreatectomy on long-term patient-reported symptoms and quality of life in recurrence-free survivors of pancreatic and periampullary neoplasms. *Journal of surgical oncology*. 2017;115:144-150.

7. Smith AB and Basch E. Role of Patient-Reported Outcomes in Postsurgical Monitoring in Oncology. *Journal of oncology practice / American Society of Clinical Oncology*. 2017;13:535-538.

8. Cowan RA, Suidan RS, Andikyan V, Rezk YA, Einstein MH, Chang K, Carter J, Zivanovic O, Jewell EJ, Abu-Rustum NR, Basch E and Chi DS. Electronic patient-reported outcomes from home in patients recovering from major gynecologic cancer surgery: A prospective study measuring symptoms and health-related quality of life. *Gynecol Oncol*. 2016;143:362-366.

9. Basch E, Deal AM, Kris MG, Scher HI, Hudis CA, Sabbatini P, Rogak L, Bennett AV, Dueck AC, Atkinson TM, Chou JF, Dulko D, Sit L, Barz A, Novotny P, Fruscione M, Sloan JA and Schrag D. Symptom Monitoring With Patient-Reported Outcomes During Routine Cancer Treatment: A Randomized Controlled Trial. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2016;34:557-65.

10. Kanai M, Izawa KP, Kobayashi M, Onishi A, Kubo H, Nozoe M, Mase K and Shimada S. Effect of accelerometer-based feedback on physical activity in hospitalized patients with ischemic stroke: a randomized controlled trial. *Clin Rehabil*. 2018;0:269215518755841.

11. Symer MM, Abelson JS, Milsom J, McClure B and Yeo HL. A Mobile Health Application to Track Patients After Gastrointestinal Surgery: Results from a Pilot Study. *Journal of gastrointestinal surgery : official journal of the Society for Surgery of the Alimentary Tract*. 2017;21:1500-1505.

12. Semple JL, Sharpe S, Murnaghan ML, Theodoropoulos J and Metcalfe KA. Using a mobile app for monitoring post-operative quality of recovery of patients at home: a feasibility study. *JMIR Mhealth Uhealth*. 2015;3:e18.

13. Jaensson M, Dahlberg K, Eriksson M, Gronlund A and Nilsson U. The Development of the Recovery Assessments by Phone Points (RAPP): A Mobile Phone App for Postoperative Recovery Monitoring and Assessment. *JMIR Mhealth Uhealth*. 2015;3:e86.

14. Dawes AJ, Reardon S, Chen VL, Kaiser W, Russell MM, Ko CY and Lin AY. Wireless Technology to Track Surgical Patients after Discharge: A Pilot Study. *The American surgeon*. 2015;81:1061-6.

15. Sun V, Dumitra S, Ruel N, Lee B, Melstrom L, Melstrom K, Woo Y, Sentovich S, Singh G and Fong Y. Wireless Monitoring Program of Patient-Centered Outcomes and Recovery Before and After Major Abdominal Cancer Surgery. *JAMA surgery*. 2017;152:852-859.

16. In H and Rosen JE. Primer on outcomes research. *Journal of surgical oncology*. 2014;110:489-93.

17. Birkmeyer JD, Dimick JB and Birkmeyer NJ. Measuring the quality of surgical care: structure, process, or outcomes? *Journal of the American College of Surgeons*. 2004;198:626-32.

18. Swanson RS, Pezzi CM, Mallin K, Loomis AM and Winchester DP. The 90-day mortality after pancreatectomy for cancer is double the 30-day mortality: more than 20,000 resections from the national cancer data base. *Annals of surgical oncology*. 2014;21:4059-67.

19. Stephens RJ, Hopwood P and Girling DJ. Defining and analysing symptom palliation in cancer clinical trials: a deceptively difficult exercise. *British journal of cancer*. 1999;79:538-44.

20. Waljee JF and Dimick JB. Do Patient-Reported Outcomes Correlate with Clinical Outcomes Following Surgery? *Advances in surgery*. 2017;51:141-150.

21. Yu HY, Friedlander DF, Patel S and Hu JC. The current status of robotic oncologic surgery. *CA: a cancer journal for clinicians*. 2013;63:45-56.

22. Oliveira M, Oliveira G, Souza-Talarico J and Mota D. Surgical Oncology: Evolution of Postoperative Fatigue and Factors Related to Its Severity. *Clinical journal of oncology nursing*. 2016;20:E3-8.

