Medical University of Gdańsk

Thesis for doctoral degree in Health Sciences

Assessment of the utility of mobile application for monitoring adverse effects of therapy and its impact on the satisfaction of patients treated with chemotherapy for breast cancer

Ocena użyteczności aplikacji mobilnej do monitorowania działań niepożądanych terapii i jej wpływu na satysfakcję pacjentów leczonych chemioterapią z powodu raka piersi

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Gdańsk 2023

To my supervisor – Dr Habil. Elżbieta Senkus-Konefka, Assoc. Prof.
Thank you for believing in me. You gave me the confidence to pursue this project
and overcome any obstacles that came my way,
and there were many…

To my beloved Family – thank you for your ongoing support
and patience beyond the limits.

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Mobile applications for early breast cancer chemotherapy-related symptoms reporting and management: a scoping review

Cancer Treat. Rev. 2022: vol. 105, s. 1-9

DOI: 10.1016/j.ctrv.2022.102364

IF 11.8 | MNiSW 140|Q1| scoping review

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Are all societies ready for digital tools? Feasibility study on the use of mobile application in Polish early breast cancer patients treated with perioperative chemotherapy

Healthcare 2023: vol. 11, nr 14, s. 1-16

DOI: 10.3390/healthcare11142114

IF 2.8 | MNiSW 40|Q2| original article

Total

Impact Factor 14.6 |MNiSW 180

II. ABBREVIATIONS

ALND	axillary lymph nodes dissection, *limfadenektomia pachowa*
BCS	breast-conserving surgery, *operacja oszczędzająca pierś*
BCT	breast conserving therapy, *leczenie oszczędzające pierś*
COPD	chronic obstructive pulmonary disease, *przewlekła obturacyjna choroba płuc*
CTCAE	Common Terminology Criteria for Adverse Events, *Wspólne Kryteria Terminologiczne Dotyczące Zdarzeń Niepożądanych*
ECOG PS	Eastern Cooperative Oncology Group Performance Status, *Stan Sprawności wg Eastern Cooperative Oncology Group*
EORTC-QLQ C30	European Organization for Research and Treatment of Cancer-Quality of Life Questionnaire, *Kwestionariusz Jakości Życia Europejskiej Organizacji Badań i Leczenia Raka*
ePROMs	electronic patient-reported outcome measures, *elektroniczne mierniki subiektywnej oceny pacjenta*
ePROs	electronic patient-reported outcomes, *elektroniczna subiektywna ocena pacjenta*
ER	oestrogen receptor, receptor estrogenowy
FACT-B	Functional Assessment of Cancer Treatment-B, *Ocena Funkcjonalna Leczenia Raka – wersja dla raka piersi*
HADS	Hospital Anxiety and Depression Scale, *Szpitalna Skala Lęku i Depresji*
HER2	human epidermal growth factor receptor 2, *ludzki receptor naskórkowego czynnika wzrostu typu 2*
HLS-14	14-item Health Literacy Scale, *14-punktowa Skala Kompetencji Zdrowotnych*
Ki67	proliferative fraction, *frakcja proliferacyjna*
MSAS	Memorial Symptom Assessment Scale, *Skala Oceny Objawów wg Memorial*
MSPSS	Multidimensional Scale of Perceived Social Support, *Wielowymiarowa Skala Odczuwanego Wsparcia Społecznego*
PBI	partial breast irradiation, *częściowe napromienianie piersi*
PgR	progesterone receptor, *receptor progesteronowy*
PPI	patient and public involvement, zaangażowanie pacjentów i opinii publicznej

PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses, *Zestaw Elementów Niezbędnych do Prawidłowego Raportowania Przeglądów Systematycznych i Meta-analiz*
PRISMA-ScR	Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews, *Zestaw Elementów Niezbędnych do Prawidłowego Raportowania Przeglądów Systematycznych i Meta-analiz - rozszerzenie dla przeglądu literatury*
PRO-CTCAE	Patient-Reported Outcome Common Terminology Criteria for Adverse Events, *Wspólne Kryteria Terminologiczne Dotyczące Zdarzeń Niepożądanych oparte na Wynikach Zgłaszanych przez Pacjentów*
PROMs	patient-reported outcome measures, *mierniki subiektywnej oceny pacjenta*
PROs	patient-reported outcomes, *subiektywna ocena pacjenta*
QoL	quality of life, *jakość życia*
RCT	randomised controlled trial, *randomizowane badanie kliniczne*
SICPA	Stanford Inventory of Cancer Patient Adjustment, *Kwestionariusz Dostosowania Pacjenta Onkologicznego wg Stanford*
SLNB	sentinel lymph node biopsy, *biopsja węzła wartowniczego*
TNBC	triple negative breast cancer, *potrójnie ujemny rak piersi*
UCC	University Clinical Centre, *Uniwersyteckie Centrum Kliniczne*
WBRT	whole breast radiotherapy, radioterapia całej piersi

III. SUMMARY

Two manuscripts included in this doctoral thesis explore the topic of mobile applications utilised for monitoring and management of chemotherapy-related symptoms among patients treated for early-stage breast cancer. To best of our knowledge, we were the first to perform literature review in this field and assess the utility of a mobile app designed to monitor adverse effects of chemotherapy among Polish breast cancer patients.

The first manuscript identified mobile apps available for patients treated with chemotherapy for early-stage breast cancer. We presented the summary of main characteristics of identified research, including description of tested mobile apps, study aims, outcome measures and results, and concluded that, although mobile applications are feasible and have ability to improve symptom management during cancer treatment, the knowledge about the use of ePROMs for monitoring patients treated for early-stage breast cancer is still limited.

The second article presented results of a study assessing the utility of the *Centrum Chorób Piersi UCK* app in Polish early breast cancer patients treated with perioperative chemotherapy. During the study, 55 (76%) participants completed the in-app questionnaire at least once and generated a total of 553 responses, reporting 1808 chemotherapy-related side effects. Fatigue was reported as the most frequent and distressing symptom, followed by sensation of pins and needles in hands and feet, pain and dizziness. 73.5% reported symptoms were mild, 21.7% - moderate, 4.4% - severe and 0.4% - debilitating. 29% of participants triggered alerts with questionnaire responses containing symptoms with critical value assessment, submitting 58 responses with 89 side effects of severity over the predefined critical threshold, resulting in 58 nursing interventions.

We examined correlations between the number of reported side effects and participants' characteristics, and found age to be the only factor determining the number of communicated symptoms. Together with possible digital exclusion among older (>60 years) patients observed during the enrolment process, our findings suggest that patients older than 60 years of age not only find it difficult to engage with mobile technology, but also are at a higher risk of experiencing problems caused by the cancer treatment and thus, may potentially derive most benefit from development of accessible eHealth technologies.

Significant negative correlation between the number of forms submitted by study participants and time from the first chemotherapy administration was observed, albeit the number of responses was not influenced by any sociodemographic or medical factors.

Next, we presented details of nursing interventions performed in response to app alerts. We described topics covered during those interventions and suggested management solutions, as well as specified indications when participants were advised to use emergency care services.

Lastly, we analysed results of patients' satisfaction survey and discovered that vast majority of study participants was satisfied with the support and care received in response to submitted questionnaires, and felt somewhat empowered by the possibility of reporting bothersome symptoms via the in-app questionnaire. However, although acceptance of eHealth solutions is widely recognised in cancer care, the uptake of the *Centrum Chorób Piersi UCK* app was poor, especially after the time of active recruitment to the study. Surprisingly, in the study follow-up period, when patients' in-app activity was monitored for additional year, the use of the app dropped substantially, resulting in only two patients using the in-app questionnaire to report their treatment-related symptoms.

KEYWORDS

Early breast cancer, chemotherapy, mobile application, eHealth, symptom management, symptom reporting

IV. SUMMARY IN POLISH/*STRESZCZENIE*

Dwie prace naukowe zawarte w niniejszej rozprawie doktorskiej badają temat wykorzystania aplikacji mobilnych do monitorowania i zarządzania objawami związanymi z chemioterapią u pacjentów leczonych z powodu wczesnego raka piersi. Zgodnie z naszą najlepszą wiedzą, jako pierwsi przeprowadziliśmy przegląd literatury w tej dziedzinie oraz oceniliśmy przydatność aplikacji mobilnej zaprojektowanej do monitorowania działań niepożądanych chemioterapii u polskich pacjentów z rakiem piersi.

Pierwsza praca naukowa zidentyfikowała dostępne aplikacje mobilne dla pacjentów leczonych chemioterapią z powodu wczesnego raka piersi. Przedstawiliśmy podsumowanie głównych cech zidentyfikowanych badań naukowych, w tym opis testowanych aplikacji mobilnych, cele badania, narzędzia pomiarowe oraz uzyskane rezultaty. Doszliśmy do wniosku, iż, mimo że aplikacje mobilne są praktyczne i mogą poprawić zarządzanie objawami podczas leczenia onkologicznego, to wiedza na temat wykorzystania elektronicznych mierników subiektywnej oceny pacjenta (ePROMs) do monitorowania chorych leczonych z powodu wczesnego raka piersi jest wciąż ograniczona.

Drugi artykuł przedstawił wyniki badania oceniającego użyteczność aplikacji "Centrum Chorób Piersi UCK" u polskich pacjentek leczonych chemioterapią okołooperacyjną z powodu wczesnego raka piersi.

Podczas badania 55 (76%) uczestników wypełniło kwestionariusz w aplikacji co najmniej raz i wygenerowało ogółem 553 odpowiedzi, zgłaszając 1808 skutków ubocznych związanych z chemioterapią. Najczęstszym i najbardziej uciążliwym objawem było zmęczenie, a następnie uczucie mrowienia w dłoniach i stopach, ból oraz zawroty głowy. 73.5% zgłoszonych objawów miało nasilenie łagodne, 21.7% umiarkowane, 4.4% ciężkie i 0.4% bardzo ciężkie. 29% uczestników wywołało alert, poprzez przesłanie odpowiedzi zawierających objawy, których nasilenie przekroczyło wartość krytyczną, generując 58 alertów informujących o 89 ciężkich lub bardzo ciężkich objawach, czego rezultatem było 58 interwencji pielęgniarskich.

Zbadaliśmy korelacje między liczbą zgłoszonych działań niepożądanych a wybranymi cechami uczestników badania i stwierdziliśmy, że wiek jest jedynym czynnikiem determinującym liczbę zgłaszanych objawów. Wraz z możliwym wykluczeniem cyfrowym wśród starszych pacjentów (>60 lat), zaobserwowanym podczas procesu rekrutacji, nasze wyniki sugerują, że pacjenci powyżej 60 roku życia nie tylko mają trudności z korzystaniem z technologii mobilnych, ale także są bardziej narażeni na problemy związane z leczeniem onkologicznym. Z tego względu, potencjalnie mogliby oni czerpać największe korzyści z rozwoju przystępnych rozwiązań eZdrowia.

Ponadto zauważyliśmy istotnie ujemną korelację między liczbą wypełnionych przez uczestników badania formularzy a czasem od pierwszego

podania chemioterapii. Niemniej jednak liczba odpowiedzi nie była uzależniona od żadnych czynników socjodemograficznych ani medycznych. W okresie obserwacji po zakończonym badaniu, gdy aktywność pacjentów w aplikacji była monitorowana przez dodatkowy rok, zainteresowanie aplikacją znacząco spadło, co skutkowało jedynie dwiema pacjentkami, które korzystały ze zgłaszania objawów związanych z leczeniem za pomocą zawartego w aplikacji kwestionariusza.

W następnej kolejności przeanalizowaliśmy wyniki badania satysfakcji pacjentów i zauważyliśmy, że ogromna większość uczestników badania była zadowolona ze wsparcia i opieki otrzymanych w odpowiedzi na przesłane zgłoszenia oraz czuła się w pewnym stopniu pewniej dzięki możliwości zgłaszania uciążliwych objawów za pomocą kwestionariusza w aplikacji. Niemniej jednak, mimo, że zastosowanie rozwiązań eZdrowia jest powszechnie akceptowane w opiece onkologicznej, użycie aplikacji "Centrum Chorób Piersi UCK" było niezadowalające, zwłaszcza po okresie aktywnej rekrutacji do badania.

Na końcu przedstawiliśmy szczegóły interwencji pielęgniarskich przeprowadzonych w odpowiedzi na alerty z aplikacji. Opisaliśmy omawiane tematy, proponowane rozwiązania problemów, których dotyczyły interwencje oraz wskazaliśmy sytuacje, w których uczestnikom zalecono skorzystanie z pomocy szpitalnego oddziału ratunkowego.

SŁOWA KLUCZOWE

Wczesny rak piersi, chemioterapia, aplikacje mobilne, eZdrowie, zarządzanie objawami, zgłaszanie objawów

V. INTRODUCTION

1. Breast cancer in Poland

According to the Polish National Cancer Registry, 23.8% of primary cancer registrations in women in 2020 were breast cancers. It remains the most frequent cancer diagnosis and the second most common cause of cancer-related deaths among Polish women [1]. Number of breast cancer diagnoses is increasing and while its mortality has decreased across Europe in the past three decades, an opposite trend has been reported in some transitional European countries, including Poland [2–4]. Breast cancer occurs predominantly in females; in males is rare, contributing to less than 1% of overall cases [5]. After sex, age is the most important known risk factor for breast cancer. Its incidence increases significantly with age, reaching its peak among women between 65 and 69 years and then decreases gradually [1]. Additional risk factors include: early menarche and late menopause, long-term hormone replacement therapy, low parity, genetic predisposition, history of atypical hyperplasia, exposure to ionising radiation, obesity, and excessive alcohol consumption [6,7]. Around 5% of breast cancers and up to 25% of familial breast cancer cases are caused by *BRCA1* or *BRCA2* mutations [8].

2. Treatment methods of breast cancer

Breast cancer is a heterogenous disease and its treatment should be carried out in dedicated breast centres and provided by multidisciplinary specialised teams, including medical oncologists, breast surgeons, radiation oncologists, breast radiologists, breast pathologists and breast nurses. Additionally, patients should have access to plastic surgeons, psychologists, physiotherapists and genetic counselling when appropriate [9]. Breast cancer treatment strategy depends on factors such as: tumour size and location, number of lesions, extent of lymph node involvement, biology of cancer, general health of the patient, their menopausal status and age [10].

Breast cancers can be grouped into subtypes categorised according to oestrogen receptor (ER), progesterone receptor (PgR) and human epidermal growth factor receptor 2 (HER2) expression. Features of particular breast cancer

subtypes are presented in Table 1. Each subtype has distinct risk profile and its management is associated with specific treatment strategy [11].

Table 1. Distinctive features of breast cancer subtypes.

SUBTYPE	SURROGATE DEFINITION	FEATURES
Luminal A	Luminal A-like	All of: ER and PgR positive HER2 negative Ki-67 low (<20, local laboratory specific)
Luminal B	Luminal B-like (HER2 negative)	ER positive HER2 negative and at least one of: Ki-67 high (≥20) PgR negative or low (≤20%)
	Luminal B-like (HER2 positive)	ER positive HER2 over-expressed or amplified Any Ki-67 Any PgR
HER2 over-expressed	HER2 positive (non-luminal)	HER2 over-expressed or amplified ER negative PgR negative
Basal-like	Triple negative (TNBC)	HER2 negative ER negative PgR negative

ER – oestrogen receptor, HER2 – human epidermal growth factor receptor 2, Ki67 – proliferative fraction, PgR – progesterone receptor, TNBC – triple negative breast cancer

Treatment methods of early stage breast cancer include surgery, systemic therapies (endocrine therapy, chemotherapy, targeted therapy, immunotherapy) and radiotherapy, delivered in diverse sequences [6,12].

2.1. Surgery

The majority of breast cancer patients will be offered surgery as primary method of treatment, however among some patients a neoadjuvant approach, where appropriate systemic treatment is given before the surgery, is recommended [6]. Patients selected for preoperative systemic therapy include mostly those with

so called "aggressive" breast cancer subtypes, which are highly sensitive to chemotherapy (e.g. TNBC, HER2 positive), with larger tumours or with metastases in axillary lymph nodes. The surgical techniques for breast cancer include breast-conserving surgery (BCS) or mastectomy, which can be combined with immediate or delayed breast reconstruction. BCS, which is always combined with postoperative radiotherapy to the breast, together named "breast conserving therapy" (BCT), aims to remove the tumour with free margins around it, but not the breast itself, while mastectomy removes the tumour as well as the breast. BCT is the preferred treatment option for the majority of early stage breast cancer patients, however mastectomy may be required due to tumour size, tumour multicentricity, inability to achieve negative surgical margins after multiple resections, prior radiation to the breast or chest wall, other contraindications to radiotherapy or patient's choice [13]. Status of axillary lymph nodes determined during the diagnostic process determines the extent of axillary surgery. Sentinel lymph node biopsy (SLNB) is a standard procedure for axillary staging in early, clinically node-negative breast cancer. Sentinel node is the first lymph node that drains lymph from a primary tumour. It is identified by injecting a radioactive isotope and/or blue dye close to the tumour. In higher risk patients, including those with clinically positive axillary lymph nodes at the time of surgery decision making, initial bulky nodal involvement and inflammatory breast cancer complete axillary lymph nodes dissection (ALND) is recommended [6,13,14].

2.2. Radiotherapy

Radiotherapy is an integral part of early stage breast cancer treatment. It uses ionising radiation to destroy cancer cells by damaging their DNA. Two main types of radiotherapy include teletherapy, where the radiation comes from an external source (linear accelerator) and brachytherapy, in which a radiation source is placed into the breast tissue to provide internal radiotherapy [14].

