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Ambulatory Cancer Care Electronic Symptom Self-Reporting (ACCESS) for Surgical Patients – A Randomized Controlled Trial

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Manuscripts

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3 **Ambulatory Cancer Care Electronic Symptom Self-Reporting (ACCESS) for Surgical Patients – A**
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5 **Randomized Controlled Trial**
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ABSTRACT

Introduction:

An increasing proportion of cancer surgeries are ambulatory procedures requiring a stay of one day or less in the hospital. Providing patients and their caregivers with ongoing, real-time support after discharge aids delivery of high-quality postoperative care in this new health care environment. Despite abundant evidence that patient self-reporting of symptoms improves quality of care, the most effective way to monitor and manage this self-reported information is not known.

Methods and analysis:

This is a two-armed randomized, controlled trial evaluating two approaches to the management of patient-reported data: (1) Team Monitoring, symptom monitoring by the clinical team, with nursing outreach if symptoms exceed normal limits, or (2) Enhanced Feedback, real-time feedback to patients about expected symptom severity, with patient-activated care as needed.

Breast, gynecologic, urologic, and head and neck cancer patients undergoing ambulatory cancer surgery (n=2,750) complete an electronic survey for up to 30 days after surgery that includes items from a validated instrument developed by the National Cancer Institute, the Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE). Information provided to patients in the Enhanced Feedback group is procedure-specific and based on updated PRO-CTCAE data from previous patients. Qualitative interviews are also performed. The primary study outcomes assess unplanned emergency department visits and symptom-triggered interventions (e.g., nursing calls and pain management referrals) within 30 days, and secondary outcomes assess the patient and caregiver experience (i.e., patient engagement, patient anxiety, and caregiver burden).

Ethics and dissemination:

This study is approved by the Institutional Review Board at Memorial Sloan Kettering Cancer Center.

The relationships between the study team and stakeholders will be leveraged to disseminate study findings. Findings will be relevant in designing future coordinated care models targeting improved health care quality and patient experience.

Trial Registration: NCT03178045

STRENGTHS AND LIMITATIONS OF THIS STUDY

1. This study is a large randomized, controlled trial that will help determine an effective mechanism for patient-reported data collection and symptom monitoring after ambulatory surgery.
2. Optimal integration of self-reported symptom data into health care systems has the potential to improve surgical outcomes and enhance patient-clinician communication.
3. Patient engagement is a major driver of study design, implementation, and future dissemination, as this study includes former patients and caregivers as members of the core study team.
4. The study population consists largely of patients with high health and computer literacy, which may be a potential threat to external validity.
5. Performance bias by clinicians who may be aware of patient arm assignment is a potential limitation of this study.

INTRODUCTION

Increasing numbers of surgical procedures, including major cancer procedures (e.g., mastectomies, hysterectomies, and prostatectomies), are being performed as short-stay (one midnight) or ambulatory surgeries [1,2,3]. Although there are many advantages to shorter hospital stays, this model adds complexities to the delivery of high-quality, patient-centered care, particularly for cancer patients and their caregivers, who are often still struggling with a new cancer diagnosis. Patients often leave the surgical center while experiencing symptoms that were previously attended to by the health care team [4]. Managing symptoms at home can be challenging for patients and caregivers who may have difficulty distinguishing normal and expected symptoms from potentially serious adverse events [5]. Without information and risk awareness, patients may delay seeking care, with severe consequences, or they may experience unnecessary anxiety and seek unnecessary care [6]. In focus groups and interviews conducted to inform the design of the current study, patients and caregivers conveyed feelings of stress and reported feeling unprepared to interpret and monitor postoperative symptoms.

Patient-reported outcome (PRO) measurement is rapidly becoming a standard of care throughout medicine that can aid in monitoring symptom burden. However, the best way to integrate and act on patient-reported data is unclear [7]. There is abundant and broad evidence that PRO data can improve communication with the clinical team, symptom control, quality of life, and patient satisfaction [8-10]. One large randomized trial comparing routine collection of PROs with usual care during chemotherapy showed that among patients who received the PROs intervention, quality of life improved (34% vs. 18%), and these patients were less likely to be seen in the emergency department (34% vs. 41%; $P = 0.02$) or hospitalized (45% vs. 49%; $P = 0.08$) [7]. Although progress has been made to better understand how symptom data might be best incorporated into clinical care among non-surgical patients, little work has been done among patients having surgery. Routine

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3 monitoring of symptoms in surgical patients, with outreach by the clinical team when severity
4 exceeds an expected range, may identify problems at an earlier stage and avoid or minimize adverse
5 events. Providing patients with feedback about expected symptom severity and allowing them to
6 activate care as needed may allow for the identification of these adverse events before they
7 progress, while also decreasing patient anxiety and unplanned care, such as unnecessary visits to the
8 emergency department. It is unknown whether providing this kind of feedback to patients would
9 affect care patterns and patient outcomes. This evidence gap provides motivation for the design of
10 the current study as well as the selection of its outcome measures.
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23 This randomized controlled trial will assess two approaches to the management of patient-reported
24 symptoms and their potential impact in decreasing emergency department visits, patient anxiety,
25 and caregiver burden up to 30 days after ambulatory cancer surgery. One approach is called Team
26 Monitoring, in which symptoms are monitored by the clinical team, with nursing outreach if
27 symptoms exceed normal limits. The second approach is called Enhanced Feedback, which provides
28 patients with real-time feedback about expected symptom severity, with patient-activated care as
29 needed. The study aligns with the Institute of Medicine's goal of determining how to deliver an ideal
30 patient care experience that is safe, effective, efficient, patient-centered, timely, and equitable [11-
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45 The study model (Figure 1) is predicated on the hypothesis that daily, patient-driven symptom reporting
46 with normative data feedback about expected symptom burden relative to previous patient reports
47 (Enhanced Feedback) will increase patients' self-efficacy [14] and their confidence that they can manage
48 their symptoms during the recovery period [15]. This has been shown to be a predictor of decreased
49 symptoms and better physical function [15,16]. On the basis of this model, patients may avoid
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unnecessary emergency department visits by better understanding expected symptoms and by achieving more efficient and effective communication with their health care team.

The study will garner important information for incorporating PROs into postoperative care and aiding in the development of tailored perioperative care pathways for cancer patients. The key lessons learned may be used to support the implementation of strategies for population health management for non-cancer treatments that can also cause burdensome symptoms. Utilizing a similar patient-reporting mechanism may benefit smaller outpatient facilities that do not have the personnel resources necessary to provide intensive monitoring of patient symptoms. It is expected that this study will also be highly relevant in designing coordinated care models targeting improved health care value, such as the Oncology Care Model and the Perioperative Surgical Home.

METHODS AND ANALYSIS

Study Design

This is a parallel group randomized, controlled trial with 1:1 procedure-stratified randomization between two arms, Team Monitoring and Enhanced Feedback. The study design follows Patient-Centered Outcomes Research Institute (PCORI) standards, including patient engagement, research methods, data integrity and analysis (including stratification by surgical procedure), handling of missing data, and heterogeneity of treatment effect.

