A feasibility trial using remote patient-reported outcomes and wearable technology-reported step data to compare engagement, utilization, and functional status in patients with incurable lung and gastrointestinal cancers

Study Protocol

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1. Abstract

Telemedicine allows clinicians to utilize modern telecommunication technology to provide healthcare services to patients including remote symptom monitoring. Given the spread of COVID-19 both locally and globally, is crucial to adapt accordingly in order to safely provide vulnerable cancer patient populations with optimal care while minimizing risk of exposure to COVID-19. In this study, we will utilize remote monitoring of patients with cancer via weekly patient-reported outcome (PRO) collection through the Way to Health (W2H) smartphone application and step data through wearable Fitbit devices. Patients with incurable lung and gastrointestinal cancers will be recruited based on whether they receive their care in-clinic or remotely. They will respond to weekly phone-based symptom surveys and wear Fitbits that track step data. This data will be collated in a Palliative Care Assessment Dashboard (PROStep Dashboard) sent to clinicians prior to each oncology visit to help inform patient management. In this feasibility study, two arms of patients will be monitored with symptom surveys and Fitbits; the study will randomize these patients to either 1) receive text feedback or 2) receive no text feedback. A third arm of patients will be randomized to receive no feedback, symptom surveys, or Fitbit device. Clinicians for patients in each arm will receive the PROstep Dashboard. The study will determine feasibility of this monitoring approach, and compare patient adherence to symptom surveys and step data collection between the two intervention arms.

2. Overall objectives

The objective of the study is to assess the feasibility of remote symptom and activity monitoring of patients with incurable lung and gastrointestinal cancers, determine the clinical utility of these remote monitoring tools and compare adherence to the intervention based upon the feedback that patients receive.

3. Outcomes

3.1 Primary outcome

Patient utility surveys will use a 5-point Likert scale for responses scored 1-5. The two co-primary outcomes will compare the scores for the following two questions, **measured at 6 months (or 3 months if the patient did not complete their 6 month survey)**, between **intervention patients** (Arms B + C) and **control patients** (Arm A).

- How well do you feel your oncology team understands your symptoms (e.g. nausea, vomiting, weight loss, etc.)?
- How well do you feel your oncology team understands your activity level and ability to function?

3.2 Secondary outcomes

The following secondary outcome will compare the same questions:

- **Measured at 3 months**, between **intervention patients** (Arms B + C) and **control patients** (Arm A).

We will compare cumulative adherence for patients in the intervention group (arm B and arm C). Each week, adherence will be defined as each week where the patient submits the weekly survey (i.e. adherence to PRO) and has step data for 4 of 7 days of the week (i.e. adherence to Fitbit platform), divided by the total number of weeks that the patient is enrolled in the trial.

- Comparison of mean patient adherence at three months for patients in arm B vs arm C
- Comparison of mean patient adherence at six months for patients in arm B vs arm C

We will analyze trends in the PROStep data (PRO surveys and Fitbit step data).

- Comparison of PRO scores between patients in arm B vs. arm C. These will be measured using mean and median composite symptom scores as reported by patients in their PRO surveys. The composite score is the sum of the scores for each domain in the PRO survey, and the mean or median composite symptom score is the mean or median of all composite scores collected during the study.
- Fitbit step data will be measured using mean daily step counts for all days in which Fitbit data is collected. Days where the patient does not have Fitbit data will be excluded from these calculations.

3.3 Exploratory outcomes

- The following exploratory outcomes will make the following comparisons for responses to the two questions in the primary outcomes:
    - Measured at 6 months (or 3 months if the patient did not complete their 6 month survey)
        - Between Arm B and Arm A
        - Between Arm C and Arm A
        - Between all Arms.
    - Measured at 3 months:
        - Between Arm B and Arm A
        - Between Arm C and Arm A
        - Between all Arms.
- Number of palliative care consults
- Number of documented advanced care planning (ACP) notes
- Number of documented serious illness conversations (SIC)
- Correlation between step, heart rate, distance, pace, elevation and sleep data trends, patient reported outcomes, patient and clinician ECOG assessment, and patient hospitalization and survival