Radiotherapy is strongly recommended after BCS and should also be given after mastectomy for high-risk patients, including those with involved resection margins, involved axillary lymph nodes and large (>5cm) tumours [6]. Adjuvant radiotherapy significantly reduces local recurrence and improves overall survival [15].

Radiotherapy after BCS is usually given as whole breast radiotherapy (WBRT). The treatment consists of specific number of fractions given over days or weeks. In patients considered to be at higher risk of local recurrence boost radiotherapy is recommended. This is an additional dose of radiation directed specifically to the area of tumour bed, where the risk of recurrence is the highest. This may be delivered with external radiotherapy or with brachytherapy. Patients who are considered to be at low risk of recurrence, for example those who are at least 50 years old, with negative resection margins, negative axillary lymph nodes and small tumours (<3cm) may be eligible for partial breast irradiation (PBI), which reduces the radiation exposure of healthy breast tissue and other organs in the chest, decreasing the risk of long-term side effects [6].

2.3. Systemic therapies

Systemic therapies for early-stage breast cancer can be given as neoadjuvant (preoperative, induction) therapy, administered prior to definitive surgery, with intention to shrink the tumour to enable less extensive surgery and assess the sensitivity of the tumour to anticancer therapy or as adjuvant treatment, to eliminate cancer cells that might be left after the surgery and prevent distant recurrence [6,16]. The decision on perioperative systemic treatment is based on several factors related to bulk and biology of the disease. Each breast cancer subtype has a predicted sensitivity to particular treatment types. Luminal A-like breast cancers in the majority of cases can be treated with endocrine therapy alone. Most of luminal B-like breast cancers should be treated with chemotherapy followed by endocrine therapy. HER2 positive breast cancers (luminal B-like HER2 positive, non-luminal HER2 positive) require additional targeted anti-HER2 treatment and TNBCs are treated with chemotherapy alone [6,17] or combined with immunotherapy [18,19]. The final decision about systemic treatment should also consider the predicted treatment toxicities, patient's age, general health status, comorbidities and preferences [6].

2.3.1. Perioperative chemotherapy

The majority of breast cancer patients referred for perioperative chemotherapy receive the treatment in outpatient hospital units. Patients are admitted for few hours for chemotherapy infusion and discharged home on the same day.

Chemotherapy is given in cycles. Each cycle starts with the day when cytotoxic drug is administered and lasts for a certain time. In breast cancer treatment, chemotherapy is commonly given weekly, every other week or every third week. The number of cycles and intervals between them depend on the type of cytotoxic drugs used and recovery time for the patient. The total length of chemotherapy can vary between 12 and 24 weeks [6].

Outpatient chemotherapy allows patients to continue with most of their usual daily activities and minimises risks associated with inpatient hospital admissions. However, shortening hospital stay results in patients experiencing the majority of chemotherapy-related side effects at home, without direct medical supervision. Therefore, remote symptom monitoring measures and accessible self-management strategies are important for patients to cope with the treatment burden between chemotherapy administrations [20]. Furthermore, several studies report, that to improve recognition and management of therapy-induced adverse effects, feasible tools are required for patients to communicate their outcomes [21–23]. Instruments that facilitate capturing patient-reported outcomes (PROs) are known as patient-reported outcome measures (PROMs).

3. eHealth and electronic patient-reported outcomes in breast cancer

World Health Organisation defines eHealth as "cost-effective and secure use of information and communications technologies in support of health and health-related fields, including health-care services, health surveillance, health literature, and health education, knowledge and research" [24]. eHealth technologies involve use of computers, smartphones and video conferences, as well as wide variety of mobile and Webb applications (apps), that are utilised in cancer care for screening, diagnostic, therapeutic and educational purposes [21,25–27].

Patient-reported outcomes play fundamental role in understanding patients' symptom experience, including perception of the frequency, intensity, distress, and

meaning of symptoms [20]. However, identification of treatment-related side effects relying mainly on retrospective patient recollection may be of limited benefit because of recall bias and inaccuracy, and most importantly, because of delays in reporting of clinically significant and potentially life-threatening symptoms. Ineffective management of treatment-related toxicities degrades patients' quality of life (QoL) and increases supportive care needs [28–31].

Electronic PROMs (ePROMs) in the form of various in-app questionnaires facilitating capturing electronic PROs (ePROs), such as symptom burden, physical function, mental status and QoL, can be particularly useful in cancer care, as they allow patients to communicate their current health status and enable healthcare professionals to respond accordingly without unnecessary delays [32]. Specific eHealth solutions offer automated feedbacks and self-care recommendations apart from physician alerting algorithms, and direct nursing advice [33]. Altogether, implementing ePROMs into routine breast cancer care decreases the chemotherapy-induced symptom burden, improves patient-clinician communication, symptom management, self-efficacy and quality of life [34–38].

4. *Centrum Chorób Piersi UCK* mobile application

The *Centrum Chorób Piersi UCK* mobile app (Figure1) was developed to improve breast care awareness, promote breast cancer prevention and screening programmes, and provide evidence-based information for people affected by breast cancer. Healthcare professionals devoted to breast care were involved in the app development. Components of the app dedicated to patients diagnosed with breast cancer explain details of this particular disease and provide information on current treatment methods. Moreover, the electronic questionnaire for treatment-related symptoms embedded in the app facilitates the unique functionality of real-time symptom reporting.

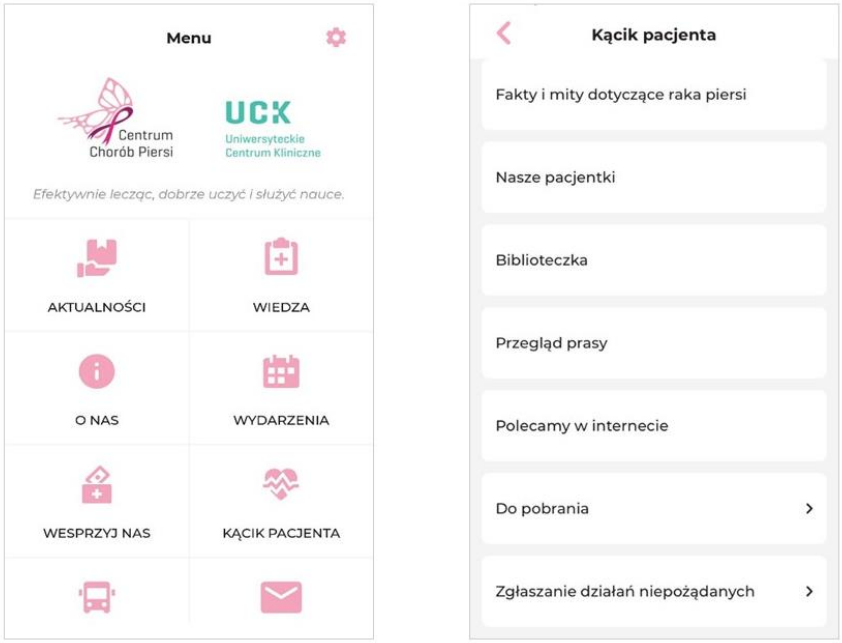


Figure1. Screen views of *Centrum Chorób Piersi UCK* mobile app

4.1 Electronic questionnaire for reporting treatment-related symptoms

The questionnaire (Figure 2) consists of 14 questions about the most common chemotherapy-related side effects, based on the Common Terminology Criteria for Adverse Events v.4 [39]. Detailed symptom assessment scale used in the studied app can be found in supplementary materials of publication no 2. Patients assess relevant symptoms on a 5-point scale, where 0 means no symptom, 1 - mild, 2 - moderate, 3 - severe and 4 - debilitating symptom. Replies including symptoms with critical value (≥3, apart from fever, which activates alerts when rated as 1 or above) trigger automatic email alerts to breast care nurses, who monitor patients' in-app activity. The application does not allow omitted questions or free-text responses in the questionnaire. Safety information emphasising that in the case of an emergency or sudden health deterioration patient must seek medical help through emergency services or an appointment with a physician or nurse, as appropriate, is displayed on the questionnaire's summary screen before submission.

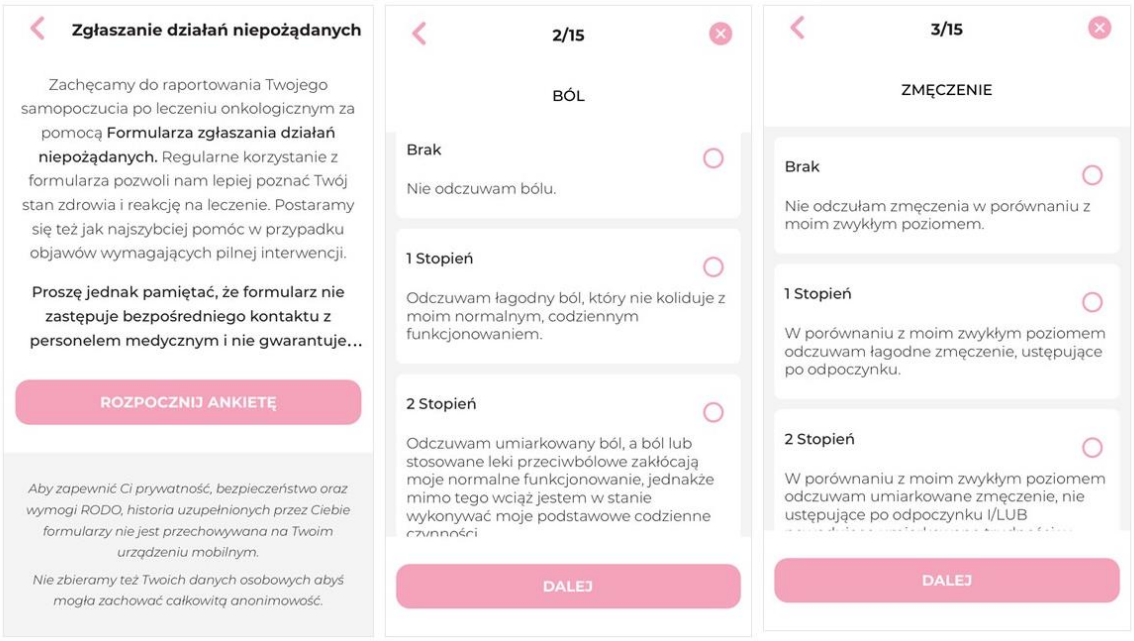


Figure 2. Screen views of the in-app questionnaire for reporting treatment-related symptoms

Patients who express their interest in using the questionnaire are informed that after reporting symptom(s) triggering an alert they will be contacted by the breast care nurse within one working day during office hours. All alerts are responded to with a nurse telephone consultation leading to further advice as necessary.

VI. AIMS OF THE STUDY

The *Centrum Chorób Piersi UCK* mobile app was the first and remains the only Polish app allowing real-time symptom reporting for breast cancer patients treated with perioperative chemotherapy. The primary objective of this project was to assess the utility of the *Centrum Chorób Piersi UCK* app for monitoring adverse effects of therapy and its impact on the satisfaction of patients treated with chemotherapy for breast cancer.

Detailed objectives included:

- assessment of patient-reported chemotherapy-related symptoms,
- analysis of treatment toxicity and adverse events reporting, depending on specific medical and sociodemographic factors,
- overview of nursing interventions performed in response to generated app alerts,
- evaluation of the satisfaction of patients using the *Centrum Chorób Piersi UCK* app.

VII. DESCRIPTION OF PUBLICATIONS INCLUDED IN THE DOCTORAL THESIS

1. *Mobile applications for early breast cancer chemotherapy-related symptoms reporting and management: a scoping review*

To explore the topic and identify literature providing information on development and use of mobile applications for adult patients undergoing chemotherapy for early stage breast cancer, a literature review was performed. Process of identification and inclusion of articles is presented in figure 3.

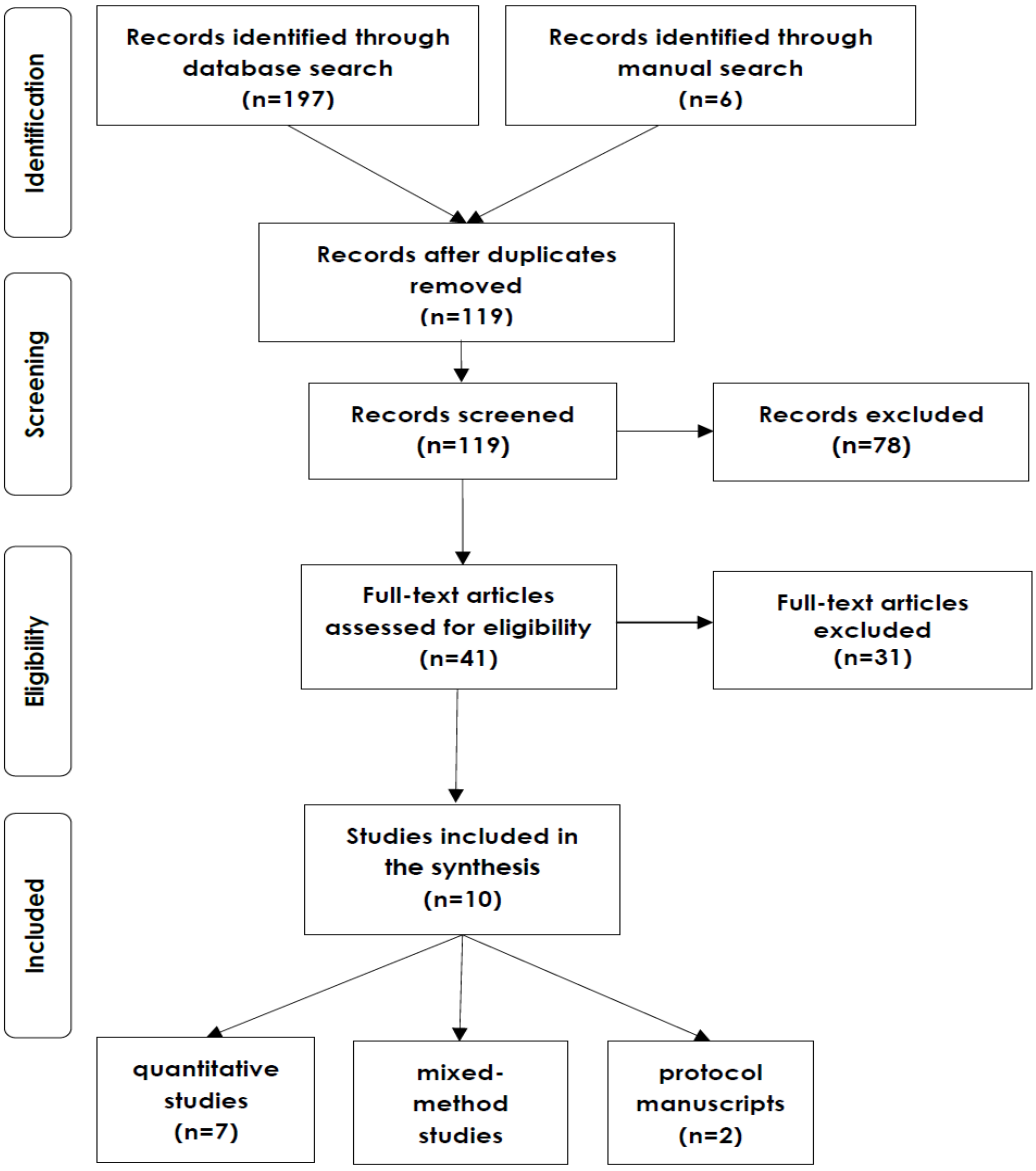


Figure 3. PRISMA Diagram – identification and inclusion of articles.

The review was conducted in compliance with Joanna Briggs Institute guidelines [40] and Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) recommendations [41]. Following research questions were asked to facilitate the process:

- what mobile applications have been developed and tested for monitoring chemotherapy-related side effects in early breast cancer and what are their specific features?
- what research, focusing on development and implementation of mobile apps addressing monitoring chemotherapy-related side effects in early breast cancer patients, is available?
- what clinical outcomes have been achieved in trials testing mobile apps for monitoring chemotherapy-related side effects in early breast cancer patients?

Electronic databases: Web of Science, PubMed and SCOPUS were searched for full text journal articles, written in English and published between 1st January 2011 and 31st January 2021. The search resuleted in 197 papers qualified for abstract screening, leading to 41 articles considered for full text review. Free online softwares were used: Rayyan for the screening process and Mendeley Reference Manager (version 1.19.8) for further data extraction. Manual search of reference lists of selected articles was performed and revealed six additional eligible papers. Overall, 10 out of 41 articles met eligibility criteria and were accepted for this review.

Five articles presented results of randomised controlled trials (RCTs) and one was a secondary data analysis of RCT. Additionally, one mixed method study, one nonrandomized controlled prospective cohort study and two study protocols were identified. All articles focused on adult patients receiving chemotherapy for early-stage breast cancer.

Six different mobile applications (Table 2) were identified within reviewed articles; all of them were developed specifically for research purposes.

