Using Stakeholder Engagement to Overcome Barriers to Implementing Patient-reported Outcomes (PROs) in Cancer Care Delivery

Approaches From 3 Prospective Studies

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Introduction: Patient-reported outcome (PRO) measures used during cancer care delivery improve communication about symptoms between patients and clinicians and reduce service utilization for uncontrolled symptoms. However, uptake of PROs in routine cancer care has been slow. In this paper, we describe stakeholder engagement activities used to overcome barriers to implementing PROs. Implementation occurred in 2 study settings: PROs completed in the waiting room and reviewed during clinical visits to guide symptom management for multiple myeloma (visit-based PROs); and weekly PROs completed by cancer patients between chemotherapy visits to monitor symptoms at home (remote PROs).

Methods: PRO implementation steps across studies included: (1) clinician and patient input on key symptoms, PRO measures, and identifying which PRO responses are clinically concerning to better target nursing actions; (2) developing PRO-based clinical decision support (CDS) for responding to concerning PROs; (3) training clinicians and clinical research assistants to interpret PROs and use software; and (4) describing implementation impact (frequency of concerning PRO responses and nursing actions).

Discussion: Clinician and patient input was critical for identifying key symptoms, PRO measures, and clinically concerning response options. For the visit-based PRO observational study, all symptom scores appeared on a clinician dashboard, and those rated ≥1 by patients (on a 0–4 or 0–10 scale) had PRO-based CDS available for access. For the 2 remote PROs trials, stakeholders recommended that the 2 "worst" response options (eg, PRO responses of "often"/"always" or "severe"/"very severe") would trigger an automated email alert to a nurse along with PRO-based CDS. In each study, PRO-based CDS was tailored based on clinician input. Across studies, the most common nursing response to concerning PROs was counseling patients on (or providing care plans for) self-management of symptoms. In the trials, the percentage of weekly remote PROs generating an alert to a nurse ranged from 13% at an academic center to 36% in community oncology practices.

Key Points: Across 3 prospective studies, PROs implemented into cancer care enabled tailored care based on issues identified on PROs. Stakeholder engagement was critical for successful implementation. This paper assists in addressing important PRO implementation challenges by describing a stakeholder-driven approach.

Key Words: patient-reported outcomes, cancer care delivery, clinical decision support

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KEY POINTS

- Across 3 prospective studies, patient-reported outcome (PROs) collected during cancer care delivery enabled tailored care based on issues identified on PROs.
- PROs completed at clinic visits (visit-based) or at home between visits (remote PROs) had overlapping implementation barriers that were overcome with stakeholder engagement.
- Across studies, there was a multistep implementation process:

Clinician and patient input on selecting key symptoms, PRO measures, and PRO responses indicating clinically concerning symptoms.

Developing PRO-based clinical decision support (CDS) with clinician input.

Training clinicians and research assistants to use PROs and software.

Describing frequency of concerning PRO responses and clinical actions taken.

- This paper assists in addressing important challenges for implementing PROs into care delivery.

INTRODUCTION

Symptoms experienced during cancer care contribute to patients' distress, functional disability, and service utilization,[1–4] yet half of symptoms go undetected and unaddressed.[5,6] PRO measures used during cancer care improve communication about symptoms between patients and clinicians.[7,8] Randomized trials have shown that symptom monitoring during care—via PROs—improves clinician awareness of symptoms, yielding significant benefits such as reduced emergency room (ER) visits, better satisfaction with care, and improved survival.[2–4] However, uptake of PROs in cancer care has been slow.[9,10]

In this paper, we describe stakeholder engagement activities used to overcome barriers in 3 prospective studies. Implementation occurred in 2 study settings: PROs completed in the waiting room and reviewed during clinical visits to guide symptom management for multiple myeloma (visit-based PROs); and weekly PROs completed by cancer patients between chemotherapy visits to monitor symptoms at home (remote PROs).

Barriers to PRO implementation were anticipated at the practice, clinician, and patient levels.[9,10] For example, PROs need to be brief and easily interpretable. It was also necessary to determine clinician and patient perceptions of which PRO responses are clinically concerning, in order to better target nursing actions. A related barrier was the lack of CDS for PROs. CDS (sometimes called "clinical pathways") is guidance provided to clinicians about care that a typical patient should receive based on evidence-based practices.[11,12] Conventionally, CDS has been developed based on clinician impressions of symptom grade.[11] Few examples of PRO-based CDS are in the literature,[13,14] and none of these were developed for US care delivery systems.