Patient and Public Involvement

The study team recruited a group of committed stakeholders that include clinicians, researchers, hospital leadership, and advocates from patient and caregiver support groups, as well as former patients and caregivers who join the team as Patient Partners. The Patient Partners have been engaged since the

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3 beginning of study development, and they offer their experiences to help inform the design, conduct,
4 and dissemination of the research. The Patient Partners and study stakeholders contributed to the
5 development of data collection tools (including the enhanced feedback reports given to patients) and to
6 the creation of study information sheets, recruitment letters, and qualitative interview guides. They also
7 helped to refine recruitment initiatives that ensured minimal burden to participants, which resulted in
8 increased enrollment over the first year of recruitment. Through their engagement, the study will
9 ultimately be more patient-centered and will lead to a greater application of results by the larger health
10 care community.
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23 **Objectives and Scientific Aims**

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25 The primary study outcome is to determine if providing enhanced reporting to patients regarding their
26 symptoms will impact patient-centered outcomes, including urgent care and emergency department
27 visits, readmissions, and symptom-triggered interventions (pain management referrals, nursing calls) up
28 to 30 days after ambulatory cancer surgery. Secondary outcomes include patient engagement, patient
29 anxiety, and caregiver burden, using validated PRO measures and qualitative interviews.
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39 **Cohort 1: Team Monitoring**

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41 Team Monitoring is the current standard of care for patients at the Josie Robertson Surgical Center
42 (JRSC) at Memorial Sloan Kettering Cancer Center (MSK). Patients report their symptoms via an
43 electronic questionnaire called the Recovery Tracker, delivered through an in-house informatics
44 platform known as the ambulatory cancer care electronic symptom self-reporting (ACCESS) system.
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46 The health care team receives portal-secure message alerts if patients report symptoms above a
47 specified threshold and contact the patient by phone during business hours. Given the need for real-
48 time feedback for some symptoms, patients who report very severe symptoms receive a bold red
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3 alert instructing them to immediately call the office (or the call team outside business hours) or seek
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5 medical attention. The response thresholds (i.e., when to give which alert) for each question are set
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7 individually and have been refined based on feedback from the clinical teams (i.e., surgeons and
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9 office practice nurses). For example, mild-moderate pain on three days after surgery is expected, but
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11 moderate shortness of breath three days after surgery is not expected and potentially concerning.
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16 **Cohort 2: Enhanced Feedback**

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18 In the Enhanced Feedback cohort, the ACCESS system provides tailored normative data visualizations
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20 that offer context and education to patients regarding expected symptom severity (Figure 2). This
21
22 Enhanced Feedback report was generated using an iterative rapid application development process by
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24 the research team in collaboration with MSK surgeons and nurses, former patients and caregivers, the
25
26 study's Patient Partners, and patient advocates from cancer support groups. Details regarding the
27
28 optimization of the feedback report are described elsewhere [17].
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34 The feedback report consists of periodically updated PRO data from previous patients that are stratified
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36 by surgical procedure and postoperative date. As a result, patients can see their recovery trajectories
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38 relative to others who have undergone the same procedure. Care is "patient-activated" in that patients
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40 use the information about expected symptoms to decide whether they should call the care team, for
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42 instance, if they experience symptoms that are more severe or more prolonged than expected. Similar
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44 to the Team Monitoring cohort, patients who report very severe symptoms are instructed to
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46 immediately contact their physician's office, and the care team receives an alert. Alerts to the clinical
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48 team can only be monitored during business hours, so for care after hours, all patients must call the
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50 doctor on call.
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Participants, Setting, and Recruitment

Patients older than 18 years who are scheduled for ambulatory cancer surgery at the JRSC at MSK are eligible for study participation. Disease types include breast, gynecologic, urologic, and head and neck cancers or benign tumors. Patients must be able to access a computer, tablet, or mobile phone to complete the electronic surveys. Caregivers of eligible patients are also eligible for study participation; they must be older than 18 years, be willing to provide an email address, and have access to a computer, tablet, or mobile phone to complete electronic surveys. A total of 2,750 patients and 1,375 caregivers will be recruited for this study over a period of three years.

Eligible patients receive written educational materials that describe the study via the MyMSK patient portal, email, or a letter mailed to their home. The study team then attempts to contact patients by phone before surgery to obtain their verbal consent to participate in the study. If the study team is unable to contact the patient prior to the day of surgery, the patient is approached at one of their clinic appointments or in the waiting room when they arrive for surgery. At the time of consent, patients are also asked to identify a caregiver who will be actively involved in their recovery. If permitted by the patient, the study team obtains the caregiver's contact information to invite them to participate in the study as well.

Randomization is implemented through the MSK Clinical Research Database, a fully secure, password-protected database that ensures full allocation concealment. It will be performed within one week of the patient's surgical visit. Randomization is stratified by procedure (e.g., breast: mastectomy [with or without sentinel and axillary nodal dissection], tissue expander placement, or other; gynecologic: laparoscopic or robotic procedure, laparotomy, or other; urologic: laparoscopic or robotic

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3 prostatectomy, laparoscopic or robotic partial or total nephrectomy, laparotomy, or other; head and
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5 neck: thyroidectomy) and will be implemented by randomly permuted blocks of random length. The
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7 trial will not be blinded, as it relies on patient knowledge (i.e., how a patient's scores compare with
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9 other patients' scores) as a key part of the intervention.
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14 **Study Measures and Data Collection**

15 **The ACCESS System and Recovery Tracker**

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17 The ACCESS system is designed to enable real-time postoperative symptom monitoring. Patients
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19 undergoing surgery at the JRSC, an ambulatory surgery center at MSK, are invited to complete the
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21 Recovery Tracker through the MyMSK patient portal. The interface was built with a responsive
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23 design, so patients can complete the Recovery Tracker via computers, tablets, or mobile phones.
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25 Patients are prompted to report on 11 items adapted from a validated symptom assessment
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27 instrument, the National Cancer Institute (NCI)'s Patient-Reported Outcomes version of the Common
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29 Terminology for Adverse Events (PRO-CTCAE) [18], three additional surgical symptom questions, and
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31 two questions about seeking urgent care or a doctor during the first 10 days after surgery. Over the
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33 following 20 days, patients have the option to complete additional surveys on demand, but they are
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35 not prompted to do so. Patients, caregivers, nurses, surgeons, and anesthesiologists participated in
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37 the selection of these items. See Table 1 for the study assessment schedule.
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Table 1. Study assessment schedule

		Preoperative (pre-op) time point	Postoperative time point			
Item	# of Items	Pre-Op (day of consent – POD1)	POD 1–10	POD14 (+7/-3 days)	POD30 (+/- 10 days)	POD60 (+/- 14 days)
Patient						
Recovery Tracker (including PRO- CTCAE symptoms and anxiety items, and additional questions)	20		Daily		Available to complete, if desired (POD11-30)	
Emergency Department Visits					X	
Readmission					X	
Adverse Events					X	
Patient	10	X		X		X

Activation Measure						
Patient Interviews					X	
Caregiver						
Caregiver Reaction Assessment and Demographics*	24			X		X
Caregiver Interviews					X	

POD, postoperative day

*Caregiver demographics collected include date of birth, sex, race/ethnicity, education level, employment status, relationship to patient, and basic caregiving information. Demographic information is collected at POD14 (+7/-3 days).

Emergency Department Visits and Adverse Events

The study team evaluates the frequency of urgent care center visits, readmissions, and symptom-triggered interventions (e.g., pain management referrals, nursing calls through triggers generated from the ACCESS system, as well as through chart extraction for 30 days after surgery).

Patient Engagement, Patient Anxiety, and Caregiver Burden

Patient engagement is evaluated preoperatively, as well as at 14 days (window of 11 to 21 days) and 60 days (window of 46 to 74 days) postoperatively using the Patient Activation Measure (PAM), a validated PRO measure developed to assess the engagement of patients in their care [19]. This measure was selected because it evaluates a key concept of interest in the study, was rigorously developed with qualitative and quantitative methods, and has strong psychometric properties. The PAM yields only a total score that will be used in the analysis. Patients are sent the PAM through the MyMSK patient portal. Patient anxiety is measured daily for 10 days following surgery using three PRO-CTCAE anxiety questions on the Recovery Tracker.