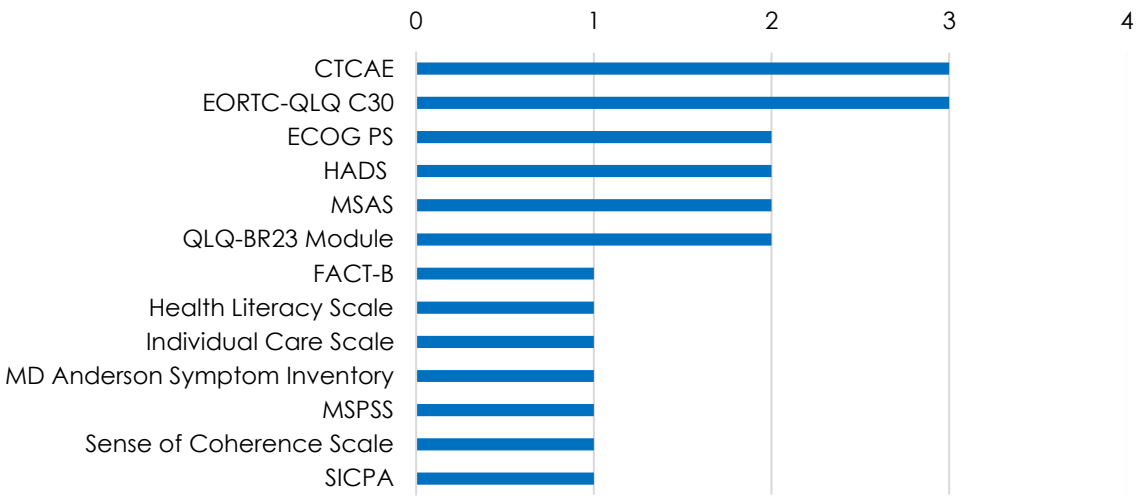
Table 2. Main characteristics of mobile apps identified in the review

Application name, country	Application language/s	Application type/ operating system	Application feature
Interaktor, Sweden	Swedish	Mobile app/ iOS and Android	– 14 symptoms based on MSAS – automatic text message alerts to contact nurses at the clinic – continuous patient access to evidence-based self-care advice and relevant web-sites related to assessed symptoms and other areas of concern; – possibility to monitor own reported symptom history over time in graphs – PPI in app development process
mPRO Mamma, Slovenia	Slovenian, English	Mobile app/ Android only	– 50 symptoms and symptom severity based on PRO-CTCAE – reminder notifications for patients – specified descriptions and recommendations depending on reported symptom level – encrypted reports to the patient's oncologist (optional) – no PPI in app development process
Breast Cancer Patient Support System, Japan	Japanese	App-based support program/ iOS and Android	– 12 symptoms and symptom severity based on PRO-CTCAE – blank fields to indicate unlisted symptoms – tips on self-care and management of side effects depending on reported severity – no PPI in app development process
Consilium, Switzerland	German	Mobile and Web app/ iOS and Android	– 48 symptoms from CTCAE listing with "quick list" of patient preselected symptoms – subjective well-being and adverse events monitoring – additional symptoms as free text – horizontal slider scale to indicate symptom severity – no reminders for patients

			– no PPI in app development process
Msemptom, Turkey	Turkish, English	Mobile app/ iOS and Android	– 32 symptoms based on MSAS – patient notifications via short message – reminder messages to the patients not reporting any symptoms – healthcare professional response within 1 hour – no PPI in app development process
Mobile Breast Cancer e-Support Program, China	Mandarin Chinese, English	Internet-based interactive program application/ iOS and Android	– 13 symptoms and symptom severity based on MD Anderson Symptom Inventory – Learning Forum - information about breast cancer and symptom management strategies – Discussion Forum – anonymous support group, moderated by healthcare professional – Ask-The-Expert Forum – online consultations facilitated by clinical oncologists – Personal Stories Forum – recorded interviews with women, who have successfully overcame difficulties during their course of cancer diagnosis and chemotherapy – PPI in app development process

CTCAE - Common Terminology Criteria for Adverse Events, MSAS - Memorial Symptom Assessment Scale, PPI - Patient and Public Involvement, PRO-CTCAE - Patient-reported Outcome Common Terminology Criteria for Adverse Events

Monitoring and management of ePROs varied significantly across described mobile applications. 13 different ePROMs (Figure 4) were used, most frequently, Common Terminology Criteria for Adverse Events (CTCAE) and European Organization for Research and Treatment of Cancer-Quality of Life Questionnaire (EORTC-QLQ) C30.



CTCAE – Common Terminology Criteria for Adverse Events, EORTC-QLQ C30 – European Organization for Research and Treatment of Cancer-Quality of Life Questionnaire, ECOG PS – Eastern Cooperative Oncology Group Performance Status, FACT-B – Functional Assessment of Cancer Treatment-B, HADS – Hospital Anxiety and Depression Scale, HLS-14 – 14-item Health Literacy Scale, MSAS – Memorial Symptom Assessment Scale, MSPSS – Multidimensional Scale of Perceived Social Support, SICPA – Stanford Inventory of Cancer Patient Adjustment

Figure 4. Patient-reported outcome measures used within reviewed articles

Professional interventions identified within reviewed reseach included: immediate automatic self-care advice and instructions for patients to aleviate reported symptoms, automatic alerts to the care team in response to severe symptoms reports, unlimited access to various educational resources and interactive expert forums.

Four out of six mobile applications recognised in this review demonstrated interventional value for management of chemotherapy-related side effects. Study participants randomised to intervention groups testing mobile apps inluding Consilium, Interactor, mPRO Mamma and Msemptom not only had better QoL, but also experienced lower symptom prevalence and symptom burden, comparing with participants in control groups receiving standard care alone. No significant differences were observed in studies assessing Breast Cancer Patient Support System and Mobile Breast Cancer e-Support Program.

2. Are all societies ready for digital tools? Feasibility study on the use of mobile application in Polish early breast cancer patients treated with perioperative chemotherapy

This article presents main results of the study conducted to achieve goals set for my doctoral project. The primary objective of the study was to analyse the results of using the questionnaire, contained within the *Centrum Chorób Piersi UCK* mobile app, to assess and monitor chemotherapy-related symptoms in patients treated for early-stage breast cancer.

Patients admitted to the Breast Cancer Chemotherapy Day Unit of the University Clinical Centre (UCC) in Gdańsk, who met the following inclusion criteria were eligible for participation in this study: referral for perioperative chemotherapy for early-stage breast cancer, possession of their own smart device, and an ability to navigate the device and download mobile applications independently; these patients completed a signed informed consent form. 93 early-stage breast cancer patients were assessed for eligibility. A total of 20 women refused, and a single eligible man was excluded from the analysis by the research team, resulting in 72 women being included in the study.

Enrolled patients were asked to download the free app *Centrum Chorób Piersi UCK* and instructed by breast care nurse to complete the in-app questionnaire weekly and on occasions when they experienced distressing symptoms. To ensure participants' safety, they were reminded that the questionnaire does not substitute for the usual way of contact with the care team in case of sudden health deterioration or emergency situation. Medical data (cancer stage and phenotype, setting of chemotherapy (preoperative vs. postoperative), type of cytotoxic drugs used, number of cycles, coexisting medical conditions and use of granulocyte colony-stimulating factors) were collected from patients' health records. Sociodemographic details including: age, sex, place of residence, education, employment, economic and marital status were self-reported by participants in the patient' satisfaction survey.

The first outcome measure used in this study was the in-app questionnaire that facilitated collecting information about chemotherapy-related side effects, and the second outcome measure was the proprietary survey that participants

completed after finishing the chemotherapy. Detailed symptom assessment scale used in our study can be found in the supplementary table 1 of this publication. The survey completed after finishing the last chemotherapy cycle or after the physician's decision to terminate the treatment included 10 questions relating to: the difficulty level of using the in-app questionnaire, safety during treatment, satisfaction from received care, sense of control, well-being during treatment, hospital admissions and free text option for additional participant suggestions.

Data collection lasted from December 2019 to June 2021, which was six months longer than first planned, due to the COVID-19 pandemic. Data were managed with Microsoft Excel and free RStudio (version 4.2.2) softwares. Nonparametric statistical methods were used to analyse the results of this study due to the small population and non-normally distributed outcome data. An α level of 0.05 was set for all tests. Correlations were assessed with the ρ-Spearman's correlation coefficient and its significance test. The Mann–Whitney U test was used to describe differences in continuous variables between two groups and the Kruskal–Wallis test for multiple (>2) groups. Post hoc Wilcoxon tests were performed to determine which groups were significantly different. For comparison between two categorical variables, Chi-square tests (for values >5) and Exact Fisher's test (for values <5) were used. Additionally, Wilcoxon Rank sum tests were performed to check differences between the median number of reported problems and two selected qualitative characteristics. Benjamini–Hochberg p-value correction for multiple comparisons was used for all performed tests.

The study acceptance was significantly higher among younger women (p=0.00006) and patients originating from rural areas (p = 0.00114). Possible digital exclusion among patients >60 years was observed during the enrolment process. Similar digital inequalities between age groups were discussed in several studies involving participants with diabetes [42], irritable bowel syndrome [43], asthma and COPD [44] and heart failure [45].

During the study, 55 (76%) participants completed the in-app questionnaire at least once and generated a total of 553 responses (competed questionnaires), reporting 1808 chemotherapy-related side effects. Patients who used the electronic questionnaire and those who submitted no responses did not differ in terms of sociodemographic or medical characteristics.

The prevalence of particular symptoms reported during our project is consistent with other studies, where fatigue was recognised as the most frequent and distressing symptom for breast cancer patients [46–48]. In our study, fatigue accounted for the majority (n=428) of overall problems reported, and triggers activating app alerts. The second most reported problem was the sensation of pins and needles in hands and feet (n=226), followed by pain (n=208) and dizziness (n=196). The least common symptoms reported included vomiting (n=6) and fever (n=5). 1329 (73.5%) symptoms were mild, 392 (21.7%) - moderate, 80 (4.4%) - severe and 7 (0.4%) - debilitating.

21 (29%) participants triggered alerts with questionnaire responses containing symptoms with critical value assessment. There were no statistically significant differences in sociodemographic or medical characteristics between patients who triggered alerts and the remaining participants. In total, 58 responses presenting 89 side effects with values over the predefined critical threshold were collected, resulting in 58 nursing interventions. Topics covered during those interventions included: physical activity and sleep (74%), pain management (24%), drug compliance (16%) and dietary needs (10%). 36% of nursing consultations related to alerts about multiple side effects; mostly consisting of combinations of severe fatigue, pain, shortness of breath and dizziness. Overall, five (7%) study participants in 23 consultations were advised to use emergency care services due to severe dyspnoea (n=10), dizziness (n=8), diarrhoea (n=3) and fever (n=2); however, no hospital admissions were required.

There were no statistically significant differences in the number of forms completed by each individual in relation to collected sociodemographic and medical factors. Nevertheless, a statistically significant negative correlation ($R= -0.3999$, $p<0.001$) was observed between the number of responses and time from first chemotherapy administration.

For the purposes of analysis of correlations identified between communicated symptoms and specific participant characteristics, the treatment-related side effects were arranged into five categories (Figure 5).

Figure 5. Categories of treatment-related side effects

The participants' age was found to be the only factor determining the number of reported symptoms. Statistically significant positive correlations were observed between age and the number of reported respiratory problems (R=0.3428, p=0.01), gastrointestinal problems (R=0.3168, p=0.018) and problems categorised as other (R=0.3661, p=0.006).

All participants completed the patient satisfaction survey. The majority (89%) of respondents assessed using the in-app questionnaire as very easy. Furthermore, most of them believed that the possibility of reporting symptoms via the questionnaire not only improved their safety and well-being during the treatment, but also made them feel in control of the situation in which they found themselves. Most participants felt satisfied with the support they received in response to the submitted forms. More than half of respondents thought that completing the in-app questionnaire improved the treatment of bothersome symptoms. According to the vast majority of participants, the overall care and support provided by medical staff met their expectations, with only a small percentage feeling that their expectations were not met. Ten patients suggested adding extra questions about nail problems (n=4), cardiac complications (n=1) and other unspecified unincluded symptoms (n=5).

VIII. CONCLUSIONS

Attempts of integrating mobile applications into standard cancer care have become increasingly popular over recent decades, and their beneficiary impact on people affected by cancer has been recognised. With continuously rising demand for oncology services not only due to growing number of breast cancer patients, but also the increasing complexity of breast cancer care, combined with workforce shortages, the implementation of feasible and accessible eHealth solutions may facilitate greater access to better, more sustainable and convenient care, improving overall patient and staff experience. Nevertheless, utilistaion of innovative eHealth solutions among Polish breast cancer patients, especially among those older than 60 years of age, treated with perioperative chemotherapy requires further exploration. Possibly, additional support should be provided to improve patients' awareness of the beneficiary potential of mobile interventions.

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X. PUBLICATIONS

Cancer Treatment Reviews 105 (2022) 102364

Contents lists available at ScienceDirect

Cancer Treatment Reviews

journal homepage: www.elsevier.com/locate/ctrv

General and Supportive Care

Mobile applications for early breast cancer chemotherapy-related symptoms reporting and management: A scoping review

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ARTICLE INFO

Keywords:
Early breast cancer
Chemotherapy
Mobile application
Patient-reported outcomes
Symptom management
Symptom reporting

ABSTRACT

Background: Mobile applications are more and more often integrated into standard cancer care. Nevertheless, knowledge about the use of mobile applications for monitoring patients during treatment for early breast cancer is still limited.
Methods: A scoping review of literature was performed based on Joanna Briggs Institute guidelines to identify articles providing information on development and use of mobile applications for adult patients undergoing chemotherapy for early breast cancer.
Results: Five randomized controlled trials (RCT), nonrandomized controlled prospective cohort study, secondary data analysis of RCT, mixed method study and two protocol manuscripts were reviewed. Four out of six mobile applications recognized in this review were demonstrated to have interventional value for management of chemotherapy-related side effects. Clinical outcomes achieved among mobile apps users included improved quality of life, lower symptom prevalence and symptom burden.
Conclusions: Mobile applications are feasible and have ability to improve symptom monitoring during cancer treatment. However, more research is needed to validate these resources, ensuring effectiveness and safety for their users.

Introduction

Rapid development of digital technologies resulted in wide variety of mobile and Webb applications (apps) being used in cancer care for screening, diagnostic, therapeutic and educational purposes [1]. Some of them provide solutions for capturing patient-reported outcomes (PROs) like symptom burden, function and quality of life. Introducing electronic PROs (ePROs) into routine cancer care not only improves symptom management and quality of life [2-4], but also in some settings increases patients' survival [5,6]. Additional advantages of integrating ePROs are enhanced patient–clinician communication [7] and detailed data collection with less information missing [8].

Utilization of mobile apps for symptom reporting has increased, however knowledge about the use of mobile apps for monitoring patients during treatment for early breast cancer (who form the majority of breast cancer patients treated in chemotherapy units - potentially affected with adverse effects of treatment and in a need for support with management of these symptoms) is still limited [9].

The primary objective of this review was to identify studies on mobile apps for monitoring chemotherapy-related side effects among patients treated for early-stage breast cancer. The secondary aim was to provide a summary with detailed description of mobile applications

Abbreviations: AE, Adverse Event; ASyMS, Advanced Symptom Management System; AYA, Adolescent and Young Adults; BCS, Breast Cancer e-Support; BPSS, Breast Cancer Patients Support System; CTCAE, Common Terminology Criteria for Adverse Events; d, average deviation; ECOG PS, Eastern Cooperative Oncology Group Performance Status; EORTC-QLQ, European Organization for Research and Treatment of Cancer-Quality of Life; ePRO, electronic Patient-reported Outcome; FACT-B, Functional Assessment of Cancer Treatment-B; GDI, Global Distress Index; HADS, Hospital Anxiety and Depression Scale; HLS-14, 14-item Health Literacy Scale; HRQoL, Health-related Quality of Life; IQR, Interquartile Range; MSAS, Memorial Symptom Assessment Scale; MSPSS, Multidimensional Scale of Perceived Social Support; p, probability value; PCC, Population Context Concept; PPI, Patient and Public Involvement; PRISMA, Preferred Reporting Items for Systematic reviews and Meta-Analyses; PRISMA-ScR, Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews; PRO, Patient-reported Outcome; PRO-CTCAE, Patient-reported Outcome Common Terminology Criteria for Adverse Events; QoL, Quality of Life; r, correlation coefficient; RCT, Randomized Controlled Trial; SICPA, Stanford Inventory of Cancer Patient Adjustment.

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https://doi.org/10.1016/j.ctrv.2022.102364
Received 8 January 2022; Received in revised form 18 February 2022; Accepted 19 February 2022
Available online 23 February 2022

tested in studies included in this review and the impact of their use on outcomes related to patients' safety, quality of life and satisfaction with treatment.

The review questions were:

- What mobile applications have been developed and tested for monitoring chemotherapy-related side effects in early breast cancer and what are their specific features?
- What research, focusing on development and implementation of mobile apps addressing monitoring chemotherapy-related side effects in early breast cancer patients, is available?
- What clinical outcomes have been achieved in trials testing mobile apps for monitoring chemotherapy-related side effects in early breast cancer patients?

Methods

A scoping review of literature was performed based on Joanna Briggs Institute guidelines; PCC (population, context, concept) mnemonic was used to form a primary question for this review [10]. Recommendations described in Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) were followed to organize the information [11].

