Original Study

Electronic Patient-reported Outcomes During Breast Cancer Adjuvant Radiotherapy

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Abstract

Patient-reported outcomes (PROs) have become extremely important in following patients' health-related quality of life during cancer treatments. The present study assessed electronic PROs during adjuvant radiotherapy in a real-world setting. The study was conducted with a total of 253 patients with early breast cancer. The patients have started actively using the ePRO system, and the response rates were high (82.6%).

Introduction: Patient-reported outcomes (PROs) have become extremely important in following patients' health-related quality of life during cancer treatments. The aim of this study was to assess the usefulness of electronic PROs (ePROs) during adjuvant radiotherapy (RT) in patients with early breast cancer. **Materials and Methods:** A registry trial was conducted with a total of 253 patients with breast cancer receiving RT. Adverse event data were collected from 9 items on the ePRO questionnaires that were administered before RT (N = 253), at the end of RT (± 3 days; N = 234), 1 month after RT (N = 230), and 3 months (N = 225) after RT. The patient characteristics and treatment details were collected from the medical records. **Results:** The patients have started actively using the ePRO system, and the response rates were high (82.6%). During RT, 39.3% of the ePRO responses were about symptoms, and 60.7% were about treatment-related questions or advice. Patients treated with hypofractionated RT reported fewer local adverse events such as skin symptoms ($P = .001$) and pain ($P = .002$) than those who received conventional RT. One of the main findings of this study was that tiredness, fatigue, and anxiety were commonly reported on the patients' ePRO questionnaires, but they were rarely recorded in the medical records. **Conclusion:** Patients were motivated to use the ePRO system, and the response rates were high. Additionally, patients seemed to find that the ePRO system was an easy way to contact their own health care professionals. More attention should be paid to mental well-being during visits to the clinic.

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Introduction

Breast cancer is the most common cancer in women worldwide.[1] In Finland, nearly 5000 new breast cancers were diagnosed, and 923 patients died owing to breast cancer in 2018.[2] This mortality rate is one of the lowest in the world.[1,2] The treatment of early breast cancer consists of surgery, radiotherapy (RT), and systemic treatments and their combinations.[3-7] Radiotherapy effectively reduces the risk of recurrence and mortality.[6,8,9] Therefore, even today, over 80% of new patients with breast cancer will receive adjuvant RT in our country.

Adjuvant breast cancer RT is usually delivered with conventionally fractionated or hypofractionated techniques. Patients treated with conventionally fractionated RT receive radiotherapy in various fractionation regimens (for example, 25 fractions with a daily 2.0 Gy dose). Patients treated with moderately hypofractionated RT receive radiotherapy in 15 to 16 fractions with a daily dose of 2.66 to 2.67 Gy. Clinical studies have shown that hypofractionated RT is as safe and effective as conventional RT.[6] The most common early side effects of RT are skin irritation, fatigue, and swelling of the irradiated area.[10,11]

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Traditionally, side effects of RT have been recorded by clinicians or nurses. A patient-reported outcome (PRO) is an outcome directly reported by the patient. PROs have been suggested to increase patient satisfaction and discussions between patient and health care professionals.[12-15] In addition, PROs have been shown to reduce the risk of treatment-related complications and to enhance health-related quality of life.[16] Research on the use of PROs has been done more in the field of chemotherapy and palliative care than in connection with RT. Furthermore, PROs are widely used to measure health-related quality of life during prospective clinical trials and to obtain real-world data from different types of interventions in health care.[14,17,18]

Noona (Varian Medical Systems, Inc, Palo Alto, CA), a modular digital cancer follow-up application (CFUA), was taken into clinical routine for patients with breast cancer at our university hospital in October 2016. It is used to improve communication between patients with cancer and health care providers and to collect data on the patients' symptoms at different phases of their cancer care. By implementing this system during everyday care, we aimed to increase the quality of our treatment processes and patient rehabilitation. The primary outcome of this retrospective study was to assess the usefulness of this application and these electronic PROs (ePROs) during adjuvant RT for early breast cancer in clinical routine.

Material and Methods

Patients with breast cancer who initiated intensity-modulated RT at the Department of Oncology in the Tampere University Hospital and used Noona,[19] a modular digital CFUA, between December 20, 2016 and May 14, 2018 were selected for this registry study (N = 307). A 3-dimensional RT treatment planning computer tomography with 3-mm slices was done in supine position for all patients. Field-in-field intensity modulated technique was used to improve target volume homogeneity. The fractionation schedule was either 25 × 2 Gy (conventional fractionation) or 15 to 16 × 2.66 to 2.67 Gy (hypofractionation).

All patients were offered the opportunity to start using the CFUA as a voluntary and complimentary communication method during their first visit to the radiotherapy unit, and 307 (46.9%) patients adopted the application. A personal email address and a smartphone or a computer with internet access were required to use the application. The application can be used anywhere. The application automatically sent questionnaires before RT, at the end of RT, and 1 and 3 months after RT. Data were collected from medical records and the CFUA. Patients who received neoadjuvant treatment (N = 27) were excluded. Additionally, patients who did not respond to the pre-radiotherapy questionnaire (N = 24) and patients with metastatic cancer (N = 3) were excluded; thus, the study population consisted of 253 patients.

PROs were surveyed through the CFUA before RT (N = 253), at the end of RT (± 3 days; N = 234), 1 month after RT (N = 230), and 3 months (N = 225) after RT. Additionally, the patients, if they needed, could be in contact with their radiotherapy unit through the CFUA between routine questionnaires during the follow-up time. A coordinator radiotherapist received notifications whenever a patient completed items. An automated reply was sent to the patient when the caregiver closed the questionnaires. All additional questions by the patients were answered either via the CFUA, by phone, or at on-site visit to the radiotherapy unit. If necessary, the radiotherapist consulted the physician. We collected the data from the routine questionnaires and other contacts during the RT and follow-up time.

The questionnaires included 9 different items: performance status, anxiety, edema, skin symptoms, pain in the radiated area, tiredness and fatigue, respiratory symptoms, and other symptoms. Performance status was assessed by Eastern Cooperative Oncology Group (ECOG) performance status.[20] Side effects were assessed by the Common Terminology Criteria for Adverse Events (CTCAE 4.0) grading system.[21] Anxiety was assessed by the Edmonton Symptom Assessment System (ESAS).[22] Patients were asked if they had edema, and if so, did they have it on the operated or non-operated side. Possible skin symptoms were redness, desquamation, or other skin symptoms. Pain was measured on the Visual Analogy Scale (VAS) from 0 to 10, where 0 meant no pain and 10 meant the most possible pain.[23] Fatigue and tiredness were assessed on a 4-step scale from none to mild, moderate, and severe symptoms. Respiratory symptoms were subdivided into shortness of breath, tightening or constriction in the chest, cough, and cold. The Noona adverse event questionnaires were tailored to patients with breast cancer receiving RT. All of the questionnaires had identical structures (see Supplemental Figures 1-5 in the online version).

The local district Ethics Committee of Tampere University Hospital approved this study (R17077). The statistical analysis (the χ^2 test, t test, and Fisher exact test) was performed with SPSS Statistics for MacOS Mojave (version 24.0) (IBM, Armonk, NY). A P-value $< .05$ was considered statistically significant.

Results

The median age of the patients was 58 years (range, 30-82 years), and the mean age was 57.6 years. Over one-half (57.3%) of the patients were treated with conventional RT, and 42.7% were treated with hypofractionated postoperative RT (Table 1). The most common operation type was breast-conserving surgery (68.7%). In addition, more than one-half (56.1%) of the patients had received adjuvant chemotherapy, and 75.5% of the patients received adjuvant hormonal treatments. Study demographics are shown in Table 1.

During RT, 39.3% of the patient-derived reports in the CFUA dealt with treatment-related symptoms or questions. The most common treatment-related symptoms were pain (18.8%) and edema (12.5%). Over one-half (60.7%) of the responses consisted of treatment-related questions or the need for advice.

Most (82.6%) patients responded to all 4 scheduled questionnaires. On average, patients reported at least 2 symptoms per questionnaire. The mean reported number of symptoms was 1.9 (range, 0-6) before RT, 3.2 (range, 0-8) at the end of RT, 2.5 (range, 0-7) 1 month after RT, and 2.5 (range, 0-7) 3 months after RT. The number of symptoms and the severity of the symptoms are shown in Table 2.

Before RT, in most (84.6%) of the patients, the performance status was good (0 or 1). The performance status of a few (N = 6; 2.4%) patients was 3 or more before RT. Of these patients, 4 had received chemotherapy before RT. Three months after RT, the performance status was 0 or 1 in 95.5% of patients, and only 2 patients (0.9%) had a performance status ≥ 3.

