Design and evaluation of a digital health intervention with proactive follow-up by nurses to improve healthcare and outcomes for patients with breast cancer in Mexico: protocol for a randomised clinical trial

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ABSTRACT

Introduction Nearly 30 000 Mexican women develop breast cancer annually, frequently presenting unmet supportive care needs. In high-income countries, incorporating electronic patient-reported outcomes (ePROs) into cancer care has demonstrated potential for increasing patient-centred care and reducing unmet needs. No such ePRO interventions have been implemented in Mexico. This paper presents the study protocol for designing and evaluating an ePRO digital health application combined with proactive follow-up by nurses.

Methods and analysis We designed a two-component intervention for women receiving breast cancer treatment: a responsive web application for monitoring ePROs and clinical algorithms guiding proactive follow-up by nurses. We will conduct a pilot test of the intervention with 50 patients with breast cancer for 6 weeks to assess feasibility and adjust the application. We will conduct a parallel arm randomised controlled trial assigning 205 patients each to intervention and control in one of Mexico’s largest public oncology hospitals. The intervention will be provided for 6 months, with additional 3 months of post-intervention observation. The control group will receive usual healthcare and a list of breast cancer information sources. Women diagnosed with stages I, II or III breast cancer who initiate chemotherapy and/or radiotherapy will be invited to participate. The primary study outcome will be supportive care needs; secondary outcomes include global quality of life and breast symptoms. Information on the outcomes will be obtained through web-based self-administered questionnaires collected at baseline, 1, 3, 6 and 9 months.

Ethics and dissemination The National Research and Ethics Committees of the Mexican Institute of Social Security approved the study (R-2021-785-059). Participants will sign an informed consent form prior to their inclusion. Findings will be disseminated through a policy brief to the local authorities, a webinar for patients, publications in peer-reviewed journals and presentations at national and international conferences.

Trial registration number NCT05925257.

INTRODUCTION

Breast cancer is the leading cause of cancer morbidity and mortality in Mexico, with nearly 30 000 incident cases and 8000 deaths in 2020.1 Age-standardised mortality from breast cancer has doubled since 2000 and...
continues to increase annually. Patients with cancer who receive healthcare in public hospitals report multiple unmet supportive care needs and deficiencies in the quality of their care: over half report receiving incomplete information, preventing their participation in decision-making and 7 in 10 receive care they consider inadequate to address their physical and emotional needs. Unmet supportive care needs negatively affect patients’ quality of life and are associated with a higher probability of using emergency services and unscheduled hospitalisations.

Patient-centred care is intended to meet the needs, expectations and preferences of patients. To be patient-centred, healthcare providers must be aware of and proactively address patients needs as they arise; therefore, design and evaluation of care models should be informed by assessing patient-reported outcome (PRO) measures. However, previous studies have found that physicians frequently underestimate the severity of patients’ symptoms during cancer treatment, causing unnecessary patient suffering, excess use of emergency services and hospitalisations. Orienting cancer care delivery around PROs has the potential to better address patients’ needs and to reduce the use of emergency services and avoidable hospitalisations. making care more efficient in resource-constrained settings. In Mexico, research has demonstrated that those receiving patient-centred care report notably better health outcomes, but that the major health systems have not integrated PROs within clinical care. Locally validated models focused on PROs are currently lacking.

Digital health information and communication technologies have emerged as a flexible and scalable approach to increasing patient-centred care. When deployed correctly, digital interventions can reduce patient travel time, facilitate access to clinical information and remote monitoring, improve communication between patients and health personnel to detect and address the treatment side effects in a timely manner and promote active participation of patients in their self-care. Digital interventions for patients with cancer have included symptom monitoring, self-care support and digital communication with providers and other patients. In high-income countries, these interventions have demonstrated high patient acceptance and adherence, as well as positive effects on PROs including symptom management.

Research on the design and implementation of digital interventions in Mexico is limited and has not addressed cancer care. It is not yet known whether incorporating PROs within cancer treatment, using digital interventions to support PRO reporting and using clinical care guidelines to respond to patient-reported needs may be feasible and effective within public oncology services in Mexico.

The objectives of this paper are to describe: (1) the design of a two-component intervention for monitoring electronic patient-reported outcomes (ePROs) among patients with breast cancer using a responsive digital application and proactive follow-up by nurses, (2) intervention pilot testing and (3) an individual randomised clinical trial to assess usability and effectiveness of the intervention.

METHODS AND ANALYSIS

The study protocol development was guided by the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) reporting guideline and the SPIRIT-PRO extension. The study will include women between 20 and 75 years, who have been diagnosed with breast cancer, who have just started or will start neoadjuvant or adjuvant treatment with chemotherapy or radiotherapy within 4 weeks before or after enrolment; who have access to the internet in mobile phone, computer or tablet; and who provide written informed consent (see online supplemental material 1: Consent form). The study will exclude illiterate women and those, who at the time of enrolment, have stage IV breast cancer, blindness or low vision not corrected with glasses, cognitive disability (eg, Alzheimer’s disease, other dementias or other mental illness with intellectual disability) or severe depression (≥12 points on the Hospital Anxiety and Depression Scale).

Study population and eligibility criteria

The study will include women between 20 and 75 years, diagnosed with breast cancer, who have just started or will start neoadjuvant or adjuvant treatment with chemotherapy or radiotherapy within 4 weeks before or after enrolment; who have access to the internet in mobile phone, computer or tablet; and who provide written informed consent (see online supplemental material 1: Consent form). The study will exclude illiterate women and those, who at the time of enrolment, have stage IV breast cancer, blindness or low vision not corrected with glasses, cognitive disability (eg, Alzheimer’s disease, other dementias or other mental illness with intellectual disability) or severe depression (≥12 points on the Hospital Anxiety and Depression Scale).

Intervention design

We designed an ePRO application to capture patient supportive care needs and a clinical care model to proactively meet such needs. We were guided by the Patient Engagement Framework proposed by the National eHealth Collaborative of the USA and focused on informing, involving, empowering, accompanying and supporting patients with cancer through electronic applications. The intervention design also followed Jensen et al recommendations for successful monitoring of
patients with cancer’s ePROs and the ePRO monitoring workflow proposed by Basch et al. As shown in figure 1, we adapted this workflow to the resources and processes within IMSS oncology services.

Based on these recommendations, we defined our ePRO intervention as a weekly register of patients with breast cancer’s symptoms and supportive care needs combined with proactive follow-up by nurses guided by predefined clinical algorithms and a weekly cell-phone message providing an educational video from a recognised cancer association or health institution. The study ePRO application uses a responsive web application design emphasizing easy-to-use electronic records with a clear interface, clinically relevant health outcomes and automated communication, including reminders to patients to record data and alerts to health professionals regarding moderate-to-severe or worsening symptoms.