Caregiver burden is evaluated postoperatively at 14 and 60 days (with similar windows) using the Caregiver Reaction Assessment (CRA). The CRA is designed to assess the impact of caregiving on disrupted schedules, self-esteem, and financial and health problems [20]. It was selected because it is well-targeted to the outcomes of interest and was developed among partners of patients with cancer [21]. Caregivers are sent the CRA and a brief demographic questionnaire through REDCap, a secure web application for building and managing online surveys and databases.

Qualitative Patient and Caregiver Interviews

Patient engagement and caregiver burden are also being evaluated using qualitative interviews, with a sample of each of the randomized cohorts. Qualitative interviews are conducted in a subsample of patients and their caregivers throughout the study. Patients and their caregivers from both randomized cohorts are selected, with the goal to interview a heterogeneous patient sample. Participants selected for qualitative interviews represent a range of procedure types and ages. The interviews will continue

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3 until data saturation is reached (i.e., no new themes identified). It is anticipated that data saturation will
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5 be reached after approximately 30 patient and 30 caregiver interviews.
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10 **Data Analysis**

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12 Sample size and power calculations were based on the primary outcome, the difference in
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14 emergency department visits without admission, between the Enhanced Feedback and Team
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16 Monitoring arms. Based on current MSK data, we expect that for every 1,000 eligible patients
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18 treated surgically at JRSC, 69 patients will make emergency department visits. We also estimate
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20 that of these 69 patients, 28 will require readmission, and hence 41 will have visited the emergency
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22 department unnecessarily. The majority of such unnecessary visits are related to concerns about
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24 symptoms, which might be avoided if patients have a better understanding of expected symptom
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26 severity. Using a traditional alpha of 5% and an event rate of 4.1% in the control group, a sample size
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28 of 2,750 will provide a power of 85% to detect a 50% relative risk reduction.
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35 The primary analysis will compare, between groups, the proportion of patients with at least one
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37 emergency department visit without admission within 30 days of surgery by logistic regression with
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39 randomization strata as covariates. A difference between proportions will be calculated along with a
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41 95% confidence interval (CI) by applying the odds ratio from the regression to the event rate in
42
43 the control group. A similar statistical approach will be taken for the proportion of patients referred
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45 to pain management and unplanned clinic visits. For nursing follow-up calls, phone referrals, and
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47 rates of adverse events, we will use both a binary approach (e.g., at least one nursing call vs. no
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49 nursing call) and analysis of count data using negative binomial regression with randomization
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51 strata as covariates. For all binary endpoints, an event will be counted only if it occurs within 30
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53 days of surgery.
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5 For the endpoints of patient engagement and caregiver burden, linear regression with randomization
6 strata as covariates for each subscale separately will be performed. For all analyses, an estimate of
7 the difference between groups along with a 95% CI and a two-sided P value for the null hypothesis of
8 no difference between groups will be reported. For the endpoint of patient anxiety, daily anxiety
9 scores will be entered as a continuous outcome variable into a longitudinal mixed effects model with
10 time, treatment, and treatment-by-time interaction as predictors and randomization strata as
11 covariates. As all data are collected after randomization, both the treatment term and the treatment-
12 by-time interaction term are indicators of a treatment effect.
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25 In exploratory analysis, the mean of each PRO-CTCAE item (0–4 scale) will be compared between
26 groups during the 10-day postoperative daily reporting period using the same longitudinal mixed-
27 effects model described above for anxiety with time, treatment, and treatment-by-time interaction as
28 predictors and randomization strata as covariates. All available data will be used in these models. This
29 likelihood-based approach to the analysis of longitudinal PRO data provides valid estimates of
30 intervention effects in the presence of ignorable missing data and is known to be robust to
31 nonignorable missing data if covariates and previous values of the outcome explain much of the
32 missingness.
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45 Supplemental analysis will also employ longitudinal mixed-effects ordinal logistic models to compare
46 ordinal PRO-CTCAE scores between arms. Qualitative interviews will be recorded and transcribed
47 verbatim. The data will be coded using a line-by-line approach, where all concepts will be labeled by
48 major and minor themes. Coding will take place as soon as possible after an interview so that findings
49 can inform subsequent interviews in an iterative fashion. Codes (i.e., patient quotations) and their major
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3 and minor themes will be organized and analyzed using NVivo qualitative analysis software (QSR
4 International). Patient characteristics (e.g., age, disease condition, procedure) will also be incorporated
5 into the qualitative database to help identify groups that might experience the system differently (e.g.,
6 elderly patients or those with lower education levels).
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11 Approach to Missing Data, Data Safety, Monitoring, and Quality Assurance 12 13

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15 Baseline characteristics between those with and those without missing data will also be compared to
16 assess for bias. The rate of missing data is expected to be low. The main threat to data completion
17 involves the caregiver and patient questionnaires obtained at 2 weeks and 2 months, respectively. In
18 addition to automated electronic reminders, a research assistant follows up with patients who have
19 missing data. Routine data quality reports are generated to assess missing data and inconsistencies.
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21 Accrual rates and accuracy of assessments are monitored periodically throughout the study period.
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23 Data are available immediately when a patient or caregiver completes a survey, which allows for
24 follow-up collection of missing and incorrect data as needed.
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37 Death, life-threatening events, and adverse events that result in inpatient hospitalization (other than
38 for planned procedures or admissions) are classified as serious adverse events (SAEs). All SAEs are
39 reviewed by the Data and Safety Monitoring Committee (DSMC) annually. The DSMC also monitors
40 the study for safety and study conduct to ensure that study conduct, accrual, and participant data
41 collection are adequate.
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50 **ETHICS AND DISSEMINATION** 51

52 The MSK Institutional Review Board reviewed and approved this study. Participants are informed of
53 their right to refuse or withdraw at any point during the study without compromising medical and other
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3 care. They are also assured that all information collected during study participation is considered
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5 confidential. Though there are minimal risks to participants, they are instructed to immediately contact
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7 their physician's office or seek medical attention if they experience distress when they complete the
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9 surveys.
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14 The routine collection of PROs creates new pathways to enhance patient-centered care by fostering
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16 more effective patient-clinician communication, education and expectation setting, and improved
17
18 patient outcomes. Although data collection is currently underway to answer the main study questions,
19
20 this study has also opened new doors to patient engagement in clinical research. By creating dynamic
21
22 partnerships with former patients and caregivers, the study team will ensure that findings are
23
24 understandable not only to scientific and health care audiences, but to patients, caregivers, and their
25
26 advocates. The study team is committed to the rapid dissemination and implementation of study
27
28 results, which will be presented at relevant scientific conferences and will be published in a peer-
29
30 reviewed scientific journal. Findings will also be disseminated to other NCI-designated Cancer Centers by
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32 presenting at the Comprehensive Cancer Center Consortium for Quality Improvement. Further, the
33
34 American College of Surgeons has recently embarked on the development of a national-scale PROs
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36 initiative, into which this system could be embedded.
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3 **Ethics approval:** This study was approved, as described in the text, in May 2017 (with subsequent minor
4 amendments) by the Memorial Sloan Kettering Cancer Center Institutional Review Board (approval
5 number 17-293). Please see the full Institutional Review Board-approved protocol included with
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3 **Patient consent:** Obtained
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6 **Data sharing statement:** Data are available upon request
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9 **ClinicalTrials.gov identifier:** NCT03178045
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FIGURE LEGENDS