The final 2 anticipated barriers included PRO training needs for clinicians and staff, and estimating nursing workload for responding to concerning PRO responses. These barriers have hindered widespread adoption of PROs into routine cancer care.[9,10] This paper addresses these limitations by describing implementation approaches, stakeholder engagement activities, and lessons learned.

METHODS

Studies Illustrating Visit-based and Remote PROs

A single-arm intervention study is used to illustrate a visit-based PRO approach. The study, "Multiple Myeloma Patient Care Plans" (MM-PCP) enrolled 90 adults in active treatment at 3 cancer centers (Table 1).[15,16] The main study outcome was provider adherence to evidence-based practices for symptom management. Electronic PROs were completed in the waiting room at 2 visits over a 12-week period using Carevive Systems Inc.'s cloud-based platform.[17] Care plans and PRO-based CDS were automatically generated based on patients' PRO responses, and accessible from a clinician dashboard.

Two randomized trials illustrate a "remote PROs" approach (Table 1). Both trials used a 2-arm design of usual care versus remote PROs completed at home with automated email alerts to nurses for concerning symptoms. Trial outcomes include survival, service utilization, and quality of life. The first trial, "Symptom Tracking and Reporting" (STAR), randomized 766 advanced cancer patients at one academic medical center.[3,4] The second trial, "PROs to Enhance Cancer Treatment" [PRO-TECT (AFT-39)] is actively recruiting adults with advanced cancer at 50 community oncology practices and is cluster-randomized (clinicaltrials.gov #: NCT03249090). As of August, 2018, 380 patients have enrolled out of a targeted 1000.

Multistep Implementation Process

Across visit-based and remote PROs studies, a common implementation process was used. PRO implementation steps included: (1) clinician and patient input on key symptoms, PRO measures, and which PRO responses are clinically concerning; (2) clinician input on PRO-based CDS; (3) training for clinicians and clinical research assistants (CRAs) to interpret and use PROs; and (4) describing implementation impact (frequency of concerning PRO responses and nursing actions). Examples from the 3 prospective studies described above are used to show implementation considerations in each step.

Stakeholder Input on Key Symptoms, PRO Measures, and Clinically Concerning PRO Response Options

In the MM-PCP study using visit-based PROs, clinical expert panels and industry experts identified 6 key symptoms for multiple myeloma during focus groups and web-based workshops (diarrhea, neuropathy, pain, fatigue, drowsiness, and sexual function). A combination of PRO measures was used to assess these symptoms: PRO version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE) diarrhea item[18–20]; Edmonton Symptom Assessment Scale—revised (ESAS-r),[21] the Functional Assessment of Cancer Therapy—General (FACT-G) sexual function,[22] and chemotherapy-induced peripheral neuropathy[23] (Table 1). Response scales were either 0–4 or 0–10. These PROs were chosen because they were developed with patient and clinician input, have validity and reliability evidence in cancer samples, and are quick to complete.[18–20,21–23] The clinical expert panels and industry experts recommended that a PRO response of ≥ 1 on any item should result in the symptom being shown on the clinician dashboard with linked PRO-based CDS available (Table 2).

The 2 trials engaged cancer patients and clinicians to choose key symptoms, PRO measures, and clinically concerning response options. Additional stakeholders in PRO-TECT included health services researchers, a scientific advisory board, and committees from the Alliance for Clinical Trials in Oncology (nursing, health

TABLE 1. Overview of 3 Prospective Studies

	Visit-Based PROs	Remote PROs	
	MM-PCP: Multiple Myeloma Patient Care Plans	**STAR Trial:** Symptom Tracking and Reporting	**PRO-TECT Trial:** Patient-Reported Outcomes to Enhance Cancer Treatment
Study	MM-PCP: Multiple Myeloma Patient Care Plans	STAR Trial: Symptom Tracking and Reporting	PRO-TECT Trial: Patient-Reported Outcomes to Enhance Cancer Treatment
Study Progress	Complete	Complete	Recruiting
Study Type	Single-Arm Intervention	Patient-randomized	Cluster-randomized
Sites	3 academic practices	1 academic medical center	>50 community practices
# Patients	N=90	N=766	N=380/1000
Primary Study Outcome(s)	• Level of provider adherence to evidence-based practices for symptom management	• Survival • Service utilization (ER, hospitalized) • Quality of life	• Survival • Service utilization (ER, hospitalized) • Quality of life and physical function
Intervention Arm	Care plans and clinical decision support automatically generated based on patients' PRO responses, and reviewed with patients during visit	Usual care vs. weekly PROs completed at home with automated alerts to nurses for concerning symptoms	Usual care vs. weekly PROs completed at home with automated alerts to nurses for concerning symptoms
PRO Frequency	2 office visits over 3 months	Weekly (between visits) up to 1 year	