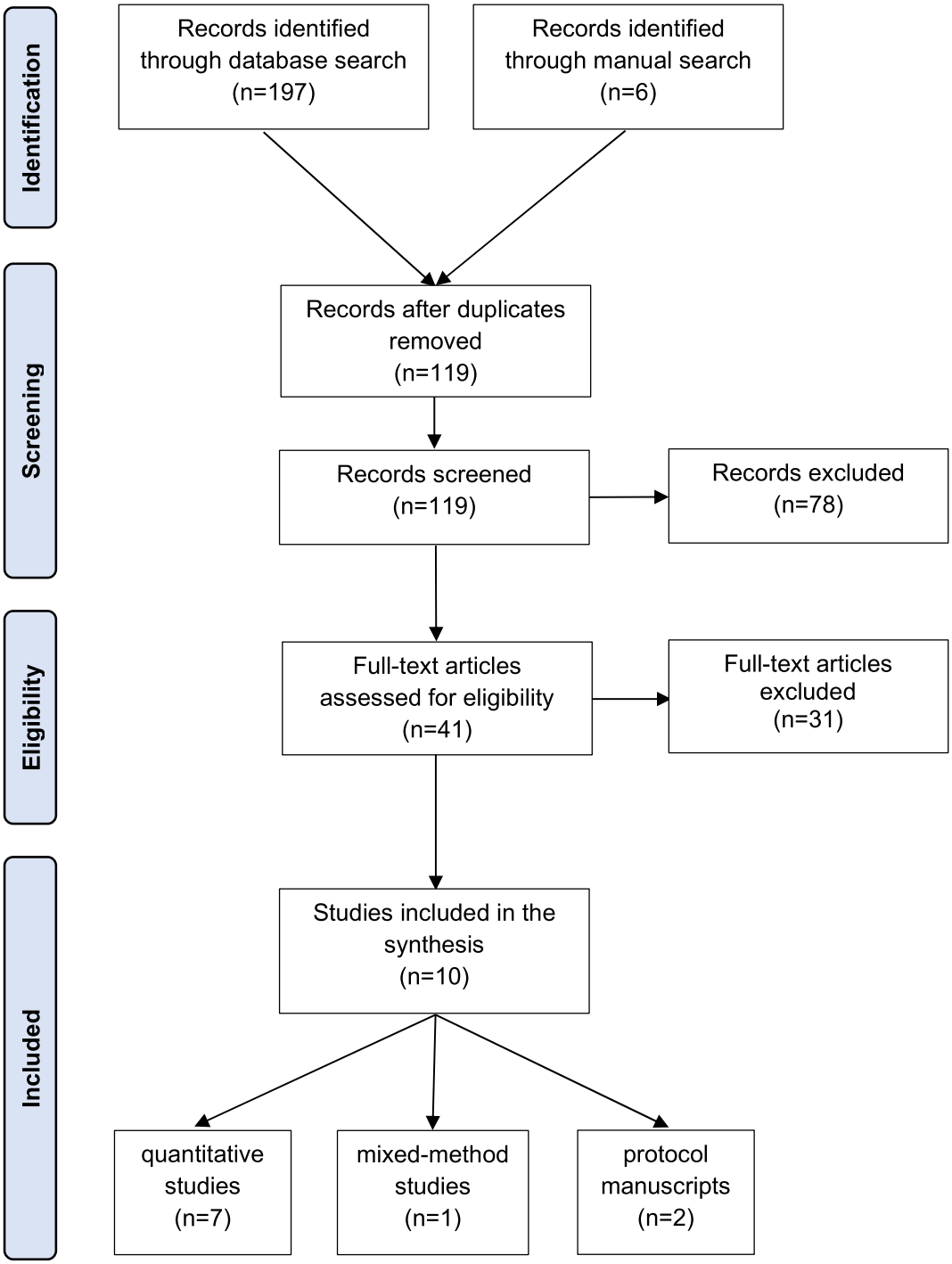

Fig. 1. PRISMA Diagram – identification and inclusion of articles.

Electronic databases: Web of Science, PubMed and SCOPUS were searched for full text journal articles, published between 1st January 2011 and 31st January 2021. The following search strings were used: breast AND cancer AND chemotherapy AND m-health; breast AND cancer AND chemotherapy AND mobile AND application OR app; mobile AND app AND symptom AND management AND breast AND cancer.

First search was performed on 14th February 2021 and final search was accomplished on 7th of July 2021. Articles written in English, providing information on development and use of mobile applications for adult patients undergoing chemotherapy for early breast cancer were considered. Furthermore, a manual search of reference lists of identified articles was performed to detect any additional relevant studies.

Results

Total of 197 articles were extracted. Free online software (Rayyan) was used for title and abstract screening. After duplicates removed, 119 papers were selected for abstract review to identify articles addressing development and utilization of mobile apps in care of early-stage breast cancer patients. Systematic and scoping reviews were removed during title screening. A total of 35 full text articles were recognized. Manual search of reference lists of those articles was performed to detect any additional papers and led to six additional eligible articles. Retrieved articles were exported to the Mendeley Reference Manager software. Articles presenting research focusing on monitoring breast cancer patients without mobile app involvement were excluded, as well as articles describing mobile apps specific for other than breast cancer malignancies. Overall, ten papers met eligibility criteria and were selected for this review. The PRISMA flow diagram of the literature search and screening process is presented in Fig. 1.

Most studies selected for this review were quantitative [12-18]. There was one mixed-method study [19] and two study protocols [16,20]. Five randomized controlled trials (RCTs) [13-15,17,18], one nonrandomized controlled prospective cohort study [12], as well as one secondary data analysis of RCT [21] were identified. The earliest study dated from 2016 [13], and the most recent was published in 2021 [15]. As per inclusion criteria, all studies concentrated on patients receiving chemotherapy for early-stage breast cancer.

In total, six mobile applications were identified within reviewed articles. All of them were developed specifically for research purposes. Detailed description of the applications, including application name, type and operating system, country where it was developed, language and main features is presented in Table 1.

In all studies applications were made available to participants, however no electronic equipment was provided by the investigators. Monitoring and management of patient-reported treatment-related symptoms varied significantly across described mobile applications. Symptom reporting was followed-up with instant healthcare professional advice in Interaktor app. Symptoms of concern generated alerts by text message to monitoring nurse at the clinic. Patients with less severe symptoms were contacted during the same day, and patients reporting symptoms of greater severity were contacted within 1 h [17]. Similar solution was offered to Msemptom app users, who were responded to within 1 h, however process of triggering health professional reaction was not specified [15]. In mPRO Mamma app and Japanese Breast Cancer Patients Support System (BPSS), instant automatic healthcare professional's advice, adapted for each grade of symptom severity, was available [12,14]. Additionally, to alleviate mild and moderate symptoms, instructions were displayed on the screen. For severe symptoms, application advised to visit general practitioner or an emergency department [12]. BPSS offered designating hospital contact details for patients who recorded grade $\geq$ 3 symptoms [14]. Mobile Breast Cancer e-Support Program for Chinese women included information about symptom management strategies in Learning Forum, moreover patients had opportunity to ask treatment related questions in Ask-The-Expert Forum, where responses were received within 24 h [18].

Table 1
Summary of main characteristics of identified applications including main features, operating system, language and country of origin.

Application name, country	Application language/s	Application type/ operating system	Application feature
Interaktor, Sweden	Swedish	Mobile app/iOS and Android	• 14 symptoms based on MSAS • automatic text message alerts to contact nurses at the clinic • continuous patient access to evidence-based self-care advice and relevant websites related to assessed symptoms and other areas of concern; • possibility to monitor own reported symptom history over time in graphs • PPI in app development process
mPRO Mamma, Slovenia	Slovenian, English	Mobile app/ Android only	• 50 symptoms and symptom severity based on PRO-CTCAE • reminder notifications for patients • specified descriptions and recommendations depending on reported symptom level • encrypted reports to the patient's oncologist (optional) • no PPI in app development process
Breast Cancer Patient Support System, Japan	Japanese	App-based support program/iOS and Android	• 12 symptoms and symptom severity based on PRO-CTCAE • blank fields to indicate unlisted symptoms • tips on self-care and management of side effects depending on reported severity • no PPI in app development process
Consilium, Switzerland	German	Mobile and Web app/iOS and Android	• 48 symptoms from CTCAE listing with "quick list" of patient preselected symptoms • subjective well-being and adverse events monitoring • additional symptoms as free text • horizontal slider scale to indicate symptom severity • no reminders for patients • no PPI in app development process
Msemptom, Turkey	Turkish, English	Mobile app/iOS and Android	• 32 symptoms based on MSAS • patient notifications via short message • reminder messages to the patients not reporting any symptoms • healthcare professional response within 1 h • no PPI in app development process

(continued on next page)

Table 1 (*continued*)

Application name, country	Application language/s	Application type/ operating system	Application feature
Mobile Breast Cancer e-Support Program, China	Mandarin Chinese, English	Internet-based interactive program application/iOS and Android	• 13 symptoms and symptom severity based on MD Anderson Symptom Inventory • Learning Forum - information about breast cancer and symptom management strategies • Discussion Forum – anonymous support group, moderated by healthcare professional • Ask-The-Expert Forum – online consultations facilitated by clinical oncologists • Personal Stories Forum – recorded interviews with women, who have successfully overcome difficulties during their course of cancer diagnosis and chemotherapy • PPI in app development process

CTCAE - Common Terminology Criteria for Adverse Events, MSAS - Memorial Symptom Assessment Scale, PPI - Patient and Public Involvement, PRO-CTCAE - Patient-reported Outcome Common Terminology Criteria for Adverse Events

In Consilium app there was no interaction between patients and medical professional. Only in one intervention group, and only during scheduled visits, treating physician was involved in discussing electronically reported symptoms [13]. Despite of recent increase of Patient and Public Involvement (PPI) in clinical research [22], only two applications included in this review were developed with consideration of patients' opinion and suggestions [17,18].

The tested patients sample size varied between 57 [15] and 149 [17]. In total, 652 patients were recruited, of which 352 were included in intervention and 300 in control groups. Fig. 2 demonstrates numbers of patients randomized and excluded before randomization in each clinical trial. Reasons for exclusion are presented in Supplementary Table 1.

In all clinical trials reviewed, a number of patients discontinued prematurely due to different reasons, the most frequent being consent withdrawal and untraceable contact. Summary of reasons for patients' exclusion after randomization is presented in Table 2.

In the process of app utility and engagement assessment, authors of Interaktor app and the Mobile Breast Cancer e-Support Program, enrolled participants from intervention groups of previous RCTs [17,18] to additional follow-up studies [19,21]. Interaktor, Breast Cancer Patient Support System (BPSS), Consilium and Breast Cancer e-Support (BCS) applications were tested on female patients, whereas for mPRO Mamma and Msemptom apps, gender of participants was not indicated. Table 3. summarizes aims and results for all reviewed research, except protocol manuscripts [16,20].

Thirteen different measurement tools were used within reviewed papers (Fig. 3), most frequently, Common Terminology Criteria for Adverse Events (CTCAE) and European Organization for Research and Treatment of Cancer-Quality of Life Questionnaire (EORTC-QLQ) C30. Every study utilized at least one international symptom monitoring scale. Collection and analysis of the results were performed, as stated by the purpose and methodological design of each study. In clinical trials [12-15,17,18], results were compared between intervention and control groups. All patients included in RCTs received standard care, but only those in intervention groups were asked to use particular mobile app. One study (Consilium) [13], apart from control group, included two intervention groups, where one group was reviewing reported data with treating physician, comparing to second group using the app without physician follow-up. In two studies [13,18], health care professionals collecting data were blinded to the participants group allocation.

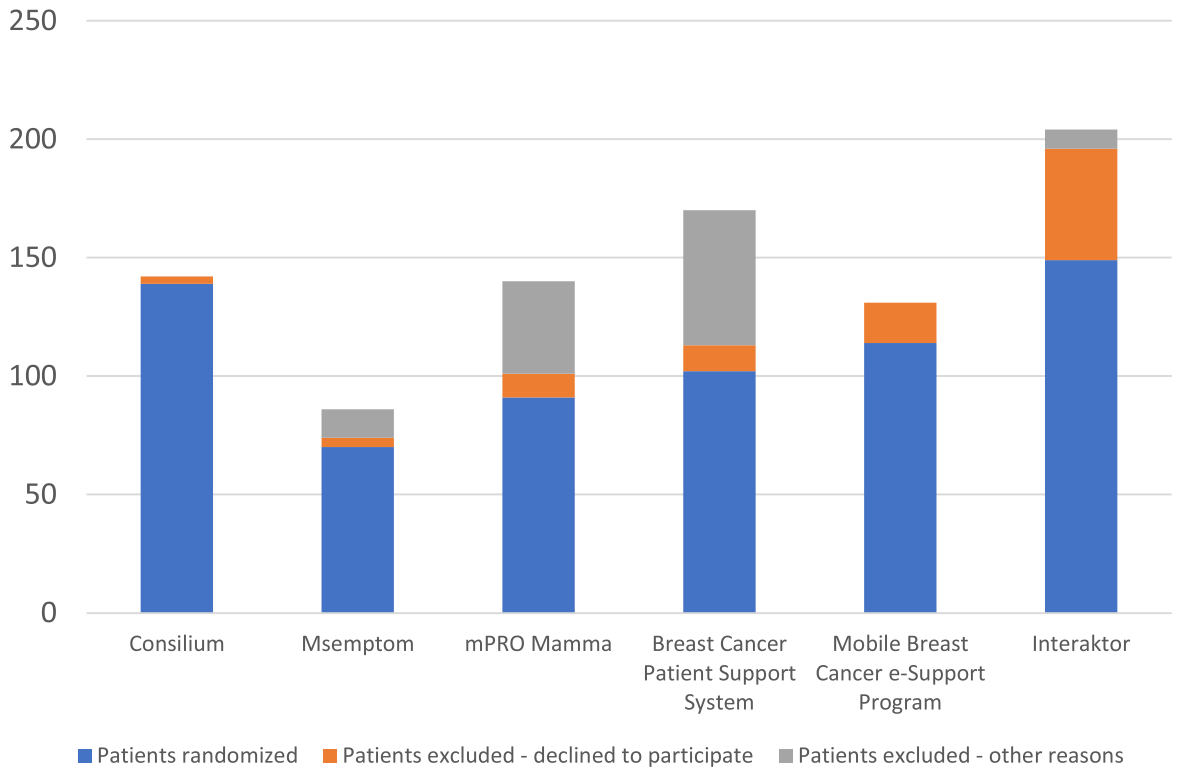

Fig.2. Distribution of patients randomized and excluded from randomization in each clinical trial.

Table 2
Summary of reasons for premature discontinuation in each clinical trial.

Reasons for exclusion after randomization	Consilium	Msemptom	mPRO Mamma	Breast Cancer Patient Support System	Mobile Breast Cancer e-Support Program	Interaktor	All
Untraceable contact	0	0	9	1	1	0	11
Consent withdrawal	4	4	0	0	5	2	15
Changes in treatment protocol because of complications	0	4	2	0	1	0	7
Disease progression (metastatic disease)	0	0	2	0	0	0	2
Transfer to another hospital	0	5	0	0	1	0	6
Software malfunction	6	0	0	0	0	0	6
All	10	13	13	1	8	2	×

Results of four out of six trials included in this review confirmed that mobile applications have interventional value for management of chemotherapy-related side effects. Patients randomized to intervention groups using mobile apps including Interactor, mPRO Mamma, Consilium and Msemptom had better global quality of life (QoL) in comparison to patients in control groups receiving standard care alone. Moreover, patients in the intervention groups experienced significantly lower symptom prevalence and symptom burden [12,13,15,17]. Higher quality of life was initially observed in the intervention group of Chinese women using Mobile Breast Cancer e-Support Program, nevertheless, this was not sustained after six-month follow-up [18].

Discussion

Results from four out of six trials included in this review confirmed that patients using designated mobile apps during chemotherapy for early breast cancer have better QoL [12,13,15,17]. Similarly, an "Ilovebreast" game-based application, addressing educational needs of adult patients, was demonstrated to improve QoL of metastatic breast cancer patients undergoing chemotherapy [23]. Additional benefits included better patient education, improved drug compliance, and decreased prevalence of physical side effects. Nevertheless, there was no impact on anxiety and depression. Another game-based application with built-in reward system, targeting adolescent and young adult (AYA) patients with non-specified cancers, was demonstrated to improve pain-related outcomes (pain intensity, pain interference) and QoL [24]. Further applications addressing AYA demonstrated improved monitoring and management of mucositis [25], nausea, vomiting, fatigue, and sleep [26].

Overall, patients value the use of mobile applications supporting symptom reporting and management. A complementary study, assessing users' engagement in the Interactor app, demonstrated high adherence to the app. Furthermore, daily symptom reporting was perceived as convenient and highly valued, especially at the beginning of the treatment [19]. High acceptance of another digital system for remote monitoring of patients' symptoms during cancer treatment was demonstrated by both patients and clinicians in PRO-TECT trial [27]. A pilot study of breast cancer survivors assessing utilization and satisfaction of electronic symptom and adherence monitoring app [28] demonstrated improved drug compliance, higher satisfaction with communication and follow-up in the intervention group versus the usual care group, however, difference in anxiety scores assessed in both groups was not significant.

The BPSS app study suggests, that it might be useful as a support tool for information sharing between patient and healthcare professionals. Importantly, it also indicated underestimation of the severity of treatment side effects, particularly fatigue and appetite loss, by the medical staff. Surprisingly, albeit similarly to other studies, the BPSS app did not improve anxiety, depression or health literacy in patients using the app additionally to standard care [14]. Similar results were observed for Mobile Breast Cancer e-Support Program users – anxiety and depression was not reduced in the intervention group [18].

Real-time symptom monitoring by a web-based symptom reporting system was demonstrated to improve a number of outcomes, most importantly patients' overall survival in patients treated for metastatic breast, lung, genitourinary and gynecologic cancers [6]. Improved QoL, less frequent emergency room visits, fewer hospital admissions and longer duration of palliative chemotherapy were amongst further benefits observed in the intervention group.

Significant survival improvement was also observed among high risk lung cancer patients, reporting self-scored symptoms in web-based follow-up application, compared to standard follow-up care [5]. Moreover, the application led to reduction of routine imaging and hospital visits per patient and earlier supportive care involvement resulting in higher performance status at relapse.