Figure 1. Study conceptual model

Figure 2. Example of Enhanced Feedback Report

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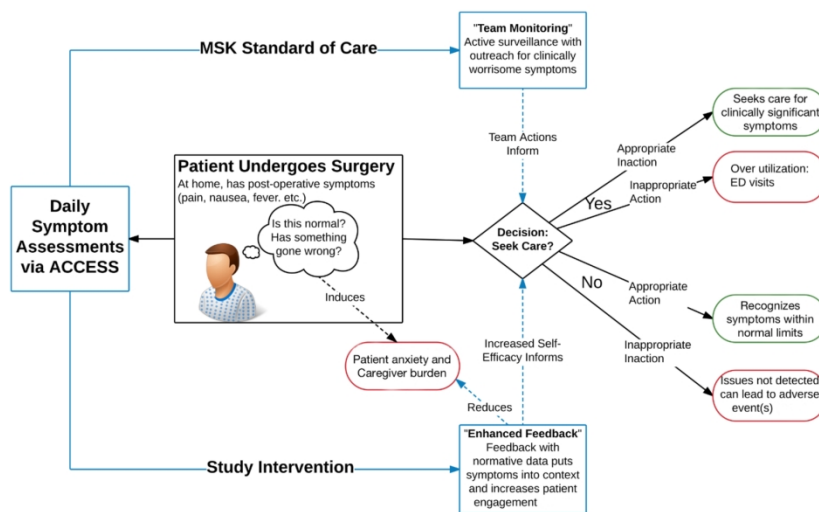


Figure 1. Study conceptual model

173x150mm (300 x 300 DPI)

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Figure 2. Example of Enhanced Feedback Report



SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	Protocol Face Page (pg 1); Full study title also on file with PCORI
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	NCT03178045
	2b	All items from the World Health Organization Trial Registration Data Set	NA
Protocol version	3	Date and version identifier	All pages
Funding	4	Sources and types of financial, material, and other support	Section 13.0.1 (pg 24); Additional info on file with PCORI
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	Protocol Face Page (pg 1); On file with PCORI
	5b	Name and contact information for the trial sponsor	On file with PCORI
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	On file with PCORI

1		5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	Section 13.0 (pg 23); Section 13.0.1 (pg 24); Section 13.1 (pg 25); Section 14.1 (pg 26); Section 14.2 (pgs 26-27);
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9	Introduction			
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11	Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	Section 1.0 (pg 3); Section 2.0 (pg 4); Section 3.0 (pgs 5-8)
12				
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16		6b	Explanation for choice of comparators	Section 3.0 (pgs 5-6); Section 4.1 (pg 9)
17				
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19	Objectives	7	Specific objectives or hypotheses	Section 2.0 (pgs 4-5); Section 3.0 (pg 5); Section 4.1 (pgs 9, 10)
20				
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24	Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	Section 2.0 (pg 4); Section 4.0-4.1 (pgs 8-10)
25				
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29	Methods: Participants, interventions, and outcomes			
30				
31	Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	Section 1.0 (pg 3); Section 5.0 (pg 15); Section 6.0 (pg 15)
32				
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35	Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	Section 5.0 (pg 15)
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39	Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	Section 4.2 (pgs 10-15); Section 6.0 (pgs 15-17)
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1	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	Section 8.0 (pg 17); Section 10.0 (pg 18); Section 14.2.1 (pgs 28-30)	
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5	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	Section 7.0 (pg 17); Section 11.0 (pg 20); Section 13.1 (pg 24-25)	
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9	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	NA	
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11	Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	Section 4.1 (pg 10); Section 4.2 (pgs 13-15); Section 7.0 (pg 17); Section 11.0 (pgs 18-19)
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17	Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Section 4.2 (pgs 12-14); Section 6.0 (pgs 15-16); Section 7.0 (pg 17)
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22	Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	Section 1.0 (pg 3); Section 11.0 (pgs 18-19)
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26	Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	Section 6.0 (pgs 15-16)
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29	Methods: Assignment of interventions (for controlled trials)			
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31	Allocation:			
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33	Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	Section 11.0 (pg 21); Section 12.2 (pg 22)
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1 2 3 4	Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	Section 12.2 (pg 22)
5 6 7	Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	Section 6.0 (pgs 15-16); Section 13.0 (pg 23)
8 9 10	Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	Section 11.0 (pg 21); Section 12.2 (pg 22)
11 12 13 14		17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	NA
15 16	Methods: Data collection, management, and analysis			
17 18 19 20 21 22 23 24 25	Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	Section 4.1 (pg 10); Section 4.2 (pgs 10-15); Section 7.0 (pg 17); Section 13.0 (pg 23); Section 13.1 (pg 24); Section 17.0 (pg 32)
26 27 28 29		18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	Section 11.0 (pg 20); Section 13.1 (pgs 24-25); Section 14.0 (pg 25)
30 31 32 33 34	Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	Section 12.0 (pg 22); Sections 13.0-13.2 (pgs 23-25); Section 14.0 (pg 25-27)
35 36 37	Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	Section 11.0 (pgs 18-19)
38 39 40 41 42		20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	Section 11.0 (pgs 19-21)

	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	Section 11.0 (pgs 20, 21)
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	Section 13.2 (pg 25)
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	NA
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	Section 14.2 (pgs 26-28)
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	Section 13.0 (pgs 23-24); Section 13.1 (pgs 24-25); Section 13.2 (pg 25)
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	Section 13.0.1 (pg 24)
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	Section 13.0.1 (pg 24) applies to amendments as well as original protocol; On file with PCORI
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	Section 6.0 (pg 16); Section 12.1 (pg 22)
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	NA

1 2 3	Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	Section 14.0 (pgs 25-26); Section 15.0 (pgs 28-30)
4 5 6	Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	On file with PCORI
7 8 9 10	Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	Section 13.0 (pg 23); Section 13.0.1 (pg 24); On file with PCORI
11 12 13 14	Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	Section 8.0 (pg 17); Section 14.0 (pg 26)
15 16 17 18	Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	On file with PCORI
19 20		31b	Authorship eligibility guidelines and any intended use of professional writers	NA
21 22 23 24		31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	NA
25 26	Appendices			
27 28 29 30 31 32 33	Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Section 17.0 (pg 32); All supplemental IRB-approved study documents (i.e. appendices) can be provided upon request.
34 35 36 37	Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	NA

38 *It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items.
39 Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons
40 ["Attribution-NonCommercial-NoDerivs 3.0 Unported"](https://creativecommons.org/licenses/by-nc-nd/3.0/) license.
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BMJ Open

Ambulatory Cancer Care Electronic Symptom Self-Reporting (ACCESS) for Surgical Patients – A Randomized Controlled Trial Protocol

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2019-030863.R1
Article Type:	Protocol
Date Submitted by the Author:	26-Jul-2019
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Primary Subject Heading:	Patient-centred medicine
Secondary Subject Heading:	Surgery, Oncology, Health informatics
Keywords:	SURGERY, ONCOLOGY, Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Health informatics < BIOTECHNOLOGY & BIOINFORMATICS, Patient-reported outcomes

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3 **Ambulatory Cancer Care Electronic Symptom Self-Reporting (ACCESS) for Surgical Patients – A**
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5 **Randomized Controlled Trial Protocol**
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10 **Cara Stabile,¹ Larissa K Temple,² Jessica S Ancker,³ Ethan Basch,⁴ Jeanne Carter,^{5,6,7} Magen Miranda,⁸**

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ABSTRACT

Introduction:

An increasing proportion of cancer surgeries are ambulatory procedures requiring a stay of one day or less in the hospital. Providing patients and their caregivers with ongoing, real-time support after discharge aids delivery of high-quality postoperative care in this new health care environment. Despite abundant evidence that patient self-reporting of symptoms improves quality of care, the most effective way to monitor and manage this self-reported information is not known.

Methods and analysis:

This is a two-armed randomized, controlled trial evaluating two approaches to the management of patient-reported data: (1) Team Monitoring, symptom monitoring by the clinical team, with nursing outreach if symptoms exceed normal limits, or (2) Enhanced Feedback, real-time feedback to patients about expected symptom severity, with patient-activated care as needed.