- We will report descriptive statistics for the remaining questions on the patient utility surveys (mean and standard deviation) followed by t-tests between each individual arm and between all intervention patients (Arms B + C) and control patients (Arm A). Patient utility surveys include the following (the intervention arms receiving additional questions):
    - How well do you feel that your oncology team has addressed your symptoms?
    - How well do you feel that your oncology team has addressed your activity level and ability to function?
    - I feel that the PROStep data prompted better communication with my oncology team about my symptoms. **(arm b and arm c)**
    - I feel that the PROStep data prompted better communication with my oncology team about my activity level. **(arm b and arm c)**
    - My oncology team has discussed the PROStep data during my appointments. **(arm b and arm c)**
    - I feel that the PROStep data changed how my oncology team addressed my symptoms and/or ability to function. **(arm b and arm c)**
    - I feel that the PROStep data changed my oncology team's treatment of my cancer, such as decisions to start, continue, or stop cancer treatments like chemotherapy. **(arm b and arm c)**
    - I feel that the PROStep data triggered discussions with my oncology team about my prognosis or goals of my cancer care. **(arm b and arm c)**
    - I feel that regularly wearing my Fitbit is burdensome. **(arm b and arm c)**
    - I feel completing my weekly symptom surveys is burdensome. **(arm b and arm c)**
    - On a scale of 0-10, how likely is it that you would recommend PROStep to other patients with cancer? **(arm b and arm c)**
- The utility to clinicians will be measured using survey data at three and six months. These similarly use a 5-point Likert scale (1-5) and we will report descriptive statistics for this survey data. Clinician survey questions include:
    - To what extent was the information provided in the PROstep Dashboard helpful for you to better understand:
        - your patient's symptoms?
        - your patient's functional status?
    - To what extent did the PROstep dashboard change your management of the patient?
    - To what extent did the PROstep dashboard prompt you to have goals of care conversations with this patient?
    - To what extent did the PROstep dashboard have any adverse effect on the patient?
    - Please indicate any ways that the PROstep dashboard has been useful or harmful in the management this patient (open ended)

4. Background

Patients with incurable lung and non-colorectal gastrointestinal (GI) cancers benefit from earlier palliative care interventions. Early palliative care in patients with incurable lung and GI cancers has been shown to improve quality of life, reduce anxiety and depression, decrease end-of-life utilization, and possibly improve survival.[1-3] Furthermore, PROs such as shortness of breath, weight loss, and appetite loss are independently associated with higher mortality in incurable lung and GI cancers.[4,5] Limited life expectancy has been recognized as a potential trigger for early palliative care interventions.[6,7] Improved identification of patients at risk of short-term mortality using patient-generated health data (PGHD) may allow better targeting of palliative care interventions to improve quality-of-life in incurable lung and GI cancers.

Recently available PGHD may improve performance of mortality prediction algorithms, but is captured on a low-scale. PGHD are health-related data generated by a patient; they include routinely collected information about patient symptoms, functional status, and activity levels out of the clinic.[8-11] PRO assessment may allow clinicians to identify patients with high symptom burden or functional status decline who would also benefit from timely palliative care interventions.[12,13] Regular PRO assessment in oncology has been associated with improved health-related quality of life and survival. Passively collected step counts and activity levels are proxies for functional status.[14] In large prospective cohort studies of patients with cancer, both higher PRO scores for depression, fatigue, and pain and lower daily step counts have been independently associated with lower overall survival.[5,15] While PROs and activity levels may be independently associated with prognosis, collection may be infeasible for large populations of patients. PROs may be collected via paper surveys, automated telephone systems, tablets or downloadable applications.[16,17] Step counts and activity levels are usually passively collected via accelerometers (ex. Fitbits). However, there are few examples of large-scale collection of PRO or accelerometer data due to low response rates, inadequate resources, and suboptimal clinician and patient training.[16]

Given the severity of the recent COVID-19 pandemic, efforts to reduce in-clinic visits via telehealth and increase remote monitoring have become urgent. Patients with active cancer, and those with a history of cancer, are at increased risk to develop complications from COVID-19 and are more likely to experience negative outcomes; thus, it is of high operational importance to safely monitor this patient population. [18-20] The benefits of telehealth during this pandemic include limiting the exposure to other acutely ill patients and reducing provider burnout. [21-23] As a result, CMS has opened up coverage for telehealth services and early data from New York shows telemedicine visits increasing from 369.1 daily to 866.8 daily (135% increase) in urgent care after the system-wide expansion of virtual health visits in response to COVID-19, and from 94.7 daily to 4,209.3 (4345% increase) in non-urgent care post expansion. [24,25]

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5. Study design

5.1 Design

This prospective cohort study will evaluate the effect of remotely collected PROs and step data derived from wearable Fitbit devices, and remotely presenting those data to clinicians and patients at each oncology visit. We will enroll patients who are diagnosed with incurable lung or gastrointestinal cancer who are receiving (or planning to receive) chemotherapy. Eligible patients can have in-person or virtual visits with their oncology clinician prior to chemotherapy, which is of particular importance as many visits are now being done via telemedicine. Patients will be randomized into one of three arms – a control (arm a), an intervention with no patient feedback (arm b), and an intervention with patient feedback (arm c) – at a 1:1:1 allocation **(Figure 1: Patient Arms)**. All intervention patients will receive 1) weekly PRO surveys for five symptoms administered through the W2H text platform and 2) a Fitbit wearable device that can track patient step, distance, active minutes, sleep, and heart rate data. At each subsequent medical oncology visit (either in-person or via telemedicine), oncology clinicians will receive a PROStep Dashboard that reports the patient's 1) trends in the home-based PROs and step data, 2) acute care utilization in the prior six months (Oncology Evaluation Unit, emergency department or inpatient admissions), and 3) whether the patient has a documented Serious Illness Conversation (a type of Advance Care Planning note that is standard practice at PCAM). Arm C will receive a brief text message feedback including an active nudge question on their upcoming appointment.

