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BRIEF REPORT

Online Symptom Monitoring During Pelvic Radiation Therapy: Randomized Pilot Trial of the eRAPID Intervention

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Purpose: Radiation therapy (RT) and chemoRT for pelvic cancers increase survival but are associated with serious treatment-related symptoms. Electronic-patient self-Reporting of Adverse-events: Patient Information and aDvice (eRAPID) is a secure online system for patients to self-report symptoms, generating immediate advice for hospital contact or self-management. This pilot study aimed to establish feasibility and acceptability of the system.

Methods and Materials: In a prospective 2-center randomized parallel-group pilot study, patients undergoing radical pelvic RT for prostate cancer (prostateRT) or chemoRT for lower gastrointestinal and gynecological cancers were randomized to usual care (UC) or eRAPID (weekly online symptom reporting for 12, 18, and 24 weeks). Primary outcomes were recruitment/attrition, study completion, and patient adherence. Secondary outcomes were effect on hospital services and performance of patient outcome measures. Missing data, floor/ceiling effects, and mean change scores were examined for Functional

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This protocol is registered with ClinicalTrials.gov and may be viewed online at https://clinicaltrials.gov/ct2/show/NCT02747264.

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Research data are stored in an institutional repository and will be shared upon request to the corresponding author.

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[1] Statistical analysis

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Assessment of Cancer Therapy (FACT-G), European Organisation for Research and Treatment of Cancer, Quality of Life (EORTC QLQ C-30), self-efficacy, and EuroQol (EQ5D).

Results: From 228 patients approached, 167 (73.2%) were consented and randomized (83, eRAPID; 84, UC; 87, prostateRT; 80, chemoRT); 150 of 167 completed 24 study weeks. Only 16 patients (9.6%) withdrew (10, eRAPID; 6, UC). In the eRAPID arm, completion rates were higher in patients treated with prostateRT compared with chemoRT (week 1, 93% vs 69%; week 2, 93% vs 68%; week 12, 69% vs 55%). Overall, over 50% of online reports triggered self-management advice for milder adverse events. Unscheduled hospital contact was low, with no difference between eRAPID and UC. Return rates for outcome measures were excellent in prostateRT (97%-91%; 6-24 weeks) but lower in chemoRT (95%-55%; 6-24 weeks). Missing data were low (1%-4.1%), ceiling effects were evident in EQ5D-5L, self-efficacy-scale, and FACT−Physical Wellbeing. At 6 weeks, the chemoRT-eRAPID group showed less deterioration in FACT-G, EORTC QLQ-C30, and EQ5D-Visual Analogue Scale than UC, after baseline adjustment.

Conclusions: eRAPID was successfully added to UC at 2 cancer centers in different patient populations. Acceptability and feasibility were confirmed with excellent adherence by prostate patients, but lower by those undergoing chemoRT for gynecological cancers.

Introduction

Radiation therapy (RT) and chemoRT are key components of curative treatment for pelvic malignancies.[1,2] However, during and after RT, patients may experience significant short and longer-term treatment-related bowel, urinary, and sexual side effects.[3,4] Traditionally measured in clinical trials using the Common Terminology Criteria for Adverse Events (CTCAE),[5] there is evidence that patients can robustly self-report on symptomatic toxicity using standardized questionnaires (known as patient-reported outcome measures [PROMs]).[6] When integrated into routine practice, PROMS can improve the timing and accuracy of symptom reporting, communication, and decision making.[7-9] Online PROMS reporting with symptom alerts delivered to the clinical team may also facilitate earlier intervention, preventing more serious complications and resulting in improved survival,[10] with this approach having the potential to transform patient care by improving the monitoring and management of symptoms.[11] However, currently the research into use of PROMS for routine symptom monitoring has mainly focused on patients treated with systemic therapies, with a paucity of data in patients treated with RT.[12-14] Notable exceptions are studies describing electronic reporting of late-effect postpelvic RT (bowel toxicity)[15] and post-RT toxicity in patients with lung cancer.[16]

The electronic patient self-Reporting of Adverse-events: Patient Information and aDvice (eRAPID) system was developed by the Patient Centered Outcomes Research group in Leeds (UK) The system utilizes a severity- dependent algorithm to advise patients to self-manage symptoms or contact the hospital when symptoms are severe, supporting patient self-management in reducing symptom severity and improving quality of life (QoL).[17] The system enables real-time transfer and display of the patient responses for clinical use within the electronic records, generating clinical alerts for severe symptoms.[18] As part of the program, eRAPID RT was successfully integrated into the electronic patient record (EPR) systems of 2 NHS trusts in the UK.[17] A definitive single-center randomized trial of eRAPID with patients undergoing systemic oncological treatments showed improved physical well-being during treatment and increased patient self-efficacy.[19,20]

In this pilot study, the eRAPID system was adapted to support patient care during and immediately after pelvic RT.[21] The aims of this study were to determine the feasibility and acceptability of the eRAPID system in this patient population.

Methods and Materials

Study design and participants

This pilot study was a prospective randomized 2-arm parallel group trial over 24 weeks with repeated outcome measures conducted across 2 centers (the Leeds Cancer Centre, Leeds Teaching Hospitals NHS Trust (L) and the Christie NHS Foundation Trust (C) in Manchester).

We tested the eRAPID intervention in 2 distinct treatment groups: (1) radical external beam RT (EBRT) for prostate cancer (prostateRT) and (2) chemoRT for lower gastrointestinal (anal, rectal; neoadjuvant) and gynecological cancers (cervical, vaginal, vulval, endometrial; adjuvant EBRT alone).

Trial procedures are described in the published protocol.[21] In brief, eligible patients had a diagnosis of prostate cancer requiring radical RT (± brachytherapy boost and ± hormone therapy) or anal, rectal, cervical (± brachytherapy), vaginal, or vulval cancer requiring chemoRT or adjuvant EBRT for endometrial cancer; were ≥18 years; had access to home Internet or mobile devices; and were able to read and understand English. Patients were excluded if participating in other clinical trials with extensive PROM completion or if they exhibited cognitive dysfunction. Consenting patients were randomized 1:1 to usual care (UC) or eRAPID intervention (supplementing UC), randomized by center (the Leeds Cancer Centre, Leeds

Teaching Hospitals NHS Trust (L) and the Christie NHS Foundation Trust (C) in Manchester) and stratified by treatment (prostateRT and chemoRT). Clinicians who took part (senior oncologists, trainees, senior nurses, radiographers) saw patients in both study arms. Randomization was performed centrally by the University of Leeds Clinical Trials Research Unit via a 24-hour automated system.

