BMJ Open

Electronic Patient-Reported Outcome Measures integrated in treatment and care of women diagnosed with Breast Cancer: A Feasibility Study Protocol

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2022-065110
Article Type:	Protocol
Date Submitted by the Author:	27-May-2022
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Keywords:	Breast surgery < SURGERY, Breast tumours < ONCOLOGY, Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT

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Word count: 3762

ABSTRACT

Introduction

The use of patient-reported outcome measures (PROMs) in clinical practice has the potential to promote person-centred care and improve patients' health-related quality of life. We aimed to develop an intervention centred around electronic PROMs (ePROMs) for systematic follow-up in patients diagnosed with breast cancer and to evaluate its feasibility.

Methods and analysis

We developed a nurse- and surgeon-oriented intervention on PROMs, including 1) an education program for nurses and surgeons; 2) administration of BREAST-Q as an ePROM during follow-up in patients diagnosed with breast cancer, and 3) feedback to nurses and surgeons on PROM scores and a guidance manual for health care practitioners. Subsequently, we designed a non-controlled feasibility evaluation. The feasibility evaluation includes qualitative ethnographic studies exploring the user perspectives of patients, nurses, and surgeons, and quantitative studies to explore the characteristics of the patient population regarding demographic background, response rates, and response patterns. The feasibility study was initiated in September 2021, is being conducted until 2024, and will include approximately 900 patients. ePROMs are collected at baseline, 1-year follow-up, and 3-year end-point.

Ethics and dissemination

The study will be conducted according to the General Data Protection Regulation and the 5th version of the Helsinki Declaration. The National Committee on Health Research Ethics approved the study according to the law of the committee § 1, part 4.

All data will be anonymised before its publication. The results of the feasibility study will be published in peer-reviewed, international journals.

Keywords: breast cancer, person-centred care, BREAST-Q, breast surgery, Patient-Reported Outcome Measures

Strengths and limitations of this study

- Breast cancer has a profound negative impact on the long-term well-being of women after treatment.
- Patient-reported outcome measures may support a systematic approach for improved person-centred care, including targeted, individual, psychosocial support and assessment of candidates for reconstructive and/or corrective breast surgical therapy. A digital approach to assessing surgery-related outcomes must be explored to prove its feasibility in patients with breast cancer.
- To our knowledge, this is the first study to investigate the proactive use of the BREAST-Q as ePROMs in (clinical practice for) women diagnosed with breast cancer undergoing different types of reconstructive breast cancer surgeries.

INTRODUCTION

Breast cancer is one of the most common cancers, with 2.3 million women globally diagnosed with breast cancer in 2020 [1]. The survival rate of these women is 75% in most developed countries [2] and 90% in Denmark [3]. In Denmark, national screening programs and improvements in breast cancer treatment have high priority in the healthcare system, and patients have several options for treatment [4]. The treatment of breast cancer is complex, multidisciplinary, and refers to standardised national guidelines by the Danish Breast Cancer Group to guarantee the highest standard of treatment and care [5].

Standard treatments in the curative setting of breast cancer include surgery and medical treatment as key components. The spectrum of surgical approaches for treating breast tumours includes breast-conserving therapy with or without the use of oncoplastic techniques, or mastectomy alone or with primary or delayed reconstruction. Treatments may further include chemotherapy, radiation therapy, and hormone therapy [6–8]. Furthermore, follow-up with reconstructive corrective plastic surgery may support an increased self-rated quality of life [9,10]. Irrespective of the treatment intensity, patients are often long-term impaired by multiple side effects, including fatigue, sleep problems, pain, reduced mobility in the shoulder, and lymphedema in the arm [11]. Psychosocially, breast loss or changes in the appearance of the breast influence individual patients [12] who may experience negative psychological impacts, such as body image and sexuality concerns, worry, anxiety, depression, and stress [13–18]. Put together, these circumstances negatively affect the patients' self-rated Health-Related Quality Of Life (HRQOL) [19]. Hence, the assessment and monitoring of individual patient experiences are important in breast cancer surgery because the success of aesthetic breast surgery is

measured by the extent to which patients' physical, psychological, and social well-being are enhanced [7,18,20].

There is strong evidence that different forms of breast surgery and reconstruction positively affect patients' quality of life [21]. Previous research has identified that evaluating patients' outcomes of breast surgery and related psychosocial aspects through patient-reported outcome measurements (PROMs) might provide useful information for nurses, surgeons, and patients [22,23]. PROMs are defined as "*any report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else* [24]". Previous PROM research has found that proactive PROMs, meaning that the clinicians actively review the patients' PROM answers during consultations and use the feedback from patients to optimise the care and treatment, enable a) earlier detection of symptoms; b) improve communication between clinicians and patients about symptoms and HRQOL; and c) increase the person-centredness of consultation processes [25–29]. Being person-centred focuses on the care and treatment of the needs of individuals. Ensuring that individual preferences, needs, and values guide clinical decisions and that clinicians provide care that is respectful and responsive to patients [30]. Previous research in palliative care settings found that information on patients' perception of their state through PROMs may enable clinicians to enhance person-centred care and treatment if the perspectives and experiences of patients are revealed and integrated [31].

Research in PROMs has also identified several barriers to the implementation of PROMs in clinical practice [32–36]. Those barriers include limited time, lack of specification of use, insufficient knowledge of clinicians on how to use PROMs, lack of capacity, and electronic barriers from both patients and clinicians [32–35].