**Intervention development**

To develop the intervention content, the lead researcher (SECS) reviewed the available institutional and international evidence-based clinical guidelines for patients with breast cancer’s diagnosis and treatment and identified 20 common symptoms affecting breast cancer women during neoadjuvant and adjuvant chemo and radiotherapy and requiring supportive care from health professionals. These symptoms included (1) pain, (2) fatigue, (3) nausea and/or vomiting, (4) constipation, (5) diarrhoea, (6) anorexia, (7) dyspnoea, (8) insomnna, (9) oral mucositis, (10) pruritus, (11) acute radiodermatitis, (12) palmar-plantar erythrodysesthesia, (13) papulopustular rash, (14) lymphoedema, (15) proctitis, (16) peripheral neuropathy, (17) infusion phlebitis, (18) anxiety and depression, (19) changes in sexuality and other symptoms. After that, SECS proposed an initial set of questions for the weekly symptoms register (95 items grouped into 20 symptom-specific sections) and constructed 21 process-of-care algorithms for proactive follow-up of symptoms by nurses (1 general and 20 symptom-specific).

The study algorithms were developed based on the Dennystädt et al method for creating algorithms for clinical decision-making in oncology. This method consists of seven steps: definition of the environment, description of the existing evidence, definition of the decision strategy, selection of decision criteria, creation of the clinical algorithm, validation and optimisation.

Next, a group of experts validated the contents of the weekly symptoms record and study algorithms. This group included three medical oncologists, one radiation oncologist, two oncology nurses, one psychologist and one health services researcher, all with clinical and research experience in breast cancer treatment. The experts rated the relevance and clarity of the items in the weekly symptom reporting and each algorithm content using a Likert-type scale: (1) not relevant, (2) somewhat relevant, (3) relevant and (4) very relevant. In the case when specific content was rated as not relevant or somewhat relevant, the experts were asked to explain the reason for this negative rating and to provide suggestions for improvement. Two rounds of rating of the record and algorithm contents were conducted to obtain their final versions, for which agreement on validity was achieved (Content Validity Index (CVI) ≥ 0.70).
During the validation process, we made 31 changes to the weekly symptoms record (eg, questions rewording, or deletion, adding response options) and 91 changes to the algorithms (eg, reorganisation of processes, adding or modifying general recommendations). The final CVI for algorithm content ranged between 0.92 and 1.00, while the CVI in each symptom-specific section of the weekly record ranged from 0.82 to 1.00.

After the expert group’s validation of the study materials, we conducted two rounds of cognitive interviews, each with nine patients with breast cancer, to assess the clarity, comprehension and relevance of the content of weekly symptoms records perceived by women. The median age of women participating was 47 years in the first round and 46 years in the second round. Half of women had a post-secondary) education, while the remainder had secondary (27.8%) or primary school (22.2%). Based on the women’s feedback, seven images were added to the weekly record, including visual illustration of pain and fatigue severity using a 6-point smiley face scale and clinical pictures to illustrate symptoms such as acute radio-dermatitis (redness and swelling in the radiation therapy area). Ten terms were modified using simple wording or defining a specific term to achieve better clarity.

A professional web development service was hired to programme the responsive web application. The application was developed in HTML5 with CSS, Bootstrap, Java and PHP Style Sheets to receive and manage the collected data. It can be accessed from different electronic devices (eg, mobile phones, tablets, desktop computers) regardless of operating system (iOS, Android, Symbian, Windows Phone, etc), running through a URL that does not require downloading. The web application has interfaces for (1) intervention group, (2) control group, (3) study nurses and (4) research team (administrators). The intervention group interface includes a baseline record of socio-demographic and clinical characteristics, weekly reporting of symptoms and supportive care needs, questionnaires to assess study outcomes and access to videos on breast cancer-relevant topics on the websites of recognised cancer associations and health institutions. The control group interface includes only modules for baseline records of socio-demographic and clinical characteristics and the questionnaires to assess study outcomes. Online supplemental material 2 provides screenshots illustrating the ePRO application content.

The model of clinical care was designed to align with the ePRO application. Symptom reporting will be linked to automated alerts to the study nurses via WhatsApp/short messaging service (SMS)/email. Those who report mild symptoms or supportive care needs will receive automated messages via SMS/WhatsApp or email (based on the participant’s preference) with general recommendations on how to reduce the presented symptoms/needs. Those who report moderate or severe symptoms/needs will be contacted by phone by the study nurse, who will guide the participant based on the clinical algorithms. Examples of non-pharmacological recommendations provided by the study nurses are presented in table 1.

Two nurses will be available in the morning shift and one nurse in the evening shift to contact participants from 08:00 to 20:00, from Monday to Friday. Outside these hours, participants will receive only automated messages via SMS, WhatsApp or email (based on the participant preference) with general recommendations. All participants will be informed that if presenting severe symptoms outside these hours or not receiving a response from the study nurse within 30 min after symptom registration, they should go to the emergency room.

Study nurses will be supervised by the lead researcher and study oncologist; all breast cancer treatment decisions will continue to be handled by the IMSS oncologist following standard care procedures.

Training of the study nurses
Prior to the study fieldwork, the lead researcher (SECS) will provide a 1-week training to the three study nurses. In addition to the intervention content, the training will include information on study selection criteria, logistics of patient recruitment, informed consent procedures and retention strategies. Training will be based on a study manual finalised during intervention development.

Study outcomes
Primary and secondary outcome variables are presented in table 2.

Study covariates
Participant demographic and clinical characteristics include age, formal educational attainment (primary school or less and secondary school or higher), marital status, number of people who live in the patient’s home, number of people who provide caregiving to the patient, time since cancer diagnosis (in weeks), cancer stage (I, II or III) and type of treatment (chemo, or radiotherapy), local/regional recurrence, chronic diseases prior to cancer diagnosis (eg, diabetes, hypertension).