Approval was gained from the Yorkshire and Humber Leeds East Research EthicsCommittee on September 13th, 2016 (REC reference 16/YH/037; ClinicalTrials.gov NCT02747264).

Procedures

UC

Before starting treatment, patients were assessed by a clinician and given verbal and written information on expected treatment-related symptoms, their management, and when and how to contact the hospital, including a 24/7 telephone hotline facilitating emergency oncology admissions. During RT, patients attend for treatment Monday through Friday and are seen weekly by a clinician. On completion, prostate patients are seen in clinic 6 to 8 weeks later and then discharged. Anal, vulval, and cervix patients are reviewed at 6 weeks and 3 months, and rectal patients are referred to surgery after a 6-week scan. RT schedules varied slightly between the 2 centers (details on RT schedules are provided in Table E3).

Intervention

eRAPID is a complex intervention with a number of interactive components and was codesigned with patients and clinical teams.[21] To enable replication and transparency we have adhered to the Template for Intervention Description and Replication (TIDIER) standards.[22] Patients were asked to report online symptoms weekly (or additionally when experiencing symptoms) during and posttreatment for 12 weeks (to capture acute symptoms) and then once at 18 and again at 24 weeks to capture later side effects (Fig. E1). The baseline online symptom report was completed within 24 hours of study entry. Reminders were sent via e-mail or text message, and self-reports were immediately available within the EPRs. The Leeds Teaching Hospitals NHS Trust EPR patient pathway manager is used in several NHS trusts across the Yorkshire region. Alerts for severe symptoms were sent to a shared clinical team e-mail, monitored by senior nurses and oncologists (see Fig. E2 for overview). Immediate automated advice was provided to patients for self-management of mild symptoms or a prompt was given to contact the hospital for serious symptoms (Fig. E3). More detailed information on symptom management was available via hyperlinks to the eRAPID website.

The eRAPID self-report items were developed by adapting and developing existing validated questionnaires for each cancer site (gynecological, lower gastrointestinal, and prostate). The majority of symptom items were taken from the male and female pelvic questionnaires,[23] which were based on the The Late Effects Normal Tissue/Subjective Objective Management Analytic scales with additions from Expanded Prostate Cancer Index (EPIC),[24] European Organisation for Research and Treatment of Cancer, Quality of Life (EORTC QLQ C-30),[25] and QLQ-PR25 (prostate module).[26] Additional questions were added from the eRAPID systemic therapy item pool based on a version of the PRO-CTCAE format by translating the CTCAE into patient language.[20] For each tumor group there was a set of 25 core symptomatic toxicity items covering bowel, urinary, fatigue, and physical side effects, which takes approximately 20 to 25 minutes to complete. Participants could also select chemotherapy- relevant items (n = 9), stoma (n = 7), and sexual issues (n = 10) from an additional drop-down menu (n = 11), including social and psychological issues, hot flushes, and so on (51 items in total).

Patient-friendly and clinically accurate advice was developed and adapted for each cancer site.[21] In consultation with health care professionals and patients using consensus and discussion- based methods, key treatment-related symptoms were selected and severity levels agreed on for the patient advice and alerts scoring algorithms[27] (see Table E1 for an example). The eRAPID patient website was designed (separate versions for each participating center) collating the existing patient information at each center, available local supportive services, and reputable national web resources (NHS Direct, Macmillan Cancer Support, Cancer Research-UK).

Patients received one-to-one eRAPID user training from a researcher and were given an eRAPID "postcard" with a unique username and password and a user manual including contact numbers for technical problems. Clinicians were trained by researchers at team meetings, one-to-one sessions, or via an interactive eRAPID eLearning program. Staff were advised to discuss the symptoms reports in patient consultations without specific recommendations for actions.

Outcome measures and analysis

The primary outcome was feasibility measured by recruitment/attrition rates, study completion, and eRAPID patients' adherence to symptom reporting.

Study completion was defined in 2 ways: (1) number/proportion of patients who remained on the study at 24 weeks (ie, did not actively withdraw or die) and (2) number/proportion of expected patients who returned the paper outcome measures at 24 weeks (ie, not including those who withdrew or died).

Patient adherence to online reporting was examined by (1) proportions of expected patients completing the online reports per protocol once a week (adjusting for withdrawals/deaths) and (2) the total number of reports per participant over 24 weeks, including extra completions.

The secondary outcomes were effect on hospital services, selection of appropriate patient outcome measure for a

future randomized controlled trial, and refinement of the intervention by exploring patient and staff views.

Effect on hospital services

Data were collected on the number of hospital contacts (admissions, clinic visits, phone calls) from the EPRs and the number of clinician alerts generated from eRAPID severe symptom reports. The data were summarized descriptively.

Missing items, floor and ceiling effects

Missing data items were examined as the proportion of returned questionnaires with significant number of missing items (as per questionnaire-scoring guidance), thus making the calculation of scores not possible.

Score distributions were examined to detect ceiling and floor effects on outcome questionnaires (defined as >15% of patients reporting highest or lowest scores) by study arm (eRAPID, UC), treatment group, center, and time of data collection. A pooled analysis of all returned questionnaires across all time points was also performed.

Data trends

Data trends were examined to aid selection of a primary patient outcome measure in a future trial. The mean score changes from patient outcome measures at baseline to 6, 12, and 24 weeks for eRAPID and UC arms were calculated. A post hoc exploratory analysis of covariance was performed on the raw scores of completed outcome data for both treatment groups to adjust for a single covariate (baseline scores).[28] We present mean differences with 95% confidence intervals (both adjusted and unadjusted) without *P* values, as suggested by the CONSORT (Consolidated Standards of Reporting Trials) statement for pilot studies.[29]

Analyses were performed separately for the 2 patient treatment groups (prostateRT and chemoRT). Analyses were carried out using SAS version 9.4 and SPSS version 26 on the intention to treat population (unless stated otherwise).

Sample size

A sample of 30 participants per study arm per treatment group (prostateRT and chemoRT) was set according to Lancaster et al's[30] recommendations for pilot studies. Allowing for 30% overall attrition, the recruitment target was n = 84 per study arm (total n = 168). Analyses were performed separately within the 2 patient cohorts (prostateRT and chemoRT).

