BMJ Open  Patient and clinician nudges to improve symptom management in advanced cancer using patient-generated health data: study protocol for the PROStep randomised controlled trial

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ABSTRACT

Introduction Patients with advanced cancers often face significant symptoms from their cancer and adverse effects from cancer-associated therapy. Patient-generated health data (PGHD) are routinely collected information about symptoms and activity levels that patients either directly report or passively record using devices such as wearable accelerometers. The objective of this study was to test the impact of an intervention integrating remote collection of PGHD with clinician and patient nudges to inform communication between patients with advanced cancer and their oncology team regarding symptom burden and functional status.

Methods and analysis This single-centre prospective randomised controlled trial randomises patients with metastatic gastrointestinal or lung cancers into one of three arms: (A) usual care, (B) an intervention that integrates PGHD (including weekly text-based symptom surveys and passively recorded step counts) into a dashboard delivered to oncology clinicians at each visit and (C) the same intervention as arm B but with an additional text-based active choice intervention to patients to encourage discussing their symptoms with their oncology team. The study will enrol approximately 125 participants. The coprimary outcomes are patient perceptions of their oncology team’s understanding of their symptoms and their functional status. Secondary outcomes are intervention utility and adherence.

Ethics and dissemination This study has been approved by the institutional review board at the University of Pennsylvania. Study results will be disseminated using methods that describe the results in ways that key stakeholders can best understand and implement.

Trial registration numbers NCT04616768 and 843616.

INTRODUCTION

Patients with advanced cancers often face significant symptoms from their cancer and adverse effects from cancer-associated therapy.1–3 In addition to suffering from high symptom burden, patients with incurable cancer experience declines in functional status and quality of life due to cancer progression or treatment.4–7 Adverse symptoms, quality of life and functional status are associated with lower survival, greater acute care use and higher financial burden for caregivers and the healthcare system.8–13 Identifying patients with high symptom burden, poor quality of life or poor functional status is thus critical to ensure high-quality care for patients with advanced cancer.14–16 However, in large prospective studies, oncology clinicians assess patient symptom burden only 40% of the time. Furthermore, in nearly three-quarters of


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Strengths and limitations of this study

⇒ PROStep is one of the first randomised trials to assess the impact of clinician and patient nudges based on patient-generated health data (PGHD) on symptom and functional status understanding among patients with advanced cancer.

⇒ Our randomised study design assesses the utility of clinician-directed PGHD information display, with or without a patient-directed active choice question, on communication about symptom burden and functional decline.

⇒ Our design allows novel longitudinal evaluation of the association between objective step counts and downstream use and outcomes.

⇒ A key limitation is that relying on data from weekly symptom reports and wearable accelerometers may select for a population that is healthier and/or younger than the general population of patients with advanced cancer.
cases where patient-reported and clinician-reported symptoms are not concordant, clinicians underestimate symptom severity.\textsuperscript{11,17-19}

Patient-generated health data (PGHD) are routinely collected information about symptoms and activity levels that patients either report directly or passively recorded using devices such as wearable accelerometers.\textsuperscript{20-22} PGHD assessment may allow clinicians to identify patients with high symptom burden or poor functional status who would benefit from timely supportive care interventions.\textsuperscript{24,25} Patient-reported outcomes (PROs), health outcomes that are directly reported by a patient, are one example of PGHD.\textsuperscript{24-27} Routine PRO assessment in medical oncology can reliably improve symptom management, resulting in improvements in healthcare use, quality of life and even patient survival. As a result, PROs have been increasingly incorporated into routine oncology practice. PROs may be collected in the clinic on paper or via applications that link to the electronic medical record, with early trials suggesting high levels of adherence at 74.9\% and 79.1\% for weekly and monthly PRO questionnaires among oncology patients.\textsuperscript{28,29} However, limiting PRO collection to in-clinic visits on oncology may be too infrequent to comprehensively account for patients’ symptom burden. Technologies that enable remote PRO collection using questionnaires delivered via mobile phone applications may provide more granular and relevant information about symptom burden to clinicians.\textsuperscript{26} This is particularly timely during the COVID-19 pandemic, as remote symptom monitoring has grown, given the need to decrease face-to-face visits and subsequent exposure risk for patients with active cancer.\textsuperscript{30-32}

In addition to quality of life and symptom burden, functional status is a critical element in determining a patient’s treatment and prognosis. Accurate measurement of functional status is challenging, as assessment via questionnaires usually differs between clinicians and patients.\textsuperscript{33,34} Passive activity monitoring via accelerometer-measured step counts may provide objective measures of functional status that can be trended over time to inform discussions about treatment and prognosis. Activity monitoring among patients with advanced cancer is feasible and associated with high levels of adherence in prior trials.\textsuperscript{35-38}

While PGHD provides important clinical and prognostic data, a critical evidence gap is how to optimally integrate these data in clinical care to improve symptom management. Behavioural economic principles can inform optimal use of PGHD to improve symptom management.\textsuperscript{39} Clinician-targeted automated default email and text alerts about prognostic risk or evidence-based practice may improve guideline-based practice in oncology.\textsuperscript{40-42} Additionally, patient-targeted nudges using active choice—a behavioural economic method used to address delays in decision making by prompting an immediate decision between alternative choices—may lead to greater completion of high-value decisions such as cancer screening.\textsuperscript{43-45}

No prospective trial has compared clinician and patient nudges informed by PGHD collection to better improve symptom management.\textsuperscript{40-42} The objective of this study was to test the impact of an intervention integrating remote collection of PGHD with clinician and patient nudges to inform symptom and functional status and communication understanding for patients with advanced cancer and their oncology team.