Arm B will not receive text feedback. Arm A will receive no PRO surveys, Fitbit device, or patient feedback (arm a) **(Figure 2: Intervention by Patient Arm)**. Patients will be enrolled for a total of six months, unless they disenroll earlier, and evaluated on the outcomes described above.

Figure 1: Patient Arms

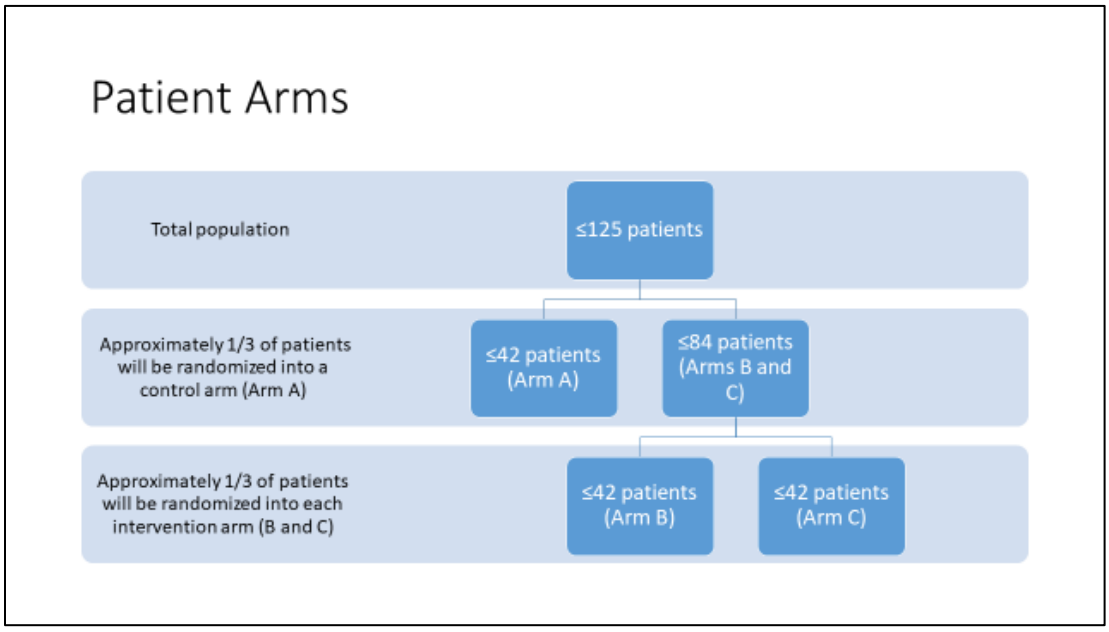
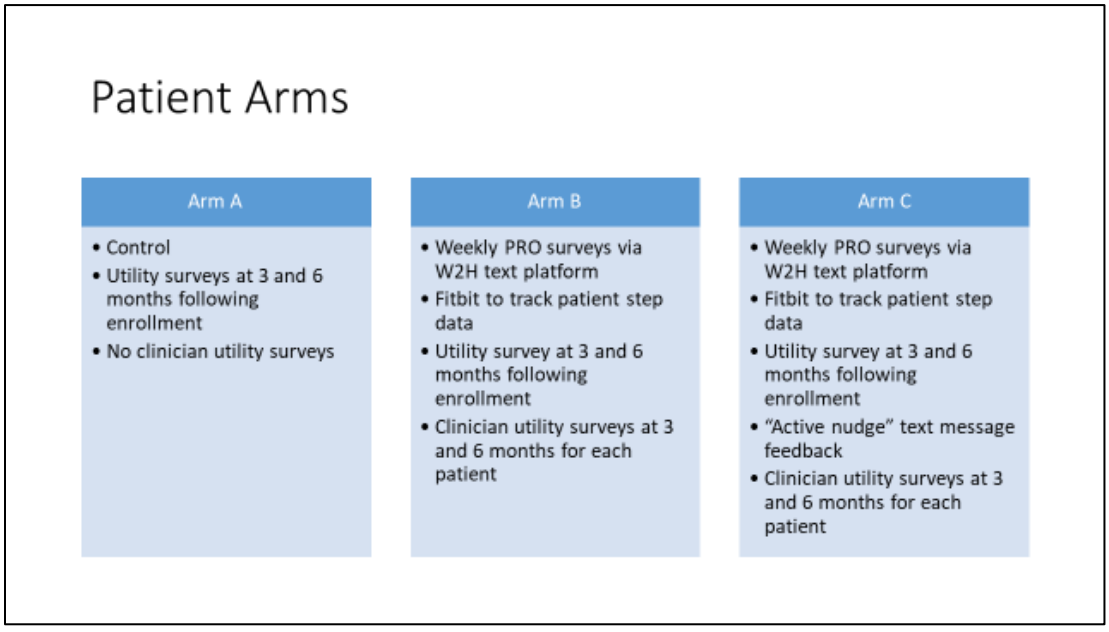


Figure 2: Intervention by Patient Arm



5.2 Study duration

The study is expected to begin in November 2020 and take 12 months to complete.

5.3 Target population

125 patients with incurable lung and gastrointestinal cancer treated at the University of Pennsylvania Health System's Perelman Center for Advanced Medicine (PCAM).