Table 1 Demographics of the Study Population

	N	%
No. patients	253	
Mean age, y (range)	57.6	30-82
Females	250	98.8
Conventionally fractionated radiotherapy	145	57.3%
Hypofractionated radiotherapy	108	47.2%
Surgical procedures for breast		
Resection, one side	171	67.6
Resection, both sides	3	1.2
Ablation, one side	73	28.8
Ablation, both sides	2	0.8
Resection & ablation (different sides)	3	1.2
No surgery	1	0.4
Surgical procedures for axilla		
Sentinel node biopsy, one side	149	58.9
Sentinel node biopsy, both sides	1	0.4
Axillary dissection, one side	95	37.5
Axillary dissection, both sides	1	0.4
Sentinel node biopsy & axillary dissection	4	1.6
No surgery	3	1.2
Chemotherapy		
3 × docetaxel & CEF	91	36.0
3 × TX & 3 × CEX	13	5.1
3 × docetaxel & 3 × trastuzumab + 3 × CEF & 14 × trastuzumab	10	4.0
3 × pertuzumab, trastuzumab, docetaxel & 3 × CEF	6	2.4
4 × TC	4	1.6
Other	17	6.7
Hormonal therapy		
Tamoxifen	55	21.7
Letrozole	121	47.8
Exemestane	9	3.6
MonarchE-study[a]	5	2.0
T-category		
pT0	3	1.2
pTis	12	4.7
pT1 (a/b/c)	8/55/97	3.2/21.7/38.3
pT2	63	24.9
pT3	14	5.5
pT4	1	0.4
N-category		
pNX	2	0.8
pN0	123	48.6
ITC	11	4.3
pN1/pN1mi	42/20	16.6/7.9
pN1a/pN1c	25/1	9.9/0.4
pN2/pN2a	10/4	4.0/1.6
pN3/pN3a	10/5	4.0/2.0
Receptor status		
HER2 (positive/negative)	23/215	9.1/85.0
ER (positive/negative)	225/15	88.9/5.9
PR (positive/negative)	209/31	82.6/12.3
Triple negative	12	4.7

Abbreviations: CEF = Cyclophosphamide, epirubicin, 5-fluorouracil; CEX = cyclophosamide, epirubicin, capesitabine; ER = estrogen receptor; HER2 = human epidermal growth factor receptor 2; ITC = isolated tumor cells in the lymph nodes; PR = progesterone receptor; TC = docetaxel, cyclophosamide; TX = docetaxel, capesitabine.
[a]Study protocol, which compares standard hormonal therapy against a combination of hormonal therapy and abemaciclib.

Before RT, most (82.2%) of the patients did not report any arm edema. At the end of RT and on the follow-up questionnaires, the proportion of patients reporting edema remained roughly the same (range, 19.6%-24.0%) (Table 2). On the questionnaire at the end of RT, patients treated with hypofractionated RT reported less arm edema than patients treated with conventional RT (12.0% vs. 29.9%; $P = .001$). This difference remained stable at the 1-month survey (10.0% vs. 25.4%; $P = .007$), and then was increased at the 3-month survey (9.4% vs. 32.6%; $P = .001$). Additionally, an association between the type of surgery and edema was observed ($P < .001$). Most of the patients with breast-conserving surgery and sentinel lymph node biopsy did not have 1-sided edema (88.4%) at the end of RT. In contrast, 37.1% (N = 33) of the patients who had axillary lymph node dissection had ipsilateral edema at the end of RT. The difference persisted at 3 months after RT (13.5% vs. 36.0%; $P < .001$).

At the end of RT, 20.9% of the patients did not have any skin irritation at all, 64.1% of the patients had redness of the skin, and 11.1% of the patients had redness of the skin and ulceration. One month after RT, the incidence of skin irritation was much lower, and 49.1% did not have any skin irritation. The incidence was even lower 3 months after RT, as 80.9% of the patients did not have any skin irritation (Table 2). Patients treated with hypofractionated RT reported fewer skin symptoms than patients treated with conventional RT (69.0% vs. 86.6%; $P = .001$) on the ePRO questionnaire at the end of RT. The difference between the groups decreased on the 1-month and 3-month follow-up questionnaires (Table 2).

Most (77.1%) of the patients reported no pain before RT. The amount of pain increased after treatment was initiated; 55.6% did not have pain 3 months after RT. Patients treated with hypofractionated RT reported less pain on average than patients treated with conventional RT. These differences were most evident at the end of RT (1.25 on the VAS scale; 95% confidence interval, 0.47-2.03; $P = .002$) and on the 3-month questionnaire (0.9 on VAS scale; 95% 95% confidence interval, 0.17-1.65; $P = .016$). Patients who had received chemotherapy before RT reported slightly more severe pain than patients who did not receive chemotherapy before RT ($P = .074$), and this difference remained at the end of RT ($P = .001$).

Fatigue was reported least often in the survey before RT and most often in the survey at the end of RT (Table 2). One of the most

Table 2 Key Results in PROM Questionnaires/Timing of Questionnaires

	Before RT, n (%)	At the End of RT, n (%)	1 Month After RT, n (%)	3 Months After RT, n (%)
Response rate	253 (100)	234 (92.5)	230 (90.9)	225 (88.9)
1. Performance status[a]				
ECOG 0	83 (32.8)	71 (30.3)	80 (34.8)	95 (42.2)
ECOG 1	131 (51.8)	137 (58.6)	130 (56.5)	120 (53.3)
ECOG 2	33 (13.0)	23 (9.8)	16 (6.9)	8 (3.6)
ECOG 3	5 (2.0)	3 (1.3)	2 (0.9)	2 (0.9)
ECOG 4	1 (0.4)	0 (0.0)	2 (0.9)	0 (0.00)
2. Anxiety	159 (62.8)	157 (62.1)	156 (61.7)	174 (68.8)
Anxiety scale 0-10, mean (range)[b]	3.3 (0.1-9.3)	3.3 (0.1-8.5)	3.1 (0.1-8.7)	3.1 (0.1-9.0)
3. One-sided edema				
None	208 (82.2)	180 (76.9)	185 (80.4)	171 (76.0)
Edema on the operated side	43 (17.0)	52 (22.2)	43 (18.7)	51 (22.7)
Edema on the non-operated side	2 (0.8)	2 (0.9)	2 (0.9)	3 (1.3)
4. Skin symptoms on the irradiated area				
None	242 (95.7)	49 (20.9)	113 (49.1)	182 (80.9)
Redness	1 (0.4)	150 (64.1)	51 (22.2)	16 (7.1)
Desquamation	–	1 (0.4)	15 (6.5)	–
Redness and desquamation	1 (0.4)	25 (10.7)	32 (13.9)	1 (0.4)
Other	9 (3.6)	9 (3.8)	19 (8.3)	26 (11.6)
5. Pain of the radiated area				
None	195 (77.1)	137 (58.5)	152 (65.9)	125 (55.6)
Rarely (0-14 days per month)	12 (4.7)	40 (17.1)	15 (6.6)	17 (7.6)
Intermittent (15-30 days per month)	3 (1.2)	6 (2.6)	7 (3.1)	6 (2.7)
Consistent	43 (17.0)	51 (21.8)	56 (24.5)	77 (34.2)
6. Pain on irradiated area, scale 0-10, mean (range)[c]	5.0 (0.8-9.7)	4.8 (1.1-9.1)	4.7 (0.2-9.0)	4.8 (0.5-8.7)
7. Fatigue and tiredness				
No fatigue or tiredness	155 (61.3)	69 (29.5)	119 (51.7)	109 (48.4)
Mild fatigue and tiredness	61 (24.1)	119 (50.9)	73 (31.7)	78 (34.7)
Moderate fatigue and tiredness	36 (14.2)	44 (18.8)	37 (16.1)	36 (16.0)
Severe fatigue and tiredness	1 (0.4)	2 (0.9)	1 (0.4)	2 (0.9)
8. Respiratory symptoms				
None	217 (85.7)	177 (75.8)	188 (81.6)	185 (82.1)
Yes	36 (14.3)	76 (24.2)	65 (18.4)	68 (17.9)

Abbreviations: ECOG = Eastern Cooperative Oncology Group performance status ([a]0 = fully active, 4 = completely disabled); PROM = patient-reported outcome measures; RT = radiotherapy.
[b]0 = no anxiety, 10 = most anxiety.
[c]0 = no pain, 10 = most pain.

interesting findings was that, 3 months after RT, one-half of the patients still reported tiredness and fatigue. Patients who had received chemotherapy reported more fatigue before RT than patients who had not received chemotherapy (46.5% vs. 28.8%; $P = .02$). There was no association between fatigue and the type of RT fractionation. Additionally, patients who received endocrine treatment reported more fatigue on the follow-up surveys, but the difference was not statistically significant.

Most of the patients did not report any respiratory symptoms on the questionnaires (Table 2). The medical records of patients with respiratory symptoms (N = 64) were examined for the possibility of radiation pneumonitis (RP). Of these patients, 6 (9.4%) were diagnosed with RP; thus, only 2.4% of the total population had RP. Most (N = 51; 79.7%) of the patients with respiratory symptoms did not have RP. Information regarding RP was not available for 7 (10.9%) patients.

