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Social and Behavioral Sciences Human Research Protocol

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PROTOCOL TITLE:
Behavioral Economic Strategies to Improve PRO adherence (BEST-PRO)

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ABSTRACT

Routine monitoring of patient-reported outcomes (PROs) for patients with advanced solid malignancies is an evidence-based practice that improves symptoms and quality of life, reduces unplanned acute care, and extends overall survival. However, patient-level adherence and clinician-level adoption to PRO monitoring is suboptimal. We will conduct a three-arm randomized pragmatic trial to test the implementation and effectiveness of patient- and nurse-directed strategies to improve engagement in PRO monitoring across in-clinic and remote monitoring settings. Participants will include patients initiating systemic cancer treatment for solid malignancies at participating Implementation Laboratory sites within the Penn Implementation Science Center in Cancer Control. Eligible patients will be randomized independently to: (1) usual practice (i.e., encounter-based PRO administration via patient portal or tablet); (2) encounter-based PRO monitoring with patient reminders and nurse alerts; or (3) remote PRO monitoring with patient reminders and nurse alerts. The primary outcome will be PRO adherence, measured at the patient level as the proportion of expected PRO questionnaires completed per patient over a 3-month follow-up period. Secondary outcomes will include measures of clinical adoption of PROs, and patient health-related quality of life, duration of therapy, acute care utilization, and treatment delay/modification.

INTRODUCTION

Routine monitoring of patient-reported outcomes (PROs) for patients with advanced solid malignancies is an evidence-based practice that improves symptoms and quality of life, reduces unplanned acute care, and extends overall survival.[1-8] Still, there is variation in adoption of and adherence to routine PRO monitoring, owing to multilevel barriers to implementation and concerns among clinicians regarding the utility of PROs in actual practice.[9-14] While high levels of patient adherence to PRO monitoring have been reported in clinical trials,[2,7,8,15-17] real-world adherence is

suboptimal. Our preliminary research shows that in a large, multi-site rollout of PROs, patient-level adherence was less than 50 percent, with patients from racial and ethnic minority groups even less likely to complete PRO questionnaires and more likely to report uncontrolled symptoms. Moreover, only half of Penn medical oncologists report that routine PRO monitoring is useful in practice. There is critical need to develop, test, and disseminate strategies to improve patient-level PRO adherence to ensure optimal and equitable symptom management, quality of life, and survival for patients with advanced cancer.

Implementation strategies informed by behavioral economics are ideally suited to address this challenge, as it is fundamentally one of clinician and patient behavior change. For PRO monitoring programs to succeed in transforming cancer care, patients must longitudinally complete PRO questionnaires and clinicians must use the resultant patient-reported data in clinical decision-making. Clinician engagement and use of PRO data begets patient engagement,[9-12] in part by signaling an approved behavior (injunctive norm) to which patients desire to conform. Repeated feedback is important for sustaining other health-promoting behaviors such as medication adherence.[18] In particular, gamification strategies, which harness game design elements and patient heuristics to motivate behavior change, have shown promise.[19-25] However, little research has harnessed these insights to promote longitudinal PRO adherence.

OBJECTIVES:

(1) Evaluate the implementation and effectiveness of patient- and nurse-directed strategies across in-clinic and remote monitoring settings, using a three-arm pragmatic cluster RCT.
- H1a: Nudges to patients and alerts to nurses will improve patient-level PRO completion and clinician-level PRO engagement

(2) Evaluate moderators of implementation effects, using a quantitative evaluation of secondary data from the electronic health record, area-level data via geocoding, and clinician surveys.
- H2a: The impact of nudges will be moderated by clinician, patient, and outer setting factors.
- H2b: Baseline PRO adherence rates will differ by race, ethnicity, and socioeconomic status.
- H2c: The nudge arms will not be significantly differentially effective across subgroups.