A RCT involving patients with early breast, lung and colorectal cancer, which assessed advanced symptom management system (ASyMS) demonstrated more precise reflection of treatment toxicity and a potential to decrease chemotherapy induced symptom burden among ASyMS users [29]. Consequently, recent international multicenter RCT evaluating ASyMS in non-metastatic breast cancer, colorectal cancer, Hodgkin's disease, or non-Hodgkin's lymphoma confirmed significant reduction in symptom burden in the intervention group [30]. Furthermore, significant improvements in anxiety, health related quality of life, self-efficacy, and supportive care needs were also achieved. The ASyMS is being investigated further, as its subtypes have been developed for use in palliative care [31] and teenagers with cancer [32]. One application (Consilium), included in this review, is also being investigated further in patients undergoing anti-PDL1 treatment [33]. However, despite positive feedback from patients, healthcare professionals reported that the application increased their workload without improving patient care [33].

Practical implementation of ePROs into routine cancer care can be challenging and therefore is still limited [34,35]. None of mobile applications reviewed in this article were adopted in standard care. The need for additional studies of healthcare professionals' perception and healthcare costs was acknowledged only in the Interaktor app clinical trial [17]. Possible logistic challenges, while integrating mobile applications into ePROs collection, need further investigation. Nevertheless, significant clinical outcomes discussed, most importantly improved patients' overall survival, observed in some studies on metastatic breast, lung, genitourinary and gynecologic cancers, have potential to outbalance expectable organizational issues.

The first open eHealth platform for oncology (CANKADO), that is meant to support standard care and research projects, is currently being investigated in locally advanced and metastatic breast cancer patients treated with targeted and endocrine therapy [36]. Primary outcome measure is QoL and secondary endpoints include progression-free survival, overall survival, drug intake and global health status. Preliminary results of this study demonstrated that CANKADO is well accepted and regularly used by patients. Moreover, possibly clinically relevant reduction in serious adverse events has been shown in the intervention group [37]. Another study, which utilized CANKADO for patients undergoing therapy for gastric, pancreatic, and colorectal cancers, demonstrated high acceptance of the app and improved patient participation in care. Additionally, regular assessment of psycho-social and

Table 3
Summary of main characteristics of identified research, including study aims, outcome measures and results.

Year/country	Study type	Sample size	Application name	Study aim	Outcome measuretools	Results
2020, Sweden [17]	Non-blinded RCT	149 intervention group (n = 74) control group (n = 75)	Interaktor	To evaluate whether the use of the interactive app Interaktor improves patients' levels of symptom burden and HRQoL during chemotherapy for breast cancer	EORTC-QLQ -C30 MSAS Individual Care Scale Sense of Coherence Scale Health Literacy Scale	In the intervention group: lower prevalence of nausea (p = .041), vomiting (p = .037), feeling sad (p = .003) two weeks after end of treatment; less overall symptom distress (p = .004); lower scores in the total MSAS physical symptom distress (p = .033) (effect size between 0.26 and 0.34)
2020, Sweden [19]	Mixed Method Study	74 intervention group from RCT [17]	Interaktor	To describe engagement with the Interaktor app	Semi-structured interviews	All patients reported with the app at least once during the study period. Median adherence was 83% (IQR 36%), 96% (71/74) of patients triggered at least one alert. Patients viewed a median of 11 (IQR 15) self-care advice topics at least once during the study period, out of 17 self-care advices available. 100% (74/74) viewed self-care advice at least once.
2020, Slovenia [12]	Nonrandomized Controlled Prospective Cohort Study	91 intervention group (n = 46) control group (n = 45)	mPRO Mamma	To evaluate whether use of an app for symptom management was associated with any change in patient quality of life or use of health resources	EORTC-QLQ C30 QLQ-BR23 Module PRO-CTCAE	10.1 (95% CI 1.8 to 18.5, p = .02) mean difference in favour of the intervention group in global quality of life after the first week Significantly higher summary scores in the intervention group: difference of 8.9 (95% CI 3.1 to 14.7, p = .003) after the first week and of 10.6 (95% CI 3.9 to 17.3, p = .002) at the end of treatment Improvements (indicated by EORTC C-30 or BR-23 scores) in social, physical, role, and cognitive function and reduction in pain, appetite loss, and systemic therapy side effects.
2020, Japan [14]	Single-centre RCT	102 intervention group (n = 52) control group (n = 50)	Breast Cancer Patient Support System (BPSS)	To examine whether the BPSS app is an effective tool for supporting patients undergoing chemotherapy	HADS CTCAE 14-item Health Literacy Scale (HLS-14)	No significant differences between before and after 4 courses of chemotherapy in the HADS score for anxiety, depression symptoms, and total scores (1.66 (95% CI 0.92 to 2.40, p = .08), 0.09 (95% CI −0.70 to 0.87, p = .35), and 1.74 (95% CI 0.39 to 3.09, p = .08) for the intervention group, respectively and 0.46 (95% CI −0.43 to 1.34, p = .08), −0.42 (95% CI −1.21 to 0.37, p = .35), and 0.04 (95% CI −1.44 to 1.52, p = .08), for the control group respectively). The medical staff underestimated the severity of 471 (25%) AEs, 51 (3%) of which were grade 3: 14 cases of fatigue, 7 cases of appetite loss, 7 cases of nausea, and 6 cases of muscle/joint pain. No significant differences in the HLS-14 scores for total health literacy from before to after 4 courses of chemotherapy 1.72 (95% CI 0.48 to 3.93, p = .82) in the intervention group vs 1.06 (95% CI 0.97 to 3.09, p = .82) in the control group), indicating that BPSS was not effective at improving health literacy.
2016, Switzerland [13]	Single centre, prospective, three-arm RCT	139 unsupervised intervention group (n = 46) supervised intervention group (n = 49) control group (n = 44)	Consilium	To evaluate the effects of a mobile app on patient-reported daily functional activity in a supervised and unsupervised setting	CTCAE ECOG PS	No significant difference in ECOG score between the first (median 90.85, IQR 30.67) and the third visit (median 84.76, IQR 18.29, p = .72) in the supervised group Numerically more distinct adverse events reported in the app than indicated in the CTCAE questionnaire at the standard care visit (supervised: n = 1033 vs n = 656; unsupervised: n = 852 vs n = 823), in both intervention groups; higher overall number of symptoms in the app reported by the unsupervised group (n = 4808) than the supervised group (n = 4463).
2021, Turkey [15]	Single-centre RCT with two parallel groups	57 intervention group	Msemptom		EORTC-QLQ C30 QLQ-BR23 Module	No statistically significant difference in total MSAS (p = .138), GDI (p = .761), and psychological subdimensions (p = .075)

(*continued on next page*)

Table 3 (*continued*)

Year/country	Study type	Sample size	Application name	Study aim	Outcome measuretools	Results
		(n = 28) control group (n = 29)		To determine the effect of the mobile application-based symptom monitoring process on symptom control and quality of life in breast cancer patients	MSAS ECOG PS GDI	between the intervention and control groups, improvement in the physical sub-dimension (p = .028) in the intervention group. Improvement in EORTC QLQ-C30 subdimensions of functional scale, physical function, social function, symptom scale, weakness (all p < .001); general health score, nausea-vomiting, pain and financial difficulty (all p = .001); loss of appetite, diarrhoea (both p = .003), and constipation (p = .021) in the intervention group.
2018, China [18]	Multicentre, single-blinded RCT	114 intervention group (n = 57) control group (n = 57)	Mobile Breast Cancer e-Support Program (BCS)	To determine the effectiveness of an app-based breast cancer e-support program to address women's self-efficacy (primary outcome), social support, symptom distress, quality of life, anxiety, and depression To explore the association between the breast cancer e-support usage data and women's health outcomes	SICPA MSPSS MD Anderson Symptom Inventory FACT-B HADS	Significantly better health outcomes at 3 months regarding self-efficacy (+21.05; 95% CI 1.87 to 40.22; p = .03; d = 0.53), symptom interference (−0.73; 95% CI − 1.35 to − 0.11; p = .02; d = 0.51), and quality of life (+6.64; 95% CI 0.77 to 12.50; p = .03, d = 0.46) in the intervention group; not sustained at 6 months follow-up. No difference in social support, symptom severity, anxiety and depression between intervention and control groups. Positive correlation of Cancer e-Support Program usage duration with self-efficacy (r = 0.290, p = .03), social support (r = 0.320, p = .02), and quality of life (r = 0.273, p = .04) at 3 months.
2020, China [21]	Secondary data analysis of the multicentre, single-blinded, RCT [18]	Intervention group from RCT [18]	Mobile Breast Cancer e-Support Program	To examine the usage data of the mobile Breast Cancer e-Support Program	N/A	The total usage duration per participant ranged from 0 to 9371 min (mean 1072.33), and the login frequency per participant ranged from 0 to 774 times (mean 54.7). The most popular were the Discussion Forum and Learning Forum of Breast Cancer e-Support Program. Breast Cancer e-Support Program usage duration and/or login frequency were associated with age, education, family monthly income and employment.

AE – Adverse Event, CTCAE – Common Terminology Criteria for Adverse Events, d – average deviation, ECOG PS – Eastern Cooperative Oncology Group Performance Status, EORTC-QLQ – European Organization for Research and Treatment of Cancer-Quality of Life, FACT-B – Functional Assessment of Cancer Treatment-B, GDI – Global Distress Index, HADS – Hospital Anxiety and Depression Scale, HLS-14 – 14-item Health Literacy Scale, HRQoL – Health-related Quality of Life, IQR – Interquartile Range, MSAS – Memorial Symptom Assessment Scale, MSPSS – Multidimensional Scale of Perceived Social Support , p – probability value, PRO-CTCAE – Patient-reported Outcome Common Terminology Criteria for Adverse Events, r – correlation coefficient, RCT – Randomized Controlled Trial, SICPA – Stanford Inventory of Cancer Patient Adjustment

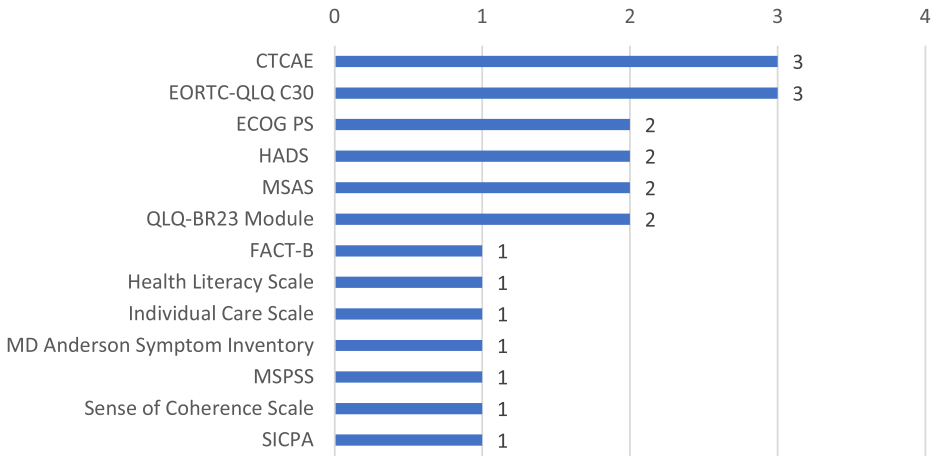

Fig. 3. Measurement tools used within reviewed articles.

nutritional aspects of care via the app was efficiently integrated in clinical routine [38].

The review possesses some limitations. The primary aim for this paper was to identify studies on mobile apps for monitoring chemotherapy-related side effects among patients treated for early-stage breast cancer, which comprise the majority of workload of breast cancer chemotherapy units. Therefore, population tested is likely to be homogenous in terms of age, comorbidities and overall performance status, which may limit the applicability of these results to the setting of more advanced disease, as in general early breast cancer patients tend to be younger and with better performance status. In addition, the perspective of being cured after completing their treatment does also lower the psychologic burden as compared, for example, to a metastatic setting.

Additional weakness is that according to methodology used we did not attempt to assess included studies for quality and possible risk of bias. The value of the conclusions drawn from our review may be also limited due to significant heterogeneity of the PRO tools used in particular studies.

Conclusions

Further work to refine optimal strategies for engaging not only patients, but also healthcare professionals in adopting digital technology to improve cancer care should be considered. Number of studies have demonstrated feasibility and benefits of using mobile applications to enhance symptom monitoring during cancer treatment, although some of the studies were possibly underpowered to detect some clinically meaningful differences. Only six applications dedicated to patients undergoing chemotherapy for early breast cancer were identified in this review. More research is needed to validate these resources, ensuring effectiveness and safety for their users.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

CRediT authorship contribution statement

Grażyna Suchodolska: Conceptualization, Methodology, Project administration, Investigation, Writing – original draft. **Elżbieta Senkus:** Investigation, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ctrv.2022.102364.

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Supplementary Table 1. Summary of reasons for exclusion in each clinical trial before randomization.

Reasons for exclusion before randomization	Consilium	Msemptom	mPRO Mamma	Breast Cancer Patient Support System	Mobile Breast Cancer e-Support Program	Interaktor	All
Untraceable contact	0	0	0	18	0	7	25
Inappropriate or no smartphone available	0	0	26	0	0	0	26
Unmet inclusion criteria	0	12	0	39	0	0	51
No internet access at home	0	0	0	0	18	0	18
Illiteracy	0	0	0	0	10	0	10
Depression	0	0	0	0	4	0	4
Refusal to participate	3	4	10	11	17	47	92
All	3	16	36	68	49	54	

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Article

Are All Societies Ready for Digital Tools? Feasibility Study on the Use of Mobile Application in Polish Early Breast Cancer Patients Treated with Perioperative Chemotherapy

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Abstract: Background: The population of individuals affected by breast cancer is growing, and with advances in cancer treatment implemented into usual care, there is an urgent need to improve the recognition, monitoring and treatment of therapy-induced adverse effects. This study aims to explore the use of an in-app electronic questionnaire to assess and monitor chemotherapy-related symptoms in early breast cancer patients treated with perioperative chemotherapy. Method: Between December 2019 and June 2021, 72 female study participants used the mobile app *Centrum Chorób Piersi UCK* and completed an in-app questionnaire about the 14 most common chemotherapy-related symptoms. Replies including symptoms with a critical value triggered automatic email alerts to the nursing team. Results: Acceptance of the study was higher among younger women and patients originating from rural areas, while possible digital exclusion among patients >60 years was observed during the enrolment process. A total of 55 participants completed the electronic questionnaire at least once and generated 553 responses with 1808 specific problems reported. Fatigue (n = 428) was the most common problem, and fever (n = 5) the least reported problem. A total of 21 participants triggered alerts with responses containing symptoms with critical value assessment (n = 89). Significant negative correlation was observed between the number of responses and time from the first chemotherapy administration; however, the number of responses was not determined by any sociodemographic or medical factors. Significant positive correlations were identified between the number of communicated problems and participants' age. The usage of our electronic symptom assessment questionnaire decreased substantially after the period of active encouragement during the study enrolment. Conclusions: Not all societies are ready for innovative eHealth solutions. Patients' age should be carefully considered when app-based interventions are introduced to usual cancer care. Additional support is suggested for older patients to improve their awareness and participation in eHealth interventions. More research involving older participants is needed to explore and address their particular needs and perspectives on eHealth solutions.

Keywords: chemotherapy; early breast cancer; eHealth; mobile app; symptom management; symptom reporting; ePROM

Citation: Suchodolska, G.; Koelmer, A.; Puchowska, M.; Senkus, E. Are All Societies Ready for Digital Tools? Feasibility Study on the Use of Mobile Application in Polish Early Breast Cancer Patients Treated with Perioperative Chemotherapy. *Healthcare* **2023**, *11*, 2114. https://doi.org/10.3390/healthcare11142114

Academic Editor: Daniele Giansanti

Received: 27 May 2023
Revised: 12 July 2023
Accepted: 22 July 2023
Published: 24 July 2023

1. Introduction

Breast cancer is the most prevalent cancer diagnosis and the second most frequent cause of cancer-related deaths among Polish women. According to the Polish National Cancer Registry in 2020, 23.8% of primary cancer diagnoses in women were breast cancers. While the population of people diagnosed with breast cancer in Poland is growing [1]

and advances in cancer treatment are being implemented into usual care [2], there is an urgent need to improve the recognition, monitoring and treatment of therapy-induced adverse effects. Electronic patient reported outcome measures (ePROMs) such as mobile and web applications (apps) offer the opportunity to address particular unmet needs of cancer patients. They can be utilised for screening, diagnostic, therapeutic and educational purposes [3]. Various in-app questionnaires facilitate capturing patient-reported outcomes, such as symptom burden, physical function, mental status and quality of life [4–8]. Implementing electronic monitoring of treatment side effects into routine breast cancer care decreases the chemotherapy-induced symptom burden, and improves symptom management, self-efficacy and quality of life [8–13]. Moreover, several studies exploring mobile apps encouraging physical activity among breast cancer patients demonstrated improved quality of life and reduced fatigue and distress levels [14–16]. Additionally, the results of research testing eHealth solutions during the COVID-19 pandemic not only confirmed that remote monitoring and management of treatment-related symptoms reduce the symptom burden and improve the quality of life, but also limit unplanned healthcare utilisation, decreasing demand on healthcare systems and improve patients' symptom experience, including perception of the frequency, intensity, distress, and meaning of symptoms [6]. Furthermore, eHealth solutions have been identified as empowering, improving patients' involvement in the continuum of cancer care [17,18].

The primary objective of this study was to analyse the results of using an in-app electronic questionnaire to assess and monitor chemotherapy-related symptoms in patients treated for early-stage breast cancer.