Patients with breast, gynecologic, urologic, and head and neck cancer undergoing ambulatory cancer surgery (n=2,750) complete an electronic survey for up to 30 days after surgery that includes items from a validated instrument developed by the National Cancer Institute, the Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE). Information provided to patients in the Enhanced Feedback group is procedure-specific and based on updated PRO-CTCAE data from previous patients. Qualitative interviews are also performed. The primary study outcomes assess unplanned emergency department visits and symptom-triggered interventions (e.g., nursing calls and pain management referrals) within 30 days, and secondary outcomes assess the patient and caregiver experience (i.e., patient engagement, patient anxiety, and caregiver burden).

Ethics and dissemination:

This study is approved by the Institutional Review Board at Memorial Sloan Kettering Cancer Center.

The relationships between the study team and stakeholders will be leveraged to disseminate study findings. Findings will be relevant in designing future coordinated care models targeting improved health care quality and patient experience.

Trial Registration: NCT03178045

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This study is a large randomized, controlled trial that will help determine an effective mechanism for patient-reported data collection and symptom monitoring after ambulatory surgery.
- Optimal integration of self-reported symptom data into health care systems has the potential to improve surgical outcomes and enhance patient-clinician communication.
- Patient engagement is a major driver of study design, implementation, and future dissemination, as this study includes former patients and caregivers as members of the core study team.
- The study population consists largely of patients with high health and computer literacy, which may be a potential threat to external validity.
- While the use of electronic patient-reported symptom monitoring, the control arm of this study, is not standard for most patients undergoing postoperative care worldwide and may limit the immediate generalizability of the results, this study may provide important guidance for the development of such systems in the future.

INTRODUCTION

Increasing numbers of surgical procedures, including major cancer procedures (e.g., mastectomies, hysterectomies, and prostatectomies), are being performed as short-stay (one midnight) or ambulatory surgeries [1,2,3]. Although there are many advantages to shorter hospital stays, this model adds complexities to the delivery of high-quality, patient-centered care, particularly for cancer patients and their caregivers, who are often still struggling with a new cancer diagnosis. Patients often leave the surgical center while experiencing symptoms that were previously attended to by the health care team [4]. Managing symptoms at home can be challenging for patients and caregivers who may have difficulty distinguishing normal and expected symptoms from potentially serious adverse events [5]. Without information and risk awareness, patients may delay seeking care, with severe consequences, or they may experience unnecessary anxiety and seek unnecessary care [6]. In focus groups and interviews conducted to inform the design of the current study, patients and caregivers conveyed feelings of stress and reported feeling unprepared to interpret and monitor postoperative symptoms.

Patient-reported outcome (PRO) measurement is rapidly becoming a standard of care throughout medicine that can aid in monitoring symptom burden. However, the best way to integrate and act on patient-reported data is unclear [7]. There is abundant and broad evidence that PRO data can improve communication with the clinical team, symptom control, quality of life, and patient satisfaction [8-10]. One large randomized trial comparing routine collection of PROs with usual care during chemotherapy showed that among patients who received the PROs intervention, quality of life improved (34% vs. 18%), and these patients were less likely to be seen in the emergency department (34% vs. 41%; $P = 0.02$) or hospitalized (45% vs. 49%; $P = 0.08$) [7]. Although progress has been made to better understand how symptom data might be best incorporated into clinical care among non-surgical patients, little work has been done among patients having surgery. Routine

1
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3 monitoring of symptoms in surgical patients, with outreach by the clinical team when severity
4 exceeds an expected range, may identify problems at an earlier stage and avoid or minimize adverse
5 events. Providing patients with feedback about expected symptom severity and allowing them to
6 activate care as needed may allow for the identification of these adverse events before they
7 progress, while also decreasing patient anxiety and unplanned care, such as unnecessary visits to the
8 emergency department. It is unknown whether providing this kind of feedback to patients would
9 affect care patterns and patient outcomes. This evidence gap provides motivation for the design of
10 the current study as well as the selection of its outcome measures.
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23 This randomized controlled trial will assess two approaches to the management of patient-reported
24 symptoms and their potential impact in decreasing emergency department visits, patient anxiety,
25 and caregiver burden up to 30 days after ambulatory cancer surgery. One approach is called Team
26 Monitoring, in which symptoms are monitored by the clinical team, with nursing outreach if
27 symptoms exceed normal limits. The second approach is called Enhanced Feedback, which provides
28 patients with real-time feedback about expected symptom severity, with patient-activated care as
29 needed. The study aligns with the Institute of Medicine's goal of determining how to deliver an ideal
30 patient care experience that is safe, effective, efficient, patient-centered, timely, and equitable [11-
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45 The study model (Figure 1) is predicated on the hypothesis that daily, patient-driven symptom reporting
46 with normative data feedback about expected symptom burden relative to previous patient reports
47 (Enhanced Feedback) will increase patients' self-efficacy [14] and their confidence that they can manage
48 their symptoms during the recovery period [15]. This has been shown to be a predictor of decreased
49 symptoms and better physical function [15,16]. On the basis of this model, patients may avoid
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3 unnecessary emergency department visits by better understanding expected symptoms and by
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5 achieving more efficient and effective communication with their health care team.
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10 The study will garner important information for incorporating PROs into postoperative care and aiding in
11
12 the development of tailored perioperative care pathways for patients with cancer. The key lessons
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14 learned may be used to support the implementation of strategies for population health management for
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16 non-cancer treatments that can also cause burdensome symptoms. Utilizing a similar patient-reporting
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18 mechanism may benefit smaller outpatient facilities that do not have the personnel resources necessary
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20 to provide intensive monitoring of patient symptoms. It is expected that this study will also be highly
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22 relevant in designing coordinated care models targeting improved health care value, such as the
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24 Oncology Care Model and the Perioperative Surgical Home.
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27 28 29 30 **METHODS AND ANALYSIS**

31 32 33 **Study Design**

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35 This is a parallel group randomized, controlled trial with 1:1 procedure-stratified randomization
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37 between two arms, Team Monitoring and Enhanced Feedback. The study design follows Patient-
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39 Centered Outcomes Research Institute (PCORI) standards, including patient engagement, research
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41 methods, data integrity and analysis (including stratification by surgical procedure), handling of missing
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43 data, and heterogeneity of treatment effect.
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48 49 **Patient and Public Involvement**

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51 The study team recruited a group of committed stakeholders that include clinicians, researchers,
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53 hospital leadership, and advocates from patient and caregiver support groups, as well as former patients
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55 and caregivers who join the team as Patient Partners. The Patient Partners have been engaged since the
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3 beginning of study development, and they offer their experiences to help inform the design, conduct,
4 and dissemination of the research. The Patient Partners and study stakeholders contributed to the
5 development of data collection tools (including the enhanced feedback reports given to patients) and to
6 the creation of study information sheets, recruitment letters, and qualitative interview guides. They also
7 helped to refine recruitment initiatives that ensured minimal burden to participants, which resulted in
8 increased enrollment over the first year of recruitment. Through their engagement, the study will
9 ultimately be more patient-centered and will lead to a greater application of results by the larger health
10 care community.
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23 **Objectives and Scientific Aims**

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25 The primary study outcome is to determine if providing enhanced reporting to patients regarding their
26 symptoms will impact potentially avoidable urgent care and emergency department visits (i.e., those
27 that do not result in hospital admission) up to 30 days after ambulatory cancer surgery. In addition, we
28 will examine readmissions and symptom-triggered interventions (pain management referrals, nursing
29 calls) up to 30 days after ambulatory cancer surgery. Secondary outcomes include patient engagement,
30 patient anxiety, and caregiver burden, using validated PRO measures and qualitative interviews.
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41 **Cohort 1: Team Monitoring**