The Danish government and regions have agreed to initiate a nationwide spread of PROM use in breast cancer hospitals [4]. Accordingly, the Danish Breast Cancer Cooperative Group initiated a single-region PROM study on late effects in women diagnosed with breast cancer [37]. This initiative is expected to become national by around 2023. However, this initiative does not include the assessment of breast surgical outcomes or systematic follow-up at the hospital, which are the core elements of this study.

PROMs in the field of breast cancer surgery have the potential to involve patients by inviting them to contribute with their pre-and postoperative expert knowledge on their own experiences, values, and concerns. PROMs may be used for systematic and person-centred follow-ups related to surgical outcomes. This has yet to be demonstrated in clinical trials [38,39].

This protocol, version 1.2, 22 February 2022, describes the organisation and methodology behind a feasibility study on electronic patient-reported outcome measures (ePROMs) that are integrated in the treatment and care of women diagnosed with breast cancer in a plastic surgery and breast surgical outpatient setting of a tertiary university hospital. Given the emphasis on person-centred care in the organisation in which the study takes place, person-centred care is an underpinning theoretical perspective that aims to be incorporated into clinical practice; thus, the hypothesis in this multimethod study is that proactive use of ePROMs during patient trajectories at the outpatient clinic improves patient care and communication by A) focusing person-centred care on individual values and concerns related to surgical outcomes and psychosocial care during surgical follow-up and B) systematic assessment of patients' potential need for supplemental breast surgery, including reconstruction or correction, to improve patients' well-being related to breasts and body image after breast cancer. Hence, the overall aim of this study is to

develop knowledge on the proactive application of ePROMs in breast surgical and breast reconstructive clinical practice.

METHODOLOGY

Study Design

This is a multi-method, non-controlled feasibility study [40,41] to investigate whether an intervention with ePROMs can be shaped to be relevant and sustainable in clinical practice. The feasibility study is divided into three sub-studies (Figure 1) with the following aims.

Study I) To explore patient's experiences related to acceptability, practicality, and demands on completion of PROMs following physical meetings at the department with nurses and surgeons.

Study II) To investigate the nurses' and surgeons' experiences related to acceptability, introduction, practicality, and proactive application of the PROM-intervention in clinical practice.

Study III) To analyse PROM data after 1 year including outcomes and demographic variables for responders and non-responders.

The multi-method study includes the development of an ePROM intervention with repeated collection of ePROMs on timings (T) T1, T2, and T3 using the BREAST-Q tool and proactive use of ePROMs during follow-up visits at the department and an evaluation of feasibility (Figure 1 and Figure 2). Studies I and II are qualitative ethnographic studies exploring the user perspectives of patients, nurses, and surgeons to gain insights into how the intervention can be refined. Additionally, Study II is complemented with a local anonymous survey study with department nurses and surgeons

to gather information on activities, beliefs, preferences, and proactive application related to the ePROM-intervention. Qualitative studies are guided by interpretive description, an inductive methodology developed to explore clinical problems that arise from practice disciplines with the objective of generating insights that inform clinical practice [42]. Quantitative study III includes the ePROM database to explore the patient population and their outcomes at T1 (Figure 2) [43]. This protocol describes only a feasibility study. The evaluations of T2 and T3 will be reported elsewhere. Guidelines for Inclusion of Patient-Reported Outcomes in Clinical Trial Protocols: The SPIRIT-PRO Extension [44] were used to report the protocol (Supplementary Material 1).

Study participants

Patient participants are women with newly diagnosed breast cancer who will be included in the multimethod study from September 2021 to September 2024, and the follow-up time will end in January 2028.

Inclusion criteria:

- Female patients age ≥18
- Newly diagnosed breast cancer is treated with curative surgical therapy to remove breast cancer
- The ability to speak and understand Danish to comprehend the given information, complete the study questionnaires, and provide written informed consent.

Exclusion criteria:

- Treated with letrozol aromatase inhibitor hormone therapy as primary treatment (nonsurgical)
- Not assigned digital information in the Danish Civil Registration System (Figure 2)

- Non-Danish speaking
- Any disability making ePROM follow-up impossible, such as blindness or mental disability, or a diagnosis of dementia.

Exclusion is assessed based on the medical record journal by a research assistant in collaboration with a breast surgeon at the department affiliated with the study. Approximately 600 women are newly diagnosed with breast cancer at the Department of Plastic and Breast Surgery of Zealand University Hospital each year. Patients will be included continuously for 3 years. A minimum sample of 900 patients is expected to be included.

For qualitative studies I and II, patient participants are purposefully sampled from consenting to the ePROM intervention using the maximum variation concept [42]. Recruited nurses and surgeons will follow the patient participants, as nurse and surgeon participants are those whom the patients met throughout their visit on the day of observation by the present researcher. The patients' visits are pre-booked, and patients visit either a nurse, surgeon, or nurse in one consultation. An anonymous survey will be distributed to all nurses and surgeons at the outpatient clinic as part of study II.

Recruitment procedures

Patients are recruited from the Department of Plastic and Breast Surgery at a large centre of plastic and breast surgery located at a tertiary Danish university hospital. The departments' research assistants are responsible for identifying and inviting patients who meet the inclusion criteria.