When comparing the ePROs reported symptoms with symptoms in the medical records during the follow-up visits to an oncologist at the end of RT and 3 months after RT, it appeared that the physicians under-recorded symptoms. At the end of RT, most (79.5%; N = 186) of the patients did not have any notes in their medical records about the symptoms they had reported through the CFUA. On the 3-month visit, one-half (52%; N = 118) of the patients had no notes in their medical record about their self-reported side

Table 3 The Symptoms That Were Unrecorded After Radiotherapy at the Outpatient Visits

Symptom	N	%
Anxiety	136	86.6
Fatigue	74	44.8
Pain	67	69.0
Respiratory tract	28	51.9
Other	22	31.9
Hemioedema	16	30.2
Skin symptoms	3	1.6

effects. One of the most interesting findings was that, at both follow-up times, the most common unrecorded symptom was anxiety (86.6%) (Table 3). Additionally, fatigue and tiredness were often unrecorded in the medical records (Table 3). Pain was the third most common symptom to be unrecorded when we compared the symptoms in the medical records with those reported by the patients through the CFUA. A summary of unrecorded symptoms at the end of radiotherapy is shown in Table 3.

During RT, 11.1% of the patients were in contact with the oncology clinic through the CFUA. In addition, after RT, 31.2% of the patients were in contact through the CFUA. Of these contacts, 34.2% were about 1 of the 6 symptoms on the questionnaires, 39.2% were about treatment-related concerns, and 26.6% were about both symptoms and treatment-related concerns. The most common reasons for contact regarding symptoms were pain (21.0%) or skin irritation (12.3%). The treatment-related concerns included questions on the schedule of follow-up appointments and mammography. The questionnaires' response rates were excellent, as up to 89% of the patients still responded at 3 months after RT.

Discussion

Our study shows that the patients who accepted and used the CFUA were motivated to report their welfare by using ePROs and answered most of the questionnaires sent via the CFUA; this is in line with the previous study.[24] The questionnaires' response rates were better than in the reported studies.[24,25] CFUA enables a 2-way communication between caregivers and patients, and therefore favors compliance and active participation.

The side effects reported through the CFUA were similar to the side effects reported in previous studies regarding RT.[11,26,27] In previous studies, the incidence of RP, one of the more serious side effects, has varied between 1% and 21% in patients with breast cancer depending on how RP was defined.[28,29] In this study, the RP incidence rate was quite similar to the reported.

The prevalence of arm edema appeared to be lower in patients treated with hypofractionated RT ($P = .001$), but this mostly reflects the selection of patients for the hypofractionated protocol. Only node-negative patients (N = 136; 53.7%) receiving solely breast RT received hypofractionated RT at the time of our study. Patients with node-positive breast cancer who required additional RT to lymph node regions were treated with conventional 25 × 2 Gy RT. Axillary lymph node dissection, which is known to be the strongest risk factor for arm edema,[30,31] was performed solely among this group of patients (N = 100; 39.5%).

One of the most interesting findings was that tiredness, fatigue, and anxiety were quite commonly reported on the patient-reported questionnaires but rarely mentioned in the Electronic Patient Record (EPR). This might indicate that these symptoms were not discussed during the appointments with the physician. On the other hand, psychological symptoms are not easy to report. One can speculate that it is not easy for Finnish patients to talk about their feelings, or our doctors are unable to open the discussion because in previous studies, psychological outcomes appear to be unchanged when using PROs.[32-35] Additionally, psychological symptoms usually must be quite severe before they are reported in the EPR. Although these symptoms and feelings were commonly reported in the questionnaires, none of the patients initiated direct contact to report them, either via the CFUA or phone, to their health care professionals. Our results showed that patients receiving chemotherapy had significantly more tiredness and fatigue.

The results might indicate that patients suffer from side effects more than clinicians have expected. In particular, mental well-being might often be overlooked. With the help of PROs, it will be easier to detect all the different symptoms so that they can be brought up in discussion. PROs have also been shown to be helpful in enhancing patient awareness of their symptoms,[12,36,37] and patients have felt more reassured that their symptoms were well-monitored.[33,38] Additionally, it has been shown that PROs have a positive impact on patient-clinician communication.[13,15,39-41] Recently, a study was published in which PROs were also shown to have a positive effect on the quality of life of patients with advanced cancer.[16]

During the time of this study, the clinicians needed to log in to the CFUA separately from the EPR, which could have been one reason why some of the symptoms were rarely mentioned in the EPR. It is known that doctors are dissatisfied with the current EPR, which might also be one major hindrance to CFUA usage.[42]

In addition, 11.1% of the patients were in contact with the clinic through the CFUA outside of the routine questionnaires even at the time when patients visited the RT unit on a daily basis, so it seems that patients found the CFUA to be an easy and helpful way to contact their own health care professionals. Similar findings were in a recent prospective and systematic survey regarding the acceptance of mobile applications for the surveillance and follow-up of patients with cancer undergoing radiotherapy was high in the study by Shafie et al.[24] However, only 46.9% of the patients adopted the application.

It has been suggested that, to optimize the efficacy of the CFUA, both patients and health care providers should be trained properly.[14] Additionally, patient recruitment needs to develop a more efficient, properly timed, and systematic process that is integrated into normal health care practice, especially in oncology, because cancer and its treatments have many side effects and concerns. In the future, ePROs could help create more individualized treatment and follow-up and increase patients' health-related quality of life.

The current practice in breast cancer clinics is individualized based on tumor biology and multimodality treatments to avoid unnecessary appointments. It has been hypothesized that patients should be more active in reporting their health concerns and contacting their health care providers when needed, and our study seems to support this position.

This is one of the first studies providing real-world data on the implementation and use of ePROs in clinical routine in a radiotherapy unit. Noona is a new CFUA that provides better communication between health care providers and patients and thus improves patient-centered care and empowers patients to become active participants in their care.

Clinical Practice Points

- PROs have become extremely important in following patients' health-related quality of life during cancer treatments. PROs have been suggested to increase patient satisfaction and discussions between patients and health care professionals. In addition, PROs have been shown to reduce the risk of treatment-related complications and to enhance health-related quality of life. Research on the use of PROs has been done more in the field of chemotherapy and palliative care than in connection with radiotherapy (RT). The aim of this study was to assess the usefulness of ePROs during adjuvant RT in patients with early breast cancer.
- In this study, patients were motivated to use the ePRO system, and the response rates were high (82.6%). Additionally, patients seemed to find that the ePRO system was an easy way to contact their own health care professionals. One of the main findings of this study was that tiredness, fatigue, and anxiety were commonly reported on the patients' ePRO questionnaires, but they were rarely recorded in the medical records. More attention should be paid to mental well-being during visits to the clinic.
- In the future, PROs could help create more individualized treatment and follow-up and increase patients' health-related quality of life. This is one of the first studies providing real-world data on the implementation and use of ePROs in a radiotherapy unit.

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Disclosure

The authors have stated that they have no conflicts of interest. The authors did not have any commercial relationship with the Varian Medical Systems, Inc company, and the company was not involved in planning, analyzing, or interpretation of the results of this study.

Supplemental Data

Supplemental figures accompanying this article can be found in the online version at https://doi.org/10.1016/j.clbc.2020.10.004.