Patient outcome measures

Validated measures of QOL (European Organisation for Research and Treatment of Cancer, Quality of Life [EORTC QLQ-C30], Functional Assessment of Cancer Therapy [FACT-G]) and health utility (EuroQol [EQ5D-5L], EQ5D-Visual Analogue Scale [VAS])[25,31,32] were collected on paper at baseline (before randomization), and at 6, 12, and 24 weeks; measures for patient self-efficacy and engagement (Self-Efficacy Scale for Managing Chronic Disease questionnaire; Patient Activation Measure [PAM])[33,34] were collected at baseline and 12 weeks; and satisfaction with the eRAPID technology at 24 weeks (eRAPID only). See Table 1 for details on patient outcome measures and the published protocol.[21] All measures were administered intact (including all subscales; see Table 1 for more detail).

Results

Primary outcome

Recruitment

Between December 1, 2016, and May 14, 2018 (17.5 months), 253 patients were identified (Fig. 1), and 25 patients did not meet eligibility criteria. Of 228 fully eligible patients, 61 declined participation (26.8%) (reasons: no Internet access, personal circumstances, and not having treatment), and 167 patients consented and were randomized. Recruitment rate was 73.2% (167 of 228).

Baseline characteristics

Baseline patient demographic, clinical characteristics, and patient outcomes scores are presented in Table 2. Patients undergoing chemoRT were younger (≤40 years) than those on prostateRT, had a lower education level (33.8% with university/professional degree vs 47.1%, respectively), and fewer comorbidities (51.3% no comorbidity vs 37.9%).

Within the prostateRT group, patient characteristics were well balanced between eRAPID and UC, with a small trend in the baseline patient outcome measures scores being better in the UC arm. Within the chemoRT group there were imbalances; a higher proportion of eRAPID patients had basic school education (42.5%) than those in UC (22.5%), and importantly, eRAPID patients reported higher (better) baseline scores than UC on almost all outcome measures completed before randomization (except EQ5D-5L).

Attrition rate and study completion

Sixteen patients (16 of 167; 9.6%) actively withdrew from the trial (eRAPID: 10 of 83 [12.0%]; UC: 6 of 84 [7.1%]), and 1 patient from the chemoRT UC arm died (Fig. 1). Most eRAPID withdrawals (n = 8) were from the chemoRT group (n = 7 gynecological cancers) and in the first 6 weeks; 2 withdrawals from prostateRT eRAPID were after 12 weeks. From the UC arm, there were 3 withdrawals from chemoRT and 3 from prostateRT. Reasons for withdrawals included "too ill" (n = 3), "too much to think about/too busy" (n = 2), "being well, no symptoms" (n = 1), "wanting to move on" (n = 2), and "not confident using Internet/prefer paper" (n = 2).

Table 1 Outcome measures: Scoring, interpretation, and time scale

Outcomes	Instrument/method	Item information/ data collection	Score range	High score	Time points
Patient self-efficacy					
Self-management	Self-Efficacy Scale for Managing Chronic Disease questionnaire[31]	6 items with 10-point question response scale from 1-10 (not at all confident to totally confident)	0-10	Better outcome	Baseline and 12 wk
Patient engagement in their own health care	Patient Activation Measure[32]	13 items, 5-point response scale: 1, disagree strongly, to 5, strongly agree	0-100	Better outcome	Baseline and 12 wk
Health-related QOL					
	FACT-G questionnaire (physical, social, emotional, and functional well-being scales)[29]	27 items 5-point response scale from 0, not at all, to 4, very much	0-108	Better outcome	Baseline and 6, 12, 18, 24 wk
	EORTC QLQ-C30 (symptom and functional scales)[25]	30 items 4-point response scale from 1, not at all, to 4, very much Summary score used, calculated using 2 items on overall QOL/health: score 1 (worse QOL) to 7 (best QOL)	0-100	Better outcome	Baseline and 6, 12, 18, 24 wk
Health utility measure	EQ5D-5L[30]	5 items 5-point response scale from no problems to extreme problems	Utility score 1 to −0.285	Better outcome	Baseline and 6, 12, 18, 24 wk
	EQ-5D VAS	Vertical 100-point response scale: 0, worst health you can imagine, to 100, best health you can imagine	0-100	Better outcome	Baseline and 6, 12, 18, 24 wk
Delivery of eRAPID intervention/fidelity					
	Patient adherence to online reporting	Downloaded from the online software (QTool)	0%-100%		During the 24-wk study period
	Type, frequency, severity of self-reported symptoms	Downloaded from the online software (QTool)	0%-100%		During the 24-wk study period
	Frequency of activated clinical algorithms and alerts	Downloaded from the online software (QTool)	0%-100%		During the 24-wk study period

Abbreviations: EORTC QLQ C-30 = European Organisation for Research and Treatment of Cancer, Quality of Life; EQ5D = EuroQol; eRAPID = Electronic-patient self-Reporting of Adverse-events: Patient Information and aDvice; FACT-G = Functional Assessment of Cancer Therapy; QOL = quality of life; VAS = visual analogue scale.