PRO Symptom Domains Assessed	• Diarrhea frequency
	• Dyspnea severity
	• Neuropathy
	  ○ Yes/no
	  ○ Severity
	  ○ Related pain
	• Fatigue severity
	• Drowsiness severity
	• Sexual function
		• Diarrhea (frequency & need fluids)
		• Pain (severity & interfere with activities)
		• Constipation (frequency & interfere with activities)
		• Nausea (severity & fluids)
		• Vomiting (frequency & fluids)
		• Appetite loss, eating & drinking less, and weight loss (same item)
		• Fatigue (severity & interfere with activities)
		• Physical function & interfere with activities (same item)
		• Additional items based on cancer type (e.g., dyspnea for lung cancer)
			• Diarrhea frequency
			• Pain
			  ○ Frequency, Severity
			  ○ Interfering with activities
			• Constipation Severity
			• Nausea
			  ○ Frequency, Severity
			  ○ Vomiting frequency
			• Eating/drinking decreases
			• Insomnia severity
			• Dyspnea
			  ○ Severity
			  ○ Interference with activities
			• Physical function decrements
			• Depression frequency
			• Falls (yes/no)

PRO Measures	• PRO-CTCAE (diarrhea) • ESAS-r • FACT-G sexual function • Chemotherapy-induced peripheral neuropathy	• Items written by STAR research team	• PRO-CTCAE • Physical function: 1 item from Scored Patient-Generated Subjective Global Assessment© (PG-SGA, permission granted by developer) • Questions on eating/drinking and falls written by PRO-TECT research team and cognitively interviewed with patients
PRO-Based CDS	Yes	No	Yes

CDS indicates clinical decision support; ER, emergency room; ESAS-r, Edmonton Symptom Assessment Scale—revised; FACT-G, Functional Assessment of Cancer Therapy—General; PRO-CTCAE, PRO version of the Common Terminology Criteria for Adverse Events; PROs, patient-reported outcomes; #, number.

TABLE 2. Percentage of Patients Reporting Concerning Symptoms and Nursing Responses

Study	Visit-Based PROs	Remote PROs	
	MM-PCP N=90	STAR Trial N=766	PRO-TECT Trial N=380/1,000
Thresholds for Concerning PRO Responses (Selected *a priori* by each study)	• PRO-based CDS (based on severity) triggered if a patient reported ≥1 on any item • PRO measures varied from response scales of 0-4 to 0-10	• Items on 0-4 scale. Nurse alert automatically triggered by PRO responses of: ○ "Frequently"/"almost always" ○ "Quite a bit"/"very much" or "severe"/"very severe" ○ Worsening symptom (moving from 0-2 response over 7 days)	
Percent of patients reporting at least 1 concerning symptom during any study week	• N = 90/90 patients (100%)	• N = 278/441 (63%) • [441/766 patients were randomized to PRO intervention arm]	• N = 319/380 patients (84%)
Most Common Symptoms Meeting Concerning Threshold	• Fatigue (119/161 visits [74%]) • Dyspnea (61/161 visits [38%]) • Diarrhea (52/161 visits [32%]) • Neuropathy (40/161 visits [25%])	• 1,070/8,498 weeks (13%) had alerts • Of 1,070 weeks with alert, ○ 662 had fatigue (62%) ○ 342 pain (32%) ○ 171 appetite (16%)	• 1,109/3,103 weeks (36%) had alerts • Of 1,109 weeks with alert, ○ 543 included pain (49%) ○ 333 physical function (30%) ○ 189 diarrhea (17%)
Total Number of Nursing Responses (Denominator)	• 684 nursing responses during 161 visits	• Not reported in prior publication[3]	• 616 nursing responses recorded for 1,109 weeks with an alert ○ 392/616 (64%) nursing responses reported clinical action taken ○ 224/616 (36%) responses, no clinical action taken
Most Common Clinical Actions Taken in Response to Concerning PROs	• Counseling patients on home care strategies (515/684 [75%]) • Referrals (96/684 [14%]) • Changing medications (73/684 [14%])	• Counsel on symptom self-management (77%)[3] • Change meds (12%) • ER/hospital (8%) • [Numerators and denominators not reported in prior publication[3]]	• Counsel patients on self-management of symptoms (135/392 responses [34%]) • Assessed symptom over phone and plan to discuss at next visit (90/392 responses [23%]) • Change medications (46/392responses [12%])