Patients eligible for inclusion are informed and invited through a digital postbox (e-Boks) to the ePROM intervention [45]. The invitation is supported by a four-minute video developed by the research assistant and a patient and public representative

providing patient information about the aims of the ePROM-intervention. Furthermore, the patients receive a postcard at the outpatient clinic, informing them about the ePROM intervention when they are diagnosed. Patients receive a link to the ePROM questionnaires in their digital postbox via the secure encrypted electronic system Research Electronic Data Capture (REDCap) [46]. Patients' may consent or decline through invitation by mail. Patients may complete questionnaires on a PC, tablet, or smartphone. The questionnaire is open for completion 14 days after invitation. After 2 days, a notification is automatically forwarded if no response is received. After 4 days, the research assistant calls and asks patients who do not respond to the invitation if they need assistance with the questionnaire. A research nurse assistant may assist with technical issues, if any. Patients included in the study can withdraw consent to participate without affecting the present or future treatment at any time, without justification. Patients withdrawing consent will be considered as 'lost to follow-up". Patients who decline to participate are registered within an encrypted database as non-responders. Nurses and surgeons at outpatient clinics have access to patients' ePROM data through REDCap, including detailed responses and the total score of each questionnaire.

Strategies for the introduction of ePROMs

This study acknowledges the introduction of ePROMs as a dissemination process: "Dissemination is the active spread of new practices to the target audience using planned strategies [47]", as implementation goes beyond feasibility [41]. The introduction strategies aim to enable systematic and flexible implementation of ePROMs in an outpatient setting [15]. The strategy includes establishing an ePROM-intervention support group, a nurse education program, and a surgeon education program. As part of the strategy, ePROM-intervention is described in detail within a clinical guideline

developed with the ePROM-intervention supporting group. The guideline includes instructions for nurses, surgeons, and secretaries on their specific responsibilities related to the ePROM intervention. A part of the strategy is a steering group plus education programs for the departments' nurses and surgeons.

Patient and public involvement

The study is supported by a patient and public representative from the Danish Cancer Society who is an equal member of the study steering group. The representative was involved throughout the design phase, research questions and agreeing plans for dissemination of the study to participants. The representative continuously informed the study with patients' and public priorities, experiences and preferences and the representative will participate for the analysis of data.

The ePROM steering group

The ePROM intervention is delivered by a steering group of experts who assist in the introduction. The group consists of an outpatient nurse from the department, a breast surgeon, a secretary, the patient and public representative, a nurse research assistant, a leading head nurse, a leading chief surgeon, and a responsible nurse researcher. In addition, three external researchers are affiliated with the intervention study as supervisors and are experts in PROMs, statistics, qualitative methodology, and person-centred practice.

Nurse education program

Before the PROM intervention, all nurses at the breast surgical outpatient clinic participated in face-to-face training on the use of ePROMs. The educational sessions were

guided by person-centred care theory and included a brief lecture on person-centredness and person-centred communication, supporting previous departmental education for nurses, whereas person-centred values have been inherent.

Training on the application of ePROMs during consultations was mandatory and provided by departments' clinical nurse specialist and research assistant for 4 hours. The education program included a broad introduction to PROMs and examples of proactive use of PROMs from other departments and research [48,49]. The educational program was planned with didactical consideration to research-based teaching and teaching for learning, with a focus on interaction and activation during sessions with case-based learning [50,51]. The trainings included: how to access the timely and relevant individual patients' ePROMs linked to nurse consultations; how to respond to ePROMs in terms of caring for individuals with psychosocial support and symptom management; how to proactively engage in ePROMs with patients; and how to document nurses' application of PROMs in patient care. The intervention is associated with continuous, monthly, 1-hour trainings that address issues related to the proactive use of ePROMs in clinical practice to improve outpatient nurses' knowledge and skills in relevant issues such as body image-related distress [52]. Nurses' use of ePROMs is evaluated every third month using a paper questionnaire and a 1-hour dialogue with the responsible researcher.

Surgeons' education program

Prior to the PROM-intervention kick-off, surgeons from the department participated in a 1-hour mandatory education program about the ePROM-intervention, aiming to inform about its objectives and processes. Surgeons participate in further follow-up training on PROMs once a month by the responsible researcher and a clinical nurse specialist. The sessions include practical training on how to access the timely and

relevant individual patients' ePROMs linked to surgeons' consultations as a comparison of the T1 and T2 questionnaires (Table 1), how to engage with and respond to ePROMs in terms of person-centred surgical follow-up on ePROMs with patients, and how to document surgeons' application of PROMs in the medical record journal. Didactical considerations correspond to those mentioned in the nurses' education programs.

Table 1. Study assessment times, measures and tasks

Data Collection		**Baseline (T1*)**	**Follow-up[1] (T2)**	**Endpoint (T3)**
All patient participants (ePROM group)	Informed consent	●		
	Demographic data[2]	●		
	Breast Cancer Core Scale (Preoperative): Satisfaction with Breasts[3]	●	❷❸	
	Breast Cancer Core Scale (Preoperative): Physical Well-Being: Chest[3]	●		
	Breast Cancer Core Scale (Pre and Postoperative): Psychosocial Well-Being[3]	●	❶❷❸	●
	Breast Cancer Core Scale (Pre and Postoperative): Sexual Well-Being[3]	●	❶❷❸	●
	Breast Conserving Therapy Module (Postoperative): Satisfaction with Breasts[3]		❶	
	Breast Conserving Therapy Module (Postoperative): Physical Well-Being: Chest[3]		❶	
	Breast Cancer Core Scale (Pre- and Postoperative): Physical Well-Being: Chest[3]		❷❸	●
	Reconstruction Module (Postoperative): Satisfaction with Breasts[3]			●
	[A]Reconstruction Module (Postoperative): Satisfaction with Nipple Reconstruction[3]			●
	[A]Reconstruction Module (Postoperative): Satisfaction with Implants[3]			●
	[A]Latissimus Dorsi Module (Postoperative): Satisfaction with Back[3]			●
Invited non-respondents	Reasoning for study drop out			
User perspectives	Participant observations during patient consultations	◊	◊	
	Individual interviews with patients			
	Individual interviews with nurses	◊	◊	
	Survey with nurses and surgeons		◊	