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43 Team Monitoring is the current standard of care for patients at the Josie Robertson Surgical Center
44 (JRSC) at Memorial Sloan Kettering Cancer Center (MSK). Patients report their symptoms via an
45 electronic questionnaire called the Recovery Tracker, delivered through an in-house informatics
46 platform known as the ambulatory cancer care electronic symptom self-reporting (ACCESS) system.
47 The health care team receives portal-secure message alerts if patients report symptoms above a
48 specified threshold and contact the patient by phone during business hours. Given the need for real-
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3 time feedback for some symptoms, patients who report very severe symptoms receive a bold red
4 alert instructing them to immediately call the office (or the call team outside business hours) or seek
5 medical attention. The response thresholds (i.e., when to give which alert) for each question are set
6 individually and have been refined based on feedback from the clinical teams (i.e., surgeons and
7 office practice nurses). For example, mild-moderate pain on three days after surgery is expected, but
8 moderate shortness of breath three days after surgery is not expected and potentially concerning.
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19 **Cohort 2: Enhanced Feedback**

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21 In the Enhanced Feedback cohort, the ACCESS system provides tailored normative data visualizations
22 that offer context and education to patients regarding expected symptom severity (Figure 2). This
23 Enhanced Feedback report was generated using an iterative rapid application development process by
24 the research team in collaboration with MSK surgeons and nurses, former patients and caregivers, the
25 study's Patient Partners, and patient advocates from cancer support groups. Details regarding the
26 optimization of the feedback report are described elsewhere [17].
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37 The feedback report consists of periodically updated PRO data from previous patients that are stratified
38 by surgical procedure and postoperative date. As a result, patients can see their recovery trajectories
39 relative to others who have undergone the same procedure. Care is "patient-activated" in that patients
40 use the information about expected symptoms to decide whether they should call the care team, for
41 instance, if they experience symptoms that are more severe or more prolonged than expected. Similar
42 to the Team Monitoring cohort, patients who report very severe symptoms are instructed to
43 immediately contact their physician's office, and the care team receives an alert. Alerts to the clinical
44 team can only be monitored during business hours, so for care after hours, all patients must call the
45 doctor on call.
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Participants, Setting, and Recruitment

Patients older than 18 years who are scheduled for ambulatory cancer surgery at the JRSC at MSK are eligible for study participation. Disease types include breast, gynecologic, urologic, and head and neck cancers or benign tumors. Patients must be able to access a computer, tablet, or mobile phone to complete the electronic surveys. Caregivers of eligible patients are also eligible for study participation; they must be older than 18 years, be willing to provide an email address, and have access to a computer, tablet, or mobile phone to complete electronic surveys. A total of 2,750 patients and 1,375 caregivers will be recruited for this study over a period of three years. Enrollment began in August 2017 and is projected to end in September 2019.

Eligible patients receive written educational materials that describe the study via the MyMSK patient portal, email, or a letter mailed to their home. The study team then attempts to contact patients by phone before surgery to obtain their verbal consent to participate in the study. If the study team is unable to contact the patient prior to the day of surgery, the patient is approached at one of their clinic appointments or in the waiting room when they arrive for surgery. At the time of consent, patients are also asked to identify a caregiver who will be actively involved in their recovery. If permitted by the patient, the study team obtains the caregiver's contact information to invite them to participate in the study as well.

Randomization is implemented through the MSK Clinical Research Database, a fully secure, password-protected database that ensures full allocation concealment. It will be performed within one week of the patient's surgical visit. Randomization is stratified by procedure (e.g., breast: mastectomy [with or

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3 without sentinel and axillary nodal dissection], tissue expander placement, or other; gynecologic:
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5 laparoscopic or robotic procedure, laparotomy, or other; urologic: laparoscopic or robotic
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7 prostatectomy, laparoscopic or robotic partial or total nephrectomy, laparotomy, or other; head and
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9 neck: thyroidectomy) and will be implemented by randomly permuted blocks of random length. The
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11 trial will not be blinded, as it relies on patient knowledge (i.e., how a patient's scores compare with
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13 other patients' scores) as a key part of the intervention.
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16 17 18 **Study Measures and Data Collection**

19 **The ACCESS System and Recovery Tracker**

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21 The ACCESS system is designed to enable real-time postoperative symptom monitoring. Patients
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23 undergoing surgery at the JRSC, an ambulatory surgery center at MSK, are invited to complete the
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25 Recovery Tracker through the MyMSK patient portal. The interface was built with a responsive
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27 design, so patients can complete the Recovery Tracker via computers, tablets, or mobile phones.
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29 Patients are prompted to report on 11 items adapted from a validated symptom assessment
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31 instrument, the National Cancer Institute (NCI)'s Patient-Reported Outcomes version of the Common
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33 Terminology for Adverse Events (PRO-CTCAE) [18], three additional surgical symptom questions, and
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35 two questions about seeking urgent care or a doctor during the first 10 days after surgery. Over the
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37 following 20 days, patients have the option to complete additional surveys on demand, but they are
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39 not prompted to do so. Patients, caregivers, nurses, surgeons, and anesthesiologists participated in
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41 the selection of these items. See Table 1 for the study assessment schedule.
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Table 1. Study assessment schedule

		Preoperative (pre-op) time point	Postoperative time point			
Item	# of Items	Pre-Op (day of consent – POD1)	POD 1–10	POD14 (+7/-3 days)	POD30 (+/- 10 days)	POD60 (+/- 14 days)
Patient						
Recovery Tracker (including PRO- CTCAE symptoms and anxiety items, and additional questions)	20		Daily		Available to complete, if desired (POD11-30)	
Emergency Department Visits					X	
Readmission					X	
Adverse Events					X	
Patient	10	X		X		X

Activation Measure						
Patient Interviews					X	
Caregiver						
Caregiver Reaction Assessment and Demographics*	24			X		X
Caregiver Interviews					X	

POD, postoperative day

*Caregiver demographics collected include date of birth, sex, race/ethnicity, education level, employment status, relationship to patient, and basic caregiving information. Demographic information is collected at POD14 (+7/-3 days).

Emergency Department Visits and Adverse Events

The study team will evaluate the frequency of urgent care center visits, readmissions, and symptom-triggered interventions (e.g., pain management referrals, nursing calls triggered by alerts generated by the ACCESS system or initiated by the patient) for 30 days after surgery. These data are available as structured fields in the MSK enterprise data warehouse and will be audited through chart review of randomly selected patient records.

Patient Engagement, Patient Anxiety, and Caregiver Burden

Patient engagement is evaluated preoperatively, as well as at 14 days (window of 11 to 21 days) and 60 days (window of 46 to 74 days) postoperatively using the Patient Activation Measure (PAM), a validated PRO measure developed to assess the engagement of patients in their care [19]. This measure was selected because it evaluates a key concept of interest in the study, was rigorously developed with qualitative and quantitative methods, and has strong psychometric properties. The PAM yields only a total score that will be used in the analysis. Patients are sent the PAM through the MyMSK patient portal. Patient anxiety is measured daily for 10 days following surgery using three PRO-CTCAE anxiety questions on the Recovery Tracker.

Caregiver burden is evaluated postoperatively at 14 and 60 days (with similar windows) using the Caregiver Reaction Assessment (CRA). The CRA is designed to assess the impact of caregiving on disrupted schedules, self-esteem, and financial and health problems [20]. It was selected because it is well-targeted to the outcomes of interest and was developed among partners of patients with cancer [21]. Caregivers are sent the CRA and a brief demographic questionnaire through REDCap, a secure web application for building and managing online surveys and databases.