CDS indicates clinical decision support; MM-PCP, Multiple Myeloma Patient Care Plans; PROs, patient-reported outcomes; PRO-TECT, Patient-reported Outcomes to Enhance Cancer Treatment.

outcomes, and patient advocate committees). Stakeholders chose common symptoms in both trials [gastrointestinal symptoms (diarrhea, constipation, loss of appetite, nausea, vomiting), pain, and physical function], which was consistent with a literature review[24,25] (Table 1). STAR also assessed fatigue, interference with daily activities, and items specific to a cancer type (eg, dyspnea for lung cancer).[3] Symptoms unique to PRO-TECT included insomnia, dyspnea, emotional distress, and falls (Table 1).

In STAR, items were written by its research team[3,26] (early version of PRO-CTCAE). In PRO-TECT, PRO measures were selected with stakeholder input and literature reviews.[27–31]

Most symptoms were assessed with PRO-CTCAE items because they mirror clinician adverse event reporting (CTCAE). The PRO-CTCAE was also developed with patient and clinician input,[18,19,32] demonstrates excellent psychometric properties,[20] has validity and reliability evidence in cancer samples,[19,20] and is quick to complete. Physical function was assessed with 1 item from the Scored Patient-Generated Subjective Global Assessment[33] (PG-SGA, permission granted by developer). Items were written by the PRO-TECT research team to assess eating and drinking decreases and falls. These items underwent cognitive interviews[34] with cancer patients from 6 cancer centers. Three rounds of interviews were

needed to rewrite items so they were comprehensible and meaningful to patients.

Stakeholders in PRO-TECT raised concerns about alert thresholds that were too high and too low. Thresholds that were too high (eg, very severe symptoms) may result in missing important changes. Stakeholders were also concerned about "alert fatigue" where clinicians would receive too many alerts that were not clinically meaningful. In both trials, stakeholders recommended that alerts be triggered by the 2 "worst" response options (eg, PRO responses of "frequently"/"almost always" or "severe"/"very severe"), which was consistent with a literature review[35-37] (Table 2). Stakeholders also felt that alerts were warranted when symptoms worsened by 2 points over the past 7 days (PRO response changed from "never" or "none" to "occasionally" or "moderate").

Clinician Input on PRO-based CDS

PRO-based CDS was developed for MM-PCP and PRO-TECT (but STAR did not use it). PRO-based CDS was based on content from the major guideline producers in oncology, such as the National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO), the Multidisciplinary Association of Supportive Care in Cancer (MASCC), and the Oncology Nursing Society (ONS).[38-41] The CDS was also consistent with ASCO's criteria for developing high-quality clinical pathways in oncology,[42] and existing PRO-based CDS used in other countries.[12,13]

Clinician input on PRO-based CDS was obtained with the same stakeholder groups described above. In both studies, feedback showed that the initial PRO-based CDS was too long for use in practice. In MM-PCP, stakeholders also reviewed the presentation and formatting of the clinician dashboard. Stakeholders in PRO-TECT recommended reformatting the one-page CDS into sections describing how to assess the symptom over the phone, grading symptoms, and selecting appropriate action (eg, dose changes) (Fig. 1).

Clinician and CRA Training on PROs and Software

Webinar training (1 h) was provided to clinicians and CRAs in all studies on interpreting PRO responses and using external software systems. PRO software platforms were not integrated into local electronic health record (EHR) systems because the necessary intervention components are not available.