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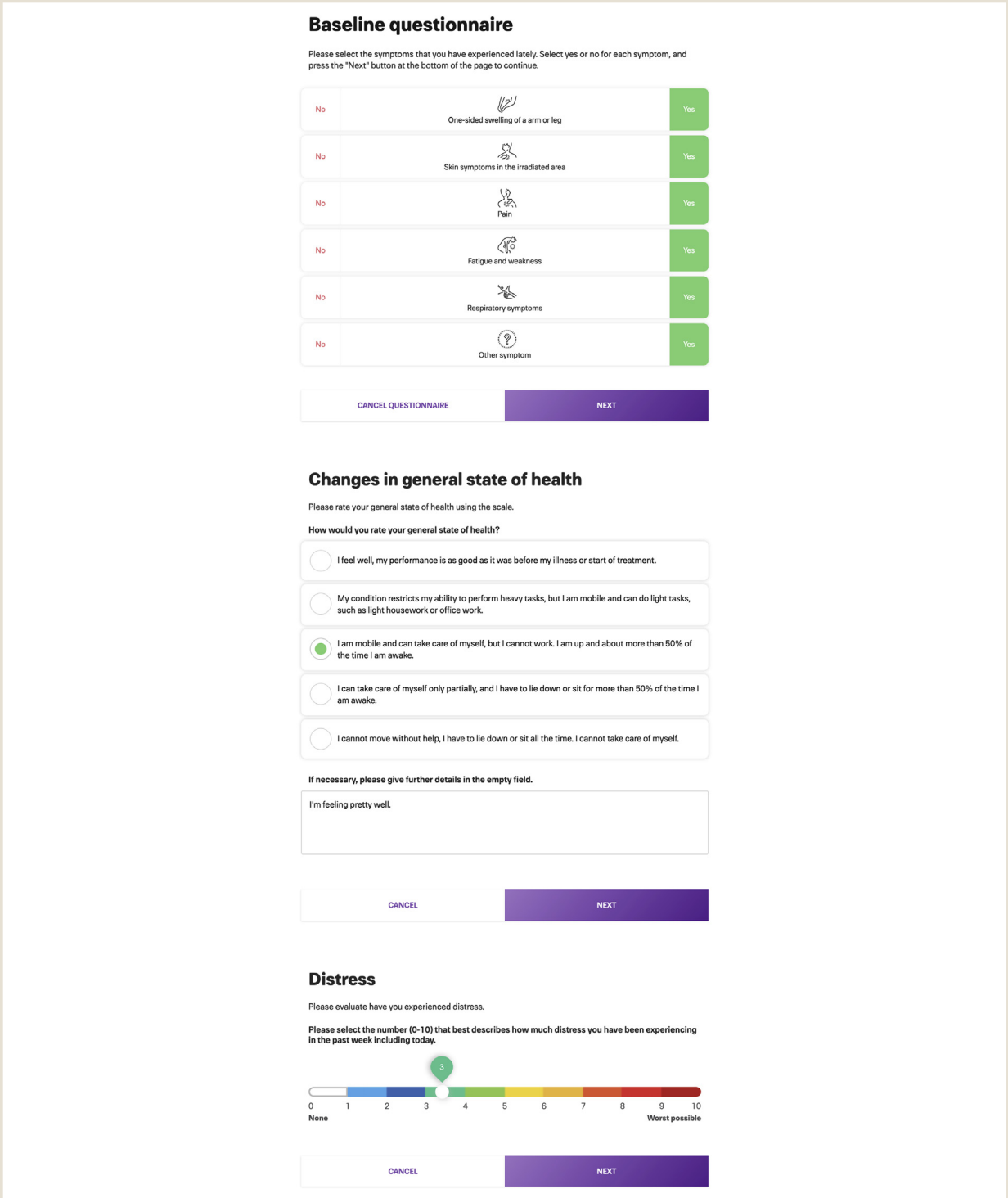
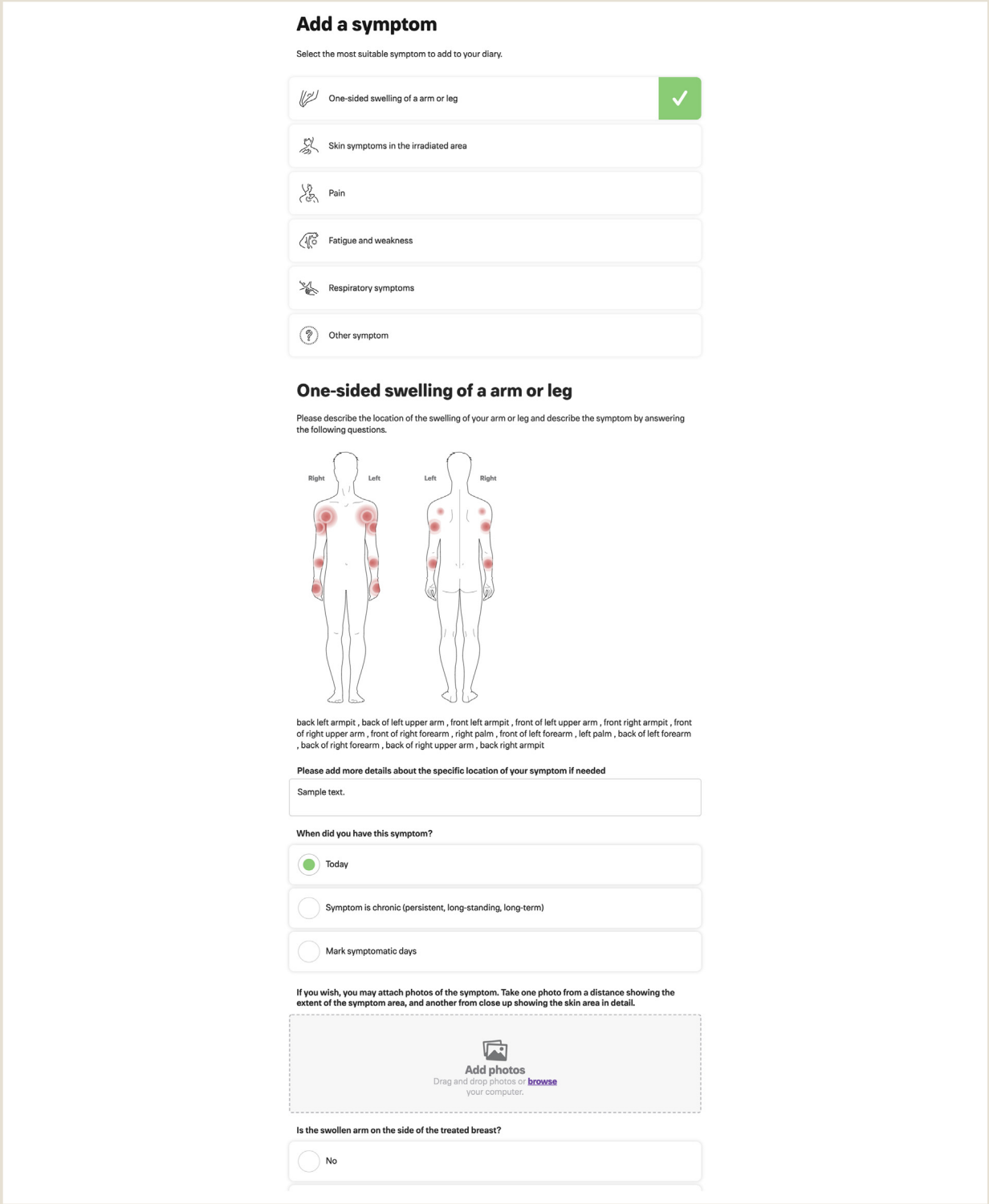
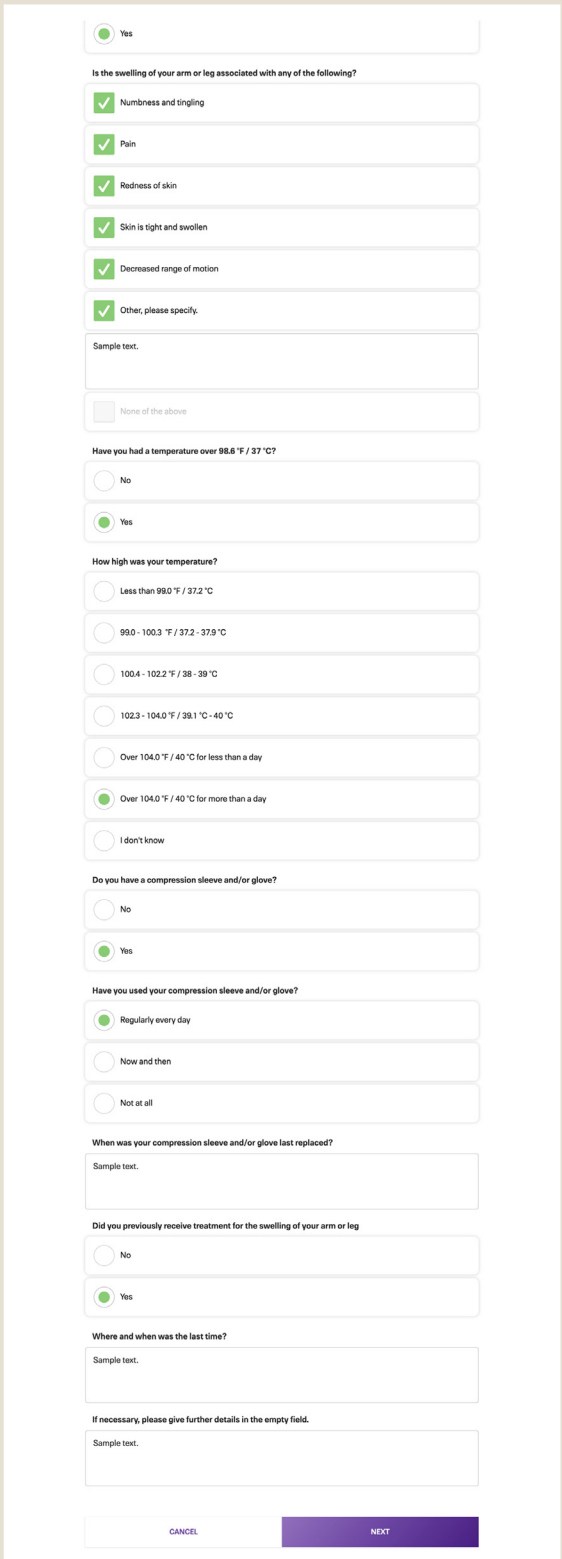
Supplemental Figure 1 Screenshot of the Patients' Side of the Cancer Follow-Up Application (CFUA) Representing the First Part of the Baseline Questionnaire. The Questionnaires Included the Most Important Symptoms Related to Breast Cancer Radiotherapy: Edema, Skin Symptoms, Pain in the Radiated Area, Tiredness and Fatigue, and Respiratory Symptoms. In Addition, Questions of Performance Status (Eastern Cooperative Oncology Group Performance Status) and Anxiety Were Included, and the Questionnaire Allowed Patients to Add Symptoms that Were Not Incorporated Into the Questionnaire (ie, Other Symptoms)