Pilot test procedures
We will conduct a pilot test of the intervention with 50 patients with breast cancer. We determined the required sample size in consideration of three planned analyses: usability of the ePRO application (primary outcome), preliminary effectiveness in reducing supportive care needs and trial feasibility in preparation for larger studies. Conservatively assuming 10% attrition, the 45 participants provide sufficient sample to yield a 95% CI of width 14% (margin of ±7) on the mHealth Application Usability Questionnaire (MAUQ) score and 90% probability that the CI width will be no larger than 14 in a future study. Based on prior studies among patients with breast cancer providing an average score of 45 (SD=29) on supportive care needs in the health system information domain (4.5), we will have 80% power to detect an improvement of at least 11 points (45 vs 34) between pre-test and post-test on a one-sided paired comparison with
Table 1 Examples of non-pharmacological recommendations

<table>
<thead>
<tr>
<th>Symptom/supportive care need</th>
<th>Non-pharmacological recommendations</th>
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<tbody>
<tr>
<td>Pain</td>
<td>Keep tracking your pain using a diary; do not self-medicate; use thermal compresses on the site of pain; practice relaxation techniques and improve sleep quality</td>
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<tr>
<td>Fatigue</td>
<td>Postpone non-essential activities; moderate activities that involve high energy use; use assistive devices to perform tiring activities</td>
</tr>
<tr>
<td>Nausea and/or vomiting</td>
<td>Practice relaxation techniques; avoid large meals and consumption of fatty, fried or very spicy foods; wear loose and comfortable clothing; avoid strong odours</td>
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<tr>
<td>Constipation</td>
<td>Consume foods high in fibre daily; increase liquid intake; avoid carbonated beverages and chewing gum; perform gentle abdominal massage</td>
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<tr>
<td>Diarrhoea</td>
<td>Drink at least one cup of fluid after each bowel movement; do not self-medicate; eat small portions of foods that are easy to digest; avoid eating dairy products, red meat and high-fat foods</td>
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<tr>
<td>Insomnia</td>
<td>Do not stay awake late; do not use a computer or other electronic devices before going to bed; avoid large meals and drinking coffee or alcohol before bedtime; practice relaxation techniques</td>
</tr>
<tr>
<td>Dyspnoea</td>
<td>Practice relaxation techniques; lie down with the upper body raised to a 45° angle by raising the bed or using pillows; use home air purifier; check your oxygenation with an oximeter</td>
</tr>
<tr>
<td>Oral mucositis</td>
<td>Do not use mouthwashes that contain alcohol; brush teeth gently or use a damp gauze pad or sponge mouth swab instead of a toothbrush; avoid acidic, fried, bitter, spicy, very salty, spicy or hot foods</td>
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<tr>
<td>Acute radiodermatitis</td>
<td>Wash the skin daily with lukewarm water and neutral soap without fragrance, without scratching; avoid excessive sun exposure; limit activities with sources that generate heat such as cooking, ironing, taking a hot bath or shower; do not use deodorants, perfumes, fragrances and powders</td>
</tr>
<tr>
<td>Lymphoedema</td>
<td>Keep the arm with lymphoedema higher than the heart whenever possible; do not sleep on the affected arm; avoid carrying weight greater than 2 kg; obtain massage performed by a trained specialist</td>
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<tr>
<td>Peripheral neuropathy</td>
<td>Avoid falls; verify daily the presence of injuries or scratches in the arms, hands, legs and feet; practice relaxation techniques</td>
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alpha set to 0.05 and within-person correlation of 0.5. Finally, the pilot study has a sufficient sample to detect study design problems with an expected prevalence of 6% or greater with 95% confidence. 

Participants will be enrolled within 2 weeks of initiating treatment, provided access and training on the ePRO application and followed for 6 weeks. Participants will also receive a voucher for 1-month prepaid data to support application use. In addition to weekly application use and symptom reporting, study measures will be assessed using questionnaires at baseline and after 4 weeks of follow-up. ePRO application use will be passively monitored for the remaining 2 weeks following the end of the prepaid internet support. Participants will continue receiving care from oncologists according to IMSS standards throughout the pilot and following the study close out. In addition, at the end of the pilot test, up to nine participants, each with incomplete and complete weekly ePRO records, will be contacted and invited to participate in semi-structured feedback interviews on their experiences and difficulties with the application and proactive care and suggestions for improvement. We will conduct structured debriefs with study nurses to identify potential changes in application of the clinical algorithms and other study procedures. At least six key stakeholders within IMSS will be contacted to explore acceptability and alignment of the intervention with organisational priorities.

We will conduct descriptive analysis of socio-demographic and clinical characteristics of initial participants and successfully retained participants compared with all patients with breast cancer within the hospital. We will describe ePRO application use and usability based on the 4-week MAUQ scores and will use paired t-tests to compare supportive care needs between baseline and 4-week assessments. We will refine the ePRO and the study procedures based on the pilot results.

Clinical trial
After finalising the pilot test and adjusting the study application, we will conduct an unblinded, parallel-arm, individual randomised controlled clinical trial. This phase 2 clinical trial focuses on exploring the effect of the intervention on outcomes presented in table 2.

Study groups
The intervention group will be given access to the ePRO application and proactive clinical care, including study
### Table 2  Study outcomes

<table>
<thead>
<tr>
<th>Variable</th>
<th>Measurement scale</th>
<th>Pilot test assessments timelines</th>
<th>Clinical trial timelines</th>
<th>Source</th>
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<tbody>
<tr>
<td><strong>Primary study outcome</strong></td>
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<tr>
<td>Supportive care needs</td>
<td>SCNS Short Form 34, previously validated in Mexico.5 This scale comprises 34 items and assesses 5 domains: (1) psychological needs, (2) health systems and information needs, (3) physical and daily living activities needs, (4) care needs and (5) needs related to sexuality. It uses a 5-point Likert scale to measure if a patient needs support and the extent of such need. Each domain score is standardised and ranges from 0 to 100, with a high score indicating a high need. The study’s primary outcome will focus on health systems and information supportive care needs domain.</td>
<td>Baseline, 4 weeks</td>
<td>Baseline, 1, 3, 6 and 9 months</td>
<td>Patient self-reported questionnaire</td>
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<tr>
<td><strong>Secondary study outcomes</strong></td>
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<tr>
<td>Global quality of life and breast symptoms</td>
<td>EORTC (European Organisation for Research and Treatment of Cancer) QLQ-C30.53  This questionnaire comprises 30 items, and it has been validated among Mexican patients with cancer54 and includes five functional scales (physical functioning, role emotional, cognitive and social), three symptom scales (fatigue, pain, nausea/vomiting), a global quality of life scale and six single items (shortness of breath, loss of appetite, insomnia, constipation, diarrhoea and economic difficulties). The complementary breast cancer questionnaire EORTC QLQ-BR2355 will also be used. This questionnaire comprises 23 items, and has been validated among Mexican patients with cancer.54 It includes five symptom scales (body image, sexual functioning, systemic therapy side effects, breast and arm symptoms) and six single items (sexual enjoyment, future perspective and upset by hair loss). For both questionnaires, linear transformation will be applied to standardise raw scores. The standardised scores range from 0 to 100 for each scale, with the higher scores representing a higher quality of life or higher intensity of symptoms.56 57 The study’s secondary outcome will focus on the global quality of life scale as measured by the EORTC QLQ-C30 and breast symptoms as measured by the EORTC QLQ-BR23.</td>
<td>Baseline, 4 weeks</td>
<td>Baseline, 1, 3, 6 and 9 months</td>
<td>Patient self-reported questionnaire</td>
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<tr>
<td>Other prespecified outcome measures</td>
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<td>Use of emergency services</td>
<td>Number of visits to the emergency room in the previous month.</td>
<td>Baseline, week 4</td>
<td>Baseline, 1, 3, 6 and 9 months</td>
<td>Patient self-reported questionnaire</td>
</tr>
<tr>
<td>Unscheduled hospitalisations</td>
<td>Number of unscheduled hospitalisations in the previous month.</td>
<td>Baseline, week 4</td>
<td>Baseline, 1, 3, 6 and 9 months</td>
<td>Patient self-reported questionnaire</td>
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</table>
nurses responding to ePROs and weekly health information videos for 6 months.