**METHODS AND ANALYSIS**

We describe the design and methods for a single-centre prospective randomised controlled trial to assess the impact of an intervention consisting of default information provision using dashboards containing PGHD to oncology clinicians (‘PROStep dashboards’), with or without a patient-directed active choice text message, on patient-reported and clinician-reported symptom understanding and communication among patients with advanced solid cancers.

**Study hypotheses**

The primary study hypothesis is that a clinician-targeted automated dashboard consisting of information about remotely collected PGHD (symptom burden, quality of life and functional status) will improve patient-perceived symptom understanding and communication compared with usual care. Secondary hypotheses are (1) the addition of a patient-directed active choice intervention based on their self-reported PGHD will improve patient-perceived symptom understanding and communication over and above PGHD dashboards to clinicians alone; (2) remote PGHD collection will be feasible and acceptable to patients and clinicians; and (3) passive activity monitoring will be feasible and acceptable to patients and clinicians.

**Study setting**

Recruitment for the trial is ongoing at the Perelman Center for Advanced Medicine (PCAM), a large tertiary academic practice at the University of Pennsylvania Health System in Philadelphia, Pennsylvania. We plan to recruit 125 patients who have incurable lung or gastrointestinal (GI) cancer and are undergoing systemic intravenous chemotherapy. Recruitment began in November 2020.

**Eligibility criteria**

The study is recruiting English-speaking patients at the PCAM who have a diagnosis of metastatic or stage IV GI or lung cancer. Patients must receive their oncology care at PCAM, be currently treated with intravenous chemotherapy (or planned receipt within 2 weeks) and have a capable smartphone (table 1). These criteria were selected with input from oncology clinicians who treat patients with GI and lung cancer to identify a population with incurable cancer who are undergoing intravenous...
Chemotherapy and are the most likely to have uncontrolled symptoms or a poor prognosis. The study cohort includes patients currently undergoing chemotherapy at PCAM. Patients seeking second opinions or undergoing their treatment at other sites are excluded as the text-based intervention cannot be delivered to other sites. Due to the intervention’s components (ie, PRO surveys, active choice text messages, utility surveys, Fitbit app, etc), we exclude non-English-speaking patients. We also exclude patients undergoing single-agent oral targeted therapy (eg, epidermal growth factor receptor antagonists) or single-agent checkpoint inhibitor monotherapy in order to enrich the study population for patients with high treatment-associated symptom burden. We exclude patients on active intervention trials—including an ongoing palliative care clinical trial among patients with thoracic malignancies—because such trials often already have a PRO collection mechanism that may confound the impact of the intervention. Finally, we exclude patients who are bedbound or wheelchair users because step data collected as a key feature of the intervention would not be expected to improve care for these patients.

**Participant screening**

On trial initiation, we obtained permission from GI and lung oncology clinicians to approach their patients regarding this trial. Each week, a trained clinical research coordinator (CRC) screens the electronic health records to identify eligible patients scheduled to see a GI or lung oncologist at PCAM in the following week. One study principal investigator (PI) (RBP) rescreens potentially eligible patients that the CRC identified to confirm eligibility. The CRC then approaches potential participants at their upcoming infusion visit.

**Recruitment and retention**

The CRC approaches patients who screen eligible during routine infusion visits at PCAM using a script to describe the purpose of the study, the randomisation process and interventions for each arm of the study. If unable to meet the patient in-clinic, the CRC can contact eligible patients via email with a similar script (see online supplemental appendices A,B). After eligibility is confirmed, the CRC uses an iPad to direct interested participants to an electronic portal to review and complete informed consent/Health Insurance Portability and Accountability Act of 1996 (HIPAA) authorisation form, enrolment form and a baseline PRO questionnaire form (see online supplemental appendix C). These are completed and stored on Way to Health (W2H), an automated information technology platform at the University of Pennsylvania that integrates wireless devices, conducts clinical trial randomisation and enrolment processes, delivers messaging (via text or email), delivers self-administered surveys and securely captures data for research purposes. W2H has been used in over 100 clinical trials inside and outside of the University of Pennsylvania. Each consenting patient completes an eight-question enrolment form that includes demographic characteristics (age, sex, race and education) and questions relevant to the trial (symptom management, activity level and comfort using text messages) (see online supplemental appendix D). The CRC asks eligible patients who decline
consent to complete a limited consent form, providing
authorisation to collect a questionnaire with an additional question (“Why did you choose not to participate in the study?”) (see online supplemental appendices E and F). This nine-question survey allows us to explore if the study design may unintentionally exclude patients of older age, specific races, lower education, or decreased email or text message access or use. The CRC also assists with setting up W2H and their Fitbit device in person or by phone or a virtual meeting (a support partner is encouraged to attend).

Randomisation and allocation concealment
Patients are randomised in a 1:1:1 fashion into arms A, B or C (Figure 1). Randomisation is completed electronically through W2H. After the patient enrolls in the study and signs the consent, the patient completes the baseline demographic survey (as described previously) and W2H generates a link to the next step. If the patient is enrolled in arm A, the iPad includes no extra links and states that enrolment is complete. If the patient is selected for arms B or C, the participant’s W2H profile is sent an option to connect their Fitbit. The arms are randomly assigned by W2H using a random number generator, and arm assignment is given to the patient if asked. One of the study PIs (CRM) and the statistician (YZ) are blinded to patient randomisation.