5.4 Accrual

The study sample will be drawn from patients who receive their cancer care from a GI or lung oncologist at the University of Pennsylvania's Perelman Center for Advanced Medicine (PCAM). We aim to enroll 125 patients. We anticipate enrolling these 125 patients over 6 months at a rate of 4 patients per week, a small fraction of the number of eligible patients with in-person or telemedicine visits at PCAM each week. A summary of recruitment mechanisms is found in Section 6 (Subject recruitment).

5.5 Key inclusion criteria

Patients must meet the following criteria to be eligible for the study:

1. English-speaking
2. Have a diagnosis of incurable or Stage IV lung or gastrointestinal cancer
3. Receive primary oncology care with a thoracic or gastrointestinal medical oncology specialist at the Perelman Center for Advanced Medicine (i.e. does not have a local oncologist that provides cancer care, including other UPHS clinic sites)
4. Currently receiving or planned receipt within 2 weeks of IV chemotherapy (see exclusions below)
5. The patient has a smart phone that can receive SMS text messages and has blue-tooth capability that can connect to Fitbit.

5.6 Key exclusion criteria

Patients will be excluded if any of the following criteria apply:

1. Age < 18 years
2. Patients has used a wheelchair, been bedbound or is unable to walk without assistance from other people every day for the past 7 days (patients are not excluded for the use of walkers or canes)
3. Patients who are receiving checkpoint inhibitor monotherapy, IV targeted therapy monotherapy (e.g. panitumumab) or oral tyrosine kinase inhibitors
4. Patients who receive chemotherapy infusions at another UPHS site or outside of UPHS or whose primary oncologist is not in thoracic or gastrointestinal oncology groups at PCAM. Notably, patients who receive part of their chemotherapy regimen at home will still be allowed to enroll.

5. Lung cancer patients enrolled in an ongoing palliative care clinical trial that may lead to better communication regarding symptoms and functional status.
6. Clinician concerns about behavioral health issues that may prevent engagement with text message prompts
7. Are enrolled in another interventional clinical trial (as clinical trials often have a substantial symptom-reporting structure; non-interventional clinical trials are permitted e.g. trials that just involve blood tests)

6. Subject recruitment

The recruitment and onboarding process can be conducted either in-person or remotely (depending on restrictions in place due to the COVID-19 pandemic). Upon trial initiation, we will obtain permission from GI and lung oncology clinicians to approach their patients regarding this trial. A clinical research coordinator (CRC) will conduct brief chart reviews of patients scheduled to see a GI or lung oncologist at PCAM to identify patients that meet eligibility criteria. The CRC will then electronically notify clinicians prior to their scheduled appointments with these patients to confirm eligibility and inform them that they will be approaching the patient. When approaching potentially eligible patients, the CRC will wear appropriate protective equipment and will meet the patient in the private clinical patient room or the private chemotherapy infusion room to describe the trial and determine eligibility. CRCs may also contact potentially eligible patients by phone and/or email to describe the trial and determine eligibility. The CRC will use a script developed by the research team when approaching patients in-clinic or by phone **(Appendix A)** or electronically based on template language provided by the Office of Clinical Research **(Appendix B)**. After eligibility is confirmed, interested participants will be directed to the online Way to Health (W2H) portal to review and provide informed consent, enroll in the study, and complete baseline questionnaires. The CRC will also inform clinicians regarding patient enrollment and ask the clinician to estimate the patient's Eastern Cooperative Oncology Group performance status. The CRC will assist with setting up W2H and their Fitbit device in-person or by phone or a virtual meeting (a support partner will be encouraged to attend).

7. Subject compensation

Patients in arms a, b, and c will be compensated with a $25 payment for completing their first utility survey at 3 months after enrollment and another $25 payment for completing their second and final utility survey at 6 months after enrollment. Patients in arms b and c will be permitted to keep the Fitbit as part of the trial.

8. Study procedures

8.1 Patient Consent

Upon recruitment, the research coordinator will contact potential participants to confirm their eligibility and explain the study's objectives, duration and requirements. Individuals who are interested in learning more about the study will be directed to the online W2H portal. Upon reaching the portal, potential participants will be led through an automated online informed consent process **(Appendix C)**. The consent document will be divided into sections, requiring the click of a button to advance from one section to the next. This will help ensure that participants read the consent form thoroughly by breaking down the form into manageable blocks of text. Successive screens will explain the voluntary nature of the study, the risks and benefits of participation, alternatives to participation, and the process for study withdrawal. The consent form will clearly state that the weekly electronic symptom surveys and step data will be shared with the patient's care team via the electronic medical record, whereas all other information collected during the study will remain confidential, available only to the study team and with appropriate privacy protections in place.

On the final consent screen, a clearly delineated button will enable patients to agree (or not) to participate in the study. Additionally, a platform electronic signature using a finger on a touch screen of a mobile phone will be required. Those who elect not to participate will be asked to grant permission (or not) for the study team to collect limited data from them. An abbreviated Study Decline Consent form will be utilized for this purpose, similarly requiring the click of a clearly delineated button to agree (or not) to limited data collection, as well as a platform electronic signature **(Appendix D)**.