Control group participants will be provided with a list of electronic links to videos on breast cancer-relevant topics on the websites of recognised cancer associations and health institutions.

All participants will continue to receive the usual health-care provided by the hospital. The intervention will last 6 months with 3 months of additional passive follow-up to allow post-intervention monitoring.

**Randomisation**

The participants will be randomly allocated to the intervention or control groups using the minimisation technique with MS-DOS Minim program. Randomisation will be conducted by a research assistant who will use a pre-prepared list of random numbers to randomise the first six participants. Starting with the seventh participant, randomisation will be carried out using the MS-DOS Minim program. The minimisation technique is recommended as a standard to ensure that clinical trial groups are similar in terms of participant characteristics, such as age, schooling, breast cancer stage and treatment modality.

**Intervention implementation**

Each week, the lead researcher will obtain a list of patients with breast cancer who have started or will start neoadjuvant or adjuvant treatment with chemotherapy or radiotherapy within 2 weeks from the oncology hospital. Study nurses will use this list to invite all eligible patients with breast cancer to participate in the study. Patients will be invited by telephone to meet at the hospital or the research unit (located within the oncology hospital) to receive study-related information and to confirm eligibility. Those who meet the inclusion criteria will be provided with the option to participate and invited to provide informed consent prior to participation.

Participants will be provided with username, password and access to the intervention or control interface of the responsive ePRO application and training on its use. All participants will be asked to answer the baseline record of socio-demographic and clinical characteristics and questionnaires to assess study outcomes. Intervention arm participants will be asked to complete the weekly register, and will receive weekly reminders via WhatsApp messaging. Study nurses will contact patients without 2 weekly records to encourage adherence to the intervention.

Study nurses will be supported by the study oncologist/oncology resident to ensure adherence to the intervention activities. Additionally, the nurses will be in regular contact with the study team and will record their activities in the corresponding interface of the responsive ePRO application.

**Confidentiality**

Consent forms with participant signatures and handwritten information such as field notes or other related research materials will be stored in a locked location only accessible by the principal and leader researchers. All electronic data will be stored on password-protected computers. Data will be anonymised prior to the statistical analysis by the research team. Only de-identified data will be used for reporting, publication and dissemination of findings. Data will be erased and destroyed after 5 years, as per IMSS Ethics and Research Committee guidelines.

**Study hypothesis**

For primary study outcome

Compared with the control group, the intervention group at the 6-month follow-up:

a. Will show lower supportive care needs in the domain of health systems and information based on a 10-point difference in this dimension of supportive care needs

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**Table 2** Continued

<table>
<thead>
<tr>
<th>Variable</th>
<th>Measurement scale</th>
<th>Pilot test assessments timelines</th>
<th>Clinical trial timelines</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use of the responsive ePRO application in the intervention group</td>
<td>Frequency of the responsive ePRO application use (site visits by IP address) and completion of a weekly report of symptoms and supportive care needs on the responsive digital application.</td>
<td>Weeks 0–6</td>
<td>1, 3 and 6 months</td>
<td>IP address</td>
</tr>
<tr>
<td>Perceived usability of the responsive ePRO application in the intervention group</td>
<td>Perceived usability will be measured by mHealth Application Usability Questionnaire translated into Spanish with content validation completed by the study expert group. This questionnaire measures the ease of use, satisfaction, system information arrangement and usefulness of the digital application.</td>
<td>Week 4</td>
<td>1, 3 and 6 months</td>
<td>Patient self-reported questionnaire</td>
</tr>
</tbody>
</table>

ePRO, electronic patient-reported outcome; IP, Internet Protocol; QLQ, Quality of Life questionnaire; SCNS, Supportive Care Needs Survey.
measured with the Supportive Care Needs Survey (SCNS) Short Form.
For secondary study outcomes
b. Will report better quality of life based on at least a 10-point difference in the global quality of life scale as measured by the European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life questionnaire (QLQ)-C30.
c. Will report lower breast symptoms based on at least a 10-point difference in the breast symptoms scale as measured by the EORTC QLQ-BR23.
For other prespecified outcome measures
d. Will report 20% less frequent use of emergency services and unscheduled hospitalisations.

Sample size
We calculated sample size using Power Analysis & Sample Size (PASS) software based on primary analysis of unadjusted outcomes at the 6-month assessment comparing control and intervention groups using two-sample t-tests allowing for unequal variance, setting alpha to 0.05, power of 80% and a dropout rate of 20%; we conservatively assume SD will be larger in the control arm than found in prior studies. Table 3 presents the additional assumptions and the number of participants to include: to address all study objectives, the required sample size is 205 participants per group.

Data collection and monitoring
Five evaluations will be performed during the trial: baseline, 1, 3, 6 and 9 months. Main study outcome variables will be measured at each evaluation, while the covariates will be collected only at the beginning of the study and application use and usability will be collected throughout the 6 months of ePRO access. We will also document reasons for dropouts and poor adherence. The information on the study variables will be gathered through the corresponding modules of the responsive ePRO application. Data monitoring will be performed by SECS and SVD to inform aspects of trial recruitment and follow-up. There will be no external data monitoring committee due to the minimal risk designation of this study.

Statistical analysis
Data quality will be assessed before statistical analysis (eg, range checks for numerical values). For the primary analysis, we will examine the effects of the intervention on each outcome variable at 6 months using a two-sample t-test. Anyone measured at 3 but not 6 months will have values carried forward or imputed as an intention-to-treat sensitivity analysis. As an additional analysis, we will use generalised estimating equations with autoregressive correlation structure to estimate time-averaged difference in each continuous outcome over all time points, adjusting for baseline measures and clinically and conceptually important baseline characteristics. The sample size required for the primary analyses is powered at 80% with alpha 0.05 to detect effect sizes of 10 points or more in supportive care needs, symptom reporting and quality of life outcomes. The analysis will be performed using Stata V.14.0 statistical software and R package V.3.6.2.