Subject compensation
Patients in arms A, Band C are compensated with a $25 gift card for completing their first utility survey at 3 months after enrollment. Patients are eligible for a second payment of $25 (uploaded to their gift card) after completing their second and final utility survey at 6 months after enrollment. Patients in arms B and C are permitted to keep the Fitbit as part of the trial; Fitbits had a value of $80 on purchase. The CRC delivers a gift card to each participant shortly after they complete their 3-month utility survey and informs them to keep the card for the remainder of the study.

Interventions
The three arms in this trial include (A) usual care, (B) remote PGHD integrated into a PROStep dashboard delivered to oncology clinicians at each visit and (C) the same intervention as arm B but with an additional text-based active choice intervention to patients. Patients randomised into arm A will not have any intervention but will complete baseline and 3 and 6-month surveys. The trial does not dictate visit frequency, and patient encounter frequency across arms will be compared and reported in the main analysis.

PGHD collection
PROs
Once enrolled, patients in arms B and C receive a baseline PRO survey after they have consented and completed their enrolment questionnaire. These eight-question PRO surveys are sent to participants weekly on Monday mornings at 10:00 via text message on their mobile phone from the W2H platform. The text messages inquire about seven symptoms, which are selected from a list of 12 validated symptoms from the National Cancer Institute’s Common Terminology Criteria for Adverse Events and are scored on a 5-point scale from 0 (no present) to 4 (disabling); the final selection of symptoms was determined after focus groups with lung and GI oncology clinicians at PCAM.52 The patients also receive a validated question asking about their activity level over the prior month (Table 2).53 For patients who do not respond to their PRO survey, automatic reminder alerts are sent on Tuesdays and Thursdays at 10:00 via W2H. If patients do not respond in 2 weeks, a CRC will follow up by phone. Weekly PRO data are reported in the dashboard delivered at each oncology visit and described as follows.

Step count monitoring
Fitbits have been shown to accurately measure step counts in previous research studies.54–56 Each patient enrolled to arms B and C is given a Fitbit Inspire HR at enrolment. The CRC instructs patients on how to set up and wear their Fitbit and periodically sync the device with their phone to send step data to W2H. As the device has a 5-day memory, patients receive a reminder to synchronise their Fitbit two times per week as well as 2 days before a clinic visit unless the data have been synchronised in the prior
For patients enrolled in arms B and C, the patient’s medical oncology clinician—physician, physician assistant or nurse practitioner—will be given a PROStep dashboard in paper or electronic form at each visit after enrolment. These dashboards include (figure 2)

1. Summary report: brief text at the top of the dashboard that describe any severe symptoms (≥3) or abrupt worsening symptoms (change in ≥2 points from the previous survey) from the PRO surveys and/or a 10% decrease in step count from the previous week.
2. The date of the patient’s last outpatient palliative care visit, if any.
3. The date of the patient’s last documented serious illness conversation, a structured conversation about patient goals and end-of-life wishes, if any.\textsuperscript{57}
4. PROs: table that displays patient responses to PRO questions over the last three surveys.
5. Step data: graph of average weekly step counts.
6. Acute care use: the number of oncology urgent care, emergency department visits and inpatient admissions in the past 90 days in the University of Pennsylvania Health System, as well as the date of the most recent event.

To create these dashboards, W2H collects the weekly PRO responses and step counts sent by patients and automatically sends data for each patient to trained research personnel in the form of an Excel (version 2016) spreadsheet 1–2 days prior to their upcoming oncology appointment. Research personnel copy these data to an Excel template that generates the personalised dashboards and physically deliver a printout of each dashboard to clinicians’ offices on the morning of their appointment. These can also be sent electronically if staff is unable to physically travel to PCAM (as was often the case due to COVID-19 restrictions in place during some of the trial period).

### Patient nudge to discuss symptoms

Patients enrolled in arm C receive an additional nudge prior to their oncology appointments. At 08:00 on the morning of every scheduled appointment, W2H automatically sends a text message summary of worsening symptoms based on their PRO surveys (ie, patient reports a severe symptom (≥3) or abrupt change in symptom severity (≥2)) and step data. This is followed by an active choice intervention consisting of the following question: ‘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’. The purpose of this active choice intervention is to encourage patients to discuss their reported symptoms with their clinician at their upcoming appointment (figure 3).

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Pro Survey</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. In the last 7 days, how often did you have nausea?</td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>Rarely</td>
</tr>
<tr>
<td>2. In the last 7 days, how often did you have loose or watery stools (diarrhea/diarrhoea)?</td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>Rarely</td>
</tr>
<tr>
<td>3. In the last 7 days, what was the severity of your constipation at its worst?</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>Mild</td>
</tr>
<tr>
<td>4. In the last 7 days, what was the severity of your pain at its worst?</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>Mild</td>
</tr>
<tr>
<td>5. In the last 7 days, how much did your shortness of breath interfere with your usual or daily activities?</td>
<td></td>
</tr>
<tr>
<td>Not at all</td>
<td>A little bit</td>
</tr>
<tr>
<td>6. In the last 7 days, how often did you have sad or unhappy feelings?</td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>Rarely</td>
</tr>
<tr>
<td>7. In the last 7 days, how often did you feel anxiety?</td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>Rarely</td>
</tr>
<tr>
<td>8. Over the past week I would generally rate my activity as</td>
<td></td>
</tr>
<tr>
<td>0, normal with no limitations</td>
<td></td>
</tr>
<tr>
<td>1, not my normal self, but able to be up and about with fairly normal activities</td>
<td></td>
</tr>
<tr>
<td>2, not feeling up to most things, but in bed or chair less than half the day</td>
<td></td>
</tr>
<tr>
<td>3, able to do little activity and spend most of the day in bed or a chair</td>
<td></td>
</tr>
<tr>
<td>4, pretty much bedridden, rarely out of bed</td>
<td></td>
</tr>
</tbody>
</table>
Data safety and monitoring