Upon agreeing to participate in the study and clicking the appropriate button, participants will have consented to enroll in the study. Participants will then be prompted to complete an online enrollment questionnaire asking for basic demographic information (e.g. age, sex, race, education, computer experience- **Appendix E)**. Additional patient characteristics (e.g. Eastern Cooperative Oncology Group performance status, Charlson comorbidity score), tumor characteristics (e.g. histology), and treatment characteristics (e.g. line/type of therapy) will be abstracted from the medical record at the time of enrollment. The patients will also receive a sample survey via text message that mimics the weekly PRO survey they will receive, but the sample survey results will be discarded. The sample will be clearly labeled to indicate that the response are not monitored.

Those who elect not to participate but consent to limited data collection, will be asked to fill out a very brief online questionnaire, asking basic demographic information, computer/mobile phone experience, and reason(s) for not wanting to participate in a de-identified manner **(Appendix F).**

After enrolling, participants will be provided with details regarding how to contact the research team via email or phone at any time if they subsequently wish to withdraw from the study or have other study-related concerns.

We request a waiver of informed consent for consenting physicians. Prior to the start of the trial, we will obtain permission from all GI cancer and lung cancer clinicians at the Perelman Center for Advanced Medicine to approach their patients. As the study does not limit clinical care in anyway (e.g. in contrast to a therapeutic intervention trial, where receipt of a treatment might make the patient ineligible for other therapies), clinician consent is not needed. The intervention simply provides additional information that clinicians can use (or choose not to use) to inform routine care of the patient.

8.2 Clinician Consent

Prior to launching the study, the research team will present a brief slide deck at a monthly meeting for relevant PCAM providers including the GI oncology and thoracic oncology tumor board meetings. The PIs will go over the study plan including the design, background, and outcomes. The investigators will obtain verbal consent from all providers to 1) recruit patients into this study and 2) answer a utility survey at 3 and 6 months following enrollment for each patient.

8.3 Procedures

Setting up patients

The CRC will assist the patient in setting up a W2H account that will deliver the weekly PRO surveys and collect Fitbit data. The CRC will be responsible for confirming the patient receives their Fitbit device at their infusion treatment (typically, the CRC will give this directly to the patient in-person, but they can be dropped off beforehand if there are restrictions in place due to the COVID-19 pandemic). Patients will be shown how to use their Fitbit and link it to their W2H account, then being asked to authorize the device to electronically transmit device data to the study database. Participants will be instructed to wear the Fitbit device as much as possible, including during sleep, for the duration of the study. Participants will be told that they need to sync their wearable device with their smartphone in order for data to be transmitted to the study team. Participants will receive regular text message reminders prompting them to wear and sync their devices.

Remote-PROs

Timing. On Monday of every week, patients will receive a series of text messages to solicit patient-reported symptoms.

Mechanism of delivery. Text messages will be sent via the W2H platform. Patients will receive the surveys in the form of text messages on their phone.

Content of the text messages. The text messages will inquire about seven symptoms, requesting a response rating the patient's response. The seven symptoms have been selected by lung and GI oncology clinicians at PCAM from a list of twelve validated symptoms from the National Cancer

Institute's Common Terminology Criteria for Adverse Events and will be scored on a five point scale from 0 (no present) to 4 (disabling). The patients will also receive a question asking about their activity level over the prior month (**Appendix G**).

Who may respond: During trial enrollment, the patient will be instructed to answer the text messages. However, a caregiver may respond for the patient if the patient needs assistance.

Safety. PRO data will be shown to clinicians in the PROStep Dashboard (see below) and will not be monitored in real time by a clinician. All study participants will be provided with the research coordinator and principle investigator's email and phone number to contact with any questions or study-related concerns. Participants will be educated at the outset and reminded throughout the study, both verbally and in writing, that the symptom-reporting tool is intended for research purposes only. If a participant feels that their symptoms warrant more urgent evaluation, s/he will be instructed to call their provider in the usual fashion. The principal investigator will be available at all times, should physician escalation be necessary.

A severe symptom (≥3), or any abrupt change in symptom severity (≥2), will trigger an alert to the participant's care team via an EPIC message to the attending clinician's symptom pool inbox, whose clinicians will be empowered to intervene at their discretion**.** Possible interventions might include a telephone call, prescription medication, home care visit, same-day office visit, urgent care, and/or acute care referral. The CRC will review all text message responses each non-holiday weekday for other responses that may warrant closer attention by clinical teams and will call the primary oncology team or send an EPIC message, as appropriate. The CRC can call the study investigators or primary oncology teams at any time to determine whether a text message requires further action.

Until 30 PRO surveys have been sent (e.g. 10 patients for 3 weeks, or 3 patients for 10 weeks), the study investigators and CRC will have a weekly meeting to review the number of responses that cross the alert threshold hold, any text message responses and identify any changes to the protocol that may be needed to ensure the adequacy of this safety mechanism. After this period, the CRC will discuss any concerning text messages to the study investigators.