Qualitative Patient and Caregiver Interviews

Patient engagement and caregiver burden are also being evaluated using qualitative interviews, with a sample of each of the randomized cohorts. Qualitative interviews are conducted in a subsample of patients and their caregivers throughout the study. Patients and their caregivers from both randomized cohorts are selected, with the goal to interview a heterogeneous patient sample. Participants selected for qualitative interviews represent a range of procedure types and ages. The interviews will continue

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3 until data saturation is reached (i.e., no new themes identified). It is anticipated that data saturation will
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5 be reached after approximately 30 patient and 30 caregiver interviews.
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10 **Data Analysis**

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12 Sample size and power calculations were based on the primary outcome, the difference in
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14 emergency department visits without admission, between the Enhanced Feedback and Team
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16 Monitoring arms. Based on current MSK data, we expect that for every 1,000 eligible patients
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18 treated surgically at JRSC, 69 patients will make emergency department visits. We also estimate
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20 that of these 69 patients, 28 will require readmission, and hence 41 will have visited the emergency
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22 department unnecessarily. The majority of such unnecessary visits are related to concerns about
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24 symptoms, which might be avoided if patients have a better understanding of expected symptom
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26 severity. Using a traditional alpha of 5% and an event rate of 4.1% in the control group, a sample size
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28 of 2,750 will provide a power of 85% to detect a 50% relative risk reduction.
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35 The primary analysis will compare, between groups, the proportion of patients with at least one
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37 emergency department visit without admission within 30 days of surgery by logistic regression with
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39 randomization strata as covariates. A difference between proportions will be calculated along with a
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41 95% confidence interval (CI) by applying the odds ratio from the regression to the event rate in
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43 the control group. A similar statistical approach will be taken for the proportion of patients referred
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45 to pain management and unplanned clinic visits. For nursing follow-up calls, phone referrals, and
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47 rates of adverse events, we will use both a binary approach (e.g., at least one nursing call vs. no
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49 nursing call) and analysis of count data using negative binomial regression with randomization
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51 strata as covariates. For all binary endpoints, an event will be counted only if it occurs within 30
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53 days of surgery.
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5 For the endpoints of patient engagement and caregiver burden, linear regression with randomization
6 strata as covariates for each subscale separately will be performed. For all analyses, an estimate of
7 the difference between groups along with a 95% CI and a two-sided P value for the null hypothesis of
8 no difference between groups will be reported. For the endpoint of patient anxiety, daily anxiety
9 scores will be entered as a continuous outcome variable into a longitudinal mixed effects model with
10 time, treatment, and treatment-by-time interaction as predictors and randomization strata as
11 covariates. As all data are collected after randomization, both the treatment term and the treatment-
12 by-time interaction term are indicators of a treatment effect.
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25 In exploratory analysis, the mean of each PRO-CTCAE item (0–4 scale) will be compared between
26 groups during the 10-day postoperative daily reporting period using the same longitudinal mixed-
27 effects model described above for anxiety with time, treatment, and treatment-by-time interaction as
28 predictors and randomization strata as covariates. All available data will be used in these models. This
29 likelihood-based approach to the analysis of longitudinal PRO data provides valid estimates of
30 intervention effects in the presence of ignorable missing data and is known to be robust to
31 nonignorable missing data if covariates and previous values of the outcome explain much of the
32 missingness.
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45 Supplemental analysis will also employ longitudinal mixed-effects ordinal logistic models to compare
46 ordinal PRO-CTCAE scores between arms. Qualitative interviews will be recorded and transcribed
47 verbatim. The data will be coded using a line-by-line approach, where all concepts will be labeled by
48 major and minor themes. Coding will take place as soon as possible after an interview so that findings
49 can inform subsequent interviews in an iterative fashion. Codes (i.e., patient quotations) and their major
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3 and minor themes will be organized and analyzed using NVivo qualitative analysis software (QSR
4 International). Patient characteristics (e.g., age, disease condition, procedure) will also be incorporated
5 into the qualitative database to help identify groups that might experience the system differently (e.g.,
6 elderly patients or those with lower education levels).
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11 Approach to Missing Data, Data Safety, Monitoring, and Quality Assurance

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16 Baseline characteristics between those with and those without missing data will also be compared to
17 assess for bias. The rate of missing data is expected to be low. The main threat to data completion
18 involves the caregiver and patient questionnaires obtained at 2 weeks and 2 months, respectively. In
19 addition to automated electronic reminders, a research assistant follows up with patients who have
20 missing data. Routine data quality reports are generated to assess missing data and inconsistencies.
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Death, life-threatening events, and adverse events that result in inpatient hospitalization (other than
for planned procedures or admissions) are classified as serious adverse events (SAEs). All SAEs are
reviewed by the Data and Safety Monitoring Committee (DSMC) annually. The DSMC also monitors
the study for safety and study conduct to ensure that study conduct, accrual, and participant data
collection are adequate.

ETHICS AND DISSEMINATION

The MSK Institutional Review Board reviewed and approved this study. Participants are informed of
their right to refuse or withdraw at any point during the study without compromising medical and other

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3 care. They are also assured that all information collected during study participation is considered
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5 confidential. Though there are minimal risks to participants, they are instructed to immediately contact
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7 their physician's office or seek medical attention if they experience distress when they complete the
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9 surveys.
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14 The routine collection of PROs creates new pathways to enhance patient-centered care by fostering
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16 more effective patient-clinician communication, education and expectation setting, and improved
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18 patient outcomes. Although data collection is currently underway to answer the main study questions,
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20 this study has also opened new doors to patient engagement in clinical research. By creating dynamic
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22 partnerships with former patients and caregivers, the study team will ensure that findings are
23
24 understandable not only to scientific and health care audiences, but to patients, caregivers, and their
25
26 advocates. The study team is committed to the rapid dissemination and implementation of study
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28 results, which will be presented at relevant scientific conferences and will be published in a peer-
29
30 reviewed scientific journal. Findings will also be disseminated to other NCI-designated Cancer Centers by
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32 presenting at the Comprehensive Cancer Center Consortium for Quality Improvement. Further, the
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34 American College of Surgeons has recently embarked on the development of a national-scale PROs
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36 initiative, into which this system could be embedded.
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3 **Ethics approval:** This study was approved, as described in the text, in May 2017 (with subsequent minor
4 amendments) by the Memorial Sloan Kettering Cancer Center Institutional Review Board (approval
5 number 17-293). Please see the full Institutional Review Board-approved protocol included with
6 submission.
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43 **Competing interests:** CS, LKT, JSA, JC, MM, DS, PS, AV, BAS, AP declare that they have no competing
44 interests. EB declares the following (please see ICMJE form for more information): Employer: University
45 of North Carolina; Research funding: NCI, PCORI; Editorial Board: Journal of the American Medical
46 Association (JAMA); Consultant on research projects: Memorial Sloan Kettering Cancer Center, Dana-
47 Farber Cancer Institute, Centers for Medicare & Medicaid Services, Research Triangle Institute; Scientific
48 advisor: Sivan Healthcare, Self Care Catalysts, Carevive
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3 **Patient consent:** Obtained
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6 **Data sharing statement:** Data are available upon request
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9 **ClinicalTrials.gov identifier:** NCT03178045
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For peer review only

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FIGURE LEGENDS

Figure 1. Study conceptual model

Figure 2. Example of Enhanced Feedback Report

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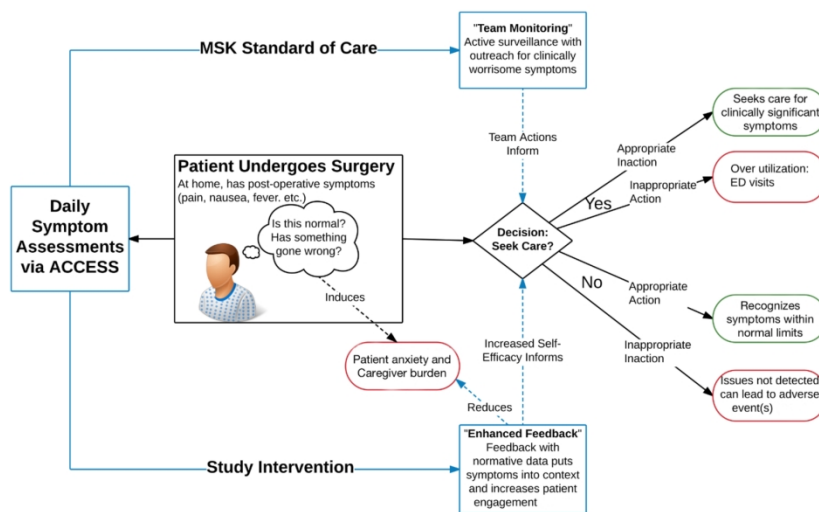