At the time of initiation of a new line of treatment, it is standard practice for patients with cancer to be given anticipatory guidance on when to seek medical attention. This practice will continue in this trial, and participants are reminded to contact their care team in the usual recommended fashion for any issues that arise during their care. They are also 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 PI and CRC are notified if a participant reports a severe symptom (≥3) or any abrupt change in symptom severity (≥2), which also triggers an alert to the patient’s care team. In this way, multiple physicians will be aware of escalating symptoms.

Consent

On recruitment, the CRC contacts 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 are directed to the W2H portal by the CRC, who uses an iPad to create a username for the new patient. On reaching the portal, potential participants are led through an automated online informed consent process (online supplemental appendix C). Successive screens explain the voluntary nature of the study, the risks and benefits of participation, alternatives to participation and the process for study withdrawal. On the final consent screen, a clearly delineated button enables 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 (online supplemental appendix D). Those who elect not to participate are asked to grant permission (or not) for the study team to complete a brief survey. An abbreviated study decline consent form is used for this purpose, similarly requiring the click of a clearly delineated button to agree (or not) to limited data collection and a platform electronic signature (online supplemental appendix E).

We received from the institutional review board (IRB) a waiver of informed consent for consenting physicians. Prior to launching the study, the research team introduced clinicians to the trial at a weekly tumour board meeting for relevant GI oncology and thoracic medical oncologists. The PIs went over the study plan including the design, background and outcomes. We obtained verbal consent from all providers to (1) recruit patients into this study and (2) answer a utility survey at 3 and 6 months following enrolment for each patient. As the study does not limit clinical care in any way, clinician consent was obtained verbally at these meetings.

Outcomes

The two coprimary outcomes will compare responses between arm A and arms B+C for the following two questions asked of patients at 6 months after enrolment (or 3 months if the patient did not complete their 6-month survey) (table 3):

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

These will be assessed on a 5-point Likert scale (1=not at all, 2=slightly, 3=moderately, 4=considerably, 5=completely). Of note, the prespecified comparison was between arm A and arm B and arm C, but the protocol was amended prior to any data review to combine the intervention arms due to slow enrolment and higher than expected dropout.

The secondary outcomes will compare these same two questions measured at 3 months between arm A and arms B+C. Another secondary outcome will be cumulative adherence between patients in the intervention arms at both 3 and 6 months. Patients are considered adherent for each week that they complete their PRO survey and sync their Fitbit step data for four or more days. Cumulative adherence is calculated when these weeks are divided by the total number of weeks that a patient was enrolled in the trial. We will also analyse trends in the PROStep data (ie, PRO survey scores and Fitbit step data) among intervention patients.

Exploratory outcomes will include multiple use metrics collected via the electronic medical record (EHR; i.e., number of ER visits, hospitalisations, palliative care consults, documented advanced care planning notes, and documented serious illness conversations. Patient utility will be another exploratory outcome measured using survey data at 3 and 6 months. Additionally, we will further analyse patient surveys by comparing the same two questions from the primary outcome between each individual arm and analyse responses to the remaining survey questions. Finally, we will measure clinician utility by comparing their survey responses at 3 and 6 months (or 3 months if the clinicians did not complete their 6-month survey for a specific patient).

**Analysis plan**

We will report descriptive statistics for patient characteristics in each arm, as well as their responses to the surveys of 3 and 6 months and PGHD.

For the two survey questions that compose the two coprimary outcomes, the study will compare the mean
score from each survey question at 6 months across all three study arms using a Kruskal-Wallis test with p<0.05 indicating statistical significance. If the result is significant, the study will use Tukey’s honestly significantly difference test to test pairwise comparisons between the study arms. If the outcomes for any arm are skewed (not normally distributed), outcomes will be log-transformed before applying all tests.

For the secondary outcomes, a similar analysis will be conducted for the secondary outcome comparing the same questions but taken from the 3-month rather than the 6-month utility survey. We will apply t-tests to compare mean response scores for the remaining secondary outcomes. We will use Kruskal-Wallis tests for continuous outcomes and χ² tests for categorical variables to compare the secondary outcomes of adherence rates and trends in PROStep data for arm B versus arm C at 3 and 6 months.

To assess whether responses in surveys of 3–6-months differ across arms, we will conduct an analysis of covariance model with the baseline score and arms as covariates, and change of score as the dependent variable.