*Timing (T) and questionnaire distribution number, [1]Patients after surgical therapy: ❶ initial breast conserving therapy, ❷ initial mastectomy, ❸ initial immediate reconstruction; [1]Demographic data (identification-number, age, marital status, educational level, body mass index, zip code); [3]BREAST-Q™ version 2.0 Questionnaire scale; [a]Individual supplementary modules.

Intervention with ePROMs

The ePROM intervention includes patients' completion of ePROMs related to satisfaction with breasts, physical well-being, psychosocial well-being, and sexual well-being to be proactively applied in patients' trajectory to monitor the individual patient's condition and accommodate individualised psychosocial and surgical follow-up based on patient preferences and values. The patients receive two to three questionnaires, depending on their trajectory, over a 3-year period (Figure 2 and Table 1). The ePROMs are to be actively reviewed by departments' nurses before the patients visit on the following times: first, prior to patients 4-day postsurgical control with a nurse (T1, baseline); second, for the 1-year follow-up (T2, follow-up), which is initially a nurse consultation. Patients in the low-risk recurrence regime have standardized 1-year postsurgical follow-up with nurses, where ePROMs are to be applied. Patients in high-risk recurrence regimes are not standard-offered breast surgical follow-up, but this is offered to patients through the ePROM-intervention. During the second follow-up, nurses are educated to proactively use patients' ePROMs for dialogue on patients' perception of body image issues related to their breasts. Based on patients' individual needs, the nurse may recommend the patient for further assessment with one of department's plastic surgeon, who will also have the ePROMs for comparison (Table 1). Patients who accept correction or reconstruction of the breasts after their 1-year follow-up receive a third ePROM (T3, endpoint).

Data collection and measurements

The outcomes of the multimethod study relate to feasibility parameters, including acceptability, proactive use of ePROMs, demand, implementation, practicality, and integration [41,53,54]. These will be conducted through multiple measurements and

outcomes in Studies I to III. The data to be analysed in sub-studies I to III are conducted as follows:

Ethnographic studies I and II

Feasibility data are collected qualitatively by exploring the user perspectives of patients, nurses, and surgeons to gain insights into how the intervention can be refined. Qualitative studies I and II investigate users' interests related to using ePROMs and practice interests that can drive or limit development. User experiences of patients, nurses, and surgeons will be qualitatively explored and guided by the interpretive description methodology for applied research [42]. Data collection includes participant observations during patient consultations with nurses and surgeons and individual interviews with patients, nurses, and surgeons to explore the application of ePROMs in clinical practice and implications for practice. An observation and interview guide is developed based on the researchers' experiences as a nurse at the department, which also allows entry into department consultations [42]. The survey with nurses and surgeons is conducted as an online survey with questions developed specifically for this study to investigate perceptions and feasibility [43] based on the principles of applied research [42].

Study III on PROMs data

PROMs are collected electronically via REDCap at time points T1, T2, and T3 (Table 1). Additional baseline demographics for Study III data are collected electronically via REDCap within T1 (Figure 2 and Table 1) and include age, marital status, educational level, height, weight, body mass index, and municipality [46]. The PROMs used for the intervention is the BREAST-Q, as recommended by the International Consortium for

Health Outcomes Measurement (ICHOM) standard order set for breast cancer patients to monitor PROMs following breast surgery [55]. The BREAST-Q was developed according to recommended guidelines through patient interviews, focus groups, an expert panel, and a literature review and has undergone thorough validation with measures of high reliability using both the paper and the electronic version [38,56–59]. The BREAST-Q was designed specifically for breast surgery and has pre- and post-operative versions in modules for mastectomy, breast-conserving therapy, breast reconstruction, breast reduction, and breast augmentation [60]. All modules contain three subdomains, including physical, psychosocial, and sexual well-being, and three sub-domains on patient satisfaction, comprising satisfaction with breasts, outcome, and care. No overall BREAST-Q scores are obtained. Each independent scale results in a score that is computed by adding the response items and then converting the raw sum scale score to a score from to 0-100 [61]. For all BREAST-Q© scales, a higher score indicates greater satisfaction or better QOL (depending on the scale). If missing data are less than 50% of the scale's items, the mean of the completed items are inserted. Each set of questionnaires, for instance BREAST-Q questionnaire 1, takes 5-10 minutes to complete. Each scale is accompanied by a conversion table to calculate a total scale score of 0-100 [22,61].

Analysis

Qualitative studies I and II

The interviews and observations will be analysed in relation to user perspectives guided by interpretive description. The analysis will be inspired by the theoretical framework of person-centred care to evaluate the feasibility of the ePROM intervention, specifically the parameter acceptability, proactive use of ePROMs, demand, introduction, practicality, and integration [30,42].