2. Materials and Methods

2.1. Study Design and Participants

This study assessed the use of a mobile app used by Polish early breast cancer patients treated with perioperative chemotherapy. The study was conducted in the Breast Cancer Chemotherapy Day Unit of the University Clinical Centre (UCC) in Gdańsk, Poland, between December 2019 and June 2021. Approval from the Independent Bioethics Committee for Scientific Research at the Medical University of Gdańsk (NKBBN/642/2019, NKBBN/642-534/2020) was obtained before the study initiation.

Patients who met the following inclusion criteria were eligible for participation in this study: referral for perioperative chemotherapy for early-stage breast cancer (all types), possession of their own smart device, and an ability to navigate the device and download mobile applications independently; these patients completed a signed informed consent form. Patients with metastatic breast cancer and those treated for other types of cancers were excluded from the study.

Perioperative chemotherapy was categorised as neoadjuvant or adjuvant with further division into specific treatment regimens (Table 1). Anthracycline-taxane regimens included combinations of doxorubicin and cyclophosphamide with paclitaxel +/− carboplatin or monoclonal antibodies (trastuzumab, pertuzumab), whereas anthracycline or taxane-based chemotherapy consisted of doxorubicin or docetaxel combined with cyclophosphamide, or combinations of paclitaxel, carboplatin and monoclonal antibodies.

2.2. Measures

During the pre-treatment preparation process, participants were asked to download the free mobile app *Centrum Chorób Piersi UCK*, which contains an electronic questionnaire (ePROM) for monitoring chemotherapy-related adverse effects. Nursing staff collected medical data (cancer stage and phenotype, setting of chemotherapy (preoperative vs. postoperative), type of cytotoxic drugs used, number of cycles, coexisting medical conditions and use of granulocyte colony-stimulating factors) from patients' health records. Sociodemographic details (age, sex, place of residence, education, employment, economic and marital status) were self-reported by participants at the end of the patient satisfaction survey.

Table 1. Medical characteristics of study participants.

Breast cancer type:		
HER2+	21	29.2%
luminal A	12	16.6%
luminal B	19	26.4%
TNBC	20	27.8%
Breast cancer stage:		
IA	11	15.3%
IB	3	4.2%
IIA	27	37.5%
IIB	14	19.4%
IIIA	6	8.3%
IIIB	6	8.3%
IIIC	5	6.9%
Chemotherapy setting:		
neoadjuvant	53	74%
adjuvant	19	26%
Chemotherapy regimen:		
anthracycline + taxane-based:	58	80.6%
neoadjuvant:	48	66.7%
12xPXL>>4xAC	15	20.8%
12xPXL>>4xddAC	15	20.8%
12xPXL+carboplatin>>4xddAC	7	9.7%
4xddAC>>12xPXL + T	5	6.9%
4xAC>>12xPXL + T	6	8.3%
adjuvant:	10	13.9%
12xPXL>>4xAC	6	8.3%
12xPXL>>4xddAC	1	1.4%
4xAC>>12xPXL + T	1	1.4%
4xddAC>>12xPXL	1	1.4%
4xddAC>>12xPXL + T	1	1.4%
anthracycline- or taxane-based:	14	19.4%
neoadjuvant:	5	6.9%
12xPXL	1	1.4%
4xddAC	1	9.7%
12xPXL + carboplatin + T + P	3	4.2%
adjuvant:	9	12.5%
12xPXL + T	4	5.6%
4xTC	4	5.6%
12xPXL	1	1.4%
Number of chemotherapy administrations:		
16	56	77.8%
12	10	13.9%
7 *	1	1.4%
4	5	6.9%
Treatment with G-CSF:		
yes	33	46%
no	39	54%
Coexisting medical conditions:		
no	36	50%
yes:	36	50%
single condition	24	33.3%
multiple conditions	12	16.7%

* patient's decision to change treating hospital. AC—doxorubicin-cyclophosphamide, dd—dose dense, G-CSF—granulocyte colony stimulating factors, P—pertuzumab, PXL—paclitaxel, T—trastuzumab, TC—docetaxel-cyclophosphamide, TNBC—triple negative breast cancer.

Enrolled patients were instructed by the breast cancer nurse (BCN) to complete the questionnaire weekly and on occasions when they experienced distressing symptoms. To ensure participants' safety, it was emphasised that in the case of an emergency or sudden health deterioration, they must seek medical help through emergency services or an appointment with a physician or nurse, as appropriate. Similar information was displayed on the questionnaire's summary screen before submission.

The questionnaire consists of 14 questions about the most common chemotherapy-related adverse events (Supplementary Table S1). The symptom severity assessment scale used in the questionnaire is based on the Common Terminology Criteria for Adverse Events v.4 [19] with its own modifications. Participants defined relevant symptoms on a 5-point scale, where 0 meant no problem at all, 1—mild, 2—moderate, 3—severe and 4—debilitating problem. The application did not allow omitted questions or free-text responses. Reports generated in connection to patients' in-app activity were closely monitored by the BCN. Figure 1 demonstrates a simplified patient–breast care team communication process via the in-app questionnaire.

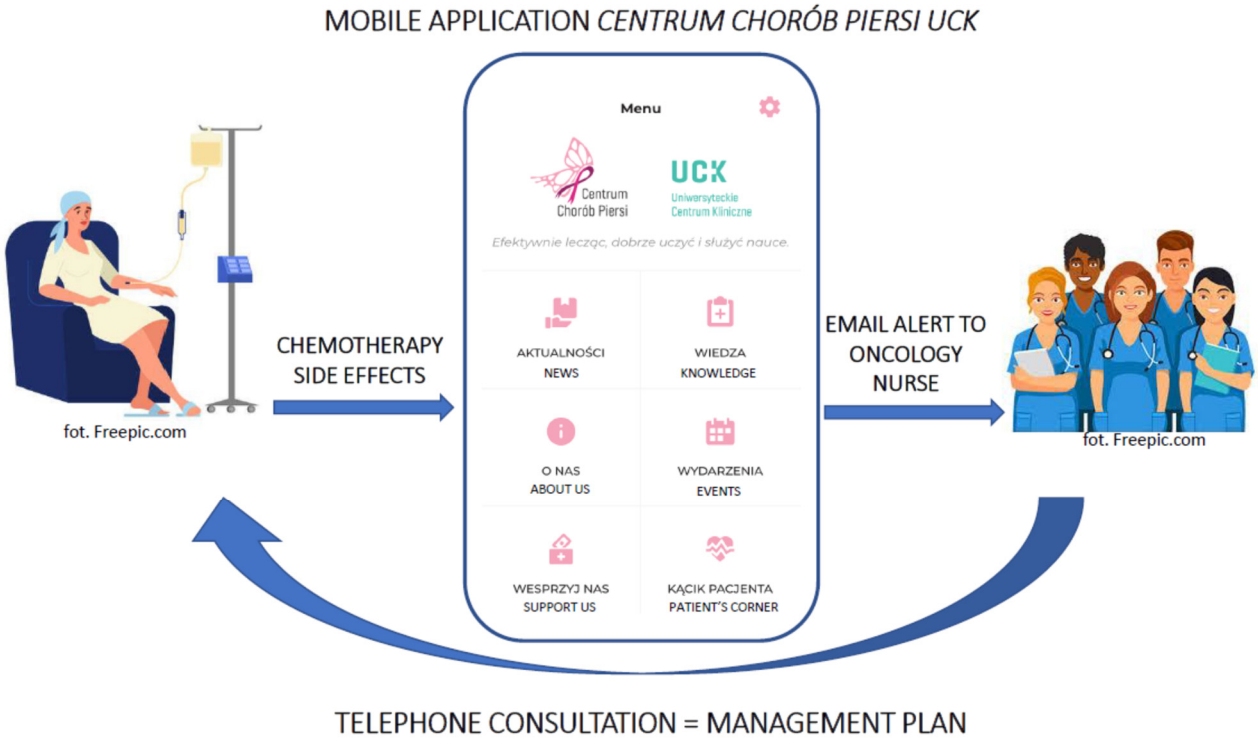

Figure 1. Patient–breast care team communication process via in-app questionnaire.

Replies including symptoms with critical value (≥3, apart from fever, which activated alerts when rated as 1 or above) triggered automatic email alerts to the nursing team. Participants were informed that after triggering an alert they will be contacted by the BCN within one working day during office hours. Nursing interventions performed in response to app alerts were recorded in patients' documentation. Every intervention began with a telephone consultation leading to further advice as necessary, and the types and outcomes of the recommended interventions were analysed. Additionally, to evaluate patients' opinions on the application, including the electronic questionnaire, participants were asked to complete a paper survey (Appendix A) after finishing the last chemotherapy cycle or after the physician's decision to terminate the treatment. The proprietary survey consisted of 10 questions relating to: the difficulty level of using the in-app questionnaire, safety during treatment, satisfaction from received care, sense of control, well-being during treatment, hospital admissions and free text option for additional participant suggestions.

2.3. Data Analysis

Data were managed with Microsoft Excel software and statistical analyses were performed with free RStudio software, version 4.2.2 (R Core Team, 2021) under the terms of the General Public License. Medians were used to report the central tendency, as the data were not normally distributed. Nonparametric statistical methods were used to analyse the results of this study due to the small population and non-normally distributed outcome data. An α level of 0.05 was set for all tests. Correlations were assessed with the ρ-Spearman's correlation coefficient and its significance test. The Mann–Whitney U test was used to describe differences in continuous variables between two groups and the Kruskal–Wallis test for multiple (>2) groups. Post hoc Wilcoxon tests were performed to determine which groups were significantly different. For comparison between two categorical variables, Chi-square tests (for values > 5) and Exact Fisher's test (for values < 5) were used. Additionally, Wilcoxon Rank sum tests were performed to check differences between the median number of reported problems and two selected qualitative characteristics. Benjamini–Hochberg *p*-value correction for multiple comparisons was used for all performed tests.

3. Results

3.1. Enrolment

Between December 2019 and December 2020, 93 early-stage breast cancer patients were assessed for eligibility. A total of 20 women refused, and a single eligible man was excluded from the analysis by the research team, resulting in 72 women being included in the study.

Acceptance of the study was higher among younger women and patients originating from rural areas (Figure 2A,B). Although the reasons for refusal were not systematically collected, the most frequently observed explanations included difficulties with navigating through mobile apps, no access to a smartphone or limited ability to use it.

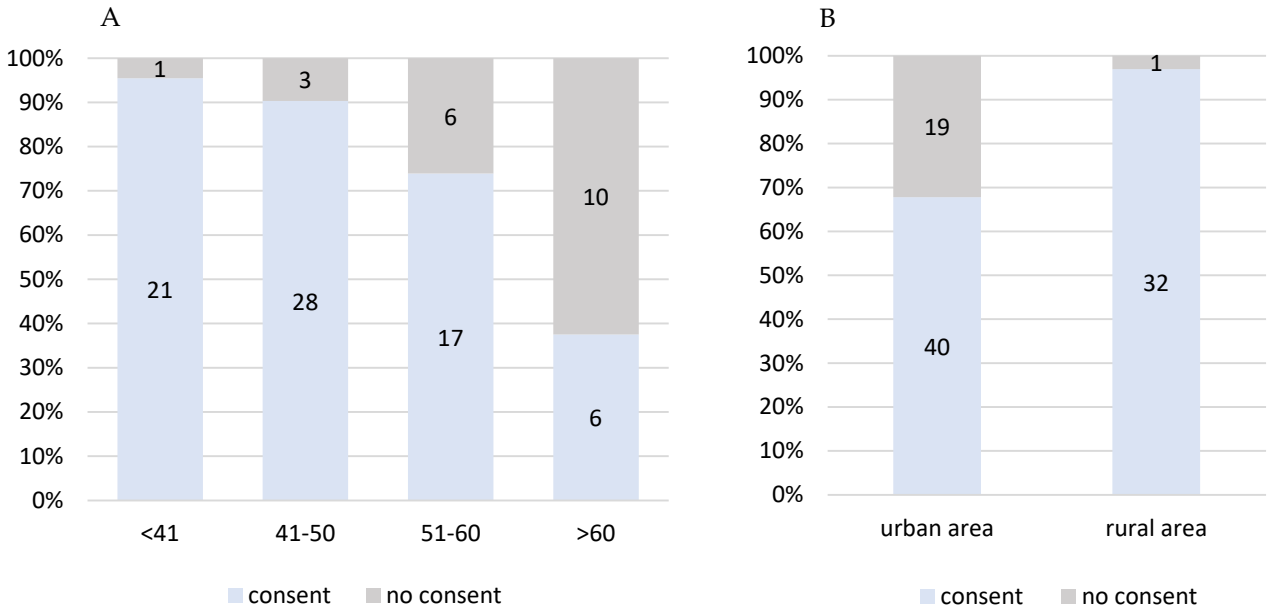

Figure 2. Study acceptance (**A**) in different age groups (p = 0.00006), (**B**) based on place of residence (p = 0.00114).

3.2. Participants' Characteristics

Medical and sociodemographic characteristics of study participants are presented in the following table (Table 2).

Table 2. Sociodemographic characteristics of study participants.

Age	**Median**	**Range**
	46	(34–70)
	Frequency (n)	Percentage (%)
Total	72	100%
Gender:		
female	72	100%
male	0	0%
Marital status:		
married	52	72.2%
single	12	16.7%
divorced	3	4.2%
in relationship	3	4.2%
widow	2	2.8%
Place of residence:		
city > 50,000	27	37.5%
city < 50,000	14	19.4%
rural area	31	43.1%
Education:		
higher	39	54.2%
secondary	17	23.6%
vocational	16	22.2%
Employment status:		
employed	63	87.5%
unemployed	5	6.9%
retired	4	5.6%
Economic status (self-assessed):		
satisfactory	58	80.6%
unsatisfactory	14	19.4%

Medical conditions reported by participants included: hypothyroidism (n = 20), hypertension (n = 7), asthma (n = 4), endometriosis (n = 3), obesity (n = 3), varicose veins (n = 3), coronary disease (n = 1), irritable bowel syndrome (n = 1), glaucoma (n = 1), nephrolithiasis (n = 1), epilepsy (n = 1) and rheumatoid arthritis (n = 1). Details of concomitant medication were not collected for the purpose of this study.

3.3. Participant Engagement with the App and Questionnaire

Data collection lasted from December 2019 to June 2021. During the study, 55 (76%) participants completed the electronic questionnaire at least once and of those 23 (42%)–10 or more times. Patients who used the electronic questionnaire and those who submitted no responses did not differ in terms of sociodemographic or medical characteristics (not reported). The number of responses generated by those who completed the questionnaire ranged from 1 to 68, median 7 (Figure 3).

Only 6 (11%) participants filled in the questionnaire as instructed by the BCN; others chose to complete it only when experiencing problematic side-effects. Overall, 553 responses were collected and some referred to more than one symptom, resulting in 1808 reported problems (Figure 4A). Fatigue (n = 428) was generally the most frequently reported problem, followed by the sensation of pins and needles in hands and feet (n = 226), pain (n = 208) and dizziness (n = 196). The least common problems reported included vomiting (n = 6) and fever (n = 5). 1329 (73.5%) symptoms were mild, 392 (21.7%)—moderate, 80 (4.4%)—severe and 7 (0.4%)—debilitating.

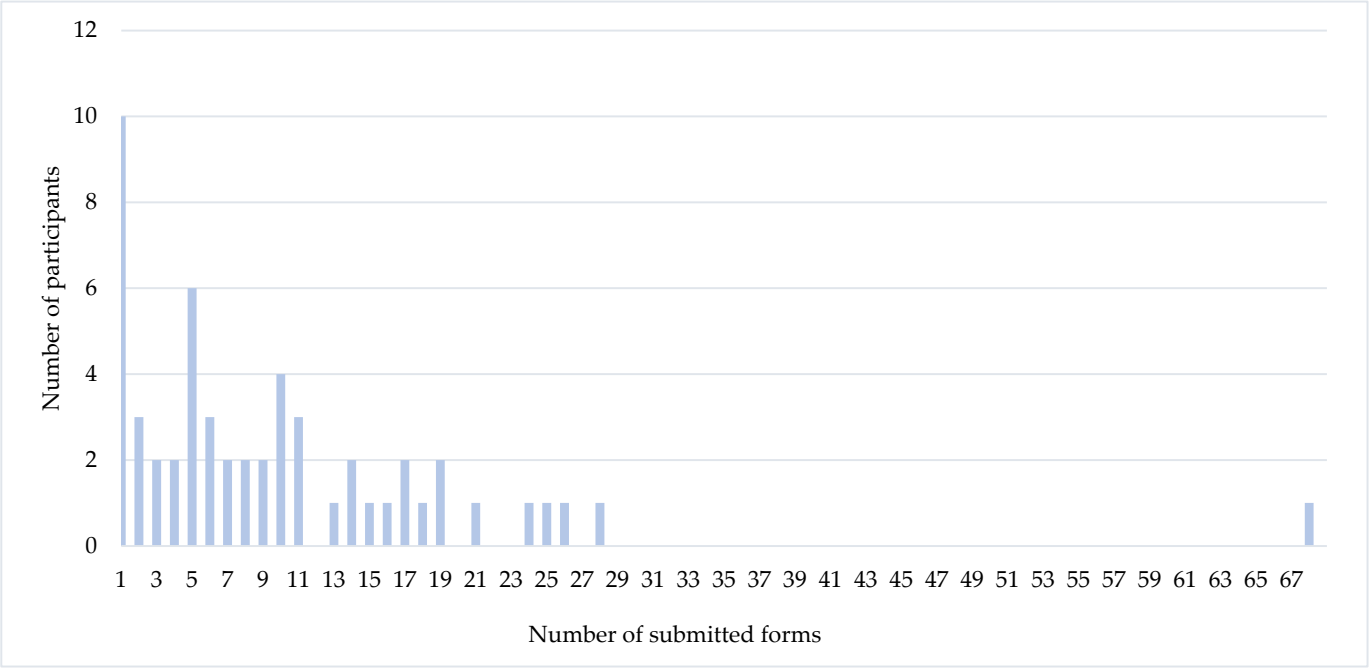

Figure 3. Responses generated during the study.