23. Brown C, Constance K, Bédard D and Purden M. Colorectal Surgery Patients' Pain Status, Activities, Satisfaction, and Beliefs about Pain and Pain Management. *Pain Management Nursing*. 2013;14:184-192.

24. Urbach DR, Harnish JL and Long G. Short-term health-related quality of life after abdominal surgery: a conceptual framework. *Surgical innovation*. 2005;12:243-7.

25. Castelino T, Fiore JF, Jr., Niculiseanu P, Landry T, Augustin B and Feldman LS. The effect of early mobilization protocols on postoperative outcomes following abdominal and thoracic surgery: A systematic review. *Surgery*. 2016;159:991-1003.

26. Reddy S, Contreras CM, Singletary B, Bradford TM, Waldrop MG, Mims AH, Smedley WA, Swords JA, Wang TN and Heslin MJ. Timed Stair Climbing Is the Single Strongest Predictor of Perioperative Complications in Patients Undergoing Abdominal Surgery. *Journal of the American College of Surgeons*. 2016.

27. Cook DJ, Thompson JE, Prinsen SK, Dearani JA and Deschamps C. Functional recovery in the elderly after major surgery: assessment of mobility recovery using wireless technology. *Ann Thorac Surg*. 2013;96:1057-61.

28. Lawrence VA, Hazuda HP, Cornell JE, Pederson T, Bradshaw PT, Mulrow CD and Page CP. Functional independence after major abdominal surgery in the elderly. *Journal of the American College of Surgeons*. 2004;199:762-72.

29. Ferriolli E, Skipworth RJ, Hendry P, Scott A, Stensteth J, Dahele M, Wall L, Greig C, Fallon M, Strasser F, Preston T and Fearon KC. Physical activity monitoring: a responsive and meaningful patient-centered outcome for surgery, chemotherapy, or radiotherapy? *Journal of pain and symptom management*. 2012;43:1025-35.

30. Mayo NE, Feldman L, Scott S, Zavorsky G, Kim do J, Charlebois P, Stein B and Carli F. Impact of preoperative change in physical function on postoperative recovery: argument supporting prehabilitation for colorectal surgery. *Surgery*. 2011;150:505-14.

31. Chung J and Lui J. Postoperative pain management: Study of patients' level of pain and satisfaction with health care providers' responsiveness to their reports of pain. *Nursing and Health Services*. 2003;5:13-21.

32. Smith AB and Basch E. Role of Patient-Reported Outcomes in Postsurgical Monitoring in Oncology. *J Oncol Pract*. 2017;0:JOP2017023838.

33. Stitzenberg KB, Chang Y, Smith AB, Meyers MO and Nielsen ME. Impact of Location of Readmission on Outcomes After Major Cancer Surgery. *Annals of surgical oncology*. 2017;24:319-329.

34. Wasif N, Etzioni D, Habermann EB, Mathur A, Pockaj BA, Gray RJ and Chang YH. Racial and Socioeconomic Differences in the Use of High-Volume Commission on Cancer-Accredited Hospitals for Cancer Surgery in the United States. *Annals of surgical oncology*. 2018;25:1116-1125.

35. Eng OS, Nelson RA, Konstantinidis I, Chao J, Erhunmwunsee L, Raz DJ and Kim JY. Disparities in survival after trimodality therapy for esophageal adenocarcinoma. *Diseases of the esophagus : official journal of the International Society for Diseases of the Esophagus*. 2018.

36. Stitzenberg KB, Chang Y, Smith AB and Nielsen ME. Exploring the burden of inpatient readmissions after major cancer surgery. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2015;33:455-64.

37. Stitzenberg KB, Sigurdson ER, Egleston BL, Starkey RB and Meropol NJ. Centralization of cancer surgery: implications for patient access to optimal care. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2009;27:4671-8.

38. Sacks GD, Lawson EH, Dawes AJ, Gibbons MM, Zingmond DS and Ko CY. Which Patients Require More Care after Hospital Discharge? An Analysis of Post-Acute Care Use among Elderly Patients Undergoing Elective Surgery. *Journal of the American College of Surgeons*. 2015;220:1113-1121.e2.

39. Jensen RE, Snyder CF, Abernethy AP, Basch E, Potosky AL, Roberts AC, Loeffler DR and Reeve BB. Review of electronic patient-reported outcomes systems used in cancer clinical care. *Journal of oncology practice / American Society of Clinical Oncology*. 2014;10:e215-22.