Patients are welcome to discontinue the trial at any time, for any reason, via text, email, phone or at a visit with their oncologist. Patients who enrol in hospice will be disenrolled and will no longer receive surveys or prompts to reduce patient burden near the end of life, but we will use their most recent survey in the analyses of 3 and 6 months. If a patient exits the study early but more than 4 weeks after enrolment or 4 weeks after the 3-month survey, they will receive the utility survey of 3 or 6 months, respectively. This may not be possible for some patients who exit the study to enter hospice or due to death. If patients die or are otherwise unable to complete a survey, they will be omitted from the analysis for the relevant outcome. For patients who disenrol from the trial for any reason (voluntary, death, etc) but meet this 4-week threshold, their clinicians will receive a utility survey.

Statistical power
Power calculations were performed for the coprimary outcomes as originally specified prior to mid-trial protocol amendment: symptom and functional status understanding at 6 months between arms C versus A and arms B versus A. We estimated that there would be at least 80% power to detect a 0.68 increase on the Likert scale scores of symptom and functional status understanding. This estimate assumes that the baseline score was 3 (moderate symptom understanding) with a common SD of 1, and a significance level with a two-sided alpha of 0.025 for each coprimary outcome.

Patient and public involvement
Patient participants were not involved in the development of the research question or outcome measures. Patient and physician participants were involved in the design of the dashboards and text message wording. The utility surveys at 3 and 6 months include a short section of questions assessing the burden of the intervention among patients in arms B and C.

DISCUSSION
Patients with advanced, incurable cancer who receive systemic therapy often have significant symptoms and declining functional status that is under-recognised and poorly managed by oncology clinicians. Remote electronic PRO and wearable step monitoring offer an opportunity to more accurately track and convey longitudinal information about symptoms and activity level for patients undergoing cancer treatment. This trial tests the impact of an intervention consisting of presenting remote PGHD via clinician dashboards, with or without a patient active choice intervention, on shared patient–clinician understanding of symptoms and functional status.

This study has several strengths, including (1) its patient-level randomised design; (2) enrolment of patients with two advanced cancers who often undergo chemotherapy and experience high symptom burden and functional decline during the course of treatment; (3) intervention that combines activity monitoring and symptom self-reporting to assess symptom burden and functional status decline; (4) use of patient and clinician behavioural prompts to improve communication about symptom management, rather than just passive measurement of symptoms; and (5) patient-centred primary outcomes that reflect patient’s perceptions of adequate clinician communication and management of symptoms and functional status.

Limitations of this pilot study include its (1) single-institution setting; (2) potential lack of generalisability to other cancers, particularly haematological malignancies; and (3) reliance on adherence to text-based PRO assessments and prompts. If successful, we plan on conducting larger, multi-institutional randomised controlled trials to test interventions consisting of PGHD collection and behavioural prompts. Additionally, real-world adherence to PRO collection is a limitation of many PRO collection programmes, and our incorporation of passive monitoring may offer an important mechanism of PGHD collection that is not dependent on a patient actively responding to a questionnaire. Thus, despite known limitations, this study is likely to provide novel data to guide the deployment of PGHD programmes in other outpatient oncology settings.

We hope that nudges to patients and clinicians based on longitudinal PGHD collection will make changes in patient symptoms, quality of life and functional status more transparent to oncology clinicians, leading to more informed discussions and decisions about the burden-some impacts of advanced cancer and its treatment. Future studies may extend this work to evaluate the role of PGHD in monitoring symptoms and functional status for populations excluded from this study, such as patients with other cancers, patients who receive non-chemotherapy anticancer drugs, patients who receive...
their chemotherapy remotely and patients who do not own a smart phone. Additionally, future studies should also assess caregiver perceptions towards this and other PGHD-related interventions, given the importance of caregivers in facilitating patient understanding of digital health tools and survey completion.

ETHICS
This study has been approved by the University of Pennsylvania IRB (protocol #843616). This trial is registered with clinicaltrials.gov with the official title 'A Feasibility Trial Using Remote Patient-reported Outcomes and Wearable Technology-reported Step Data to Compare Engagement, Utilisation, and Functional Status in Patients With Incurable Lung and Gastrointestinal Cancers'.

The potential risks to human subjects in this project include (1) risks of breach of confidentiality of personal health information, (2) risks of participants misinterpreting this tool as a means of quick communication with their care team and (3) risks of a breach of data for participating clinicians. To minimise these risks, our study employs numerous safeguards to protect human subjects. These include an experienced and well-trained study team, a robust informed consent process, state-of-the-art data security, and ongoing emphasis that the electronic symptom-reporting tool is investigational and not a replacement for usual means of communication with patients' care teams.

DISSEMINATION
We anticipate collection of data for all outcomes will be complete in December 2021. In addition to presentation at scientific meetings and publication in scholarly journals, we plan to leverage resources at Penn to place our results in the public domain where they can be openly discussed before any policy changes are recommended. This includes developing and implementing strategies to describe results in ways that key stakeholders can understand and implement.

TRIAL STATUS
At the time of manuscript submission, 105 patients from the University of Pennsylvania clinics have consented to participate and have been randomised, and 82 are currently enrolled in the trial.

Contributors RBP and CRM conceptualised the study design and obtained the funding. RBP, CRM, PEG, LMS, LNG and MSP contributed to the development of the study design. WF, JW, JW, NK, MK and MB were responsible for the development of the data collection platform, field testing of the study logistics, including clinic and subject recruitment. RBP, CRM, YZ and JC are responsible for the development of the analysis plan. WF, RBP and CRM drafted the first version of the manuscript. All authors read, edited and approved the final version.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were involved in the design, conduct, reporting or dissemination plans of this research. Refer to the Methods and analysis section for further details.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by the University of Pennsylvania institutional review board (protocol #843616). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

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in patients with advanced cancer; flipping the paradigm to improve timing of palliative and end-of-life discussions and reduce unwanted health care costs. Oncologist 2019;24:76–85.
Appendix A: PROStep Recruitment Script

Hello, am I speaking with ____________? My name is ____________ and I am a clinical research coordinator calling from the University of Pennsylvania.