Supplemental Figure 2 Screenshot of the Patients' Side of the Cancer Follow-Up Application (CFUA). Second Part of the Baseline Questionnaire. If the Patient Answered "Yes" Any of the 6 Different Symptoms (Edema, Skin Symptoms, Pain in the Radiated Area, Tiredness and Fatigue, and Respiratory Symptoms, Anxiety, Other Symptoms), the CFUA Asked Additional Questions, Which are Represented in the Screenshot



Supplemental Figure 2 Continued



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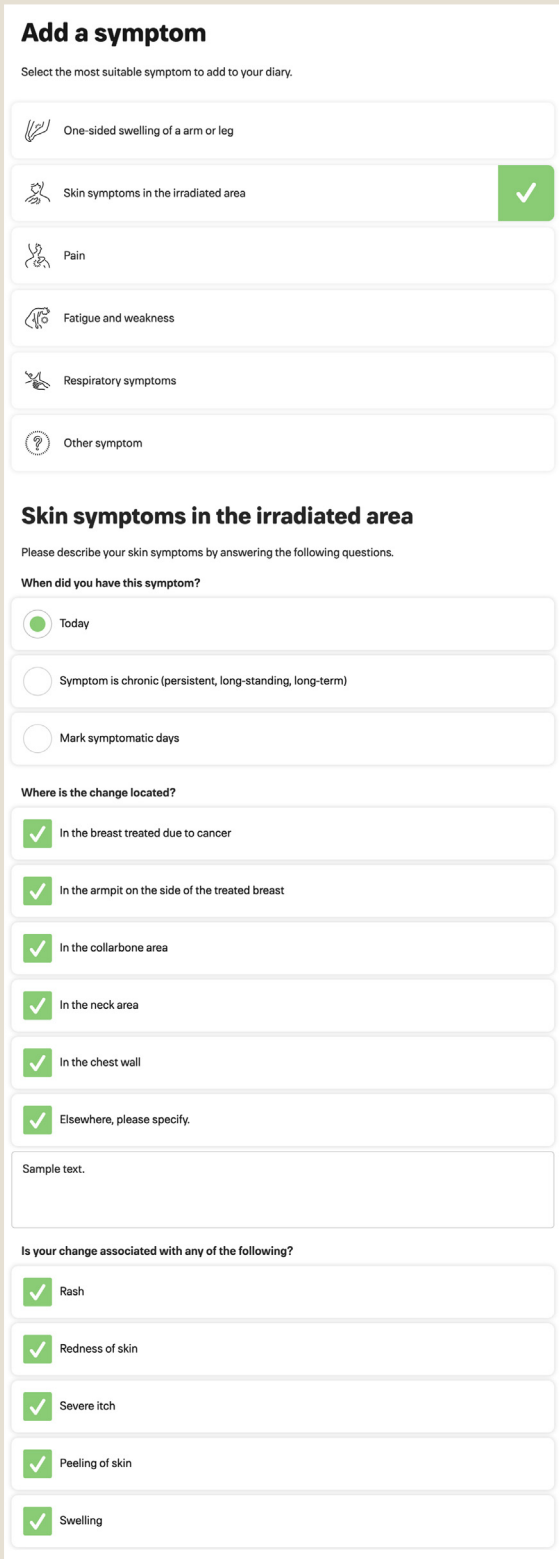


Supplemental Figure 2 Continued

- [x] Nodule(s) or lump(s)
- [x] Sore
- [x] Other, please specify.

Sample text.

- [ ] None of the above

If you wish, you may attach photos of the symptom. Take one photo from a distance showing the extent of the symptom area, and another from close up showing the skin area in detail.

Add photos
Drag and drop photos or **browse** your computer.

Do you feel burning sensation on your skin?

- ( ) No
- (•) Yes

Have you had a temperature over 98.6 °F / 37 °C?

- ( ) No
- (•) Yes

How high was your temperature?

- ( ) Less than 99.0 °F / 37.2 °C
- ( ) 99.0 - 100.3 °F / 37.2 - 37.9 °C
- ( ) 100.4 - 102.2 °F / 38 - 39 °C
- ( ) 102.3 - 104.0 °F / 39.1 °C - 40 °C
- ( ) Over 104.0 °F / 40 °C for less than a day
- (•) Over 104.0 °F / 40 °C for more than a day
- ( ) I don't know

If necessary, please give further details in the empty field.

Sample text.

CANCEL NEXT

Supplemental Figure 2 Continued

Add a symptom

Select the most suitable symptom to add to your diary.

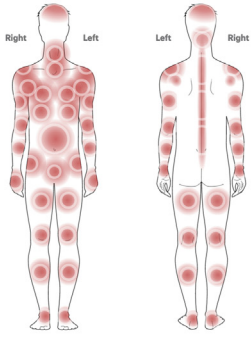
- One-sided swelling of a arm or leg
- Skin symptoms in the irradiated area
- Pain ✓
- Fatigue and weakness
- Respiratory symptoms
- Other symptom

Pain

Please determine the location of your pain and describe the pain by answering the following questions.

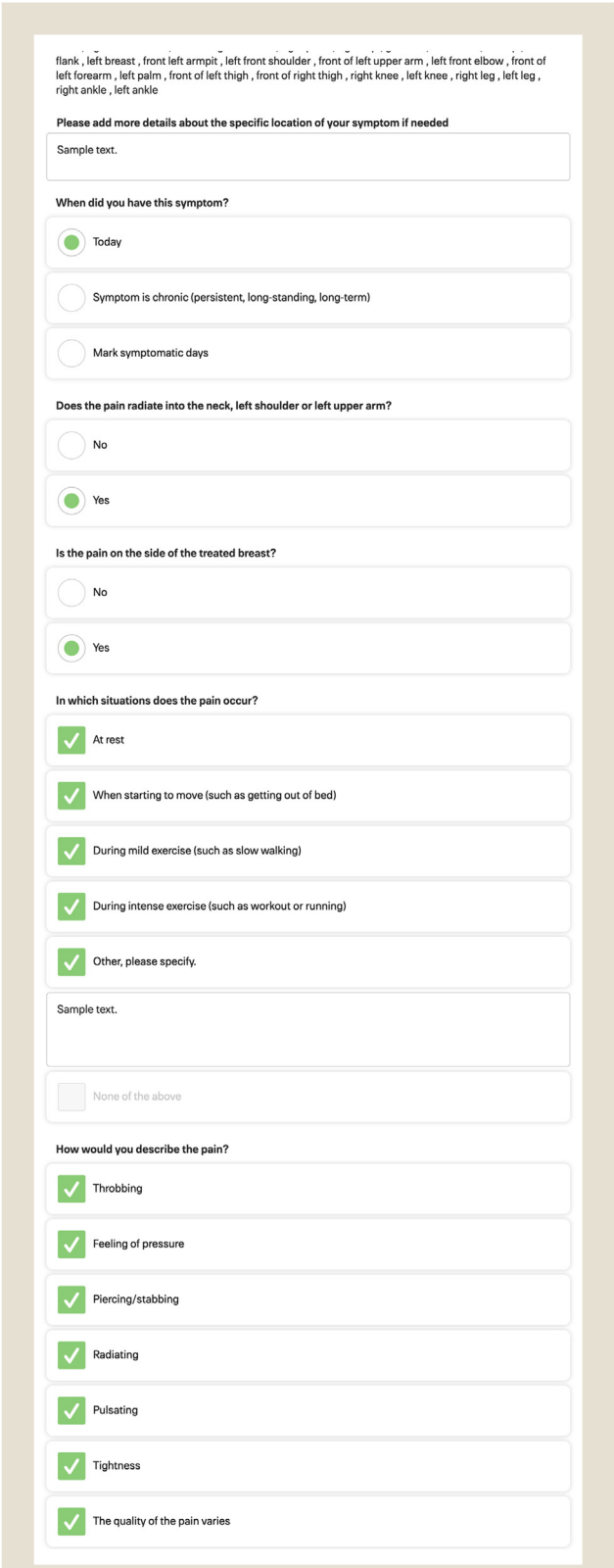
Where is the pain located?