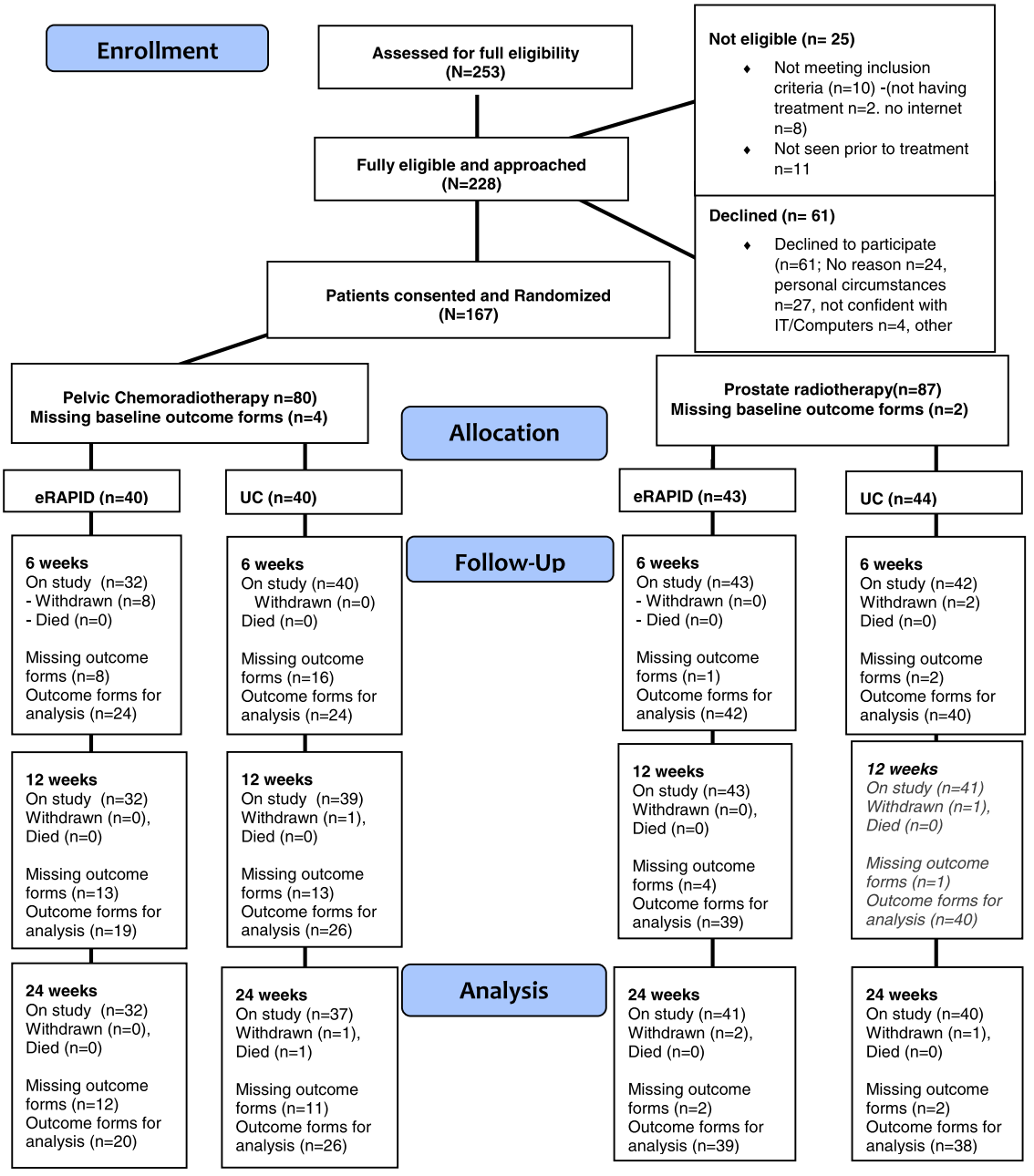

Fig. 1. CONSORT (Consolidated Standards of Reporting Trials) diagram by treatment group. *Abbreviations:* eRAPID = Electronic-patient self-Reporting of Adverse-events: Patient Information and aDvice; UC = usual care.

Thus, 150 patients completed the study, 88% (73 of 83) on eRAPID arm and 92% (77 of 84) UC. A total of 123 of those 150 patients (82%) returned the paper patient outcome measures (this included both eRAPID and UC groups). Completion rates were lower in the chemoRT group (eRAPID 32 of 40, 80%; UC 36 of 40, 90%) than in prostateRT group (eRAPID 41 of 43, 95%; UC 41 of 44, 93%). At 24 weeks, the prostateRT group had the highest outcome completion rate (eRAPID 39 of 41, 95% and 38 of 40, 95% UC), and it was lower in the chemoRT group (eRAPID 20 of 32, 63% and 26 of 37, 70% UC). Indeed, chemoRT patients had lower completion rates for the paper outcomes at all time points (between 75% and 60% of expected). In contrast, completion rates of the prostateRT patients were between 91% and 97% at all time points.

Adherence to eRAPID online symptom reports

Patients were expected to complete a minimum of 14 online reports per protocol. There were 924 completions in total, of which 791 were per protocol (from 1022 expected 77%, adjusted for withdrawals) and 133 were additional reports. The prostateRT group had high adherence to weekly online reporting, 93% in weeks 1 to 2, dropping to 69% in week 12, and 43% at week 24. The adherence was lower in the chemoRT group between at highest 74% (week 3) and 55% week 12, and 31% week 24 (Fig. 2a), particularly for patients

Table 2 Participants' baseline demographic, clinical characteristics, and outcome measures scores

	Pelvic chemoradiotherapy			Prostate radiation therapy		
	eRAPIDn = 40	Usual caren = 40	Totaln = 80	eRAPIDn = 43	Usual caren = 44	Totaln = 87
Demographic characteristics						
Age summaries (y)						
Mean (SD)	51.1 (15.9)	53.0 (14.3)	52.1 (15.1)	70.5 (7.1)	70.8 (6.9)	70.7 (7.0)
Median (range)	52.0 (22.0, 80.0)	55.0 (26.0, 78.0)	54.0 (22.0, 80.0)	70.0 (51.0, 84.0)	70.5 (55.0, 82.0)	70.0 (51.0, 84.0)
Sex						
Male	9 (22.5%)	7 (17.5%)	16 (20.0%)	43 (100.0%)	44 (100.0%)	87 (100.0%)
Female	31 (77.5%)	33 (82.5%)	64 (80.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Education						
Basic school education	17 (42.5%)	9 (22.5%)	26 (32.5%)	14 (32.6%)	10 (22.7%)	24 (27.6%)
Beyond basic school education	8 (20.0%)	15 (37.5%)	23 (28.8%)	6 (14.0%)	13 (29.5%)	19 (21.8%)
University or professional degree/qualification	13 (32.5%)	14 (35.0%)	27 (33.8%)	22 (51.2%)	19 (43.2%)	41 (47.1%)
Missing	2 (5.0%)	2 (5.0%)	4 (5.0%)	1 (2.3%)	2 (4.5%)	3 (3.4%)
Clinical characteristics						
Hospital						
Leeds Cancer Centre	21 (52.5%)	21 (52.5%)	42 (52.5%)	22 (51.2%)	23 (52.3%)	45 (51.7%)
Christie Hospital Manchester	19 (47.5%)	19 (47.5%)	38 (47.5%)	21 (48.8%)	21 (47.7%)	42 (48.3%)
Diagnosis site						
Lower GI	17 (42.5%)	16 (40.0%)	33 (41.3%)			
Gynecology	23 (57.5%)	24 (60.0%)	47 (58.8%)			
Comorbidity categories						
No comorbidities	22 (55.0%)	19 (47.5%)	41 (51.3%)	13 (30.2%)	20 (45.5%)	33 (37.9%)
1 comorbidity	10 (25.0%)	11 (27.5%)	21 (26.3%)	16 (37.2%)	13 (29.5%)	29 (33.3%)
2 comorbidities	7 (17.5%)	5 (12.5%)	12 (15.0%)	10 (23.3%)	3 (6.8%)	13 (14.9%)
3+ comorbidities	1 (2.5%)	5 (12.5%)	6 (7.5%)	3 (7.0%)	7 (15.9%)	10 (11.5%)
Missing				1 (2.3%)	1 (2.3%)	2 (2.3%)
QOL baseline scores						
Mean (SD)						
FACT-G overall	83.9 (14.3)	77.8 (20.6)		88.5 (13.8)	91.6 (12.1)	
FACT-G PWB	23.0 (4.9)	20.5 (7.5)		24.3 (3.3)	25.6 (3.1)	
EORTC QLQ C-30 summary score	81.2 (14.9)	75.3 (20.0)		86.3 (8.7)	88.0 (11.2)	
EORTC QLQ C-30 global/ QOL	69.8 (20.9)	65.8 (24.5)		76.4 (15.2)	81.7 (15.9)	
EQ5D utility	0.8 (0.2)	0.8 (0.2)		0.9 (0.1)	0.9 (0.2)	
EQ5D VAS	74.7 (18.4)	67.0 (24.0)		76.3 (17.0)	80.4 (17.7)	
SES	7.3 (1.6)	6.6 (2.4)		8.0 (1.8)	8.4 (1.5)	