ETHICS AND DISSEMINATION
The study was authorised by the National Research and Ethics Committees of the Mexican Institute of Social Security (R-2021-785-059). Potential participants will sign an informed consent form prior to joining the study. This form contains the information about study objectives, random assignment of participants to intervention or control groups, study content and duration, relevant ethical considerations (eg, voluntary participation, possible risks and benefits, data custody, security and confidentiality protections) and contact information.

<table>
<thead>
<tr>
<th>Table 3 Sample size</th>
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<tbody>
<tr>
<td><strong>Outcome</strong></td>
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<tr>
<td><strong>Primary study outcome</strong></td>
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<td>Global quality of life</td>
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<tr>
<td>Breast symptoms</td>
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<tr>
<td><strong>Other prespecified outcome measures</strong></td>
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<tr>
<td>Emergency services and unscheduled hospitalisations</td>
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of the principal investigator and IMSS Ethics Committee (online supplemental material 1).

The trial was registered at ClinicalTrials.gov. Based on the SPIRIT recommendations, any modifications to the protocol that may affect the conduct of the study or the potential benefit or risk of the study participants, such as changes of study objectives, study design, population, sample sizes or study procedures will be submitted as an IMSS IRB amendment to the protocol and modified accordingly on ClinicalTrials.gov. The pilot study began on 15 August 2023; the anticipated start date for the trial is 15 January 2024, with expected completion by the end of 2024. Study findings will be disseminated through publications in peer-reviewed journals, presentations in national and international conferences, a policy-brief to the local authorities and a webinar to patients with breast cancer and health professionals.

DISCUSSION

In Mexico, a substantial unmet need exists to improve health services and outcomes for women with breast cancer. Patient-centred ePRO digital interventions have been proven useful for breast cancer care quality improvement in other settings, but have not been tested in Mexico. The Mexican population is well equipped to adopt digital interventions: there are 86.5 million cell phone users in the country, and 79.9% of the population live in urban areas and use the internet, predominantly via smartphone. Moreover, the Mexican government has recognised the importance of implementing eHealth strategies to achieve ‘universal and effective health coverage’ in the country. The experience of the COVID-19 pandemic has increased familiarity with telemedicine among patients and providers, showing the benefits of digital approaches, and heightened interest among health system policymakers in validated, scalable models of digital, patient-centred care. Despite that, public health services for patients with cancer in Mexico lack modern and innovative options for remote monitoring and control of cancer symptoms, treatment side effects and supportive care needs. Thus, it is imperative to identify feasible and effective digital health interventions to improve cancer care in Mexico.

The proposed intervention has several strengths. We conducted a comprehensive development and validation process drawing on expert input to ensure the intervention content is complete and accurate and on patient perspectives to confirm clarity and relevance. The final content demonstrated high validity. The intervention design is structured around accessibility from the patient’s perspective, relying on a visually attractive web application that can be used on any device regardless of browser or operating system. The pilot test will provide evidence of the preliminary usability of the web-based ePRO application and generate patient and provider perspectives on necessary adjustments to the intervention or study procedures in preparation for the clinical trial. The intervention focuses on early chemotherapy and radiotherapy, representing a critical window in which patients face the most important supportive care needs.

Several limitations can be noted. First, participation is limited to those capable of interacting with the application, excluding those without access to an internet-capable device as well as illiterate patients, those with limited visual acuity and those with cognitive disability or pre-existing severe depression. Uncontrolled severe depression is characterised by persistent apathy, sadness, poor concentration and loss of interest in activities, symptoms that make it difficult to engage with study activities; women with prior diagnosis of depression receiving effective treatment (reporting Hospital Anxiety and Depression Scale <12) are eligible for participation. This prevents generalising to all patients with breast cancer in Mexico; we will report on the demographic composition of study participants compared with all IMSS patients with breast cancer. Second, the intervention does not include patients with stage IV breast cancer. Although these patients have numerous symptoms and unmet supportive care needs, they will not be included due to the more complex care needs and a limited possibility of improvement of their quality of life. Third, the limited working hours of study nurses (08:00 to 20:00) could affect the use of the ePRO application by patients and, therefore, the effectiveness of this intervention; however, 24-hour support would not be feasible for scale up within IMSS clinical care, so understanding effectiveness with this model will be more relevant to further implementation. Third, study participation and completion of assessment tools require time from women undergoing cancer treatment, who may find it difficult to participate, particularly if no benefit is perceived. Finally, the intervention procedures and evaluation will be conducted separately from routine clinical care; if demonstrated to be effective, considerations of cost and implementation feasibility would need to be addressed within IMSS.

Study materials (e.g., content of the ePRO application, clinical algorithms for nurses) are expected to guide the implementations of similar multifaceted ePRO interventions at oncology services of public health institutions in Mexico and other Latin American countries to provide remote monitoring and control of adverse symptoms and supportive care needs of patients with breast cancer, particularly for large oncology hospitals with patient populations similar to the study setting; further local adaptations may be required.

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Provenance and peer review Not commissioned; externally peer reviewed.

Patient consent for publication Not applicable.

Competing interests None declared.

Patient and public involvement Patients and/or the public were involved in the design, conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

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REFERENCES
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Supplemental material 1: Clinical trial informed consent form (Spanish version)

Instituto Mexicano del Seguro Social

Coordinación de Investigación en Salud
Unidad de Investigación Epidemiológica y en Servicios de Salud CMN Siglo XXI

CARTA DE CONSENTIMIENTO INFORMADO

Proyecto: “Diseño y evaluación de la efectividad de una intervención de salud digital para mejorar la atención y resultados en salud de pacientes con cáncer.”

Ciudad de México a ___ de ______________ 202_

Por medio de esta carta, la invitamos a participar en el estudio titulado “Diseño y evaluación de la efectividad de una intervención de salud digital para mejorar la atención y resultados en salud de pacientes con cáncer” que tiene el número de registro del Comité Nacional de Investigación R- 2021-785-059.

Justificación y objetivo del estudio: El motivo de esta investigación es conocer los beneficios que tiene una estrategia de salud digital enfocada en proporcionar información y monitoreo remoto de los síntomas de cáncer, de los efectos adversos del tratamiento (que son complicaciones inesperadas que se pueden presentar durante el tratamiento con un medicamento o terapia, como quimioterapia, o radioterapia, o cirugía) y de las necesidades de apoyo, generando alertas en tiempo real y seguimiento proactivo de las pacientes con cáncer de mama por las enfermeras.