For MM-PCP, clinicians and CRAs were taught how to use a clinician-facing dashboard for PROs. The dashboard showed concerning PRO responses, and trained CRAs were resident in clinics to ensure that providers viewed the dashboard and accessed the automatically generated PRO-based CDS available. Clinicians also reviewed a patient-friendly version of CDS (called a "care plan") with patients and revised it together to further tailor symptom management. Clinician actions (including nurses) were determined by reviewing symptom management strategies listed in the finalized care plan reviewed with the patient.

Training for clinicians and CRAs in STAR and PRO-TECT included examples of interpreting PRO responses, and how to use the PRO Core software system. Clinicians and CRAs were shown PRO items they might see in automated email alerts and which response options would trigger alerts.

Clinicians were instructed how to use PRO-based CDS and asked to follow-up with patients within 72 hours. CRAs were taught how to enter new patients in the software and track progress of weekly PRO completion. CRAs were instructed to give patients reminder calls when needed and to follow-up with clinicians 72 hours after an alert to determine nursing responses taken. CRAs also printed symptom report graphs for clinicians when patients visited the clinic.

In PRO-TECT, CRAs were also instructed that automated alerts would be sent to them that included a patient's study ID and problematic symptom(s). CRAs were asked to add identifying information to the email and forward it to the treating nurse(s). This step ensured that identifying information would only circulate through secure servers of the practice (rather than originating from an outside source—PRO Core).

Describing Implementation Impact (Frequency of Concerning Symptoms and Nursing Actions)

As described in step (2) above, stakeholders in each study determined which PRO responses were clinically concerning (Table 2). In MM-PCP, all patients [n = 90 (100%)] reported at least one concerning symptom during any visit. In STAR and PRO-TECT, 278/441 patients (63%) and 319/380 patients (84%) reported at least 1 concerning symptom during the studies, respectively.

Symptoms commonly yielding concerning responses were tracked (Table 2). In MM-PCP, the denominator was the number of visits. PRO responses of ≥ 1 were most commonly reported for fatigue [119/161 visits (74%)], dyspnea [61/161 visits (38%)], diarrhea [52/161 visits (32%)], and neuropathy [40/161 visits (25%)].

In STAR and PRO-TECT, the denominator was the number of weekly PROs with an alert. Multiple concerning symptoms could appear on the same weekly alert, and thus the weekly rate of concerning symptoms is more representative of nursing workload. In STAR, 1070/8498 weekly PROs (13%) resulted in an alert. Of the 1070 weekly PROs with alerts, 662 included fatigue (62%), 342 pain (32%), and 171 appetite (16%). In the PRO-TECT trial in community practices, the weekly PRO alert rate was considerably higher: 1109/3103 weekly PROs (36%). Of the 1109 weekly PROs with alerts, 543 included pain (49%), 333 physical function (30%), and 189 diarrhea (17%).

We conducted a sensitivity analysis to compare weekly PRO alert rates when restricted to the 6 symptoms collected in both trials (pain, nausea, vomiting, diarrhea, constipation, and appetite). In STAR, the weekly PRO alert rate reduced to 609/8496 weekly PROs (7%) versus 776/3103 weekly PROs (25%) in PRO-TECT.

Finally, nursing responses to clinically concerning PROs were tracked. In MM-PCP, there were a total of 684 nursing responses recorded during 161 visits. Common clinician responses involved counseling patients on home care strategies [515/684 responses (75%)], referrals [96/684 responses (14%)], and changing medications [73/684 responses (14%)]. In a previous STAR publication,[3] nursing interventions included telephone counseling about symptom management (77%), supportive medication initiation/change (12%), and referral to the ER/hospital (8%) (numerators and denominators were not

Clinician Symptom Management Pathway

CONSTIPATION
Constipation is the slow movement of feces through the large intestine that results in dry, hard stool and can cause discomfort/pain. Causes in patients with cancer include: 1. The cancer itself can obstruct the bowel or affect the nervous system (e.g., spinal cord compression). 2. Dehydration, immobility, changes in normal bowel habits. 3. Previous laxative abuse. 4. Cancer therapies such as vinca alkaloids, taxanes, thalidomide, platinums. 5. Supportive medications such as opioids, 5HT3 nausea medications, some antidepressants, antihistamines, anticholinergics.