Data are presented as n (%) unless otherwise indicated.

Abbreviations: EORTC QLQ C-30 = European Organisation for Research and Treatment of Cancer, Quality of Life; EQ5D = EuroQol; eRAPID = Electronic-patient self-Reporting of Adverse-events: Patient Information and aDvice; FACT-G = Functional Assessment of Cancer Therapy; GI = gastrointestinal; PWB = physical wellbeing; QOL = quality of life; SD = standard deviation; SES = Self-Efficacy Scale; VAS = visual analogue scale.

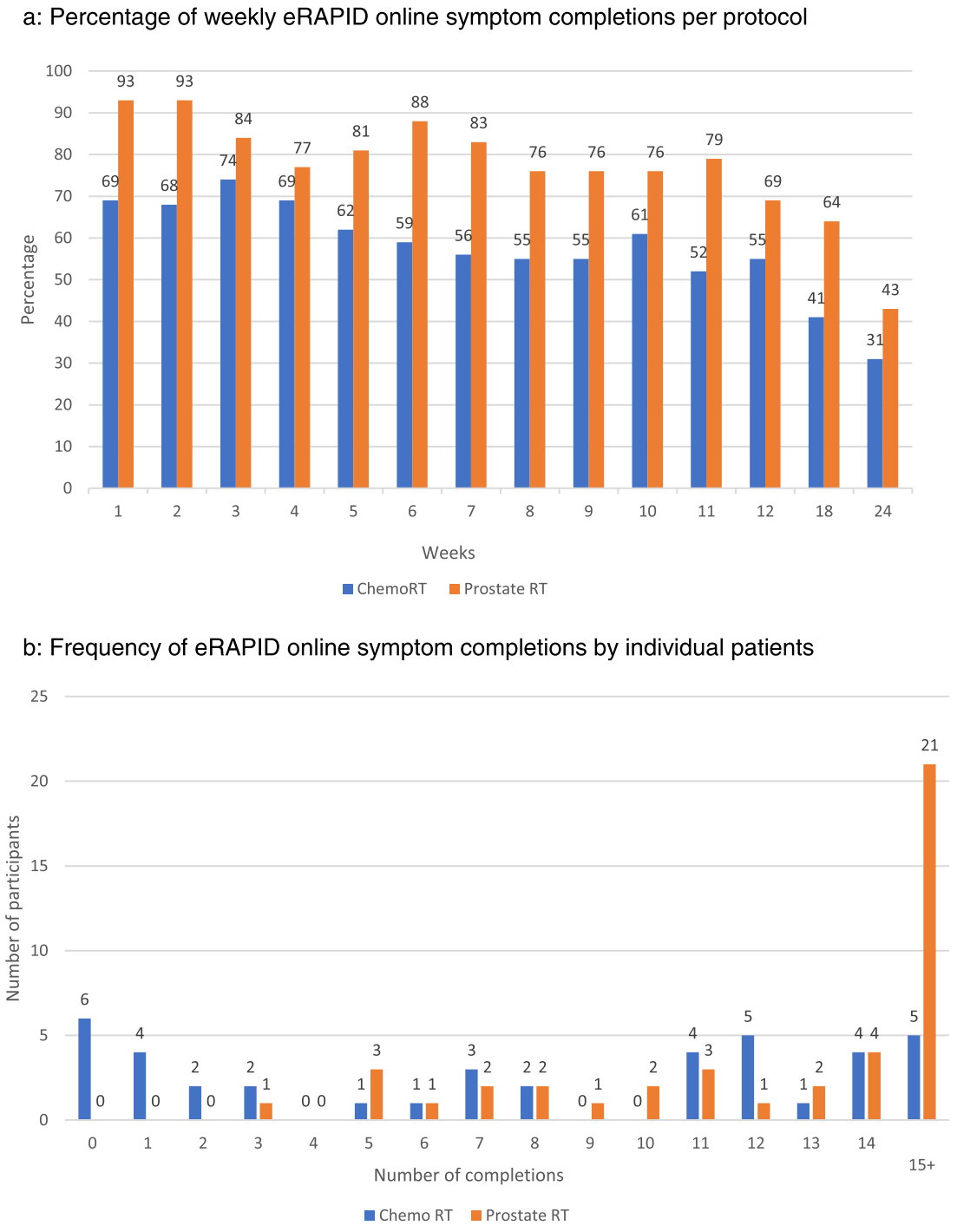

Fig. 2. Adherence to eRAPID online symptom reports. (A) Percentage of weekly eRAPID online symptom completions per protocol. (B) Frequency of eRAPID online symptom completions by individual patients. *Abbreviation:* eRAPID = Electronic-patient self-Reporting of Adverse-events: Patient Information and aDvice.

with cervix/endometrial cancer (11 of 23 patients completed 0-3 online reports). Nonadherent patients (cervical and endometrial) were younger (mean age, 35.8; 9 of 11 were <40 years) in comparison with the adherent group (prostate) (mean age, 45.2; 4 of 12 were <40 years). Completions per patient, including the extra reports, were higher in the prostateRT group (median, 14; range, 3-27; mean, 14.4; standard deviation [SD], 6.3) than in the chemoRT group (median, 8; 0-21; mean, 8.0; SD, 6.0), with lowest adherence for gynecological cancers (median, 6; 0-15; mean, 6.8; SD, 5.9) and anorectal cancers (median, 12; range, 0-21; mean, 9.6; SD, 6.1) (Fig. 2b).