Los estudios previos han encontrado que la mayoría de los pacientes con cáncer que reciben atención en hospitales públicos en México reportan múltiples síntomas de cáncer, efectos adversos de medicamentos, necesidades de apoyo no satisfechas y perciben deficiencias en la calidad de su atención. En países de altos ingresos se ha encontrado que el monitoreo remoto de los síntomas de cáncer, de los efectos adversos del tratamiento y de las necesidades de los pacientes mediante las aplicaciones en teléfonos móviles, o sitios específicos en internet permiten generar alertas en tiempo real que llegan al personal de salud y permiten que las enfermeras realicen seguimiento proactivo para disminuir los síntomas y las necesidades de apoyo de los pacientes con cáncer; sin embargo, este tipo de atención no ha sido implementada y evaluada en México.

Participación o retiro: La participación en el estudio es completamente voluntaria. Puede aceptar participar en el estudio ahora y cambiar de opinión más adelante. Si desea cambiar su opinión y no participar en este estudio, independientemente del motivo, infórmenos por favor. En caso de que tome la decisión de no participar o abandonar este estudio, no tendrá problemas para seguir recibiendo los servicios por parte del IMSS como hasta la fecha. También, le informamos que la participación en este estudio no generará ningún costo para usted, pero tampoco se le proporcionará dinero por su participación.
Quien puede participar: Mujeres con diagnóstico establecido de cáncer de mama, entre 20 y 75 años de edad, quienes hayan iniciado recientemente (hace 2 semanas o menos) con quimio y/o radioterapia y acudan a los servicios de consulta externa, quimio, o radioterapia del Hospital de Oncología del Centro Médico Nacional Siglo XXI, que tengan acceso a internet a través del teléfono móvil o computadora en su casa y que voluntariamente acepten participar en el estudio firmando la carta del consentimiento informado.

El estudio propone comparar el efecto de dos tipos de atención:
Atención/ Grupo #1 consiste en la atención habitual junto con información y monitoreo remoto de los síntomas de cáncer, de los efectos adversos del tratamiento y de las necesidades de las pacientes mediante una aplicación digital (por internet), así como seguimiento proactivo por las enfermeras del estudio.

Atención/ Grupo #2 consiste en la atención habitual, además se le entregara a la participante un listado de fuentes de información publicadas en las páginas web de las asociaciones y organizaciones civiles para pacientes/sobrevivientes de cáncer en México que brindan información sobre los efectos adversos del tratamiento del cáncer de mama y cómo mitigarlos.

Si Usted cumple con los criterios de inclusión podrá participar en uno de los dos grupos. Le asignaremos el grupo en el cual va a participar mediante un sorteo; sin opción a cambiar el grupo.

Duración del estudio: La duración total del estudio para cada participante será de 9 meses.

Actividades dentro del estudio: Las participantes de ambos grupos recibirán acceso a una aplicación móvil de registro basal de sus características sociodemográficas y clínicas como su escolaridad, duración y etapa del cáncer, etc. Las enfermeras del estudio explicarán a los participantes de como completar este registro y otros cuestionarios/registros del estudio y, si es necesario, brindarán apoyo para completar la evaluación inicial. Además del registro basal de los datos sociodemográficos y clínicos al inicio del estudio, las participantes de ambos grupos van a tener que registrar sus síntomas y necesidades de apoyo en una aplicación móvil del estudio al inicio, a los 1, 3, 6 y 9 meses. Las invitaciones/recordatorios para registrar los síntomas y necesidades se enviarán por medio del teléfono móvil, y/o correo electrónico de la participante.

Adicionalmente, las participantes del Grupo #1 recibirán el acceso y las indicaciones de monitoreo de sus síntomas y necesidades de apoyo mediante su registro semanal en una aplicación móvil y seguimiento por las enfermeras del proyecto. Las participantes del Grupo #1 durante los primeros 6 meses del estudio recibirán un recordatorio semanal para llenar el registro de los síntomas y necesidades y también recibirán un mensaje semanal con la liga de la fuente de información, según el tipo de tratamiento y problemas presentados (síntomas y necesidades). En el caso de presentar síntomas/necesidades de apoyo moderados a severos las participantes del Grupo #1 recibirán la llamada de la enfermera del proyecto (audio o video llamada según la preferencia del participante) quien les orientará de cómo atender los síntomas/necesidades presentadas. Es importante resaltar que en el Grupo #1, las enfermeras contactarán a las pacientes para ayudarles a atender los síntomas y necesidades moderadas y severas solo durante los días hábiles en un horario de 8:00 am a 19:00 pm y que en el caso de presentar síntomas severos que necesiten atención inmediata fuera de este horario, la paciente
tiene que acudir a los servicios de urgencias; la misma recomendación es aplicable si la paciente registra en su aplicación móvil que tiene algún síntoma grave que es difícil de aguantar (como dolor insoportable, o vómito intenso) y por algún imprevisto no recibe la respuesta de la enfermera del estudio en el transcurso de 30 minutos después del registro correspondiente.

**Posibles riesgos y molestias de la participación en el estudio:** Hasta el momento los estudios que aplicaron monitoreo remoto de los síntomas y necesidades de los pacientes mediante las aplicaciones para los teléfonos móviles no han reportado eventos adversos. El único inconveniente es el registro regular (semanal en el Grupo #1 y solamente a los 1, 3, 6 y 9 meses en el Grupo #2 de sus síntomas y necesidades de apoyo en una aplicación en su teléfono móvil que va a requerir entre 15 y 30 minutos de su tiempo para cada registro.

**Posibles beneficios que recibirá al participar en el estudio:** Como se ha documentado en estudios previos se espera que a nivel de la participante, el registro de los síntomas y necesidades de apoyo y su seguimiento en el caso de los síntomas y necesidades de intensidad moderada a severa por la enfermera permitirá disminuir estas problemáticas que enfrentan las pacientes con cáncer de mama, así como aumentar su calidad de vida y disminuir el uso de servicios de urgencias y hospitalizaciones no programadas. Además, en el caso de comprobar la efectividad de la atención a través del monitoreo remoto mediante una aplicación en teléfonos móviles y seguimiento proactivo de los síntomas y necesidades de las mujeres con cáncer de mama, puede ser recomendada para su implementación en México para el beneficio de otros pacientes que padecen cáncer.