BACKGROUND:

Routine PRO monitoring is an evidence-based practice that improves patient outcomes. Patients with cancer commonly experience symptoms which go unrecognized by clinical teams up to half of the time.[26,27] PROs are a powerful tool to bridge this gap, amplifying the patient experience and improving communication between patients and clinicians.[1,28,29] Basch et al. conducted a seminal clinical trial in which weekly PRO symptom assessments with care team alerts led to reduced care utilization, improved quality of life, and lengthened overall survival among patients receiving active treatment for advanced solid tumors.[2,3] Subsequent randomized trials have corroborated the quality of life and survival advantages of PRO monitoring in other cancer populations and practice settings.[4-8]

Real-world adherence to PRO monitoring is lower than in seminal clinical trials, with potential racial/ethnic disparities. Multilevel barriers to PRO implementation exist at the patient, clinician, practice, and system levels.[7,9,10,12] While patient adherence to PRO monitoring in seminal trials ranged from 70 to 90 percent,[2,8,15-17] real-world adherence is much lower and more variable. Our preliminary research (under review) demonstrates that in a large, multi-site rollout of PRO monitoring, mean patient-level adherence was less than 50 percent. Moreover, compared to non-Hispanic White patients, Black and Hispanic patients were 9% and 4% less likely to complete PRO questionnaires, respectively, but more likely to report more severe symptoms. These results highlight that historically marginalized subgroups may benefit less from current methods of PRO administration, potentially reinforcing existing disparities in symptom management if not remediated.[30]

This will be the first study to apply behavioral economic strategies to align clinicians and patients in achieving sustained patient-level PRO adherence, and addresses limitations of current PRO approaches. Current approaches to PRO collection are limited by: (1) suboptimal clinician engagement, (2) encounter-based assessments which preclude longitudinal monitoring of PROs outside of the clinic, and (3) insufficient automated effectors actively linking reported symptoms with clinical response. This proposal addresses these limitations by employing behavioral strategies directly targeting clinician engagement, utilizing novel electronic remote monitoring methods to maximize real-time PRO capture, and linking these with pathway-driven automated effectors.

CHARACTERISTICS OF THE STUDY POPULATION:

1. ***Target Population and Accrual:***
   The target population will include approximately 480 patients with solid malignancies cared for at the following practice sites of the Penn Medicine Abramson Cancer Center (ACC), referred to hereafter as the "Implementation Laboratory": **Perelman Center for Advanced Medicine (PCAM) and Princeton Health**. In this pragmatic trial, eligible patients will accrue as they initiate a new line of systemic cancer treatment.

2. ***Key Eligibility Criteria:***
   Key inclusion criteria
   Eligible patients must meet the following criteria:
   - Initiate a new line of systemic cancer therapy (ie, intravenous chemotherapy or immunotherapy) at a participating Implementation Lab site

   Key exclusion criteria
   Patients will be ineligible for ANY of the following reasons:
   - Active enrollment in a therapeutic clinical trial
   - Patient opts out of pragmatic research

3. Subject Recruitment and Screening:

Subjects will accrue to the study when initiating a new line of systemic cancer therapy (ie, intravenous chemotherapy or immunotherapy). Subject recruitment and screening will occur pragmatically via weekly queries of upcoming Epic/Beacon treatment plans, identifying patients scheduled to initiate a new line of systemic cancer therapy in the following week.

Given the pragmatic nature of this study and its objective to test implementation strategies to promote engagement in an evidence-based practice in routine cancer care, ***we are requesting a waiver of informed consent***. There are several reasons to justify this request. First, we are assessing the impact of implementation strategies delivered to patients through adjustments in existing clinical workflows using the electronic medical record and other patient communication tools. Second, it would not be feasible to consent every patient enrolled in the trial. Third, individual informed consent might impact patient behavior, thereby complicating the study design and interpretation of its findings. Fourth, none of the proposed strategies forces behavior change. No one will be coerced or forced to engage in PRO monitoring; rather, the goal of nudges is to promote evidence-based practices while preserving autonomy and freedom of choice.

4. Early Withdrawal of Subjects:

We are requesting a waiver of informed consent, so the option to withdraw early from this study is not applicable.

5. Vulnerable Populations:

We will not be targeting children, pregnant women, fetuses, neonates, or prisoners in this research study.

6. Populations vulnerable to undue influence or coercion:
We will not be targeting participants who are likely to be vulnerable to undue influence or coercion in this research study.

STUDY DESIGN:

1. Study design:
This hybrid type 2 study design[31] will simultaneously evaluate implementation and effectiveness outcomes. We will conduct a three-arm randomized pragmatic trial to test the effect of patient reminders and triage nurse alerts, in the context of remote vs encounter-based PRO monitoring, on implementation and effectiveness outcomes. Participants meeting eligibility criteria will be randomized 1:1:1 to:

(1) usual practice, consisting of encounter-based PRO monitoring;
(2) encounter-based PRO monitoring plus patient reminders and triage nurse alerts;
(3) remote PRO monitoring plus patient reminders and triage nurse alerts

Across arms, the administered PRO questionnaire will consist of 13 validated metrics spanning patient-reported symptoms, quality of life, and performance status. **[Appendix 1]** We will employ rapid cycle approaches to optimize implementation strategies prior to conducting the clinical trial.