Dr. _________________ gave us permission to contact you for a clinical trial we are currently enrolling for and I was wondering if you had a few minutes to hear a little bit about it and see if you were interested?

If YES -> Continue below

IF NO -> Thank the person for their time and end the call.

The purpose of this study is to assess the feasibility of remote symptom and activity monitoring of patients with lung and gastrointestinal cancers, facilitate the recognition and communication of a patient’s symptoms, and compare adherence to the intervention based upon the feedback that patients receive.

If you were to participate in this study, you will be randomized (like flipping a coin) to an intervention or control arm. The reason we do this is because we want to be sure to assess the impact of patient feedback.

Your study participation will take place over 6 months, with all of your study activities being conducted remotely. All patients will receive a short questionnaire at 3 and 6 months following enrollment.

If you are randomized to the control arm, you will only be asked to complete those two questionnaires.

If you are randomized into the intervention arm, you will receive short weekly surveys via text message that will ask you about your symptoms on a 1-5 Likert scale. You will also receive a Fitbit wearable device that will track your step, distance, active minutes, sleep, and heart rate data. You will be asked to wear this device on a daily basis as it will allow your care team to monitor activity trends. Some patients in this group will also receive an additional text message prior to oncology appointments describing survey and step data.

Over the 6 month trial period, you will receive approximately 24 surveys via text message. There is a compensation of up to $50 in the form of a $25 payment after completing your questionnaires at 3 and 6 months after enrollment. If you are randomized into an intervention arm, you will also be permitted to keep your Fitbit device at the end of the trial.

Do you have any questions? If you are interested, we can talk more about the details. We can also give you the consent forms to look over and we can schedule a time to call you in a few days to discuss the details and answer any questions.

Do you think that this is something that you are interested in learning more about?

IF YES -> Great, I will send you a copy of the informed consent form. I can send the information via email or if you prefer I can mail it out.

IF YES -> Study coordinator will go into more details about the study visits and/or schedule the full screening visit.

IF NO -> Thank the person for their time and end the call.
Appendix B: PROStep Email Recruitment Letter

[Date]

[Patient Name]
[Patient Address]

Dear [Patient Name],

I am writing to let you know that my office is participating in a research study called 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. We are assessing the recognition and communication of a patient’s symptoms and functional status with their clinicians. We have reviewed your medical records and determined that you may be eligible to participate in this study.

If you qualify to participate for this 6-month trial, you may be asked to do the following:

- Complete a short questionnaire via text message at 3 and 6 months following enrollment.
- Complete weekly surveys via text message that will ask you about your symptoms on a 1-5 Likert scale.
- Wear a Fitbit wearable device that will track your step, distance, active minutes, sleep, and heart rate data. You will be asked to wear this device on a daily basis as it will allow your care team to monitor activity trends.
- Receive an additional text message prior to oncology appointments describing survey and step data.

There is a compensation of up to $50. Patients who receive a Fitbit device will be permitted to keep it at the end of the trial.

If you would like to learn more about potentially participating in this research study please contact [CRC Name] at [CRC phone number].

It is important that you understand that this letter is not telling you that you should or should not join the research study. That decision is completely up to you. Your participation in this study is voluntary. Whether or not you want to participate will have no effect on your future clinical care.

If you are not interested in this study you do not need to respond to this letter. If you do not wish to participate in this study you do not need to respond to this letter but, as part of our mailing list, you may receive a brochure about this study in the future. You can disregard this or, if you change your mind, contact us in the future.

Warm Regards,

Ravi Parikh, MD, MPP
Principal Investigator
Appendix C: Informed Consent and HIPAA Authorization

UNIVERSITY OF PENNSYLVANIA
INFORMED CONSENT AND HIPAA AUTHORIZATION FORM

Protocol Title:
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

Principal Investigator:
Ravi B. Parikh, MD, MPP
1102 Blockley Hall
423 Guardian Drive
Philadelphia, PA 19104
215-746-8437

Emergency Contact:
William Ferrell, MPH
1133 Blockley Hall
423 Guardian Drive
Philadelphia, PA 19104
215 746 8671

Why am I being asked to volunteer?
You are being invited to participate in a research study. Your participation in this study is voluntary, which means that you can choose whether or not to be in the study. Before you can make your decision, you will need to know the study’s purpose, your role in the study, and possible risks and benefits from participating. The following sections will explain the study in detail. After reviewing this information, you will see an option to select whether or not you would like to participate in the study. If you choose to participate and are enrolled, you may withdraw from the study at any time.

What is the purpose of the study?
The purpose of the study is to learn more about self-reporting of symptoms via mobile phone among patients receiving treatment for lung and gastrointestinal (GI) cancers.

How long will I be in the study?
The study will last for 6 months.