Assessment
• Obtain bowel history (frequency, pattern, and consistency), dietary changes, medications, activity level. • Assess for any non-essential constipating medication. • Evaluate for potential obstruction symptoms (abdominal pain/tenderness, vomiting, abdominal fullness or bloating, excessive cramping), and impaction symptoms (pain, overflow around impaction).

Severity

Grade 1 *Mild*	Grade 2 *Moderate*	Grade 3 *Severe*	Grade 4 *Life Threatening*
Occasional/intermittent symptoms; occasional use of stool softeners, laxatives, dietary modification, or enema	Persistent symptoms w/regular use of laxatives or enemas; limiting instrumental ADL	Obstipation w/manual evacuation indicated; limiting self-care ADL	Life-threatening consequences; urgent intervention indicated

Interventions Based on Severity

Grade 1 (mild):
- Supportive medications: polyethylene glycol 1 capful/ 8 oz water 2D (takes 2 days to work), reduce dose or increase to BID as needed to achieve soft bowel movement w/o straining.
- Increase fluids, dietary fiber, exercise daily.
- Drink 8-10 glasses of clear liquids daily; drink hot beverages 30 mins before defecation.
- Discontinue any non-essential constipating medications.

Grade 2 (moderate):
- Add dose of laxative (senna, 2 tablets BID-QID) w/goal of 1 non-forced bowel movement every 1-2 days.
- Add and titrate bisacodyl 10-15 mg 1-3x/day w/a goal of 1 non-forced bowel movement (BM) every 1-2 days.
- Consider increasing polyethylene glycol (1 capful/8 oz water to BID or switch to lactulose, 30-60 mL BID-QID; sorbitol, 30 mL every 2 h x 3, then prn).
- Consider tap water enema until clear.
- Consider use of a prokinetic agent (metoclopramide, 10-20 mg PO QID). Note: use caution if fixed bowel obstruction.
- Reassess for cause and severity of constipation, check for impaction or obstruction.
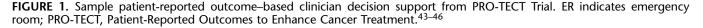
Grade 3 (severe):
- Administer glycerine suppository ± mineral oil retention enema. Avoid phosphosoda enemas.
- Consider magnesium hydroxide, 20-60 mg 1-2x/day; or magnesium citrate, 8 oz daily.
- Consider large volume polyethylene glycol (240 mL (8 oz) every 10 mins until 4 L are consumed or rectal effluent is clear.
- Consider methylnaltrexone for opioid-induced constipation, except for post-opileus and mechanical bowel obstruction, 0.15 mg/kg SQ every other day no more than once a day.
- Consider referral to ER/Urgent Care.

Consider referral to ER/Urgent Care if:
- Severe abdominal pain, swelling or vomiting, significant rectal bleeding w/no history of hemorrhoids or bleeding with constipation, signs of severe dehydration (severe lethargy/weakness, heart palpitations, decreased urine output, sunken eyes, orthostatic hypotension, dizziness).
- Consider appointment to see medical professional within 48 hrs if: no bowel movement in 5-7 days, unresponsive to interventions at home, history of diverticulitis and fever, temperature >100.4° F (38° C) with unknown cause and possible risk of neutropenia, unable to tolerate foods or fluids, signs of dehydration.

This form was developed for use by health care providers (not patients) to assist clinicians in the assessment of symptoms. It is not intended to: invite or establish a health care provider-patient relationship; furnish professional services; constitute or substitute for the advice or judgment of a medical professional; nor to serve as the sole basis for medical treatment. Update: July 2017.

FIGURE 1. Sample patient-reported outcome–based clinician decision support from PRO-TECT Trial. ER indicates emergency room; PRO-TECT, Patient-Reported Outcomes to Enhance Cancer Treatment.[43–46]

published in the article).[3] In PRO-TECT, there were a total of 616 responses recorded for potential nursing actions, where 392 (64%) indicated a clinical action had been taken. The most common responses to concerning PROs were counseling patients on self-management of symptoms [n = 135/392 responses (34%)], planning to discuss at next visit after assessing grade over the phone [n = 90/392 responses (23%)], and changing medications [n = 46/392 responses (12%)].

In most cases where no action was taken (224/616 responses), the reason provided was that a clinician was already aware of the symptom(s) [206/224 (92%)]. For example, a patient's PRO responses may have generated multiple weeks of alerts while the same symptom was being treated. The symptom was not "new," and thus a new clinical action did not need recorded. Clinicians recommended adding a software feature where they could "pause" alerts for a symptom while it was being actively treated.