Figure 1. Study conceptual model

173x150mm (300 x 300 DPI)

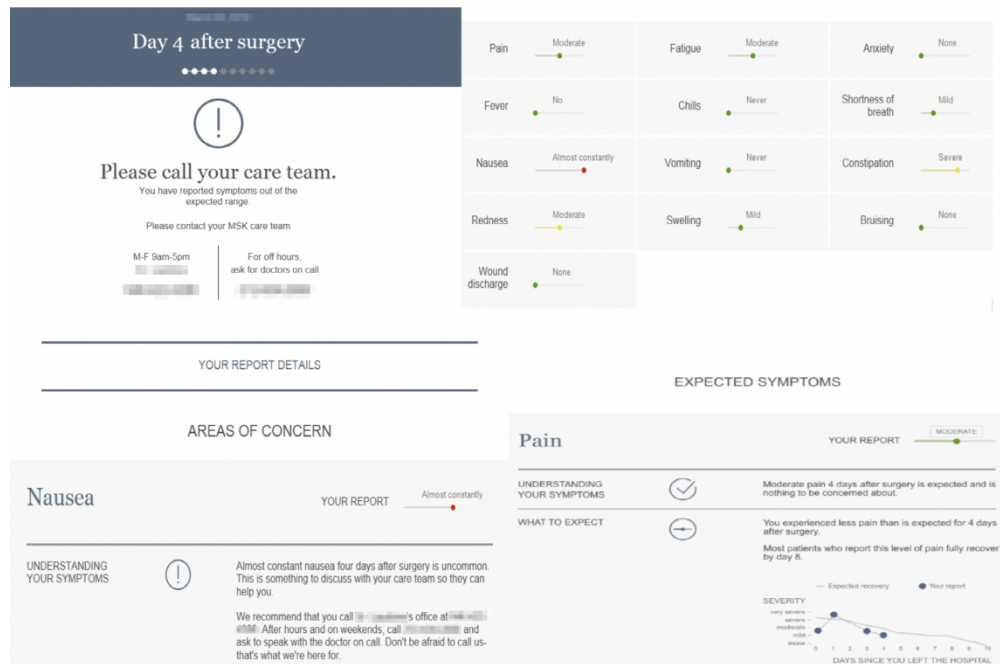


Figure 2. Example of Enhanced Feedback Report



SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	Protocol Face Page (pg 1); Full study title also on file with PCORI
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	NCT03178045
	2b	All items from the World Health Organization Trial Registration Data Set	NA
Protocol version	3	Date and version identifier	All pages
Funding	4	Sources and types of financial, material, and other support	Section 13.0.1 (pg 24); Additional info on file with PCORI
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	Protocol Face Page (pg 1); On file with PCORI
	5b	Name and contact information for the trial sponsor	On file with PCORI
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	On file with PCORI

1		5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	Section 13.0 (pg 23); Section 13.0.1 (pg 24); Section 13.1 (pg 25); Section 14.1 (pg 26); Section 14.2 (pgs 26-27);
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9	Introduction			
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11	Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	Section 1.0 (pg 3); Section 2.0 (pg 4); Section 3.0 (pgs 5-8)
12				
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16		6b	Explanation for choice of comparators	Section 3.0 (pgs 5-6); Section 4.1 (pg 9)
17				
18				
19	Objectives	7	Specific objectives or hypotheses	Section 2.0 (pgs 4-5); Section 3.0 (pg 5); Section 4.1 (pgs 9, 10)
20				
21				
22				
23				
24	Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	Section 2.0 (pg 4); Section 4.0-4.1 (pgs 8-10)
25				
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29	Methods: Participants, interventions, and outcomes			
30				
31	Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	Section 1.0 (pg 3); Section 5.0 (pg 15); Section 6.0 (pg 15)
32				
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35	Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	Section 5.0 (pg 15)
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39	Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	Section 4.2 (pgs 10-15); Section 6.0 (pgs 15-17)
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1	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	Section 8.0 (pg 17); Section 10.0 (pg 18); Section 14.2.1 (pgs 28-30)	
2				
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5	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	Section 7.0 (pg 17); Section 11.0 (pg 20); Section 13.1 (pg 24-25)	
6				
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9	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	NA	
10				
11	Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	Section 4.1 (pg 10); Section 4.2 (pgs 13-15); Section 7.0 (pg 17); Section 11.0 (pgs 18-19)
12				
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17	Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Section 4.2 (pgs 12-14); Section 6.0 (pgs 15-16); Section 7.0 (pg 17)
18				
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22	Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	Section 1.0 (pg 3); Section 11.0 (pgs 18-19)
23				
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26	Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	Section 6.0 (pgs 15-16)
27				
28				
29	Methods: Assignment of interventions (for controlled trials)			
30				
31	Allocation:			
32				
33	Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	Section 11.0 (pg 21); Section 12.2 (pg 22)
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1 2 3 4	Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	Section 12.2 (pg 22)
5 6 7	Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	Section 6.0 (pgs 15-16); Section 13.0 (pg 23)
8 9 10 11	Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	Section 11.0 (pg 21); Section 12.2 (pg 22)
12 13 14		17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	NA
15 16	Methods: Data collection, management, and analysis			
17 18 19 20 21 22 23 24 25	Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	Section 4.1 (pg 10); Section 4.2 (pgs 10-15); Section 7.0 (pg 17); Section 13.0 (pg 23); Section 13.1 (pg 24); Section 17.0 (pg 32)
26 27 28 29		18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	Section 11.0 (pg 20); Section 13.1 (pgs 24-25); Section 14.0 (pg 25)
30 31 32 33 34	Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	Section 12.0 (pg 22); Sections 13.0-13.2 (pgs 23-25); Section 14.0 (pg 25-27)
35 36 37	Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	Section 11.0 (pgs 18-19)
38 39 40 41 42		20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	Section 11.0 (pgs 19-21)

	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	Section 11.0 (pgs 20, 21)
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	Section 13.2 (pg 25)
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	NA
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	Section 14.2 (pgs 26-28)
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	Section 13.0 (pgs 23-24); Section 13.1 (pgs 24-25); Section 13.2 (pg 25)
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	Section 13.0.1 (pg 24)
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	Section 13.0.1 (pg 24) applies to amendments as well as original protocol; On file with PCORI
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	Section 6.0 (pg 16); Section 12.1 (pg 22)
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	NA

1 2 3	Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	Section 14.0 (pgs 25-26); Section 15.0 (pgs 28-30)
4 5 6	Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	On file with PCORI
7 8 9 10	Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	Section 13.0 (pg 23); Section 13.0.1 (pg 24); On file with PCORI
11 12 13 14	Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	Section 8.0 (pg 17); Section 14.0 (pg 26)
15 16 17 18	Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	On file with PCORI
19 20		31b	Authorship eligibility guidelines and any intended use of professional writers	NA
21 22 23 24		31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	NA
25 26	Appendices			
27 28 29 30 31 32 33	Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Section 17.0 (pg 32); All supplemental IRB-approved study documents (i.e. appendices) can be provided upon request.
34 35 36 37	Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	NA

38 *It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items.
39 Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons
40 ["Attribution-NonCommercial-NoDerivs 3.0 Unported"](https://creativecommons.org/licenses/by-nc-nd/3.0/) license.
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