40. Basch E, Artz D, Dulko D, Scher K, Sabbatini P, Hensley M, Mitra N, Speakman J, McCabe M and Schrag D. Patient online self-reporting of toxicity symptoms during chemotherapy. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2005;23:3552-61.

41. Taenzer P, Bultz BD, Carlson LE, Speca M, DeGagne T, Olson K, Doll R and Rosberger Z. Impact of computerized quality of life screening on physician behaviour and patient satisfaction in lung cancer outpatients. *Psycho-oncology*. 2000;9:203-13.

42. Rosenbloom SK, Victorson DE, Hahn EA, Peterman AH and Cella D. Assessment is not enough: a randomized controlled trial of the effects of HRQL assessment on quality of life and satisfaction in oncology clinical practice. *Psycho-oncology*. 2007;16:1069-79.

43. Boyes A, Newell S, Girgis A, McElduff P and Sanson-Fisher R. Does routine assessment and real-time feedback improve cancer patients' psychosocial well-being? *European journal of cancer care*. 2006;15:163-71.

44. Velikova G, Booth L, Smith AB, Brown PM, Lynch P, Brown JM and Selby PJ. Measuring quality of life in routine oncology practice improves communication and patient well-being: a randomized controlled trial. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2004;22:714-24.

45. Mooney KH, Beck SL, Friedman RH and Farzanfar R. Telephone-linked care for cancer symptom monitoring: a pilot study. *Cancer practice*. 2002;10:147-54.

46. Cleeland CS, Wang XS, Shi Q, Mendoza TR, Wright SL, Berry MD, Malveaux D, Shah PK, Gning I, Hofstetter WL, Putnam JB, Jr. and Vaporciyan AA. Automated symptom alerts reduce postoperative symptom severity after cancer surgery: a randomized controlled clinical trial. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2011;29:994-1000.

47. Weaver A, Young AM, Rowntree J, Townsend N, Pearson S, Smith J, Gibson O, Cobern W, Larsen M and Tarassenko L. Application of mobile phone technology for managing chemotherapy-associated side-effects. *Annals of oncology : official journal of the European Society for Medical Oncology / ESMO*. 2007;18:1887-92.

48. Butt Z, Wagner LI, Beaumont JL, Paice JA, Straus JL, Peterman AH, Carro G, Von Roenn JH, Shevrin D and Cella D. Longitudinal screening and management of fatigue, pain, and emotional distress associated with cancer therapy. *Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer*. 2008;16:151-9.

49. Kearney N, McCann L, Norrie J, Taylor L, Gray P, McGee-Lennon M, Sage M, Miller M and Maguire R. Evaluation of a mobile phone-based, advanced symptom management system (ASyMS) in the management of chemotherapy-related toxicity. *Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer*. 2009;17:437-44.

50. Bainbridge D, Seow H, Sussman J, Pond G, Martelli-Reid L, Herbert C and Evans W. Multidisciplinary health care professionals' perceptions of the use and utility of a symptom assessment system for oncology patients. *Journal of oncology practice / American Society of Clinical Oncology*. 2011;7:19-23.

51. Basch E, Snyder C, McNiff K, Brown R, Maddux S, Smith ML, Atkinson TM, Howell D, Chiang A, Wood W, Levitan N, Wu AW and Krzyzanowska M. Patient-reported outcome performance measures in oncology. *Journal of oncology practice / American Society of Clinical Oncology*. 2014;10:209-11.

52. Bennett AV, Jensen RE and Basch E. Electronic patient-reported outcome systems in oncology clinical practice. *CA: a cancer journal for clinicians*. 2012;62:337-47.

53. Strasser F, Blum D, von Moos R, Cathomas R, Ribi K, Aebi S, Betticher D, Hayoz S, Klingbiel D, Brauchli P, Haefner M, Mauri S, Kaasa S, Koeberle D and Swiss Group for Clinical Cancer R. The effect of real-time electronic monitoring of patient-reported symptoms and clinical syndromes in outpatient workflow of medical oncologists: E-MOSAIC, a multicenter cluster-randomized phase III study (SAKK 95/06). *Annals of oncology : official journal of the European Society for Medical Oncology / ESMO*. 2016;27:324-32.

54. Nekhlyudov L, Levit L, Hurria A and Ganz PA. Patient-centered, evidence-based, and cost-conscious cancer care across the continuum: Translating the Institute of Medicine report into clinical practice. *CA: a cancer journal for clinicians*. 2014;64:408-21.