- [x] Right breast
- [x] Right armpit
- [x] Right collarbone area
- [x] Left breast
- [x] Left armpit
- [x] Left collarbone area
- [x] Chest wall
- [x] Neck area
- [x] Elsewhere in the body

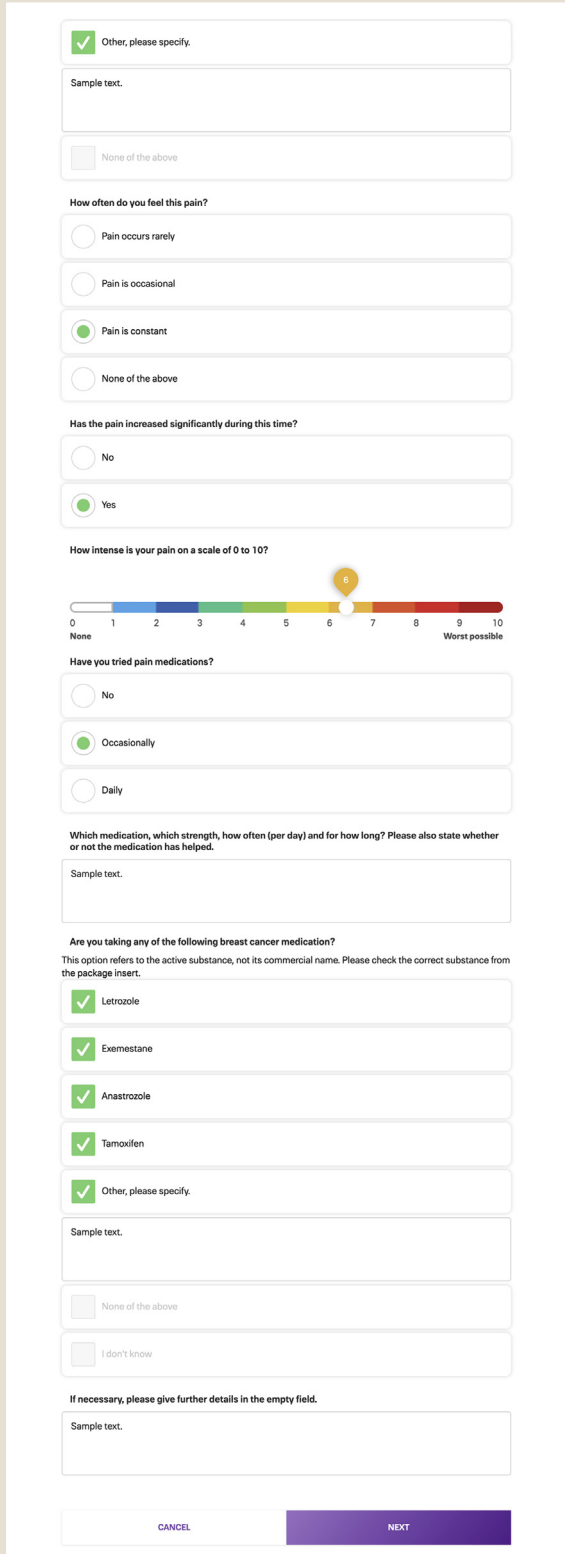


back of the head , back of the neck , left back shoulder , upper back , back left armpit , mid back , back of left upper arm , left elbow , lower back , back of left forearm , left wrist , back of left thigh , back of right thigh , back of left knee , back of right knee , left calf , right calf , left achilles , right achilles , right wrist , back of right forearm , right elbow , back of right upper arm , back right armpit , right back shoulder , head , neck , right front shoulder , breastbone , front right armpit , right breast , front of right upper arm , right flank , right front elbow , front of right forearm , right palm , right hip , genitals , abdomen , left hip , left

Supplemental Figure 2 Continued



Supplemental Figure 2 Continued



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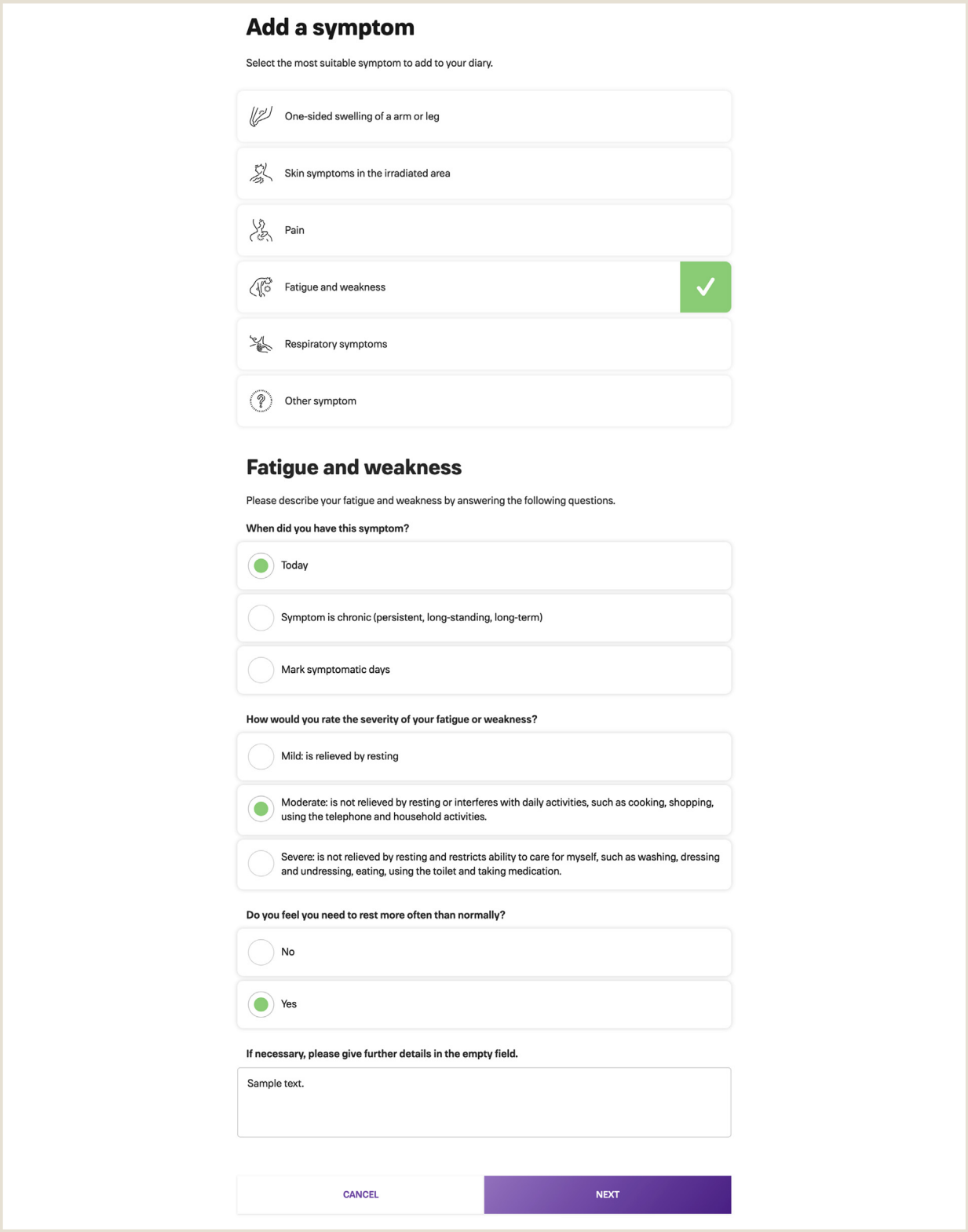

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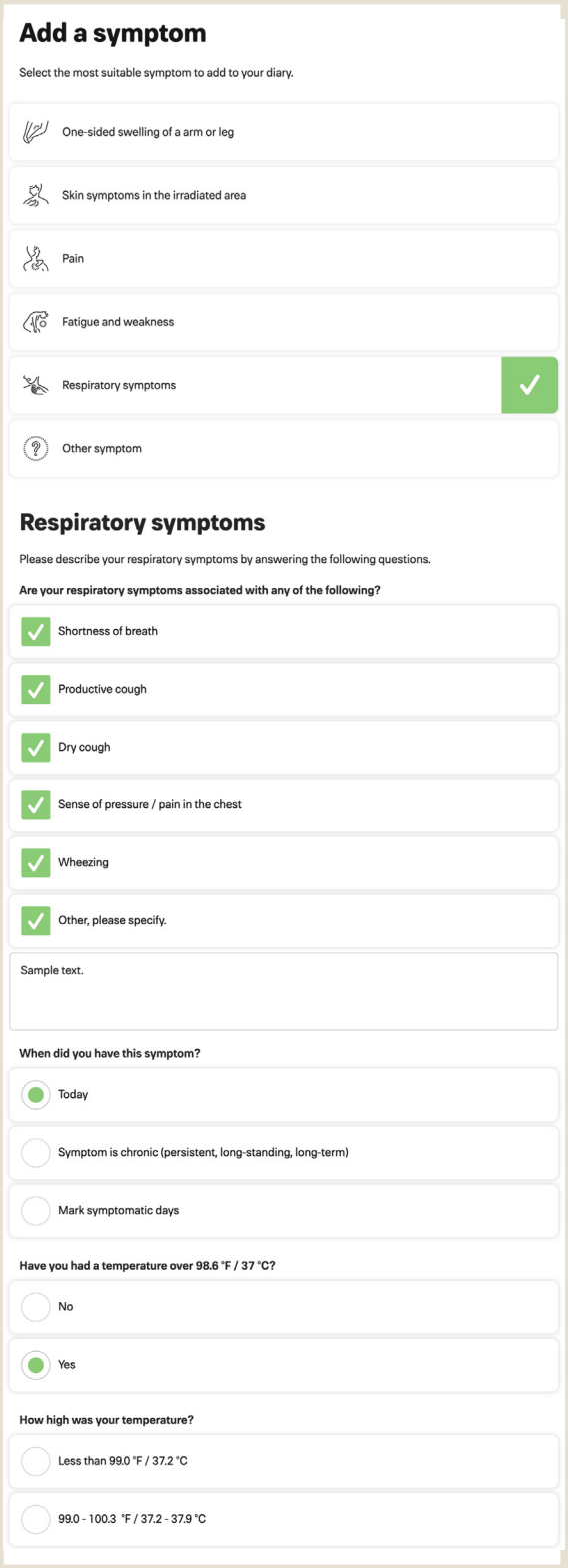