2. Study Duration:
The study duration will be approximately 6 months, including a 3-month accrual period and 3-month follow-up period per participant over which primary outcomes will be ascertained.

METHODS:

1. Study Instruments:
We do not anticipate the use of study instruments beyond the PRO questionnaire [**Appendix 1**], which is already administered in routine practice. Any additional study instruments will be submitted to the IRB as a modification prior to use.

2. Administration of Surveys and/or Process:
We do not anticipate the use of surveys beyond the PRO questionnaire [**Appendix 1**], which is already administered in routine practice. Any additional surveys will be submitted to the IRB as a modification prior to use.

3. Data Management:
To minimize the risk of breach of data and confidentiality, we will use secure, encrypted servers to host the data and conduct the analysis. The Penn Medicine Academic Computing Services (PMACS) will be the hub for the hardware and database infrastructure that will support the project. 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. 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. Data will be stored, managed, and analyzed on a secure, encrypted server behind the University of Pennsylvania Health System (UPHS) firewall. All study personnel that will use this data are listed on the IRB application and have completed training in HIPAA standards and the CITI human subjects research. Data access will be password protected. Whenever possible, data will be de-identified for analysis.

4. Subject Follow-up:
Subjects will be followed for approximately 3 months after enrollment.

STUDY PROCEDURES:

1. Detailed Description:
Eligible patients will be identified pragmatically using the criteria listed above, and will be independently randomized to study arms using a three-arm design. A description of the three study arms follows:

(1) **Usual practice.** This arm will consist of encounter-based PRO monitoring, in which patients have an opportunity to complete PRO questionnaires via patient portal in advance of clinical encounters or via tablet during clinical encounters. While clinicians will be encouraged to view and discuss PROs with patients during clinical encounters, they will not be prompted to do so in real-time, nor will there be alerts for escalating symptoms.

(2) **Encounter-based PRO monitoring <u>plus</u> patient reminders and triage nurse alerts**. This arm consists of usual practice (described above) plus the addition of patient reminders to complete PRO questionnaires and triage nurse alerts for severe symptoms. Patient reminders will be operationalized through the Epic patient portal. Triage nurse alerts will be routed to Epic symptom management pools in response to a patient reporting moderate or severe symptoms. Patients will have the opportunity to decline or opt-out of triage nurse support. Clinical interventions stemming from triage nurse alerts will be up to the discretion of clinical teams – ie, clinical responses will be neither prescriptive nor mandatory. Notably, the entry point for triage nurse alerts (ie, Epic symptom management pools), as well as resultant clinical responses, are existing standard operating procedures/practices for patients reporting symptoms by phone.

(3) **Remote PRO monitoring <u>plus</u> patient reminders and triage nurse alerts.** This arm will consist of weekly PRO questionnaires administered via the patient portal, de-linked from clinical encounters. Patient reminders and triage nurse alerts will be operationalized as described in Arm (2).

We will use rapid cycle approaches (RCA) to optimize implementation strategies to ensure face validity and maximum effect. We will focus on optimizing content, messaging, and design. RCA procedures will involve design meetings with study team, discussions with administrators and clinicians who are members of our Implementation Lab, as well as piloting of nudges with potential participants to elicit feedback.

2. Data Collection:
The electronic medical record and other Penn Medicine secondary databases used to collect data in routine care will be used to collect information on study participants. We will also collect data from the U.S. Census via publicly available datasets.

Aim 1

The primary outcome will be PRO adherence, measured at the patient level as the proportion of expected PRO questionnaires completed per patient. Secondary specifications will include:

- % patients completing at least one PRO questionnaire during study period
- % patients completing at least one PRO questionnaire per month during the study period

Secondary implementation outcomes will include:

- % patients with at least one note documenting PROs during study period
- % patients with at least one note documenting PROs per month during study period
- For Arms 2-3 only: time to alert response

Secondary effectiveness outcomes will include:

- Symptom burden, measured as a composite and for each PRO/symptom
    a. For Arms 2-3 only: % patients who trigger alert
- Acute care utilization, measured as % patients with ED visit or hospitalization
- Treatment delays/modifications, measured as % patients with treatment delay/modification
- Duration of therapy

Aim 2

Aim 2 measures, collected through the electronic medical record and using publicly available U.S. Census data, will include:

- *Patient-level data*: age, sex, race/ethnicity, education, marital status, cancer type, cancer stage, health insurance (e.g., Medicare, Medicaid, commercial);
- *Clinician-level data*: years in practice and patient panel size;
- *Practice-level data*: setting (community vs. hospital-based), urban vs. non-urban location, and health insurance mix;
- *Ecologic-level data* linked at the patient- and practice-level, including median income and educational attainment.