Study III - Statistical analysis

Descriptive statistics will be calculated for all demographic variables for both responders and non-responders to the BREAST-Q questionnaire, based on data from T1 (baseline). Depending on the normality of the numerical variables, means (SD) or medians (interquartile range) will be calculated, while categorical variables will be expressed as proportions. Differences will be analysed using t-tests, Mann-Whitney U tests, and chi-squared tests, respectively. Furthermore, among responders, linear regression models will be used to identify which demographic variables are associated with the subscale scores from the BREAST-Q questionnaire. All variables will be entered into univariate and multivariate regression models to identify demographic variables that were independently associated with the questionnaire scores. Data will be analysed using the Stata software package [62]. The significance level will be set at $p < .05$, and all tests will be two-tailed. If applicable, sensitivity analysis using multiple imputation will be conducted on item-wise missing responses if the rate of missing data exceeds 5%.

ETHICS AND DISSEMINATION

The patients provide informed consent, which they can withdraw at any time. Data will be stored in REDCap and on an encrypted regional team site for personally sensitive research data. The study is designed according to the General Data Protection Regulation (GDPR) and adheres to the principles defined by the World Medical Association in the Helsinki Declaration. The use of the BREAST-Q questionnaire, authored by Drs. Klassen, Pusic, and Cano, was licenced by the Memorial Sloan Kettering Cancer Center, New York, USA.

The findings of this study will be submitted to international peer-reviewed journals and presented at conferences.

CONCLUSIONS

The study will generate detailed information on the feasibility aspects of the ePROM intervention for person-centred follow-up. Details include the users' experiences related to the proactive use of ePROMs and the practical interests that can drive its development. Furthermore, the study will explore whether a systematic approach to the patients' experiences of satisfaction with breasts, physical well-being, psychosocial well-being, and sexual well-being through ePROMs can function as enablers and triggers for the integration of person-centred care in follow-up consultations. This study will generate evidence-based knowledge on the feasibility and effects of a digital approach to assess and integrate surgery-related well-being and aesthetic outcomes in patients with breast cancer. To our knowledge, this is the first study to investigate the proactive use of the BREAST-Q as an ePROM in clinical practice for women diagnosed with breast cancer.

DECLARATIONS

Acknowledgements

KHKarlsen for representing patients and public into the study design. JHPrüsse for building the research database.

Competing interests

Authors do not have any conflicts to declare.

Patient consent for publication

Not applicable.

Authors' contributions

STH and was responsible for the initial study design and the grant application and is responsible for supervising as project leader. STH, VJS, KML and KP did the background research and was responsible for the protocol's in-depth development and drafting of this manuscript, including its figures and tables. LBH and BHH helped supervise. KP, LBH and BHH contributed with thorough revisions to the manuscript. All authors read and approved the final manuscript.

Funding

This work was supported by Region Zealand, National Cancer Plan IV [grant number 20-082, 2020]. The Region Zealand has not been part of designing the study, nor will the region be part of the analysis or interpretation of data. The Department of Plastic- and Breast Surgery, Zealand University Hospital and The University of Southern Denmark covers STH's salary. KP, BHH, KML, and VJS are currently not receiving a salary for this work.

Ethics Approval

The study is approved by the Danish Data Protection Agency (REG-104-2021) and the National Committee on Health Research Ethics (SJ-914, EMN-2021-01530).

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Supplemental material

Supplementary material 1 - SPIRIT 2013 and SPIRIT-PRO Extension Checklist

Legends

Figure 1. Illustration of the multimethod feasibility study, the intervention and sub-studies

Figure 2. Illustration of the ePROM-intervention flowchart. Dark boxes illustrate intervention features. T1, T2, and T3 refer to the timely specific questionnaires that are sent to the patients.

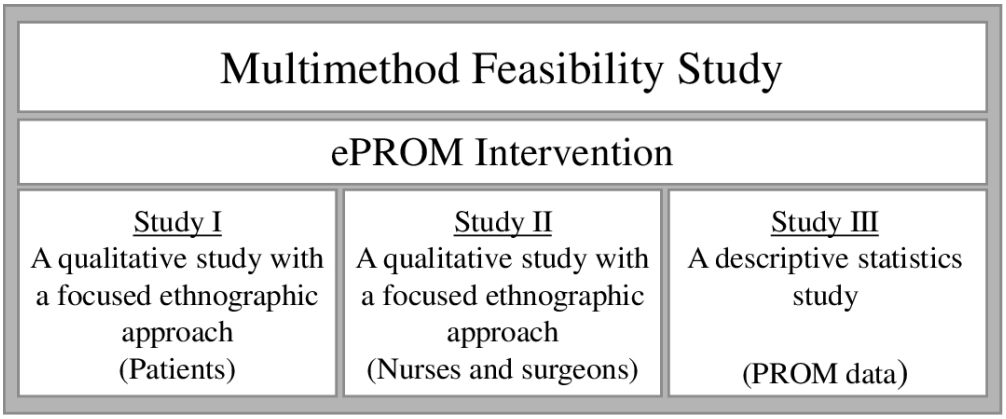

Figure 1. Illustration of the multimethod feasibility study, the intervention and sub-studies