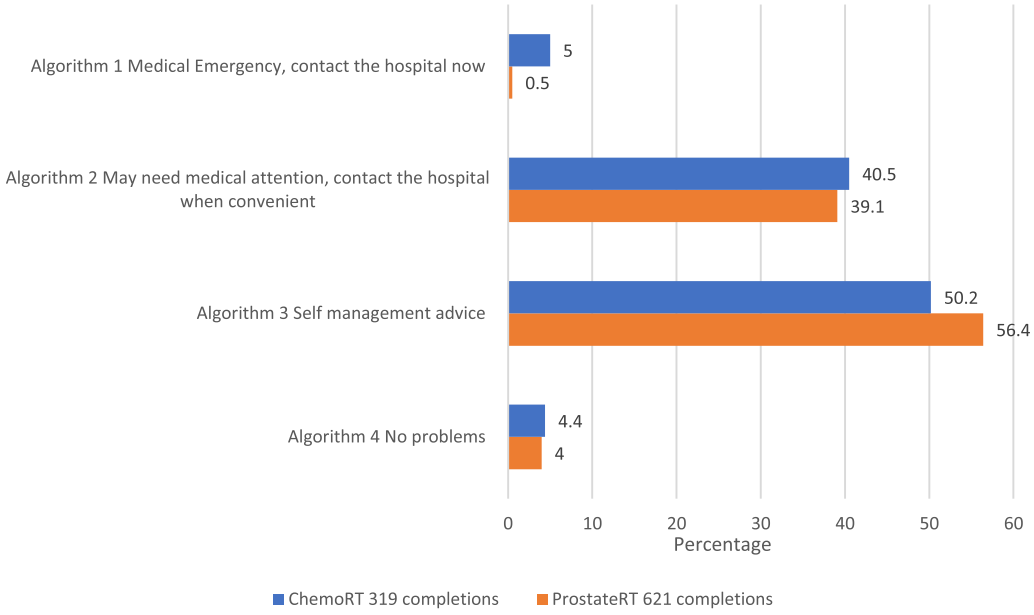

Fig. 3. Activated eRAPID algorithms during the 24-week study for both chemoRT and prostateRT. *Abbreviations:* chemoRT = chemoradiation therapy; eRAPID = Electronic-patient self-Reporting of Adverse-events: Patient Information and aDvice; prostateRT = prostate radiation therapy.

The type, frequency, and severity of online symptoms varied by week and cancer site (see Fig. E4 for examples). Typically, gynecological patients experienced significant bowel and urinary urgency (weeks 3-10), vaginal bleeding, abdominal pain, nausea, and fatigue for longer periods throughout the 24 weeks. Anal patients reported severe RT skin reactions (weeks 5 and 6), pain, and diarrhea. Prostate patients experienced predominantly mild/moderate symptoms (bowel and urinary, urgency, frequency, and hot flushes). Mild pain when passing urine was experienced throughout the 24 weeks, but more severe pain was experienced in weeks 3 to 6.

Severe symptom algorithms were activated for 5% of the online reports by the chemoRT patients and 0.5% of the prostateRT patients (Fig. 3). Moderately severe symptom combinations, triggering advice to contact the hospital when convenient, were similar between the groups (prostateRT 39.1% and chemoRT 40.5%). For mild symptoms, self-management advice was generated for 56.4% of the prostateRT group and 50.2% of the chemoRT group.

Website analytics

The number of website visits was 277 (124 at Leeds: 153 at the Christie). More detailed symptom advice could be accessed via webpages, and the most accessed (an indicator of the extent of the symptoms) were: bowel problems after radiotherapy (46 of 277, 16.6% by 20 patients), urinary problems (37 of 277, 13.3% by 17 patients), side effects of hormone therapy (14 of 277, 5.4% by 9 patients), sexual health for men after pelvic RT (14 of 277, 5.1% by 6 men), temperature/shivering (11 of 277, 4.0% by 9 patients), and abdominal pain (10 of 277, 3.6% by 8 patients). These findings also illustrate the extent to which patients were willing to self-manage symptoms.

Secondary outcomes

Effect on hospital services

Over the 24-week study the number of calls made to the hospital staff per patient was overall low, with slightly more calls from the chemoRT patients: chemoRT eRAPID mean number per patient: 1.3 (SD, 1.9) versus UC 1.6 (SD, 2.4); prostateRT eRAPID mean number per patient: 0.4 (SD, 1.1) versus UC 0.1 (SD, 0.3). The mean number of unscheduled hospital visits per patient was: chemoRT eRAPID 0.3 (SD, 0.8) versus UC 0.5 (SD, 0.9); prostateRT eRAPID mean 0.0 (SD, 0.3) versus UC 0.0 (0.0).

Selection of a future primary outcome measure

Missing items, floor and ceiling effects

Detailed analysis by study arm, chemoRT/prostateRT, center, and time points did not show any trends toward significance; therefore, only the pooled analysis across all time points is presented (Table E4). The number of returned outcome measures with missing items affecting the score calculations was low, under 2% across all measures, except FACT-G (4.1%, 22 of 538 forms had missing items, predominantly from the prostateRT; n = 16). No floor effects were seen. Ceiling effects were seen for EQ5D-5L utility score (24.1%, the 6-item SES [16.9%] and the FACT−Physical Wellbeing [PWB] [17.4%]). Measures that met all criteria were EORTC QLQ-C30 summary score, EORTC QLQ-C30 overall QOL/health score, and EQ5D-VAS.