**Privacidad y confidencialidad:** Una vez obtenido el consentimiento informado se asignará una clave numérica a una carpeta con sus datos. Toda la información proporcionada durante el estudio será manejada de manera confidencial. La identidad de cada participante será protegida y ocultada. Para proteger la identidad de las participantes se les asignará un número que se utilizará para identificar sus datos, y se utilizará ese número en lugar del nombre en las bases de datos del estudio. La información que cada participante proporcione durante el estudio y que pudiera ser utilizada para identificarla (como su nombre y teléfono) será guardada de manera confidencial en la computadora de los investigadores principales de este estudio y protegida con contraseña. Solo el personal del estudio tendrá acceso a la información que la participante nos proporcione. Sólo facilitaremos la información de la participante al personal de salud del IMSS, si fuera necesario para proteger sus derechos y bienestar (por ejemplo, si los investigadores del estudio detectan que la participante necesita cuidados de emergencia). Cuando los hallazgos de este estudio sean utilizados para informar, publicar y difundir los resultados del presente estudio, No se incluirá información que pudiera revelar la identidad de las participantes.

**Si tiene preguntas o quiere hablar con alguien sobre este estudio de investigación puede comunicarse con el investigador principal del estudio, la Dra. Svetlana Doubova al teléfono 55 56 27 69 00 ext. 20172; de 8 a 16:00 horas.; o al correo electrónico: svetlana.doubova@gmail.com, o si usted tiene dudas o preguntas sobre sus derechos al participar en un estudio de investigación puede comunicarse con los responsables del Comité de Ética en Investigación en Salud del IMSS, a los Tel. 56276900 ext. 21216, de 9 a 16:00 horas.; o al correo electrónico: comiteeticainv.imss@gmail.com. El Comité de Ética en Investigación en Salud se encuentra ubicado en el Edificio del Bloque B, Unidad de Congresos.
piso 4, Centro Médico Nacional Siglo XXI, Av. Cuauhtémoc 330 Colonia Doctores, C.P. 06725, Ciudad de México.

DECLARACIÓN DE CONSENTIMIENTO INFORMADO

Proyecto de investigación titulado: “Diseño y evaluación de la efectividad de una intervención de salud digital para mejorar la atención y resultados en salud de pacientes con cáncer.”

Se me ha explicado con claridad en qué consiste este estudio, además he leído (o alguien me ha leído) el contenido de este formato de consentimiento. Se me ha dado la oportunidad de hacer preguntas y todas mis preguntas han sido contestadas a mi satisfacción. Se me ha dado una copia de este formato.

Al firmar este formato estoy de acuerdo en participar en la investigación que aquí se describe.

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**Firma del encargado de obtener el consentimiento informado**

Le he explicado el estudio de investigación al participante y he contestado todas sus preguntas. Considero que comprendió la información descrita en este documento y libremente da su consentimiento a participar en este estudio de investigación.

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**Firma del testigo 1**

Mi firma como testigo certifica que el/la participante firmó este formato de consentimiento informado en mi presencia, de manera voluntaria.

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**Firma del testigo 2**

Mi firma como testigo certifica que el/la participante firmó este formato de consentimiento informado en mi presencia, de manera voluntaria.

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Mexican Institute of Social Security  
Health Research Coordination  
Epidemiology and Health Services Research Unit CMN Siglo XXI  

INFORMED CONSENT FORM  

Research study: “Design and evaluation of the effectiveness of a digital health intervention to improve health care and outcomes for cancer patients.”  

We invite you to participate in the study entitled "Design and evaluation of the effectiveness of a digital health intervention to improve health care and outcomes for cancer patients." which has the registration number of the IMSS National Research Committee R-2021-785-059.

Study justification and objectives: The reason for this research is to identify the benefits of a digital health strategy focused on providing information and remote monitoring of cancer symptoms and adverse effects of treatment (which are unexpected complications that can occur during cancer treatment with chemotherapy, radiotherapy, or surgery) and the supportive care needs, generating alerts in real-time and proactive monitoring of breast cancer patients by nurses.

Previous studies have found that most cancer patients who receive health care in public hospitals in Mexico report multiple cancer symptoms, adverse drug effects, unmet supportive care needs, and deficiencies in the quality of their care. In high-income countries, it has been found that remote monitoring of cancer symptoms, adverse effects of treatment, and patient needs through mobile or web applications allow generating real-time alerts sent to nurses allowing them to perform the proactive follow up of cancer patients to reduce their symptoms and supportive care needs; however, this type of care has not been implemented and evaluated in Mexico.

Participation or withdrawal: Participation in this study is entirely voluntary. You can agree to participate in the study and change your mind later. If you wish to change your mind and not participate in this study, regardless of the reason, please let us know. If you decide not to participate or to abandon this study, you will continue receiving healthcare services at IMSS. Also, we inform you that there will be no expenditure to you for participating in this study and no money paid to you for your participation.

Who can participate: Women with breast cancer between 20 and 75 years, with the established cancer diagnosis, who have been recently started (2 weeks ago or less) chemo and/or radiotherapy and attend the outpatient consultation with oncologist, or chemo, or radiotherapy services of the Oncology Hospital of the National Medical Center Siglo XXI, who have access to the internet via mobile phone or computer at home and who voluntarily agree to participate in the study by signing the informed consent form.
The study proposes to compare the effect of two types of health care:

**Health Care/Group#1** consists of usual care along with information and remote monitoring of cancer symptoms, adverse effects of treatment and patient needs through a digital application (online), as well as proactive follow-up by study nurses.

**Health Care /Group #2** consists of the usual health care provide by IMSS, in addition, the participant will receive a list of the web pages of breast cancer associations and civil organizations in Mexico that provide information on the adverse effects of breast cancer treatment and how to mitigate them.

If you meet the inclusion criteria, you can participate in one of the two groups. We will assign you to the group through a lottery; without the possibility to change the group.

**Study Duration:** The total study duration for each participant will be 9 months.

**Activities within the study:** Participants in both groups will receive access to a study web application for baseline registration of their sociodemographic and clinical characteristics, such as their age, education, duration and stage of cancer, etc. Study nurses will teach participants to complete this register and other study questionnaires/registries and, if needed, will provide the support to complete the baseline evaluation. In addition to the baseline registry of sociodemographic and clinical data at the beginning of the study, the participants of both groups will have to register their symptoms and supportive care needs in a study web application at baseline, 1, 3, 6, and 9 months. Invitations/reminders to register symptoms and supportive care needs will be sent via the participant's mobile phone and/or email.