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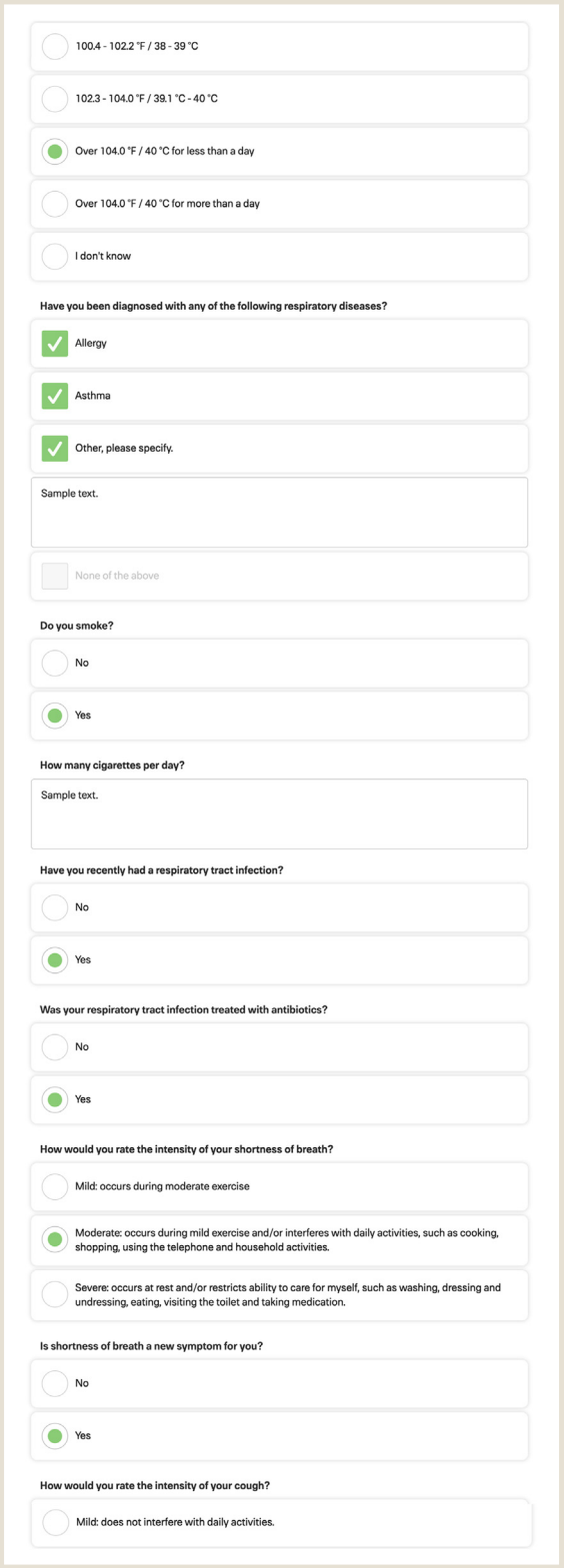

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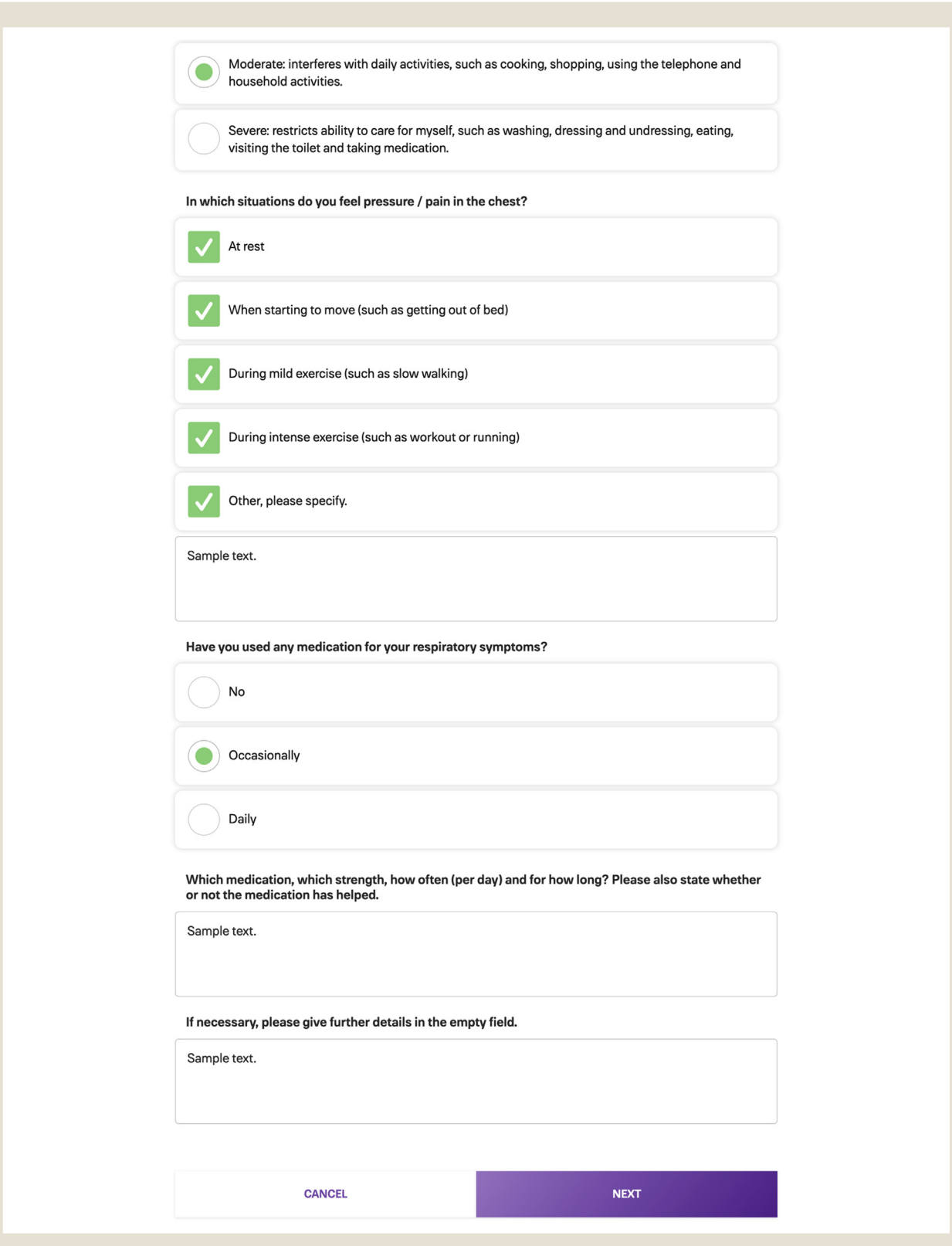