55. Dorrell RD, Vermillion SA and Clark CJ. Feasibility of real-time location systems in monitoring recovery after major abdominal surgery. *Surg Endosc*. 2017;31:5457-5462.

56. Low CA, Bovbjerg DH, Ahrendt S, Choudry MH, Holtzman M, Jones HL, Pingpank JF, Jr., Ramalingam L, Zeh HJ, 3rd, Zureikat AH and Bartlett DL. Fitbit step counts during inpatient recovery from cancer surgery as a predictor of readmission. *Annals of behavioral medicine : a publication of the Society of Behavioral Medicine*. 2018;52:88-92.

57. van der Meij E, van der Ploeg HP, van den Heuvel B, Dwars BJ, Meijerink W, Bonjer HJ, Huirne JAF and Anema JR. Assessing pre- and postoperative activity levels with an accelerometer: a proof of concept study. *BMC Surg*. 2017;17:56.

58. Wood WA and Basch E. From Intuition to Execution: Realizing the Potential of Wearables in Oncology. *Journal of Oncology Practice*. 2017;13:90-92.

59. Institute of Medicine. Best Care at Lower Cost: The Path to Continuously Learning Health Care in America. 2012.

60. Abernethy AP, Etheredge LM, Ganz PA, Wallace P, German RR, Neti C, Bach PB and Murphy SB. Rapid-learning system for cancer care. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2010;28:4268-74.

61. Sox HC, Basch EM and Berwick D. Strategies to Achieve High-Value Oncology Care-A Beginning. *JAMA oncology*. 2018;4:171-172.

62. Stover AM and Basch EM. Using patient-reported outcome measures as quality indicators in routine cancer care. *Cancer*. 2016;122:355-7.

63. Smith TG, Castro KM, Troeschel AN, Arora NK, Lipscomb J, Jones SM, Treiman KA, Hobbs C, McCabe RM and Clauser SB. The rationale for patient-reported outcomes surveillance in cancer and a reproducible method for achieving it. *Cancer*. 2016;122:344-51.

64. Beg MS, Gupta A, Stewart T and Rethorst CD. Promise of Wearable Physical Activity Monitors in Oncology Practice. *Journal of oncology practice / American Society of Clinical Oncology*. 2017;13:82-89.

65. Bennett AV, Reeve BB, Basch EM, Mitchell SA, Meeneghan M, Battaglini CL, Smith-Ryan AE, Phillips B, Shea TC and Wood WA. Evaluation of pedometry as a patient-centered outcome in patients undergoing hematopoietic cell transplant (HCT): a comparison of pedometry and patient reports of symptoms, health, and quality of life. *Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation*. 2015:1-12.

66. Pezold ML, Pusic AL, Cohen WA, Hollenberg JP, Butt Z, Flum DR and Temple LK. Defining a Research Agenda for Patient-Reported Outcomes in Surgery: Using a Delphi Survey of Stakeholders. *JAMA surgery*. 2016;151:930-936.

67. Lenz ER, Pugh LC, Milligan RA, Gift A and Suppe F. The middle-range theory of unpleasant symptoms: an update. *ANS Advances in nursing science*. 1997;19:14-27.

68. Lenz ER, Suppe F, Gift AG, Pugh LC and Milligan RA. Collaborative development of middle-range nursing theories: toward a theory of unpleasant symptoms. *ANS Advances in nursing science*. 1995;17:1-13.

69. Peterson SK, Garden A, Shinn E, Shete S, Martch S, Camero M, Baum G, Farcas E, Lin K, Raab F, Nandigam V, Yan Y, Ferrarotto R, Godino J, Patrick K and Beadle B. Using mobile and sensor technology to identify early dehydration risk in head and neck cancer patients undergoing radiation treatment: Impact on symptoms. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2018;36 suppl:6063.

70. Lafaro KJ, Raz DJ, Kim JY, Hite S, Ruel N, Varatkar G, Erhunmwunsee L, Melstrom L, Lee B, Singh G, Fong Y and Sun V. Pilot study of a telehealth perioperative physical activity intervention for older adults with cancer and their caregivers. *Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer*. 2019.

71. Kooiman TJ, Dontje ML, Sprenger SR, Krijnen WP, van der Schans CP and de Groot M. Reliability and validity of ten consumer activity trackers. *BMC Sports Sci Med Rehabil*. 2015;7:24.