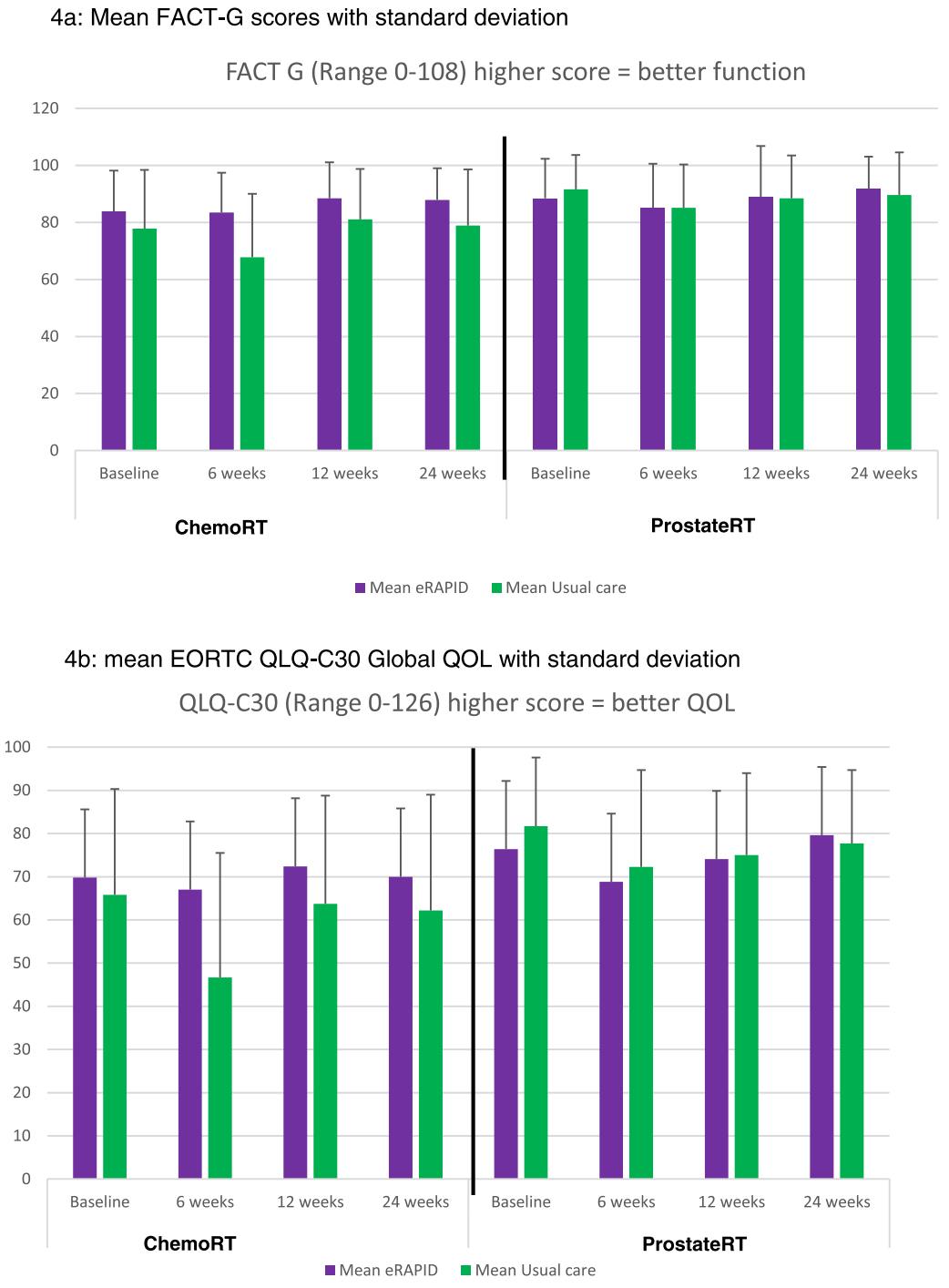

Fig. 4. Examples of outcome measures scores at baseline and 6, 12, and 24 weeks. (A) Mean FACT-G scores with standard deviation. (B) Mean EORTC QLQ-C30 global QOL with standard deviation. *Abbreviations:* chemoRT = chemoradiation therapy; EORTC QLQ C-30 = European Organisation for Research and Treatment of Cancer, Quality of Life; eRAPID = Electronic-patient self-Reporting of Adverse-events: Patient Information and aDvice; FACT-G = Functional Assessment of Cancer Therapy; prostateRT = prostate radiation therapy; QOL = quality of life.

Data trends

Table 2 shows change scores from baseline to 6, 12, and 24 weeks for outcome PROMs and the difference between eRAPID and UC scores as an indication of the intervention effectiveness. The eRAPID chemoRT group reported less deterioration over time than UC, with greater differences observed at 6 weeks for FACT-G (overall and PWB score),

EORTC QLQ-C30 summary score, QLQ-C30 global health/QOL score, and EQ5D-VAS. An overall mean difference between eRAPID and UC was evident at 6 weeks in the chemoRT group for FACT-G overall score (eRAPID 83.5 [SD, 13.9] vs 67.8 [SD, 22.2]) and the EORTC-QLQC-30 summary score (eRAPID 76.9 [SD, 14.6] vs UC 59.6 [SD, 23.4]), and this trend remained after adjustment for baseline scores (see mean difference between eRAPID and UC; Table 2). Figure 4 graphically shows this trend with examples of mean scores for FACT-G and QLQ-C30 global health/QOL scores at baseline and 6, 12, and 24 weeks. A different pattern emerged in the prostateRT group, with no changes in scores over time and no differences between eRAPID and UC. This data should be interpreted with caution as the numbers at each timepoint are small with a wide 95% confidence interval, and there was an imbalance in the outcome measure scores at baseline.

Discussion

To the best of our knowledge, this is the first study in pelvic RT to add immediate severity-dependent advice to address self-reported symptoms and to enable clinicians to view the online reports from within the EPRs. The results establish the feasibility and acceptability of this approach with patients undergoing 2 treatment modalities of pelvic RT (chemoRT for lower gastrointestinal and gynecological cancers and RT for prostate cancer).