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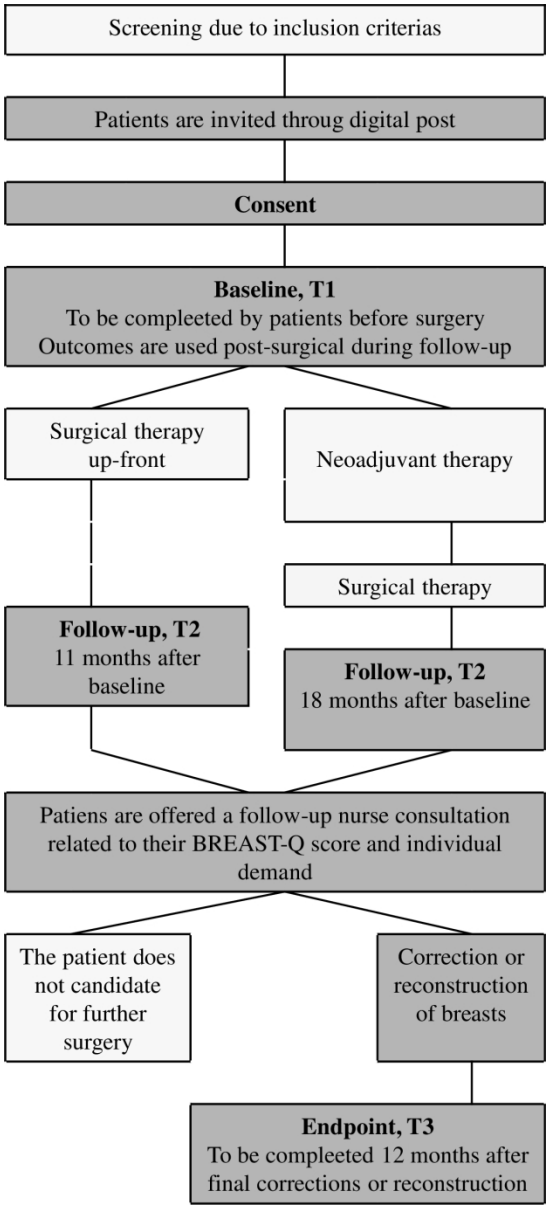

Figure 2. Illustration of the ePROM-intervention flowchart. Dark boxes illustrate intervention features. T1, T2, and T3 refer to the timely specific questionnaires that are sent to the patients.

97x215mm (300 x 300 DPI)

SPIRIT 2013 AND SPIRIT-PRO EXTENSION CHECKLIST: RECOMMENDED ITEMS TO ADDRESS IN A CLINICAL TRIAL PROTOCOL AND RELATED DOCUMENTS*

SPIRIT Section/item	SPIRIT Item No	SPIRIT Item Description	SPIRIT-PRO Item No	SPIRIT-PRO Extension or Elaboration Item Description	Page **
Administrative information					
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym			p.1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry			-
	2b	All items from the World Health Organization Trial Registration Data Set			-
Protocol version	3	Date and version identifier			p.6
Funding	4	Sources and types of financial, material, and other support			p.19
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	SPIRIT-5a-PRO elaboration	Specify the individual(s) responsible for the PRO content of the protocol	p.19
	5b	Name and contact information for the trial sponsor			-

	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities			-
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)			-
Introduction					
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	SPIRIT-6a-PRO Extension	Describe the PRO-specific research question and rationale for PRO assessment and summarize PRO findings in relevant studies.	p.6
	6b	Explanation for choice of comparators			-
Objectives	7	Specific objectives or hypotheses	SPIRIT-7-PRO Extension	State the specific PRO objectives or hypothesis (including relevant PRO concepts/domains).	p.16
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)			p.2
Methods: Participants, interventions, and outcomes					

Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained			p.6
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	SPIRIT-10-PRO Extension	Specify any PRO-specific eligbility citeria (eg, language/reading requirements or prerandomization completion of PRO). If PROs will not be collected from the entire study sample, provide a rationale and describe the method for obtaining the PRO subsample	p.8
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered			p.14
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)			-
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)			p.10
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial			-
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	SPIRIT-12-PRO Extension	Specify the PRO concepts/domains used to evaluate the intervention (eg, overall health-related quality of life, specific domain, specific symptom) and, for each one, the analysis metric (eg, change from baseline, final value, time to event) and the principal time point or period of interest.	p.15

Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	SPIRIT-13-PRO Extension	Include a schedule of PRO assessments, providing a rationale for the time points, and justifying if the initial assessment is not prerandomization. Specify time windows, whether PRO collection is prior to clinical assessments, and, if using multiple questionnaires, whether order of administration will be standardized.	Fig. 2
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	SPIRIT-14-PRO Elaboration	When a PRO is the primary end point, state the required sample size (and how it was determined) and recruitment target (accounting for expected loss to follow-up). If sample size is not established based on the PRO end point, then discuss the power of the principal PRO analyses.	p.9
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size			p.9
Methods: Assignment of interventions (for controlled trials)					
Allocation:					
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions			-
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned			-

Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions			-
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how			-
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial			-
Methods: Data collection, management, and analysis					p.15
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	SPIRIT-18a (i)-PRO Extension	Justify the PRO instrument to be used and describe domains, number of items, recall period, and instrument scaling and scoring (eg, range and direction of scores indicating a good or poor outcome). Evidence of PRO instrument measurement properties, interpretation guidelines, and patient acceptability and burden should be provided or cited if available, ideally in the population of interest. State whether the measure will be used in accordance with any user manual and specify and justify deviations if planned.	
			SPIRIT-18a (ii)-PRO Extension	Include a data collection plan outlining the permitted mode(s) of administration (eg, paper, telephone, electronic, other) and setting (eg, clinic, home, other).	p.15