Patients may opt out of the text message intervention at any time by responding to a W2H text message with the phrase "Stop". The CRC will contact the patient by the next non-holiday weekday to determine whether the patient would like to 1) resume receiving the text messages (in which case they will be reactivated), 2) continue in the trial without receiving the text messages, or 3) withdraw from the trial.

If a patient in the intervention group does not respond to two weekly surveys the CRC will contact the patient to inquire about obstacles to participation (e.g. mobile phone has changed, patient does not wish to participate, etc). Patients will be provided with the CRC's email and phone number to contact with any questions.

Step monitoring

At enrollment, the CRC will instruct patients on how to wear the Fitbit device and periodically sync the device with their phone to send step data to W2H, as described above. As the device has a 5 day memory, patients will receive a reminder to sync Fitbit twice per week as well as two days before a clinic visit unless the data was synchronized in the prior 24 hours. If patients have no step data transmitted for a two week period, the CRC will contact the patient. Note that while step data will be collected to assess activity, GPS data will not be collected or used in this study.

Presenting PROStep Dashboard to clinicians

The study team will provide an updated PROStep Dashboard (**Appendix H**) to lung or GI oncology clinicians for each patient enrolled in the intervention arms prior to their appointments. W2H will generate the dashboards and the study team will physically deliver it to their office or touchdown space or send electronically. The Dashboard will include:

1. Home-based PRO report, including the weekly survey results for each question in tabular and graphical form
2. Step data report, including a summary of number of daily steps in graphical form (with rolling weekly averages) and weekly averages in tabular form
3. A list of all acute care utilization in the UPHS system in the prior 6 months including,
    a. Oncology Evaluation Unit visits
    b. Emergency department visits
    c. Inpatient admissions
4. Whether the patient has had an outpatient palliative care visit
5. Whether the patient has had a documented Serious Illness Conversation

Active nudge text feedback

Intervention patients in arm c will receive text feedback describing worsening or severe symptoms collected from their remote PRO questionnaires (i.e. “Your following symptoms are severe or have gotten worse:”) and their step count (“Your Fitbit step count compared to last week is worse.”). They will also receive an “active nudge” question on their upcoming visit (i.e. “Do you plan on discussing these symptoms with your oncologist at your upcoming visit? Type "1" if you plan to discuss them; Type "2" if you do not plan to discuss them.").

Clinician surveys

At 3 and 6 months after patient enrollment, the patient’s oncology clinician team (the attending oncologist and associated advanced practice providers that had an encounter with the patient during the study period) will receive an emailed survey to assess the clinicians’ perspectives on the utility of the PROStep Dashboard for the specific patient (**Appendix I**). Clinicians will be surveyed for each intervention patient (arms b and c) enrolled in the study including patients who

disenroll early but were enrolled for at least 4 weeks of the enrollment period for the upcoming survey.

Patient surveys

At 3 and 6 months after enrollment, all patients (arms a, b, and c) will receive a text message with a link to a survey to assess the patients' perspectives (**Appendix J)**. Patients are eligible to receive these surveys if they are enrolled in the study for a minimum of 4 weeks.

Patient exit interviews

Upon exiting the trial, all intervention patients (arms b and c) will receive a brief exit interview to gather feedback. The CRC will conduct these interviews, and they will consist of the following questions:

1. *Overall, what did you think of the intervention?*
2. *What parts were the most helpful?*
3. *What parts were not helpful?*
4. *What should we change?*
5. *How often do you have your smart phone in your pocket when you walk around?*
    - *Never*
    - *Rarely*
    - *Sometimes*
    - *Most of the time*
    - *Always*

Data collection

Patient data for outcome determination will be obtained from W2H (for home-based PROs and Fitbit device data), Penn Data Store and Clarity (Epic's data reporting database, for the remaining outcomes).

9. Analysis plan

For each primary outcome, we will compare the mean scores from the survey questions at 6 months (see section 3.1) for all 3 groups (2 intervention, 1 control) using a Kruskal-Wallis test with $p<0.05$ indicating statistical significance. If the result is significant, we will use the Tukey's honestly significantly difference (HSD) test to test pairwise comparisons. If the outcomes for any arm are skewed (not normally distributed), we will use log-transformation before applying all tests. For

clinicians who have completed a 3-month survey for a specific patient, but do not complete a 6-month survey for that patient, we will apply their 3-month survey responses in place of their missing 6-month survey for analysis for that specific patient. For example, if Clinician A completes a 3-month survey for Patient A, but not a 6-month survey, we will use the results from their completed 3-month survey in its place for Patient A (but not for other patients). That said, we will do a sensitivity analysis only using the coded 6 month analyses (complete case analysis).

We will repeat this analysis for the secondary outcome of composite survey score at 3 months. For patients who exit the study early, we will attempt to administer their next survey and use that assessment. These will be administered if patients have been enrolled for a minimum of 4 weeks of the enrollment period leading up to their following survey. For example, if a patient dis-enrolls 4 weeks after receiving their 3-month utility survey, they will be eligible for their 6-month survey whereas a patient who dis-enrolls at 3 weeks will not). If a patient dies or is otherwise unable to complete a survey, they will be omitted from the analysis for the relevant outcome. For patients who disenroll from the trial for any reason (voluntary, death, etc.), but meet this 4 week threshold, their clinicians will receive a utility survey. To assess whether responses in 3-month to 6-month surveys differ across arms, we will run an analysis of covariance (ANCOVA) model with the baseline score and arms as covariates, and change of score as the dependent variable.