A total of 21 (29%) participants triggered alerts with responses containing symptoms with critical value assessment. Overall, 58 responses with values over the predefined critical threshold were collected, of which 21 (36%) referred to more than one symptom with a critical value (Figure 4B). Altogether, there were no statistically significant differences in sociodemographic or medical characteristics between patients who triggered alerts and the remaining participants.

Although there were no statistically significant differences in the number of generated responses in relation to sociodemographic details such as age, place of residence, education level, employment, economic or marital status, and medical factors including breast cancer stage, chemotherapy setting, chemotherapy regimen, number of treatment cycles, coexisting medical conditions or use of G-CSFs, a statistically significant negative correlation was observed between the number of responses and time from the first chemotherapy administration (Figure 5).

For the purposes of analysis of correlations identified between communicated problems and specific participant characteristics, problems were arranged into five categories: fatigue, dizziness, gastrointestinal problems (appetite loss, nausea, diarrhoea, constipation, oral mucositis, vomiting), respiratory problems (shortness of breath, cough) and others (pain, skin changes on hands and feet, sensation of pins and needles in hands and feet, fever). Detailed responses collected during the study and grouped accordingly are presented in Supplementary Table S2 and Figure 6.

The participants' age was found to be the only factor determining the number of reported problems. Statistically significant positive correlations observed between age and the number of reported specific problems are presented in Figure 6A–D.

Additionally, factors including employment status, marital status and stage of the breast cancer were initially found to be significant in the Kruskal–Wallis test; however, further analysis (Wilcoxon signed-rank tests) found these to be statistically insignificant ($p > 0.05$) (Supplementary Table S2). Separate sensitivity analyses (not reported) confirmed that results are not affected by the inclusion of a single male participant or the exclusion of participants who visibly exaggerated the number of reports (Figure 3).

All participants completed the patient satisfaction survey. The majority (89%) of respondents assessed using the in-app questionnaire for symptoms reported it to be very easy to use. Moreover, most of them believed that the possibility of reporting symptoms via

an electronic questionnaire not only improved their safety and well-being during treatment, but also made them feel in control of the situation in which they found themselves. Most participants felt satisfied with the support they received in response to the submitted forms. More than half of respondents thought that using the side-effects-reporting module improved the treatment of bothersome symptoms. According to the vast majority of participants, the overall care and support provided by medical staff met their expectations, with only a small percentage feeling that their expectations were not met. Ten participants expressed their suggestions of adding extra questions about nail problems (n = 4), cardiac complications (n = 1) and other unspecified unincluded symptoms (n = 5). Detailed responses to specific questions are presented in Table 3.

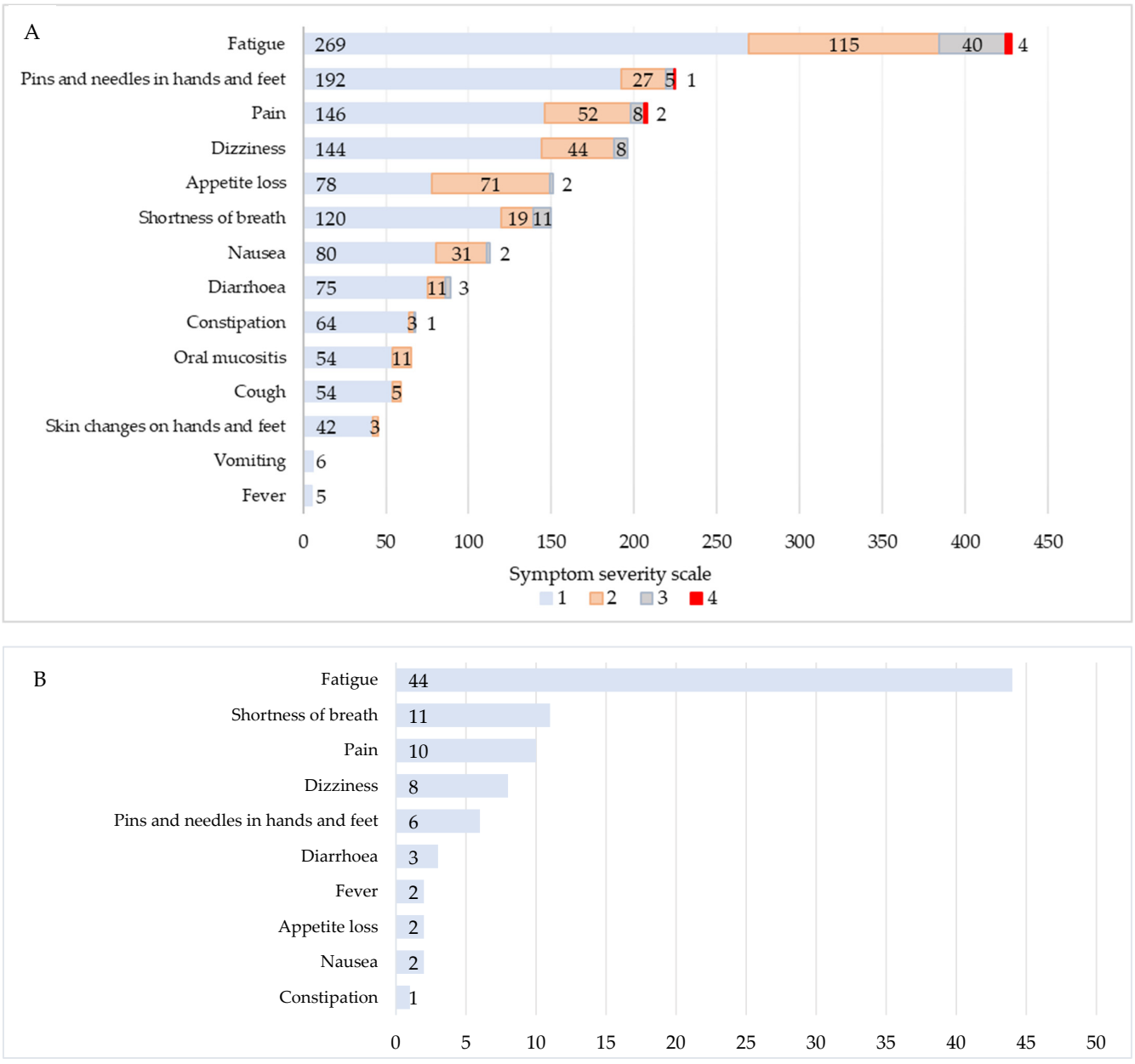

Figure 4. Summary of (**A**) specific symptoms reported during the study, (**B**) specific symptoms with critical value assessment.

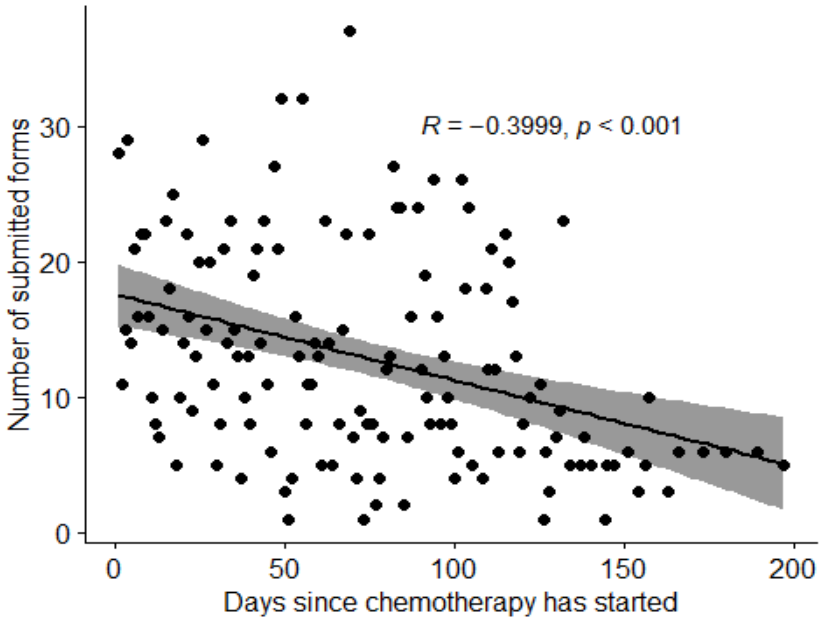

Figure 5. Distribution of responses collected during study period.

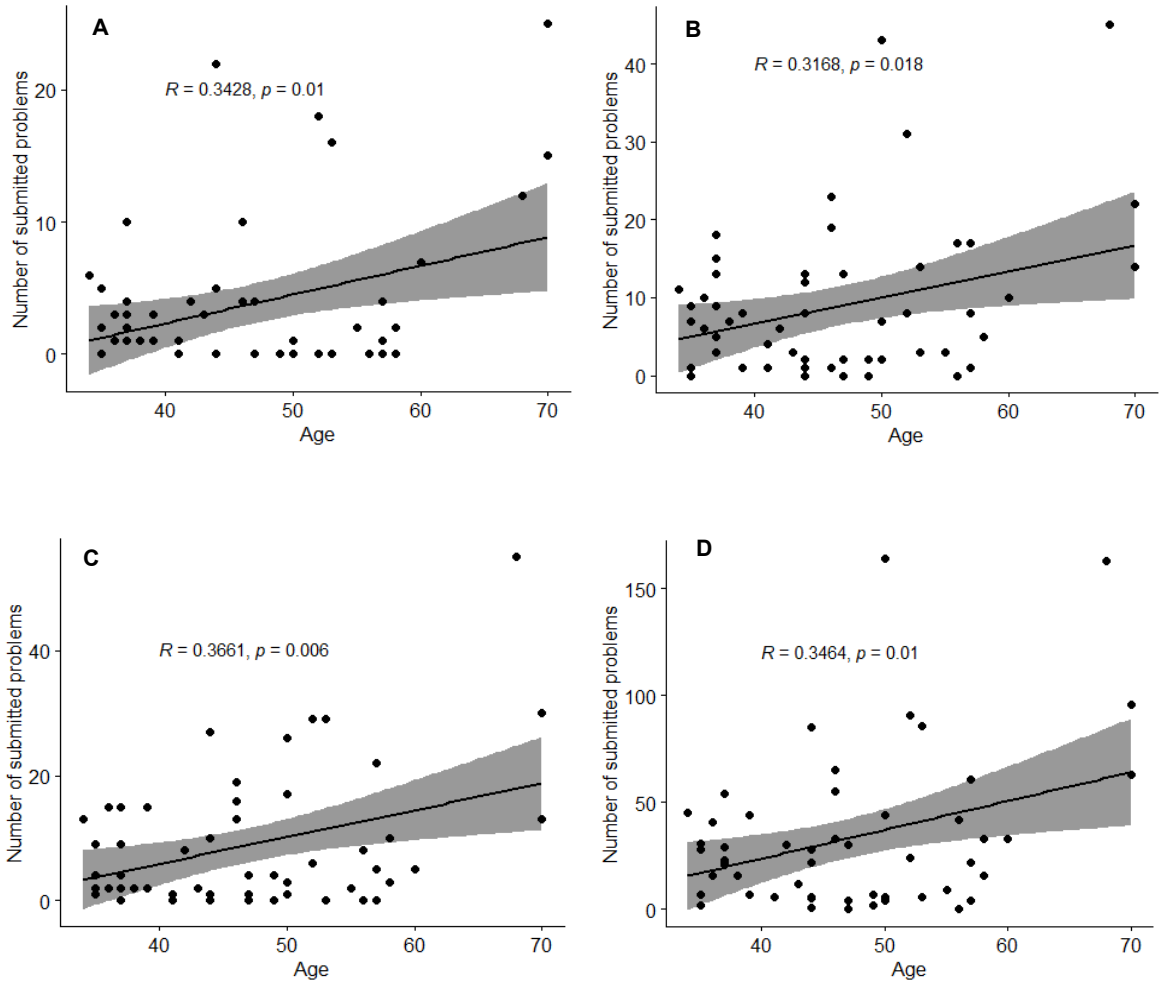

Figure 6. Correlations between age and (**A**) respiratory problems, (**B**) gastrointestinal problems, (**C**) other problems, (**D**) all problems reported.

Table 3. Detailed responses from patients' satisfaction survey.

1. In your opinion, how difficult it is to use the in-app side-effects-reporting module?					
Answer	**Very easy**	**Rather easy**	**Difficult to say**	**Rather difficult**	**Very difficult**
N	64	6	2	0	0
(%)	(89)	(8)	(3)		
2. In your opinion, did the possibility of using the in-app side-effects-reporting module improve your safety during chemotherapy?					
Answer	Definitely yes	Rather yes	Difficult to say	Rather no	Definitely no
N	44	26	2	0	0
(%)	(61)	(36)	(3)		
3. Are you satisfied with the support you received in response to submitted answers?					
Answer	Definitely yes	Rather yes	Difficult to say	Rather no	Definitely no
N	42	10	20	0	0
(%)	(58)	(14)	(28)		
4. Did you feel in control of the situation, when using the in-app side-effects-reporting module?					
Answer	Definitely yes	Rather yes	Difficult to say	Rather no	Definitely no
N	30	26	16	0	0
(%)	(42)	(36)	(22)		
5. In your opinion, did the possibility of using the in-app side effects-reporting-module improve your well-being during chemotherapy?					
Answer	Definitely yes	Rather yes	Difficult to say	Rather no	Definitely no
N	37	32	3	0	0
(%)	(51)	(45)	(4)		
6. In your opinion, did the use of the in-app side-effects-reporting module improve the treatment of bothersome side effects of chemotherapy?					
Answer	Definitely yes	Rather yes	Difficult to say	Rather no	Definitely no
N	22	23	26	1	0
(%)	(30)	(32)	(36)	(1)	
7. How do you assess the waiting time for the reaction of the medical staff in response to submitted answers about feeling unwell?					
Answer	Very short	Rather short	Difficult to say	Rather long	Very long
N	22	25	25	0	0
(%)	(30)	(35)	(35)		
8. Did the support provided to you by the medical staff meet your expectations?					
Answer	Definitely yes	Rather yes	Difficult to say	Rather no	Definitely no
N	56	11	3	2	0
(%)	(78)	(15)	(4)	(3)	
9. Did you require hospital admission due to exacerbation of chemotherapy-related side effects?					
Answer	Yes	No			
N	5	67			
(%)	(7)	(93)			
10. Is there anything that you would like to change in the in-app side-effects-reporting module?					
Answer	Yes	No			
N	10	62			
(%)	(14)	(86)			

3.4. Nursing Interventions

During the study, 58 nursing interventions (telephone consultations) were performed in response to app alerts generated by 21 participants. All interventions provided psychological support and reassurance combined with additional guidance as required. Topics covered during telephone consultations included: physical activity and sleep (74%), pain

management (24%), drug compliance (16%) and dietary needs (10%). A total of 64% of nursing interventions related to single problem reports and 36% to alerts about multiple problems; mostly consisting of combinations of severe fatigue, pain, shortness of breath and dizziness. Overall, five (7%) patients in 23 interventions were advised to use emergency care services due to severe dyspnoea (n = 10), dizziness (n = 8), diarrhoea (n = 3) and fever (n = 2); however, no hospital admissions were required. The number of follow-up contacts was flexible and tailored to the patient's needs; nevertheless, they were not analysed within this study.

3.5. Post-Study Observations

After the end of the study, we continued to provide new patients with information about the possibility of reporting chemotherapy-related symptoms via the mobile app. In the follow-up process of the study, mobile application reports were monitored for an additional year. Unexpectedly, the use of the mobile app for symptom reporting dropped substantially after the active study ended, resulting in only two patients using the in-app questionnaire to report treatment-related side effects over this period.

4. Discussion

High acceptance of digital tools in cancer care is widely recognised [3,7,9,20–22]. Nevertheless, there are still societies that prefer the traditional way of communication. Specialist breast cancer nurse-led interventions, mostly telephone consultations, tailored to patients' requirements are part of standard care for all breast cancer patients treated in UCC Gdańsk, where this study was conducted. Complex nursing interventions can significantly reduce the symptom burden [23,24], and symptom-focused education can enable patients to administer self-care more effectively [25,26]. With already well-established patient–nurse communication standards, the uptake of an additional tool to report treatment-related side effects by breast cancer patients was poor, especially after the period of active recruitment to the study. Moreover, possible digital exclusion among older (>60 yrs) patients was observed during the enrolment process, resulting in their lower interest in study participation (Figure 2), albeit the rationale for study refusal was not recorded. Similar digital inequalities between age groups were discussed in multiple studies involving participants with other diseases such as diabetes [27], irritable bowel syndrome [28], asthma and COPD [29], heart failure [30] and mental illnesses [31], and age was found to be a significant factor that influences the use of eHealth. However, although patients older than 60 years of age were generally less interested in participating in our study, once enrolled, they used the in-app questionnaire for symptoms reporting with comparable patterns of reporting, and overall, a pattern of reporting more problems than younger participants (Supplementary Table S2, Figure 6).