Moreover, the participants of Group #1 will receive access and indications for monitoring their symptoms and supportive care needs through their weekly registration in a study App and follow-up by the study nurses. During the first 6 months of the study, the participants of Group #1 will receive a weekly reminder to register their symptoms and needs and will also receive a weekly message with the link to the source of information that addresses problems (symptoms and needs) that they presented. In the case of presenting moderate to severe symptoms/needs, Group #1 participants will receive a call from the study nurse (audio or video call depending on the participant's preference), who will guide them on how to address their symptoms/needs. It is important to highlight that in the intervention group, the nurses will contact the patients to help them to address moderate and severe symptoms and needs only during business days from 8:00 a.m. to 19:00 p.m; therefore, in the case the patient presents severe symptoms that need immediate response outside these hours, the patient must go to the emergency services. The same recommendation is applicable if the patient registers severe symptoms (such as unbearable pain or severe vomiting) and does not receive a response from the study nurse for 30 minutes after symptom registration.

**Potential risks and drawbacks of participation:** To date, studies that applied remote monitoring of patient symptoms and needs using mobile or web apps reported no adverse events. The only drawback is the regular (weekly) registration of symptoms and supportive care needs by participants of Group #1 and at 1, 3, 6, and 9 months by participants of Group #2 that will require between 10 and 30 minutes of your time for each record.

**Possible benefits of the study participants:** Based on the results of the previous studies in high-income countries, it is expected that at the participant level, the recording of
symptoms and supportive care needs and their follow-up by nurses could reduce these problems faced by cancer patients, as well as increase the quality of life and reduce the use of emergency services and unscheduled hospitalizations. In addition, if this study confirms the effectiveness of the present intervention, it can be recommended for implementation at IMSS and in other public health institutions in Mexico to benefit other patients with breast cancer.

Privacy and confidentiality: All information provided during the study will be kept confidential. The identity of each participant will be protected and hidden. Once informed consent has been obtained, a numerical identifier will be assigned to the digital folder with the participant's data to protect her identity. All confidential information (such as your name and telephone number) will be kept confidential on the computer of the study's principal investigator and protected with a password. Only the study staff will have access to the information that the participants provide. We will only provide the participant's information to the IMSS health professionals responsible for the participants' treatment if it is necessary to protect their well-being (for example, if the study nurses detect that the participant needs emergency care that the study personnel cannot provide). When the study results are reported or published, the information that could reveal the identity of the participants will not be included.

If you have questions or want to talk to someone about this research study, you can contact the principal investigator of the study, Dr. Svetlana Doubova at 55 56 27 69 00 ext.20172; from 8 to 16:00 hrs.; or to the email: svetlana.doubova@gmail.com, or if you have doubts or questions about your rights as a research study participant, you can contact the staff of the IMSS Health Research Ethics Committee, at Tel. 56276900-21216, from 9 a.m. to 16:00 p.m.; or to the email: comiteeticainv.imss@gmail.com. The Health Research Ethics Committee is located in the Block B Building, Congress Unit, 4th floor, Centro Médico Nacional Siglo XXI, Av. Cuauhtémoc 330 Colonia Doctores, C.P. 06725, Mexico D.F.

DECLARATION OF INFORMED CONSENT
Research study entitled: "Design and evaluation of the effectiveness of a digital health intervention to improve health care and outcomes for cancer patients."

It has been clearly explained to me the content of the study, also I have read (or someone has read to me) the content of this consent form. I have been given the opportunity to ask questions and all of my questions have been answered to my satisfaction. I have been given a copy of this form.

By signing this form, I agree to participate in the research study described here.

________________________________________________________________________
Participant Name

________________________________________________________________________
Participant signature                                                                  Date

Signature of person who obtains the informed consent

I have explained the research study to the participant and have answered all of her questions. I believe that she understood the information described in this document and give her consent to participate in this research study freely.

Name of person responsible for obtaining informed consent

Signature of person responsible for obtaining informed consent    Date

Signature of witness 1
My signature as a witness certifies that the participant signed voluntarily this informed consent form in my presence.

Name of witness 1

Participant-witness relationship

Signature and Date

Signature of witness 2
My signature as a witness certifies that the participant signed voluntarily this informed consent form in my presence.

Name of witness 2

Participant-witness relationship

Signature and Date
Supplemental material 2: Screenshots of the study web application.

Access screen to the patient web application (intervention group) on mobile phone (A) on computer (B).

C. Patients’ interface with access to different sections.
D. Initial question of the weekly record of symptoms and supporting care needs.

Registro Semanal de Sintomas y Necesidades de Apoyo

¿Tiene algún síntoma o necesidad de apoyo en esta semana?

EnviAR el REGISTRO

E. Subsections of the weekly record of symptoms and supporting care needs.
F. Example of questions of the pain subsections of the registry of symptoms and supporting care needs.
G. Example of questions of palmo-plantar erythrodysesthesia subsection of the registry of symptoms and supporting care needs.

![Image of palmo-plantar erythrodysesthesia questions]

H. Example of questions of lymphedema subsections of the registry of symptoms and supporting care needs.

![Image of lymphedema questions]
I. Evaluation section.

J. Evaluation section. Subsections of baseline evaluation.
K. Example of quality of life questionnaire

**CUESTIONARIO SOBRE CALIDAD DE VIDA**

**INSTRUCCIONES**

“Los pacientes dicen que en ocasiones presentan los siguientes síntomas o problemas. Por favor, marque la opción que mejor describe la frecuencia en que le ocurrieron estos problemas durante la semana pasada.”

1. ¿Tiene alguna dificultad para realizar actividades que requieren de un esfuerzo importante, como llevar una bolsa pesada o una maleta?
   - [ ] No en absoluto
   - [ ] Un poco
   - [ ] Bastante
   - [ ] Mucho

2. ¿Tiene alguna dificultad para dar un paso largo?
   - [ ] No en absoluto
   - [ ] Un poco
   - [ ] Bastante
   - [ ] Mucho

3. ¿Tiene alguna dificultad para dar un paso corto fuera de casa?
   - [ ] No en absoluto
   - [ ] Un poco
   - [ ] Bastante
   - [ ] Mucho

4. ¿Tiene que permanecer en la cama o sentado en una silla durante el día?
   - [ ] No en absoluto
   - [ ] Un poco
   - [ ] Bastante
   - [ ] Mucho

L. Video section.

**Videos**

<table>
<thead>
<tr>
<th>Título</th>
<th>Intro</th>
<th>Sem.</th>
</tr>
</thead>
<tbody>
<tr>
<td>GENERALIDADES CÁNCER MAMA…</td>
<td>¿Quieres…</td>
<td>1</td>
</tr>
<tr>
<td>COMUNICACIÓN CON PERSONAL DE…</td>
<td>¿Qué pre…</td>
<td>1</td>
</tr>
<tr>
<td>TRATAMIENTO DE CÁNCER…</td>
<td>¿Sabes cu…</td>
<td>1</td>
</tr>
</tbody>
</table>