			SPIRIT-18a (iii)-PRO Extension	Specify whether more than 1 language version will be used and state whether translated versions have been developed using currently recommended methods.	p.8
			SPIRIT-18a (iv)-PRO Extension	When the trial context requires someone other than the trial participant to answer on his or her behalf (a proxy-reported outcome), state and justify the use of a proxy respondent. Provide or cite evidence of the validity of proxy assessment if available.	-
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	SPIRIT-18b (i)-PRO Extension	Specify PRO data collection and management strategies for minimizing avoidable missing data.	p.10
			SPIRIT-18b (ii)-PRO Elaboration	Describe the process of PRO assessment for participants who discontinue or deviate from the assigned intervention protocol.	p.10
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol			p.10, 17
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	SPIRIT-20a-PRO Elaboration	State PRO analysis methods, including any plans for addressing multiplicity/type I (α) error.	p.17

	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)			
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	SPIRIT-20c-PRO Elaboration	State how missing data will be described and outline the methods for handling missing item or entire assessments (eg, approach to imputation and sensitivity analyses)	p.17
Methods: Monitoring					
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed			p.11
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial			-
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	SPIRIT-22-PRO Extension	State whether or not PRO data will be monitored during the study to inform the clinical care of individual trial participants and, if so, how this will be managed in a standardized way. Describe how this process will be explained to participants; eg, in the participant information sheet and consent form.	p.12
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor			-

Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	p.19
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	p.11
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	p.17
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	-
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	p.3
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	p.18
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	p.6
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	-

Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	p.18
	31b	Authorship eligibility guidelines and any intended use of professional writers	-
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	-
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	-
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	-

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

**page numbers refers to protocol paper

BMJ Open

Electronic Patient-Reported Outcome Measures to enable systematic follow-up in treatment and care of women diagnosed with Breast Cancer: A Feasibility Study Protocol

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2022-065110.R1
Article Type:	Protocol
Date Submitted by the Author:	01-Sep-2022
Complete List of Authors:	Thestrup Hansen, Stine; Zealand University Hospital Roskilde, Department of Plastic & Breast Surgery; University of Southern Denmark Faculty of Health Sciences, Department of Regional Health Research Piil, Karin; Copenhagen University Hospital Centre for Cancer and Organ Diseases, Department of Oncology; Aarhus Universitet Sundhedsvidenskabelige Fakultet, Department of Public Health Bak Hansen, Lone; Zealand University Hospital Roskilde, Department of Plastic & Breast Surgery; University of Copenhagen Faculty of Health and Medical Sciences, Department of Clinical Medicine Ledertoug, Karen Marie; Zealand University Hospital Roskilde, Department of Plastic & Breast Surgery; Capital Region of Denmark, Copenhagen Emergency Medical Services Hølge-Hazelton, Bibi; Zealand University Hospital Roskilde, Research Support Unit; University of Southern Denmark, Department of Regional Health Research Schmidt, Volker ; Zealand University Hospital Roskilde, Department of Plastic & Breast Surgery; University of Copenhagen Faculty of Health and Medical Sciences, Department of Clinical Medicine
Primary Subject Heading:	Surgery
Secondary Subject Heading:	Nursing, Surgery, Health services research, Qualitative research
Keywords:	Breast surgery < SURGERY, Breast tumours < ONCOLOGY, Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT

TITLE: Electronic Patient-Reported Outcome Measures to enable systematic follow-up in treatment and care of women diagnosed with Breast Cancer: A Feasibility Study Protocol

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Word count: 4430

ABSTRACT

Introduction

The use of patient-reported outcome measures (PROMs) in clinical practice has the potential to promote person-centred care and improve patients' health-related quality of life. We aimed to develop an intervention centred around electronic PROMs (ePROMs) for systematic follow-up in patients diagnosed with breast cancer and to evaluate its feasibility.

Methods and analysis

We developed a nurse- and surgeon-oriented intervention in PROMs, including 1) an education programme for nurses and surgeons; 2) administration of BREAST-Q as proactive ePROMs during follow-up in patients diagnosed with breast cancer; and 3) feedback to nurses and surgeons on PROM scores and a guidance manual for healthcare practitioners. The feasibility evaluation includes qualitative ethnographic studies exploring the user perspectives of patients, nurses and surgeons, and quantitative studies to explore the characteristics of the patient population regarding demographic background, response rates and response patterns. The feasibility study was initiated in September 2021, will continue until 2024, and will include approximately 900 patients. EPROMs are collected at the following assessment time points: baseline (after diagnosis, before surgery), 1-year follow-up, and 3-year endpoint.

Ethics and dissemination

The study will be conducted according to the General Data Protection Regulation and the 5th version of the Helsinki Declaration. The National Committee on Health Research Ethics approved the study according to the law of the Committee § 1, part 4.

All data will be anonymised before its publication. The results of the feasibility study will be published in peer-reviewed, international journals.

Keywords: breast cancer, person-centred care, BREAST-Q, breast surgery, Patient-Reported Outcome Measures

Strengths and limitations of this study

- Breast cancer has a profound negative impact on the long-term well-being of women after treatment.
- Patient-reported outcome measures may support a systematic approach for improved person-centred care, including targeted, individual, psychosocial support and assessment of candidates for reconstructive and/or corrective breast surgical therapy. A digital approach to assessing surgery-related outcomes must be explored to prove its feasibility in patients with breast cancer.
- To our knowledge, this is the first study to investigate the proactive use of BREAST-Q as ePROMs in clinical practice for women diagnosed with breast cancer undergoing different types of reconstructive breast cancer surgeries.