We will use descriptive statistics to compare the secondary outcomes of adherence rates between the two intervention groups and trends in PROstep data. We will use Kruskal-Wallis tests for continuous outcomes and chi-square tests for categorical variables to compare these outcomes between all arms at 3 and 6 months.

10. Investigators

Ravi Parikh, MD, MPP, is the Principal Investigator. Dr. Parikh is an Assistant Professor in Medical Ethics and Health Policy at the University of Pennsylvania and Staff Physician at the Corporal Michael J. Crescenz VA Medical Center.

Christopher Manz, MD, is a co-Investigator. Dr. Manz is an Instructor of Medical Oncology at Dana Farber Cancer Institute.

Mitesh Patel, MD, MBA is a co-Investigator. Dr. Patel has experience implementing pragmatic clinical trials of similar scale at the University of Pennsylvania Health System.

The PI and co-investigators have experience implementing similar pilot interventions at UPHS oncology sites.

Dr. Manz and Dr. Parikh are supported by the Conversation Connect team and Abraham Cancer Center leadership, including:

Nina R. O'Connor, MD	Palliative Care
Justin E. Bekelman, MD	Penn Center for Cancer Care Innovation

Mitesh Patel, MD, MBA	Penn Nudge Unit
Mohan Balachandran, MS	Way to Health Team
Lynn M. Schuchter, MD	Hematology/Oncology
Lawrence N. Shulman, MD	Hematology/Oncology
William Ferrell, MPH, Project Manager	Medical Ethics and Health Policy
Jonathan Wakim, BA	Perelman School of Medicine
Joelle Williamson, BS, CRC	Department of Medicine Clinical Trials Unit
Lead Biostatistician (TBD)	

11. Human research protection

11.1 Data confidentiality

Computer-based files will only be made available to personnel involved in the study through the use of access privileges and passwords. Wherever feasible, identifiers will be removed from study-related information. Precautions are already in place to ensure the data are secure by using passwords and HIPAA-compliant encryption.

Computer-based records will be stored on the Way to Health (W2H) study portal, supported by the Penn Medicine Academic Computing Services (PMACS) infrastructure, and will only be made available to personnel involved in the study through the use of access privileges and passwords. Wherever feasible, identifiers will be removed from study-related information. Precautions are in place to ensure the data are secure, including use of passwords and encryption, because the research involves web-based surveys.

The W2H Team supports all research studies run on the platform. Default views within the platform for all W2H staff display de-identified participant data. As a part of support and troubleshooting, the W2H team is trained to use only these de-identified views. In rare cases where the issue involves viewing identifiable participant data, the W2H team may need to view this data to assist the study team. The W2H Team are employees of the University of Pennsylvania and Penn Medicine. All W2H team members have completed HIPAA Security training and CITI Protection of Human Subjects Research Training - ORA.

11.2 Subject confidentiality

Research material will be obtained from participant surveys, Fitbit device data and targeted review of the electronic medical record. All participants will provide informed consent for access to these materials. The data to be collected include demographic data (e.g., age, sex, self-identified race, education level), patient baseline characteristics (e.g., comorbidities, performance status), disease-related data (e.g., tumor stage, histology), treatment-related data (e.g., line/type of therapy), process data (e.g. patient adherence to the intervention), and outcome data (e.g. health-related quality of life, symptom burden, step data, acute care utilization). PRO and step

data will be presented to the patient's oncology clinician as described above. The remaining data that is obtained will be used for research purposes only. The same procedure used for the analysis of automated data sources to ensure protection of patient information will be used for the survey data and chart-abstracted data, in that patient identifiers will be used only for linkage purposes or to contact patients. The study identification number, and no other identifying information, will be used on all data collection instruments. All study staff will be reminded to appreciate the confidential nature of the data collected and contained in these databases.

The Penn Medicine Academic Computing Services (PMACS) will be the hub for the hardware and database infrastructure that will support the project and is where the W2H web portal is based. The PMACS is a joint effort of the University of Pennsylvania's Abramson Cancer Center, the Cardiovascular Institute, the Department of Pathology, and the Leonard Davis Institute. The PMACS provides a secure computing environment for a large volume of highly sensitive data, including clinical, genetic, socioeconomic, and financial information. Among the IT projects currently managed by PMACS are: (1) the capture and organization of complex, longitudinal clinical data via web and clinical applications portals from cancer patients enrolled in clinical trials; (2) the integration of genetic array databases and clinical data obtained from patients with cardiovascular disease; (3) computational biology and cytometry database management and analyses; (4) economic and health policy research using Medicare claims from over 40 million Medicare beneficiaries. PMACS requires all users of data or applications on PMACS servers to complete a PMACS-hosted cybersecurity awareness course annually, which stresses federal data security policies under data use agreements with the university. The curriculum includes Health Insurance Portability and Accountability Act (HIPAA) training and covers secure data transfer, passwords, computer security habits and knowledge of what constitutes misuse or inappropriate use of the server. We will implement multiple, redundant protective measures to guarantee the privacy and security of the participant data. All investigators and research staff with direct access to the identifiable data will be required to undergo annual responsible conduct of research, cybersecurity, and HIPAA certification in accordance with University of Pennsylvania regulations.