3. Genetic Testing:

Not applicable

4. Use of Deception:

Not applicable

5. Statistical Analysis:

Aim 1

The design is a three-arm randomized trial, resulting in three independent study arms: (1) usual practice, (2) encounter-based PRO monitoring with patient reminders and triage nurse alerts, (3) remote PRO monitoring with patient reminders and triage nurse alerts. Implementation and effectiveness outcomes will be assessed across arms. The main comparison for the purposes of power calculations will be Arm 2 vs Arm 1. Multivariable linear regression will be used to model patient PRO adherence as a function of nudge exposure (i.e., study arm assignment). Covariates will be assessed across study arms and included in the model if unbalanced across arms. Significance will be determined using the z-score corresponding to each of the estimated effects, using a two sided type 1 error of 5%. All enrolled patients will be included in the intention-to-treat analysis.

The secondary outcomes will be similarly modeled except using logistic models as appropriate for binary outcome variables. All hypothesis tests will use a two-sided alpha of 0.05 as the threshold for statistical significance.

Power and Sample Size
For our primary comparison of patient-level adherence across study arms, we expect to have 80% power to detect a 14.5 percentage point difference in patient-level adherence, assuming baseline adherence rates of 0.50 (SD 0.40) [based on our preliminary data], a two-sided alpha of 0.05, and a mean of approximately 3 opportunities for each patient to complete the survey. Based on prior trends in Beacon plan treatment starts in 2022, this assumes accrual of approximately 100 patients per month for three months totaling approximately n=300 patients. Over the course of the pragmatic trial, enrollment exceeded expectations at both participating sites. As such, the target accrual was updated to total approximately 480 patients.

Aim 2
We will evaluate for heterogeneity of implementation effects on PRO adherence by including an interaction term between study arm and, separately, patient-level age (dichotomized), sex, race/ethnicity, income, and geographic location. Evidence for effect modification will be judged based on the z-score corresponding to the ratio of hazard ratios (interaction term) using again a two-sided alpha of 0.05 as the threshold for statistical significance.

RISK/BENEFIT ASSESSMENT:

1. Risks:
There are minimal risks to participants in this trial. There is a risk of breach of data and confidentiality; however, we described the precautions in place to manage this data securely in the Data Management section of this protocol.

2. Benefits:
Strong data support routine PRO monitoring as an evidence-based practice that improves patient outcomes including health-related quality of life and overall survival. This study is designed to improve patient engagement in this practice and thus may lead to better symptom monitoring/management and improved health outcomes. However, it is possible that patients will receive no benefit from this study.

3. Subject Privacy:
Privacy will be given utmost consideration and is highly valued in the proposed research. No research activities involve any direct interaction with subjects that would pose risk to their privacy.

4. Subject Confidentiality:
Confidentiality refers to the subject's understanding of, and agreement to, the ways in which identifiable information will be stored and shared.

How will confidentiality of data be maintained?

☐ Paper-based records will be kept in a secure location and only be accessible to personnel involved in the study.
☒ Computer-based files will only be made available to personnel involved in the study through the use of access privileges and passwords.
☒ Prior to access to any study-related information, personnel will be required to sign statements agreeing to protect the security and confidentiality of identifiable information.
☒ Whenever feasible, identifiers will be removed from study-related information.

☐ A Certificate of Confidentiality will be obtained, because the research could place the subject at risk of criminal or civil liability or cause damage to the subject's financial standing, employability, or liability.
☒ A waiver of documentation of consent is being requested, because the only link between the subject and the study would be the consent document and the primary risk is a breach of confidentiality. (This is not an option for FDA-regulated research.)
☒ Precautions are in place to ensure the data is secure by using passwords and encryption, because the research involves web-based surveys.
☐ Audio and/or video recordings will be transcribed and then destroyed to eliminate audible identification of subjects.
☐ Other (specify):

To protect participant confidentiality, only the research team outlined in HSERA will have access to review identified research records. Confidentiality will be protected to the fullest extent allowable under the law. See the Data Management section for more details.