Adherence to the *Centrum Chorób Piersi UCK* app decreased with individual progress throughout chemotherapy (Figure 5). Similar observations were made in another study in early breast cancer patients [32], where the authors suggested that the reason for dropping engagement was an improvement in understanding the nature of particular side effects and the development of coping strategies; therefore, patients did not feel reporting symptoms to still be necessary. App adherence in cancer care has been explored in another study [20], where predictors of adherence were evaluated; similarly to our findings, no significant correlations were identified.

The prevalence of particular symptoms reported during our project is consistent with other studies. Fatigue is known to be the most frequent and distressing symptom for breast cancer patients [33–36]. In our study, fatigue accounted for the majority of overall problems reported, and triggers activating alerts to the BCNs. Dyspnoea was the second most common reason triggering alerts. Compared with another study testing a similar app solution [37], the average number of alerts per patient in our series was similar (2.8 vs. 2.7). However, in contrast to research led by Basch et al. [38], the proportion of individual symptoms triggering alerts in our study was higher (89/1808, 4.9% vs. 1431/84212, 1.7%),

while the type of triggers remained consistent, fatigue, dyspnoea and pain being the most common severe or debilitating problems. Multiple studies examined factors related to fatigue; however, results are ambiguous. Several reports [39–41], found no significant relationship between fatigue and age. Other studies [42,43] have observed younger patients experiencing higher levels of fatigue, which was also associated with working while in treatment. In contrast, the present study suggests that older patients are at a higher risk of experiencing cancer-related fatigue. The breast cancer stage and number of chemotherapy cycles were insignificant in our investigation, while other studies [36,44,45] indicate that patients with more advanced nonmetastatic breast cancer and those receiving more treatments are at higher risk of suffering from cancer-related fatigue. The number of responses and specific problems communicated during our study were not determined by education level, marital, employment or economic status. Nevertheless, another study [21] demonstrated that married and cohabitating participants generated more reports than those living alone. The same study evaluated patients' perceptions of using the app, and in line with the results of our study, demonstrate that the possibility of reporting treatment side effects in real-time created feelings of assurance and safety. Moreover, other research that explored the effect of eHealth apps on patient satisfaction during treatment confirmed that the use of mobile health apps could improve patient experience and overall health outcomes [22]. Recently published results of the PreCycle trial [46] present the successful utilisation of the interactive app (CANKADO), that works without any intervention by healthcare professionals to significantly delay the deterioration of quality of life among patients treated for metastatic breast cancer. The study reveals the next generation of ePRO monitoring and management, opening further discussion for patient empowerment and involvement in the continuum of cancer care.

Limitations of the Study

The present study has some limitations. Our project was performed in a single centre with a limited number of participants due to the COVID-19 pandemic. To explore participants' perception of the app, we used a proprietary survey, instead of a standardised tool; however, we achieved a 100% completion rate with overall positive feedback. Another potential drawback is that the study design did not involve automatic reminders for participants to complete the in-app questionnaire, resulting in low app adherence (e.g., only 6% of participants completed the questionnaire as instructed).

5. Conclusions

Although successful use of ePROMs for monitoring treatment-related adverse events has been described in many settings, the results of this study suggest a possible lack of trust and/or understanding of eHealth tools among Polish patients treated for early-stage breast cancer. Our findings suggest that patients older than 60 years of age find it difficult to engage with mobile technology and eHealth solutions. On the other hand, this is the population that, according to our research, is at a higher risk of experiencing not only cancer-related fatigue, but also other problems caused by the treatment. To improve patient engagement and understanding of eHealth solutions, it is essential that patients are invited to and involved in the fundamental stages of creating innovative app-based interventions. With age being a significant factor in determining the number of problems experienced during chemotherapy, we suggest that additional support be provided to older patients to enhance their awareness of the beneficiary potential of eHealth interventions. More research involving older participants is needed to explore and address their particular needs and perspectives on eHealth solutions.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/healthcare11142114/s1.

Author Contributions: Conceptualization, G.S. and E.S.; methodology, G.S. and E.S.; formal analysis, A.K., M.P. and G.S.; investigation, G.S. and E.S; data curation, G.S. and A.K.; writing—original draft preparation, G.S.; writing—review and editing, E.S., G.S., A.K. and M.P.; visualization, G.S.; supervision, E.S.; project administration, G.S. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board (or Ethics Committee) of the Medical University of Gdańsk (Project identification codes: NKBBN/642/2019 approved 3 December 2019, NKBBN/642-534/2020 approved 17 September 2020).

Informed Consent Statement: All subjects gave their informed consent for inclusion before they participated in the study.

Data Availability Statement: The data presented in this study are available on request from the corresponding author.

Conflicts of Interest: The authors declare no conflict of interest.

Appendix A. Patient's Satisfaction Survey

"Patient's Satisfaction Survey"				
1. In your opinion, how difficult it is to use the in-app side-effects-reporting module?				
Very easy	Rather easy	Difficult to say	Rather difficult	Very difficult
2. In your opinion, did the possibility of using the in-app side-effects-reporting module improve your safety during chemotherapy?				
Definitely yes	Rather yes	Difficult to say	Rather no	Definitely no
3. Are you satisfied with the support you received in response to submitted answers?				
Definitely yes	Rather yes	Difficult to say	Rather no	Definitely no
4. Did you feel in control of the situation, when using the in-app side-effects-reporting module?				
Definitely yes	Rather yes	Difficult to say	Rather no	Definitely no
5. In your opinion, did the possibility of using the in-app side-effects-reporting module improve your well-being during chemotherapy?				
Definitely yes	Rather yes	Difficult to say	Rather no	Definitely no
6. In your opinion, did the use of the in-app side-effects-reporting module improve the treatment of bothersome side effects of chemotherapy?				
Definitely yes	Rather yes	Difficult to say	Rather no	Definitely no
7. How do you assess the waiting time for the reaction of the medical staff in response to submitted answers about feeling unwell?				
Very short	Rather short	Difficult to say	Rather long	Very long
8. Did the support provided to you by the medical staff meet your expectations?				
Definitely yes	Rather yes	Difficult to say	Rather no	Definitely no
9. Did you require hospital admission due to exacerbation of chemotherapy-related side effects?				
no			yes	
10. Is there anything that you would like to change in the in-app side-effects-reporting module? Please write below:				
Age:	**Sex:**			
Place of residence:	city > 50.000 ☐	city < 50.000 ☐	rural area ☐	
Education:	primary ☐	vocational ☐	lower secondary ☐	secondary ☐ higher ☐
Marital status:	in relationship ☐	divorced ☐	widowed ☐	married ☐ single ☐
Employment status:	working ☐	unemployed ☐	retired ☐	student/pupil ☐
Economic status:	satisfactory ☐	unsatisfactory ☐		

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Table S1. Detailed symptom assessment scale

	0	1	2	3	4
Pain					
	I don't feel pain.	I feel mild pain, that doesn't affect my usual daily activities.	I feel moderate pain, that affects my usual daily activities, but I'm still able to cope.	I feel severe pain, that seriously affects my basic daily activities.	I feel completely exhausted by pain.
Fatigue					
	I don't feel fatigued, comparing to my usual state.	I feel mild fatigue, that is relieved by rest.	I feel moderate fatigue, that is not relieved by rest AND/OR is causing moderate problems with my usual daily activities.	I feel severe fatigue, that seriously affects my basic daily activities.	I feel completely exhausted. I can't cope.
Nausea					
	I don't feel nausea.	I lost appetite because of nausea but I'm able to eat as usual.	I eat and drink less than usual because of nausea, but my weight is stable and I'm not dehydrated or malnourished	I don't eat and drink enough OR I'm dehydrated or malnourished, OR nausea seriously affects my basic daily activities.	_____
Vomiting					
	I wasn't vomiting	I was vomiting, but less than 2 times per 24 hours	I was vomiting 3-5 times per 24 hours	I was vomiting more than 6 times per 24 hours OR I'm dehydrated and/or malnourished, OR vomiting seriously affects my basic daily activities.	I feel completely exhausted by vomiting.
Diarrhoea					
	I don't have more bowel movements than usual	I have 1-3 more bowel movements than usual	Every day, I have 4-6 more bowel movements than usual, but I'm not dehydrated and diarrhoea doesn't affect my basic daily activities.	I have more than 6 bowel movements per 24 hours OR diarrhoea seriously affects my basic daily activities.	I feel completely exhausted by diarrhoea.
Constipation					

	I don't have constipation.	I have occasional or intermittent constipation OR use stool softeners, laxatives, dietary modification or enema occasionally.	I have persistent constipation and use laxatives or enemas regularly.	Constipation seriously affects my basic daily activities OR manual evacuation of stool was necessary.	I feel completely exhausted by constipation.
Appetite loss					
	I don't have problems with my appetite or eating.	I lost appetite but I eat and drink as usual.	I eat less but my weight is stable and I'm not malnourished.	I eat or drink very little and I lose weight, AND/OR I'm malnourished.	I feel completely exhausted by malnutrition caused by appetite loss.
Oral mucositis					
	I don't have oral mucositis.	I have mild mucositis but it doesn't cause any discomfort and I'm able to eat as usual.	I have moderate mucositis, that is causing some discomfort but I'm able to eat soft diet.	I have severe mucositis, I'm not able to eat or drink.	I feel completely exhausted by mucositis
Pins and needles in hands and feet					
	I don't feel pins and needles in my hands and feet.	I feel mild pins and needles in my hands and feet, but it doesn't affect my daily activities like fastening buttons, feeling for small object or walking	I feel moderate pins and needles in my hands and feet OR pins and needles in hands and feet challenge my daily activities like fastening buttons, feeling for small object or walking	I feel severe pins and needles in my hands and feet OR I'm not able to do daily activities like fastening buttons, feeling for small object or walking, because of pins and needles in my hands and feet.	I spent most of the day in bed because of severe pins and needles in my hands and feet.
Cough					
	I don't have cough.	I have mild cough OR cough is relieved by over the counter medication, herbs or supplements.	I have persistent cough, that limits some daily activities OR I have to take prescription medication to relieve cough.	I have constant cough OR I have problems with basic daily activities like eating, washing, walking or sleeping.	————
Shortness of breath					
	I don't have shortness of breath.	I have mild shortness of breath with moderate exertion but I	I have moderate shortness of breath with mild exertion. I can't walk to the	I have severe shortness of breath even when resting OR it is very difficult for me to	I can't breathe. I'm not able to do anything.

		can still walk to the first floor or walk around the house without resting.	first floor or walk around the house without resting.	do daily activities like eating, washing, walking or sleeping, because of severe shortness of breath.	
Hand and foot syndrome					
	I don't observe erythema, peeling or blistering on my hands or feet.	I have erythema on my hands and feet but it doesn't affect my usual daily activities, working or walking.	I have peeling, bleeding, blistering or oedema of hands and feet, AND/OR I have difficulties with my usual daily activities, working, walking because of pain in my hands and feet.	I have serious difficulties with basic daily activities because of skin changes and pain.	_____
Fever					
	I don't have fever.	I have fever between 38.1-39^{0}C.	I have fever between 39.1-40^{0}C	I have 40^{0}C fever for less than 24 hours.	I have 40^{0}C fever for more than 24 hours.
Dizziness					
	I don't feel dizzy.	I feel mildly unstable, mildly off balance when walking.	I feel moderately unstable. It limits my usual daily activities.	I feel seriously unstable and dizzy. I'm not able to do daily activities independently.	_____

Table S2. Symptoms reported in relation to categorical sociodemographic and medical factors.

	Fatigue			Dizziness			Gastrointestinal problems			Respiratory problems			Other			All		
	n/mean	median	p	n/mean	median	p	n/mean	median	p	n/mean	median	p	n/mean	median	p	n/mean	median	p
Place of residence																		
Rural area	170/8	7	0.89	88/4	1	0.58	214/10	7.5	0.85	113/5	2	0.24	259/12	7.5	0.40	844/38	28.5	0.17
City < 50 000	47/6	5		13/2	1		43/5	5		15/2	0.5		33/4	3		151/19	19	
City > 50 000	211/8	5		95/4	1		235/9	7		81/3	1		191/8	4		813/32.5	22	
Education																		
Vocational	62/7	8	0.81	21/2	3	0.88	67/7	6	0.34	22/2	2	0.26	60/7	4	0.84	232/26	28	0.12
Secondary	80/7	4		42/4	1		91/8	2		39/3.5	0		111/10	2		363/33	7	
Higher	286/8	5		133/4	1		334/9.5	8		148/4	3		312/9	5		1213/35	28	
Employment status																		
Unemployed	32/16	16	0.22	4/2	2	0.80	18/9	9	0.51	26/13	13	0.04*	35/17.5	17.5	0.39	115/57.5	57.5	0.02*
Employed	295/7	5		149/3.5	1		343/8	5.5		110/3	1		320/8	3.5		1217/29	22	
Retired	101/9	5		43/4	1		131/12	10		73/7	4		128/12	4		476/43	30	
Marital status																		
Single	79/9	5	0.69	41/5	1	0.34	109/12	8	0.20	52/6	2	0.10	126/14	9	0.24	407/45	22	0.002*
In relationship	27/9	8		14/5	4		36/12	14		22/7	4		31/10	13		130/43	55	
Married	291/7	5		131/3	1		335/9	6		135/3	1		299/8	4		1191/30.5	23	
Divorced	18/6	1		3/1	1		5/2	0		0	0		10/3	0		36/12	2	
Widow	13/13	13		7/7	7		7/7	7		0	0		17/14	17		44/44	44	
Patient's economic status (self-assessed)																		
Unsatisfactory	100/10	9	0.27	47/5	2	0.40	102/10	6.5	0.75	46/5	2	0.48	127/13	6	0.40	422/42	28.5	0.12
Satisfactory	328/7	5		149/3	1		390/9	7		163/4	1		356/8	4		1386/31	22	
Breast cancer stage																		

I	102/8.5	3	0.40	55/5	1	0.62	88/7	4	0.40	10/1	0	0.08	76/6	2.5	0.60	331/28	14	0.03*
II	196/7	5		88/3	2		250/9	7		130/4	3		246/8	4		910/31	28	
III	130/9	8		53/4	1		154/11	7.5		69/5	2		161/11.5	6.5		567/40.5	29.5	
Coexisting medical conditions																		
No	189/9	5	1	83/4	1	0.40	150/7	5	0.11	70/3	1	0.51	162/8	2	0.50	654/31	16	0.13
Yes	239/7	5		113/3	1.5		342/10	8		139/4	2		321/9	5		1154/34	26	
Chemotherapy setting																		
Adjuvant	95/6	3	0.55	41/3	2	0.85	103/7	5	0.34	61/4	1	0.50	125/8	3	0.96	425/28	16	0.40
Neoadjuvant	333/8	5		155/4	1		389/10	7		148/4	1.5		358/9	4		1383/35	28	
Number of chemotherapy administrations																		
4	22/4	2	0.59	16/3	1	0.76	24/5	3	0.63	18/4	0	0.87	34/7	1	0.72	114/23	6	0.35
6	4/4	4		3/3	3		6/6	6		1/1	1		2/2	2		16/16	16	
12	36/9	5		5/1	0.5		22/5.5	4.5		23/6	0.5		37/9	4		123/31	15.5	
16	366/8	6		172/4	1		440/10	7		167/4	2		410/9	5		1555/35	28	
Treatment with G-CSF																		
No	234/8	6	0.41	91/3	1	0.82	246/8	6	0.40	123/4	1	0.76	283/10	5	0.73	977/34	24	0.97
Yes	194/7	5		105/4	1		246/9	7.5		86/3	1.5		200/8	3.5		831/32	22.5	
Chemotherapy regimen																		
Taxane or anthracycline	58/6	3	0.49	24/3	1	0.83	51/6	5	0.37	42/5	1	0.65	71/8	2	0.61	246/27	16	0.29
Taxane + anthracycline	370/8	5.5		172/4	1		441/10	7		167/4	1.5		412/9	4.5		1562/34	28	

* - values not confirmed by Wilcoxon signed-rank test; G-CSF- granulocyte colony stimulating factors

XI. STATEMENTS OF CO-AUTHORS

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Gdańsk, dnia 24 sierpnia 2023 roku

OŚWIADCZENIE

Jako współautor pracy pt. ***Are all societies ready for digital tools? Feasibility study on the use of mobile application in Polish early breast cancer patients treated with perioperative chemotherapy*** oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji to: przeprowadzenie wstępnych analiz statystycznych, zatwierdzenie ostatecznej wersji artykułu.

Jednocześnie wyrażam zgodę na przedłożenie w/w pracy przez Panią ***mgr Grażynę Suchodolską*** jako część rozprawy doktorskiej w formie spójnego tematycznie zbioru artykułów opublikowanych w czasopismach naukowych.

Oświadczam, iż samodzielna i możliwa do wyodrębnienia część ww. pracy wykazuje indywidualny wkład Pani ***mgr Grażyny Suchodolskiej*** przy opracowywaniu koncepcji, wykonywaniu części eksperymentalnej, opracowaniu i interpretacji wyników tej pracy.

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Gdańsk, dnia 24.08.2023

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OŚWIADCZENIE

Jako współautor pracy pt. ***Are all societies ready for digital tools? Feasibility study on the use of mobile application in Polish early breast cancer patients treated with perioperative chemotherapy*** oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji to: przeprowadzenie głównych analiz statystycznych, zatwierdzenie ostatecznej wersji artykułu.

Jednocześnie wyrażam zgodę na przedłożenie w/w pracy przez mgr *Grażynę Suchodolską* jako część rozprawy doktorskiej w formie spójnego tematycznie zbioru artykułów opublikowanych w czasopismach naukowych.

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