What am I being asked to do?
- During the enrollment process, you will be asked to fill out a brief questionnaire, which should take 2-3 minutes to complete.
- If you meet necessary requirements for the study, you will be asked to fill out a short questionnaire at the start of the study, and again at 3 and 6 months. This should take less than 5 minutes to complete each time and be conducted via text message.
- You may be asked to wear a Fitbit device throughout the study period that can track steps, distance, active minutes, sleep, and heart rate data.
- Finally, you may be asked to use your mobile phone to report information about specific symptoms you may be experiencing. A weekly text message will prompt you to fill out a short
electronic symptom survey by mobile phone, which should take only a few minutes to complete. This information will be transmitted to your electronic medical record and made available for your care team to use to help manage your symptoms; all other information collected as part of the study will be kept confidential.

**What are the possible risks or discomforts?**
The risks of participation are expected to be minimal. There is a minor risk of loss of confidentiality and privacy. The research team will take every necessary precaution to make sure your confidentiality and privacy are maintained. Information from the weekly mobile-phone based symptom surveys will be transmitted to the electronic medical record and thus made available to your clinical team; all other information will be kept confidential. Your personal information will be used only by study team members, who have been trained to use secure protocols to maintain the privacy of your data. We will use commercial-grade encryption to protect your information similar to that which is used to protect electronic health records. Whenever possible, data will be de-identified to protect your privacy.

Also, it is important to realize that self-reporting your symptoms via mobile phone as part of the study is NOT a replacement for usual means of communication with your doctor. If you are having symptoms that you think need urgent medical attention, you will need to contact your doctor directly.

**What if new information becomes available about the study?**
During the course of the study, we may find more information that could be important to you. This includes information that, once learned, might cause you to change your mind about being in the study. We will notify you as soon as possible if such information becomes available. You will always have the right to change your mind about participating in the study.

**What are the possible benefits of the study?**
Weekly self-reporting of symptoms via mobile phone may improve communication with your doctor and may help your doctor manage your symptoms over time. However, this intervention is experimental and thus its benefits are uncertain. You may not get any direct benefit from being in this research study.

**What other choices do I have if I do not participate?**
Your alternative to participating in the study is not to participate in the study. If you choose not to participate, there will be no loss of benefits to which you are otherwise entitled.

**Will I be paid for being in the study?**
Yes, there is a compensation of up to $50 in the form of a $25 payment after completing your questionnaires at 3 and 6 months after enrollment. If you are randomized into an intervention arm, you will also be permitted to keep your Fitbit device at the end of the trial.

**Will I have to pay for anything?**
There is no cost for you to participate in the study. However, you will receive weekly communications via text message, and standard text message charges may apply.

**Can I leave the study before it ends?**
Yes, participation in the study is voluntary. You can decide to stop participating at any time and for any reason. If you choose to leave the study, we will not delete information we have already collected from
you, but we will stop collecting any new information and will stop contacting you. To stop participating in the study, please contact the study staff.

**How will my personal information be protected?**
We will do our best to make sure that the personal information we collect about you is kept private and secure. Your personal information will only be given out if necessary (e.g., if required by law to prevent possible injury to you or others).

Your information will be kept in a secured, password-protected file at the University of Pennsylvania. Your information will be transmitted and stored using very secure systems. The network servers where your data are stored sit behind firewalls that do not allow unauthorized access and are physically located in a secure server room that can only be accessed by critical staff members. The investigator and staff involved with the study will keep your personal information collected for the study strictly confidential. All of these personnel will have completed research and confidentiality training.

Please refer to information below that explains more specifically how your personal information will be used:

- Way to Health (W2H) study and data storage portal supported by the Penn Medicine Academic Computing Services (PMACS) infrastructure
- Twilio Cloud Communications (to send you text messages)
- 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.

Once your personal information is disclosed to others outside the University of Pennsylvania, it may no longer be covered by federal privacy protection regulations. You can review the privacy policies of these companies here:


**What information about me may be collected, used or shared with others?**
During enrollment, you will be asked to report your name, telephone number, and date of birth, as well as background information such as gender, race, education and income level. Additional information about your medical history, including details about your cancer diagnosis and its treatment, will be collected from your electronic medical record by the study team. Finally, data will be collected during the study regarding your symptoms, quality of life and care utilization.

**Why is my information being used?**
Your information will be used by the research team to contact you during the study. Your information and results of surveys are used: a) to do the research, b) to oversee the research, c) to see if the research was done right, and d) to evaluate and manage research functions.

**Who may use and share information about me?**
Your information will be used by authorized members of the University of Pennsylvania study team. The following individuals may use or share your information for this research study:

- The investigator for the study and the study team
- Other authorized personnel at Penn, including offices that support research operations
- Other research personnel with access to the databases for research and/or study coordination and as otherwise approved by the IRB

Who, outside of the School of Medicine, might receive my information?
If required by law and/or necessary for oversight purposes, your information may be shared with 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. Once your personal health information is disclosed to others outside the School of Medicine, it may no longer be covered by federal privacy protection regulations. The Principal Investigator or study staff will inform you if there are any additions to the list above during your active participation in the trial. Any additions will be subject to University of Pennsylvania procedures developed to protect your privacy.

How long may the School of Medicine use or disclose my personal health information?
Your authorization for use of your personal health information for this specific study does not expire. Your information may be held in a research database. However, the School of Medicine may not re-use or re-disclose information collected in this study for a purpose other than this study unless:

- You have given written authorization
- The University of Pennsylvania’s Institutional Review Board grants permission
- As permitted by law

Can I change my mind about giving permission for use of my information?
Yes. You may withdraw or take away your permission to use and disclose your information at any time. You do this by sending written notice to the investigator for the study. If you withdraw your permission, you will not be able to stay in this study. Any information collected before your withdraw from the study may be used by the study team for research purposes.