If any data needs to be transmitted, it will be done through a Penn-approved secure encrypted file transfer solution as is described Penn IRB's Guidance on Electronic Data Protection Requirements for Research Involving the Use of PHI. Records will not be released without the participant's consent unless required by law (e.g., imminent risk of harm to self-suspected) or court order. When results of the research are presented at scientific meetings or published, no identifying information will be included.

All identifiable data, including the master list linking identifiers to the ID number and recordings, will be destroyed in 2031, seven years after the award period ends.

5. Protected Health Information

- Name
- Address
- Date of Birth
- Phone number(s)
- Electronic mail address
- Medical record numbers

6. Compensation:

Participants will not be compensated for participating in this study.

7. Data and Safety Monitoring:

The nature of the project poses minimal risk to participant safety and privacy. Yet, we will constitute a formal Data Safety Monitoring Board. The specific aspects of the DSMB for this study are as follows:

- The DSMB will consist of 4 members: 1) Erin Aakhus, MD, Assistant Professor of Clinical Medicine, Perelman School of Medicine, University of Pennsylvania, Associate Director of the Hematology Oncology Fellowship Program 2) Kate Courtright, MD, MSHP, Assistant Professor of Clinical Medicine at the Perelman School of Medicine of the University of Pennsylvania 3) Kit Delgado, MD, MS, Assistant Professor of Emergency Medicine at the Perelman School of Medicine of the University of Pennsylvania, Associate Director of Center for Health Incentives and Behavioral Economics 4) Meghan Lane-Fall, MD, MSHP, David E. Longnecker Associate Professor of Anesthesiology and Critical Care & Associate Professor of Epidemiology at the Perelman School of Medicine of the University of Pennsylvania, Associate Director of the Center for Health Incentives and Behavioral Economics

- The DSMB will perform several duties. First, they will review and approve research protocols and plans for data and safety monitoring prior to any study commencement. Second, they will evaluate the progress of any eligible trial. This will include assessment of data quality, participant recruitment, accrual and retention, participant risk versus benefit, and study outcomes. This assessment will be performed at meetings every six months during eligible trials and, more frequently, if decided by the DSMB. Third, they will make recommendations to ensure that all of the issues above are appropriately addressed. The corresponding project teams will be responsible for responding to all recommendations of the DSMB and submitting DSMB reports to the University of Pennsylvania IRB.

Data Safety and Monitoring Plan. Oversight and evaluation will be accomplished using standard University procedures for safety monitoring. The specific elements of our oversight plan are as above: 1) all project staff will complete certification in the protection of research participants; 2) the principal investigator will supply the IRB with annual progress reports, or more frequently as determined by the IRB, which may in turn suspend, terminate or restrict the study as appropriate; and 3) any serious adverse events will be reviewed in real time by the PI and reported to the IRB as required. Individual-level data for participants will be kept confidential and will only be stored on highly secure servers available for patient-level data. Only authorized project personnel will have access to the data and the data will only be stored on servers and not stand-alone PCs or laptops. All data will be reported at units of aggregation which make impossible the identification of individual patients or clinicians.

The data and safety monitoring plan will have 3 parts. First, the study MPIs, biostatistician, and Director of the Data Management Unit will develop and implement methods of verifying entered data and of quality control. Second, the MPIs will be directly responsible for identifying and reporting all adverse events, protocol deviations/violations and unanticipated events to the IRB and funding agency promptly, as appropriate. The PIs will also report all adverse events, accrual rates, retention rates, and all other logistical issues to the DSMB (described above) at least biannually (and more frequently if there are serious adverse events). Third, there will be a DSMB responsible for monitoring the trial.

A written research protocol will undergo formal institutional scientific and institutional review board (IRB) review at the University of Pennsylvania (Penn) to ensure protection of the rights and welfare of human research subjects. Specifically, the MPIs and the IRB will be responsible for ensuring risks to human subjects are minimized, risks are reasonable, subject selection is equitable, the research team has access to adequate resources to conduct the study, the informed consent process (or waiver) meets regulatory and ethical requirements, adequate provision is made to protect human subjects by monitoring the data collected and there are adequate provisions to protect subject privacy per HIPAA regulations and confidentiality of data.