72. Bonsignore L, Bloom N, Steinhauser K, Nichols R, Allen T, Twaddle M and Bull J. Evaluating the Feasibility and Acceptability of a Telehealth Program in a Rural Palliative Care Population: TapCloud for Palliative Care. *Journal of pain and symptom management*. 2018;56:7-14.

73. Hsieh HF and Shannon SE. Three approaches to qualitative content analysis. *Qualitative health research*. 2005;15:1277-88.

74. Sun V, Raz DJ, Ruel N, Chang W, Erhunmwunsee L, Reckamp K, Tiep B, Ferrell B, McCorkle R and Kim JY. A Multimedia Self-management Intervention to Prepare Cancer

Patients and Family Caregivers for Lung Surgery and Postoperative Recovery. *Clinical lung cancer*. 2017;18:e151-e159.

75. Raz DJ, Sun V, Kim JY, Williams AC, Koczywas M, Cristea M, Reckamp K, Hayter J, Tiep B and Ferrell B. Long-Term Effect of an Interdisciplinary Supportive Care Intervention for Lung Cancer Survivors After Surgical Procedures. *Ann Thorac Surg*. 2016;101:495-502; discussion 502-3.
76. Sun V, Ercolano E, McCorkle R, Grant M, Wendel CS, Tallman NJ, Passero F, Raza S, Cidav Z, Holcomb M, Weinstein RS, Hornbrook MC and Krouse RS. Ostomy telehealth for cancer survivors: Design of the Ostomy Self-management Training (OSMT) randomized trial. *Contemporary clinical trials*. 2018;64:167-172.
77. Balke B. A Simple Field Test for the Assessment of Physical Fitness. Rep 63-6. *[Report] Civil Aeromedical Research Institute*. 1963:1-8.
78. Lord SR and Menz HB. Physiologic, psychologic, and health predictors of 6-minute walk performance in older people. *Archives of physical medicine and rehabilitation*. 2002;83:907-11.
79. Harada ND, Chiu V and Stewart AL. Mobility-related function in older adults: assessment with a 6-minute walk test. *Archives of physical medicine and rehabilitation*. 1999;80:837-41.
80. Podsiadlo D and Richardson S. The timed "Up & Go": a test of basic functional mobility for frail elderly persons. *Journal of the American Geriatrics Society*. 1991;39:142-8.
81. Volpato S, Cavalieri M, Sioulis F, Guerra G, Maraldi C, Zuliani G, Fellin R and Guralnik JM. Predictive value of the Short Physical Performance Battery following hospitalization in older patients. *The journals of gerontology Series A, Biological sciences and medical sciences*. 2011;66:89-96.
82. Studenski S, Perera S, Wallace D, Chandler JM, Duncan PW, Rooney E, Fox M and Guralnik JM. Physical performance measures in the clinical setting. *Journal of the American Geriatrics Society*. 2003;51:314-22.
83. Cleeland CS, Mendoza TR, Wang XS, Chou C, Harle MT, Morrissey M and Engstrom MC. Assessing symptom distress in cancer patients: the M.D. Anderson Symptom Inventory. *Cancer*. 2000;89:1634-46.
84. Montoye AH, Moore RW, Bowles HR, Korycinski R and Pfeiffer KA. Reporting accelerometer methods in physical activity intervention studies: a systematic review and recommendations for authors. *Br J Sports Med*. 2016.
85. Aadland E and Ylvisaker E. Reliability of Objectively Measured Sedentary Time and Physical Activity in Adults. *PLoS One*. 2015;10:e0133296.
86. Aadland E and Ylvisaker E. Reliability of the Actigraph GT3X+ Accelerometer in Adults under Free-Living Conditions. *PLoS One*. 2015;10:e0134606.
87. Matthews CE, Hagstromer M, Pober DM and Bowles HR. Best practices for using physical activity monitors in population-based research. *Medicine and science in sports and exercise*. 2012;44:S68-76.

88. Slankamenac K, Nederlof N, Pessaux P, de Jonge J, Wijnhoven BP, Breitenstein S, Oberkofler CE, Graf R, Puhan MA and Clavien PA. The comprehensive complication index: a novel and more sensitive endpoint for assessing outcome and reducing sample size in randomized controlled trials. *Annals of surgery*. 2014;260:757-62; discussion 762-3.

89. Slankamenac K, Graf R, Barkun J, Puhan MA and Clavien PA. The comprehensive complication index: a novel continuous scale to measure surgical morbidity. *Annals of surgery*. 2013;258:1-7.