All data for this project will be stored on the secure/firewalled servers of the PMACS Data Center, in data files that will be protected by multiple password layers. These data servers are maintained in a guarded facility behind several locked doors, with very limited physical access rights. They are also cyber-protected by extensive firewalls and multiple layers of communication encryption. Electronic access rights are carefully controlled by University of Pennsylvania system managers. We believe this multi-layer system of data security, identical to the system protecting the University of Pennsylvania Health Systems medical records, greatly minimizes the risk of loss of privacy. In addition, risk of loss of confidentiality will be minimized by storing completed paper copies of the surveys and signed informed consent forms in locked file cabinets in locked offices accessible only to trained study staff. Each subject will

be assigned a unique identifier without identifying information, and data will be entered into an electronic database using only the unique identifier. Only trained study staff will have access to the code that links the unique identifier to the subject's identity. Electronic data will be stored on secure, password-protected firewalled servers at the University of Pennsylvania.

Data regarding provider performance of Serious Illness Conversations are already shared among providers and will continue to be shared in unblinded fashion as part of the trial. Data regarding acute care utilization in the last 30 days for a provider's deceased patient panel will be shared amongst providers as well. This will occur as part of the intervention but is planned to occur regardless of trial approval as part of quality improvement efforts.

11.3 Subject privacy

Interested participants will be directed to the W2H portal where they will be asked to enter data related to demographic characteristics. Enrollment will include a detailed description of the voluntary nature of participation, the study procedures, risks and potential benefits. The enrollment procedure will provide the opportunity for potential participants to ask questions and review the consent form with family and friends prior to making a decision to participate. Participants will be told that they do not have to answer any questions if they do not wish and can drop out of the study at any time, without affecting their medical care or the cost of their care. They will be told that they may or may not benefit directly from the study and that all information will be kept strictly confidential, except as required by law. Subjects will be given a copy of the consent document. All efforts will be made by study staff to ensure subject privacy.

11.4 Data disclosure

The following entities, besides the members of the research team, may receive protected health information (PHI) for this research study:

 Twilio, Inc., the company that processes study-related text messages. Twilio will store patients' phone numbers on their secure computers.

 The Office of Human Research Protections at the University of Pennsylvania

 Federal and state agencies (for example, the Department of Health and Human Services, the National Institutes of Health, and/or the Office for Human Research Protections), or other domestic or foreign government bodies if required by law and/or necessary for oversight purposes.

 Lens is used by W2H to enable data visualization. Lens is built on an open-source offering called Metabase. This offering is fully hosted within PMACS environment and follow the same guidelines and privacy / encryption procedures and policies described above.

11.5 Data safety and monitoring

At the time of initiation of a new line of treatment, it is standard practice for cancer patients to be given anticipatory guidance on when to seek medical attention. This practice will continue, and

participants will be reminded to contact their care team in the usual recommended fashion for any issues that arise during their care. They will also be reminded weekly after each symptom report that they should contact their primary oncologist with any issues for which they think urgent medical attention is warranted.

Both the principal investigator and research coordinator will be notified if a participant reports a severe symptom (≥3), or any abrupt change in symptom severity (≥2), which will also trigger an alert to the patient's care team. In this way, multiple physicians will be aware of escalating symptoms.

11.6 Risk/benefit

11.6.1 Potential study risks

A potential risk for patient participants in this study is a breach of data, as these subjects will be reporting information related to their health. This risk will be mitigated by using the platforms and security procedures described above. A second potential risk to patient participants is that they may misinterpret this tool as a means of quick communication with their care team. We will take great care to emphasize that the electronic symptom reporting tool is investigational, and not a replacement for usual means of communication with one's care team. Participants will be reminded repeatedly, both verbally and via text after each symptom report, that they should contact their care team directly if they are having any symptoms for which they think urgent medical attention is warranted. A potential risk for clinicians participating in this study is a breach of data, which will also be mitigated by using the platforms and security procedures described above. All potential risks to patient and clinicians are minimal.

11.6.2 Potential study benefits

Potential study benefits include improved recognition by the patient's oncology clinicians of poorly controlled or worsening symptoms and more nuanced perspective on current functional status and changes in functional status which may lead to an increase in discussions about patients' prognosis, goals and wishes (through a Serious Illness Conversation), improved symptom management and more informed decision-making regarding cancer treatment plans.

11.6.3 Risk/benefit assessment

Potential risks are minimal and the risk/benefit ratio of this study is very favorable. The study team will take necessary steps to maintain confidentiality and privacy throughout the study period. Participants will be reminded regularly that electronic reporting of symptoms is not a replacement for usual communication with their care team.