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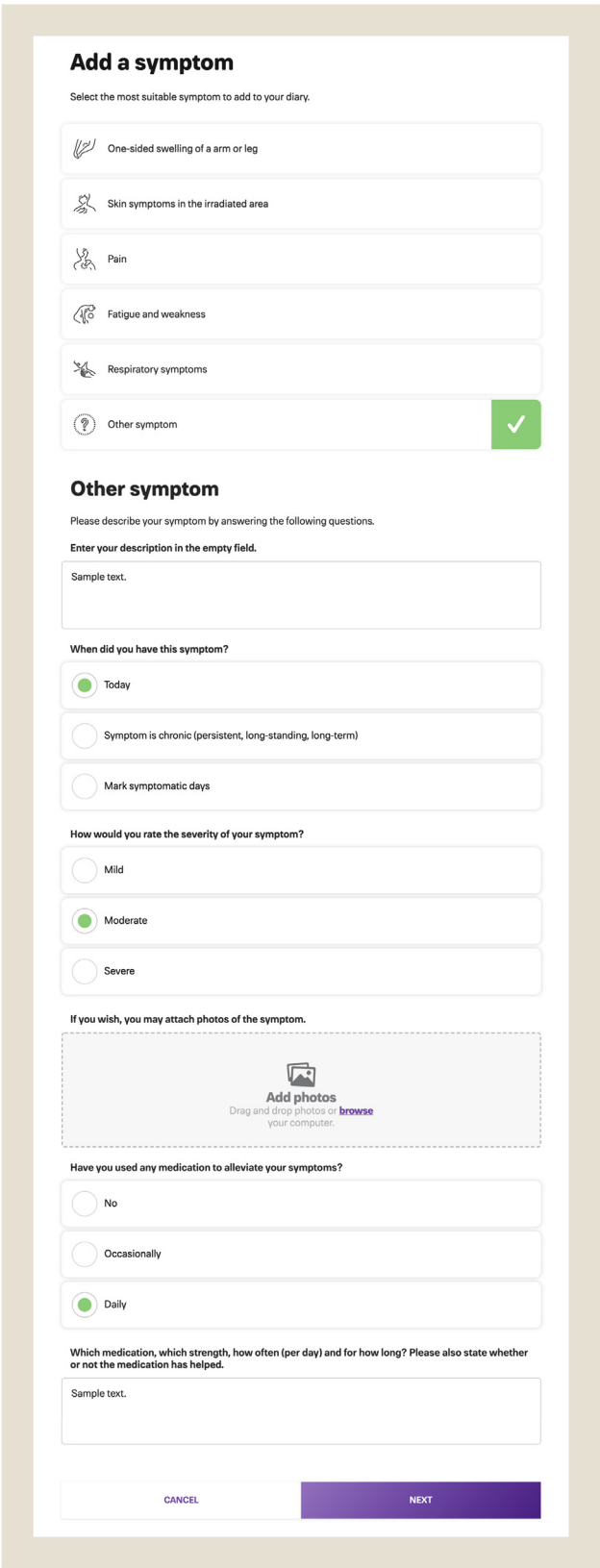
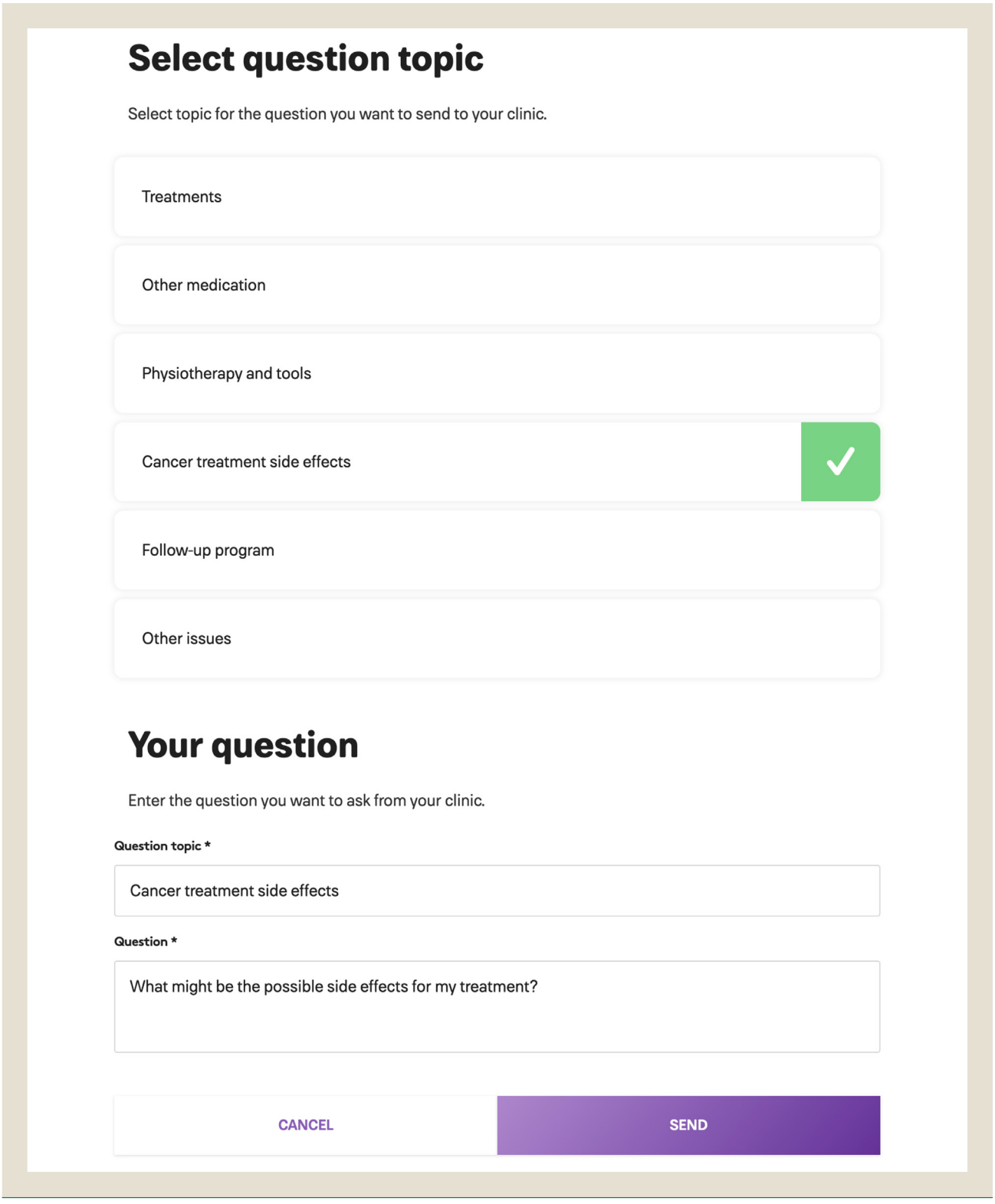
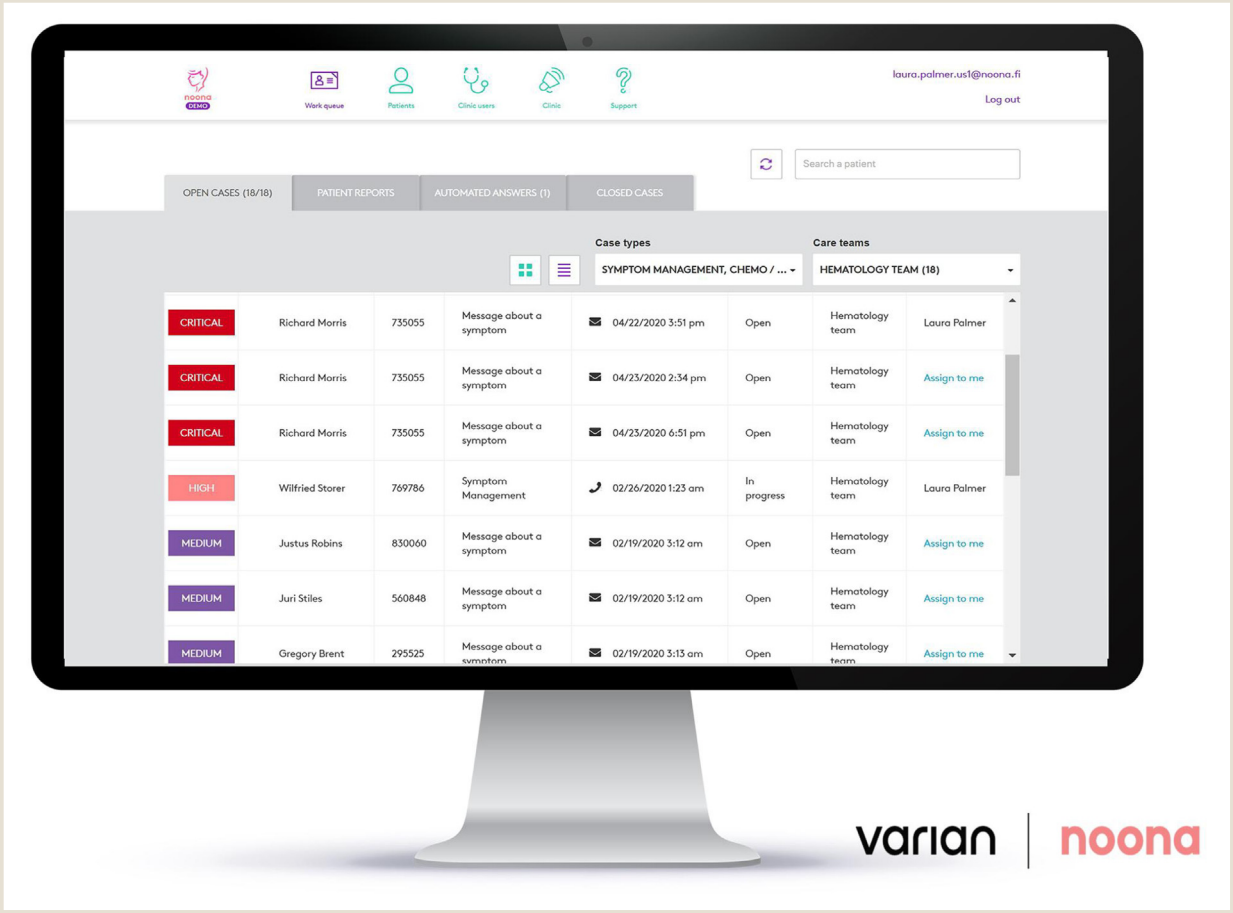


Supplemental Figure 3 Screenshot of the Patients' Side of the Cancer Follow-Up Application (CFUA) Allowing the Patients to be in Contact With the Clinic Through CFUA. The CFUA Offered Different Contact Options



Supplemental Figure 4 Screenshot of the Caregiver Side of the Cancer Follow-Up Application (CFUA). In the Caregiver's Side, the Main Functionality is a Work Queue to Monitor New Patients Who Have Requested Assistance and the Possibility to Communicate Directly With patients



Supplemental Figure 5 Screenshot of the Caregiver Side of the Cancer Follow-Up Application (CFUA). Summary View of a Patients' Questionnaire. The Symptoms Reported by the Patient are Presented on the Different Lines. The Line Shows the Grading of the Symptom, Duration of the Symptom, and the Trend of the Symptom. Each Symptom Reported Can Be Viewed in More Detail