All senior/key personnel and research staff who will be involved in the design and conduct of the study must receive education in human research subject protection from a training program that is approved by a properly constituted independent Ethics Committee or Institutional Review Board. The MPIs will be responsible for ensuring project faculty and staff have the equipment and training required to protect privacy and confidentiality and will monitor and document that these individuals are properly certified. If new senior/key personnel and staff become involved in the research, documentation that they have received the required education will be included in the annual progress reports. The UPENN Office of Regulatory Affairs currently requires HIPAA training upon designation as research investigator/staff and recertification in human research subjects protection every three years.

The Penn IRB will serve as the IRB of record for any external ethics review boards or IRBs applicable to researchers from other institutions who may have access to human research subjects identified data.

8. Investigator's Risk/Benefit Assessment:
This study presents minimal risk that is balanced by the potential benefits of the research to society.

INFORMED CONSENT:

1. Consent Process:
Since this is a pragmatic trial focused on improving implementation of evidence-based practices with minimal risk to patients, we are requesting a waiver of informed consent from patients. We have received this in the past for these types of trials.

2. Waiver of Informed Consent:
We are requesting a waiver of informed consent and HIPAA authorization from patients (see attached request for waiver of HIPAA authorization). A waiver of informed consent is requested for the following reasons. First, it is not feasible to consent every patient randomized to nudges. Second, if members of the control group were consented, they would know they were being studied and this could change their behavior. This could potentially disrupt the design of the study and make interpretation of the findings challenging. Third, patients are not being forced to engage in the PRO surveys. In all arms, care team members can still engage or refrain from using the PRO data according to their best clinical judgment, and patients can refuse to complete the PRO survey.

RESOURCES NECESSARY FOR HUMAN RESEARCH PROTECTION:
Adequate facilities are available at the ACC. The members of the research team are outlined in HSERA and include appropriate personnel to successfully implement this project. The entire team will be overseen by the PI. All personnel will complete required training before being granted access to any identifying information. This includes training on confidentiality through the Collaborative IRB Training Initiative (CITI) course. All personnel will be trained in the procedures for reporting unintentional breaches in confidentiality to the PI. All personnel will be aware that violations of participants' confidentiality, either unintentional or deliberate, may result in termination of hire. The PI will conduct training with all research personnel regarding data, limits of confidentiality, maintaining confidentiality and proper study procedures.

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APPENDICES

Appendix 1. Content of Patient Reported Outcome (PRO) questionnaire

PRO-CTCAE items	
Frequency	
Diarrhea	In the last 7 days, how often did you have loose or watery stools (diarrhea)?
Nausea	In the last 7 days, how often did you have nausea?
Scale	*0, Never | 1, Rarely | 2, Occasionally | 3, Frequently | 4, Almost constantly*
Severity	
Anorexia	In the last 7 days, what was the severity of your decreased appetite at its worst?
Constipation	In the last 7 days, what was the severity of your constipation at its worst?
Neuropathy	In the last 7 days, what was the severity of your numbness or tingling in your hands or feet at its worst?
Scale	*0, None | 1, Mild | 2, Moderate | 3, Severe | 4, Very severe*
Interference with activities of daily living	
Anxiety	In the last 7 days, how much did anxiety interfere with your usual or daily activities?
Depression	In the last 7 days, how much did sad or unhappy feelings interfere with your usual or daily activities?
Dyspnea	In the last 7 days, how much did your shortness of breath interfere with your usual or daily activities?
Fatigue	In the last 7 days, how much did fatigue, tiredness, or lack of energy interfere with your usual or daily activities?
Scale	*0, Not at all | 1, A little bit | 2, Somewhat | 3, Quite a bit | 4, Very much*
PROMIS items	
Global health	In general, would you say your quality of life is
Scale	*0, Excellent | 1, Very good | 2, Good | 3, Fair | 4, Poor*
PG-SGA items	
Activity level	In the last 7 days, how would you generally rate your activity level?
Scale	*0, Normal with no limitations* *1, Not my normal self, but able to be up and about with fairly normal activities* *2, Not feeling up to most things, but in bed or chair less than half the day* *3, Able to do little activity and spend most of the day in bed or chair* *4, Pretty much bedridden, rarely out of bed*
Final question – *randomized to be sent to patients in Arms in 2 and 3*	
Triage nurse team outreach	Would you like your triage nurse team to reach out to you regarding the symptoms you have reported in this survey?
Scale	*Yes* *No*

PRO-CTCAE™ = Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events
PROMIS® = Patient-Reported Outcomes Measurement Information System
PG-SGA© = Patient-Generated Subjective Global Assessment