What if I decide not to give permission to use and give out my health information?
Then you will not be able to participate in this research study.

Who can I contact with other questions about the study?
If you have questions, concerns or complaints regarding your participation in this research study or if you have any questions about your rights as a research subject, you should speak with the Principal Investigator listed on page one of this form. If a member of the research team cannot be reached or you want to talk to someone other than those working on the study, you may contact the Office of Regulatory Affairs with any question, concerns or complaints at the University of Pennsylvania by calling 215-898-2614.

You will be provided a copy of this Informed Consent and HIPAA Authorization Form describing your confidentiality and privacy rights for this study. By clicking the button stating that you want to participate in the study and signing your name below, you will have consented to enroll. This means you are permitting the School of Medicine to use and disclose personal health information collected about you for the research purposes as described above.
CONSENT
This consent form will be saved electronically and a copy will be provided to you for your records.

Please select your choice and then click the NEXT button on the right to continue.

☐ I want to participate

☐ I do NOT want to participate

Name: __________________________  Signature: __________________________  Date: __________
Appendix D: Enrollment Questionnaire

You have consented to participate in a study measuring the impact of weekly electronic symptom reporting by mobile phone among patients receiving treatment for lung or gastrointestinal cancer. Please answer the following questions to complete your enrollment in this study.

1. What is your age?
2. What is your sex?
   a. M
   b. F
3. Which race best describes you?
   a. White
   b. Black or African American
   c. Asian
   d. Other
4. What is the highest level of education you have completed?
   a. Some or graduated from High School / GED
   b. Vocational, technical or trade school training
   c. Some college but did not receive a college degree
   d. Associate’s degree
   e. Bachelor’s degree
   f. Post-graduate degree
5. How would you rate your current symptoms due to your cancer or it’s treatment?
   a. Well-controlled
   b. Poorly-controlled
   c. Prefer not to answer
6. How would you rate your current activity level?
   a. I am fully active and out of a bed or chair most of the day
   b. I cannot do physically strenuous activity but otherwise am active and out of a bed or chair most of the day
   c. I cannot do most activities but am out of a bed or chair most of the day
   d. I am in a bed or chair most of the day
   e. I am completely disabled
7. Do you feel comfortable using text messaging?
   a. Yes
   b. No
   c. Maybe
8. Generally, how often do you send/receive text messages?
   a. Not at all
   b. Fewer than 3 times weekly
   c. 3-5 times weekly
   d. Nearly every day
   e. Multiple times every day
Appendix E: Study Decline Consent

UNIVERSITY OF PENNSYLVANIA
STUDY DECLINE CONSENT

Protocol Title: 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

Principal Investigator: Ravi B. Parikh, MD, MPP
1102 Blockley Hall
423 Guardian Drive
Philadelphia, PA 19104
215-746-8437

You declined to participate in the PROStep research study. You are now being asked to allow us to collect limited information about you. It is voluntary to give permission. If you decide not to give permission, your care at our cancer center will not be affected in any way.

We are asking for permission to collect limited information about your health and computer/mobile phone experience. This information would help us compare patients who chose not to participate in our study to those who chose to participate.

The risks to participation include potential loss of confidentiality. We will not collect or retain any information that could link this information to you after we have recorded it for the study. Therefore, it will not be possible to withdraw your information from the study once it has been collected.

If you agree to give permission, we will collect the information from a one-time very short (2-3 minutes) survey and from your medical chart. The information we collect will remain confidential at all times and be maintained in a password protected file. Only the investigator for the study, the study team and the IRB may use your information. None of your information will be disclosed to others outside of the University of Pennsylvania Health System.

If you have questions regarding your rights or welfare as a research participant you may contact the University of Pennsylvania’s Institutional Review Board at 215-898-2614.

CONSENT
This consent form will be saved electronically and a copy will be provided to you for your records.

Please select your choice and then click the NEXT button on the right to continue.

☐ I consent to allowing the use of limited information for study purposes

☐ I do NOT consent to the use of any of my information for the study

Name: __________________________ Signature: __________________________ Date: __________
Appendix F: Decline Enrollment Questionnaire

You have chosen NOT to participate in the PROStep study but have consented to providing a limited amount of information to the study team. Please answer the following questions. You will not be contacted again after completion of this short survey.

1. What is your age?
2. What is your sex?
   a. M
   b. F
3. Which race best describes you?
   a. White
   b. Black or African American
   c. Asian
   d. Other
4. What is the highest level of education you have completed?
   a. Some or graduated from High School / GED
   b. Vocational, technical or trade school training
   c. Some college but did not receive a college degree
   d. Associate’s degree
   e. Bachelor’s degree
   f. Post-graduate degree
5. Do you feel comfortable using e-mail?
   a. Yes
   b. No
   c. Maybe
6. Generally, how often do you use e-mail?
   a. Not at all
   b. Fewer than 3 times weekly
   c. 3-5 times weekly
   d. Nearly every day
   e. Multiple times every day
7. Do you feel comfortable using text messaging?
   a. Yes
   b. No
   c. Maybe
8. Generally, how often do you send/receive text messages?
   a. Not at all
   b. Fewer than 3 times weekly
   c. 3-5 times weekly
   d. Nearly every day
   e. Multiple times every day
9. Why did you choose not to participate in the study?
   a. _____________________