DISCUSSION

Three prospective studies show that PROs used during cancer care delivery enable tailored care based on issues identified on PROs. This paper assists in addressing important implementation challenges.

Strengths and Weaknesses of Implementation Approach

An important strength of our implementation approach is stakeholder engagement. Stakeholders determined important symptoms to assess and selected PROs. We recommend that stakeholders (including adults with the health condition) be involved early in implementation decision making.[47]

Stakeholder engagement was also critical for identifying clinically concerning PRO responses. Research teams made a priori selections about concerning PRO responses, but were unique to each study. Although there is not yet a clear consensus on what a meaningful threshold is for "concerning" PRO responses, the level at which a symptom becomes clinically significant and is important to patients is a good guideline.[18,24,25,32,35–37] Evidence suggests that when symptoms are moderate or severe, they begin to meaningfully interfere with function and daily activities,[48] which are likely to be significant to clinicians and patients. Stakeholder input in the current studies supported this idea, but more research is needed on selecting and validating thresholds for use in routine care. Research is also needed on how threshold selection impacts clinician workload, false-positive rates, and patient service utilization.

In the second implementation step, PRO-based CDS was refined based on clinician feedback in MM-PCP and PRO-TECT. PRO-based CDS is typically specific to 1 symptom, and thus versions are needed to cover all symptoms assessed, but it does have the advantages of brevity and specificity for use in routine care. MM-PCP and PRO-TECT also used data visualization (eg, symptom graphs over time) at point-of-care, which may increase clinician engagement. A limitation is that PRO-based CDS needs updated as new evidence becomes available and treatment guidelines evolve.

Guidelines specific to developing PRO-based CDS are needed that include recommended minimum standards for PRO measures[27] and stakeholder engagement[47] to increase content validity. The National Institutes of Health is taking a step toward this goal by funding Small Business Innovation Research contracts to develop algorithm-based CDS for management of common cancer symptoms (https://sbir.cancer.gov/funding/contracts/377), of which Carevive is a recipient.

The third step in our implementation approach was training clinicians and CRAs on PROs and software. Research is needed to determine what additional training and resources will be needed by practices outside the research context. For example, case examples could highlight how to integrate patient preferences, PROs, and symptom management goals into shared decision making conversations.

Third-party PRO software was necessary across studies because most EHR systems lack critical features for using PROs at point-of-care (eg, alert algorithms). Some EHR vendors are working toward meaningful use of PROs at point-of-care but significant work remains to be done. In future studies, it will be important to examine characteristics of practices and EHR systems that are associated with successful PRO and CDS implementation to support replication.

The final step of our implementation approach was to evaluate implementation impact by describing the frequency of concerning PRO responses and clinical actions taken. In the trials,

nursing workload for responding to remote PRO alerts was over 20% higher in community oncology practices than at an academic center. Contextual variables may help explain this difference, but caution must be exercised in interpreting results because patients are still enrolling in PRO-TECT. Community cancer centers may have fewer resources available for symptom management[49] (eg, palliative care), and patients may be older, less educated, or have more comorbid health conditions, which are risk factors for poor chemotherapy outcomes.[50,51] Finally, the difference may be due to different PRO wording. Future implementation studies should consider choosing PRO measures with patient and clinician input and high validity and reliability evidence.

Previous publications for the STAR trial show improved survival by 5 months, reduced ER visits and hospitalizations, and better quality of life among chemotherapy patients randomized to the PRO intervention.[3,4] PRO-TECT is an ongoing trial and MM-PCP is currently analyzing data, and thus clinical processes and outcomes will be examined in future publications. PRO-TECT is also examining patient acceptability and usefulness, and clinician acceptability, satisfaction, and workload perceptions with semistructured interviews, which will be described in future publications.

Given the strengths and weaknesses of our implementation approach for visit-based and remote PROs, these methods are best applied with appropriate governance when a PRO program is being implemented for a study or in routine care.[10] Visit-based PROs may be a suitable option when symptoms are stable (eg, survivorship visits or early-stage disease with few symptoms), or when a practice is deciding whether to implement PROs for all patients. Remote PROs may be better suited when symptoms are dynamic (eg, chemotherapy), and when practices are experienced with PROs or want to reduce avoidable service utilization (eg, ER visits).

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