Although there were a number of PROMs to complete on paper (total 82 items), which could have constituted a burden, prostateRT patient completions were high (91%-97%), whereas the completions of chemoRT patients were 60% to 75%, that is, more similar to PROM completions in clinical trials. Patients undergoing prostateRT were also the most consistent weekly online reporters throughout (93% initially and 69% at week 12), perhaps reflecting greater motivation to self-manage their disease.[35] Patients undergoing chemoRT were less adherent to online reporting, largely because of poor reporting by patients with cervical cancer. These patients were much younger (under 40), had a lower level of education, and received more intensive concurrent chemoRT. It can be hypothesized that, when patients had more toxic treatment, were younger, and were likely balancing treatment with home and family life, they were less likely to adhere to online reporting, which was a key unexpected finding. From the qualitative interviews, some patients found the system required effort, particularly when feeling unwell and when they had different priorities.[36] A similar finding of low participation in younger women was seen in the NHS QOL survey.[37]

These results factors may suggest online symptom reporting may be less suitable in this group of young female patients. The benefits of eRAPID highlighted from the qualitative interviews were that patients felt supported though their treatment. The advice they accessed informed and educated them about their symptoms,[36] and they became more confident in knowing when to contact the hospital for support. Those staff who used the system found it useful in clinical practice and realized the potential of the system for capturing late effects and facilitating stratified follow-up.[36]

The eRAPID approach did not generate extra hospital visits or calls and the number of alerts for severe symptoms was low (4% chemoRT; 0.5% prostateRT). Over 50% of online reports triggered advice enabling patients to self-manage milder symptoms when they occurred rather than delaying until their next appointment. These results are similar to our randomized controlled trial (RCT) findings using eRAPID during chemotherapy,[20] despite patients having daily visits to the RT department.

The outcome measures generally performed well, with low rates of missing items or floor and ceiling effects. The EORTC QLQ-C30 overall QOL/health score and the EQ5D VAS in particular met all criteria and could be recommended for a future RCT.

Descriptive statistics demonstrated a trend toward less symptom deterioration over time for eRAPID chemoRT patients, especially earlier at the 6 weeks timepoint. No differences were seen during prostateRT, possibly because of the lower severity of RT-related symptoms. These findings enable hypothesis generation and provide effect estimates for future trials but should be interpreted cautiously because of baseline score imbalances and high proportions of missing data for gynecological patients. Further studies of potential benefits for anorectal patients could be considered. Despite limited patient benefit seen for prostate patients, high adherence and engagement are strong positives and could justify an eRAPID approach for collection of RT-related late effects. Indeed, studies have shown that ePROMs are an excellent way to collect and deliver sensitive information and provide supportive care for prostate patients.[38,39] However, we should be mindful of the lower online adherence observed at 12 and 24 weeks and the value of carefully developing all aspects of the intervention through codesign with patients to maintain high engagement, as demonstrated in our systemic therapy trial.[19,20]

Strengths and limitations

To our knowledge, this is the first complex intervention of online symptom reporting during and after completion of curative pelvic RT. This is also the first study to enable clinical staff to view patient reports within the EPR system. The eRAPID RT programme has been successfully integrated into 2 different hospital EPR systems. A user guide to facilitate integration of PROs in the EPR by Snyder and Wu[40] recommend 3 levels (full, hybrid, moderate) and a standalone low integration. Each of these offers a bespoke integration solution within disparate information technology health systems. The eRAPID system adopted a hybrid approach. Furthermore, this is the first study internationally in pelvic RT to include the generation of severity-graded extensive patient advice, beyond alerts for severe symptoms.

A key strength of the eRAPID intervention is the codesign with patients and clinicians of the online symptom items, definitions of severity levels, and the bespoke self-management advice for each cancer site and treatment. Thus, the eRAPID intervention was developed to be a close approximation of clinical practice with the addition of patient input.

The trial design evaluating 1 intervention in 2 distinct RT treatment modalities is an innovative application of the basket trial concept to a complex health intervention. This approach demonstrated important differences in feasibility, adherence, and potential benefits that will inform future research.

Conducting a randomized pilot study across 2 cancer centers is a strength, improving the diversity of the study sample and demonstrating that challenges, including variations in IT infrastructure and compatibility of systems, were overcome. Local variations in RT schedules and procedures resulted in the development of self-management advice for each center. This is an important consideration for the future development of a multicenter RCT.

Because of limited time and funding resources, this pilot study examined online monitoring of symptoms in the acute phase (<3 months) and up to 6 months afterward. However, the positive findings on feasibility and patient adherence for prostate and anorectal cancers justify further studies after treatment to enable reporting and management of persistent treatment-related symptoms. This approach may offer a potential solution to the inconsistent assessment and documentation of late RT effects because of decentralized and multidisciplinary follow-up practices.[2]

In the eRAPID chemotherapy RCT we demonstrated an association between clinician engagement and patient online adherence. In this current study, we trained clinicians but were unable to monitor their use of the online reports because of the complex and diverse nature of the clinical pathways. Further, the system does not yet have prompts to remind clinicians to utilize the data. However, the qualitative substudy (to be published separately) confirmed positive clinician and patient experiences with eRAPID. After the study, clinical oncologists in Leeds saw the benefits of routine online monitoring, and at Leeds Cancer Centre online reporting has now been introduced into the anal cancer clinical work flow. In addition, the routine collection of symptomatic toxicity data using this method provides the opportunity for future use of the PROM data in developing predictive models of RT toxicity to inform radiation treatment planning.[13,41] However, a limitation we must address is that this system is only accessible for people who have Internet access, and therefore it may exclude those in lower socioeconomic classes. However, the digital divide is narrowing, and it is estimated that by 2028, 100% of the world population will have Internet access.[42] Indeed, the necessity of digital communication during the COVID-2019 pandemic has accelerated this process.[43]

Conclusions

Online symptom monitoring was successfully added to UC at 2 cancer centers across 2 distinct patient treatment groups (chemoRT for anorectal cancers and RT for nonmetastatic prostate cancers). This approach demonstrated less effect in young patients with gynecologic cancers. We observed a trend for a beneficial effect of eRAPID for both anorectal and gynecologic cancers but not for prostateRT. However, the value of the self-management advice to patients was demonstrated as advice was generated for over half of the milder symptoms reported regardless of patient population.

Increasing evidence on the use of online symptom reporting in the RT setting is becoming available.[15,16] Nationally, the COVID- 2019 pandemic has served as a driver to the adoption of remote solutions in cancer and wider health care helping to support approaches like eRAPID.[43]

The results from this work add to the growing body of evidence supporting regular online patient self-reported symptom monitoring in cancer care, contributing valuable data for understanding in which settings this approach may work more effectively and where modifications may be required. The findings will inform future trials and health services development projects. The integration of ePROMs data into the clinical pathway for RT patients promises to be an exciting prospect for supporting patient care.

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