INTRODUCTION

Breast cancer is one of the most common cancers, with 2.3 million women globally diagnosed with breast cancer in 2020 [1]. The survival rate of these women is 75% in most developed countries [2] and 90% in Denmark [3]. In Denmark, national screening programmes and improvements in breast cancer treatment have high priority in the healthcare system, and patients have several options for treatment [4]. The treatment of breast cancer is complex, multidisciplinary, and refers to standardised national guidelines by the Danish Breast Cancer Group to guarantee the highest standard of treatment and care [5].

Standard treatments in the curative setting of breast cancer include surgery and medical treatment as key components. The spectrum of surgical approaches for treating breast tumours includes breast-conserving therapy with or without the use of oncoplastic techniques, or mastectomy alone, or with primary or delayed reconstruction. Treatments may further include chemotherapy, radiation therapy, and hormone therapy [6–8]. Furthermore, follow-up with reconstructive corrective plastic surgery may support an increased self-rated quality of life [9,10]. Irrespective of the treatment intensity, patients are often long-term impaired by multiple side effects, including fatigue, sleep problems, pain, reduced mobility in the shoulder, and lymphedema in the arm [11]. Psychosocially, breast loss or changes in the appearance of the breast influence individual patients [12] who may experience negative psychological impacts, such as body image and sexuality concerns, worry, anxiety, depression, and stress [13–18]. Put together, these circumstances negatively affect the patients' self-rated Health-Related Quality Of Life (HRQOL) [19]. Hence, the assessment and monitoring of individual patient experiences are important in breast cancer surgery because the success of aesthetic breast surgery is

measured by the extent to which patients' physical, psychological, and social well-being are enhanced [7,18,20].

There is strong evidence that different forms of breast surgery and reconstruction positively affect patients' quality of life [21]. Previous research has identified that evaluating patients' outcomes of breast surgery and related psychosocial aspects through patient-reported outcome measurements (PROMs) might provide useful information for nurses, surgeons, and patients [22,23]. PROMs are defined as "any report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else [24]". Previous PROM research has found that proactive PROMs, meaning that the clinicians actively review the patients' PRO answers during therapy and use the feedback from patients to optimise the treatment and care [25,26], enable 1) earlier detection of symptoms; 2) improve communication between clinicians and patients about symptoms and HRQOL; and 3) increase the person-centredness of consultation processes [27–32]. A person-centred approach focuses on the care and treatment of the needs of individuals and ensures that individual preferences, needs, and values guide clinical decisions and that clinicians provide care that is respectful and responsive to patients [33]. Previous research in palliative care settings found that information on patients' perception of their state through PROMs may enable clinicians to enhance person-centred care and treatment if the perspectives and experiences of patients are revealed and integrated [34].

Research in PROMs has also identified several barriers to the implementation of PROMs in clinical practice [35–39]. Those barriers include limited time, lack of specification of use, insufficient knowledge of clinicians on how to use PROMs, lack of capacity, and electronic barriers from both patients and clinicians [35–38].

The Danish government and regions have agreed to initiate a nationwide extension of PROM use in breast cancer hospitals [4]. Accordingly, the Danish Breast Cancer Cooperative Group initiated a single-region PROM study on late effects in women diagnosed with breast cancer [40]. This initiative is expected to become national by around 2023. However, this initiative does not include the assessment of breast surgical outcomes or systematic follow-up at the hospital, which are the core elements of this study.

PROMs in the field of breast cancer surgery have the potential to involve patients by inviting them to contribute with their pre- and postoperative expert knowledge on their own experiences, values, and concerns. PROMs may be used for systematic and person-centred follow-ups related to surgical outcomes. This has yet to be demonstrated in clinical trials [41,42].

This protocol, version 1.2, 22 February 2022, describes the organisation and methodology behind a feasibility study on electronic patient-reported outcome measures (ePROMs) that are integrated in the treatment and care of women diagnosed with breast cancer in a plastic surgery and breast surgical outpatient setting of a tertiary university hospital. Given the emphasis on person-centred care in the organisation in which the study takes place, person-centred care is an underpinning theoretical perspective that aims to be incorporated into clinical practice; thus, the hypothesis in this multimethod study is that proactive use of ePROMs (including dialogue on satisfaction and HRQOL outcomes), promotes mutual understanding of patients' preferences during patient trajectories at the outpatient clinic and improves patient care and communication by 1) focusing person-centred care on individual values and concerns related to surgical outcomes and psychosocial care during surgical follow-up and 2) systematic assessment of patients' potential need for supplemental breast surgery, including reconstruction or

correction, to improve patients' well-being related to breast and body image after breast cancer. Hence, the overall aim of this study is to develop knowledge on the proactive application of ePROMs in breast surgical and breast reconstructive clinical practice.

METHODOLOGY

Study Design

This is a multimethod, non-controlled feasibility study [43,44] to investigate whether an intervention with ePROMs can be shaped to be relevant and sustainable in clinical practice. In this study, the term feasibility was inspired by Bowen et al. (2009) who introduce the term *feasibility study* for a more broad use to encompass any sort of study that can help investigators prepare for full-scale research leading to intervention study [44]. We investigated and evaluated feasibility outcome variables including acceptability, demand, implementation, practicality, and integration as described by Bowen and colleagues throughout three sub-studies (Figure 1 and Table 1) with the following aims:

Study I) To explore patients' experiences related to acceptability, practicality, and demands on completion of PROMs following physical meetings at the department with nurses and surgeons.

Study II) To investigate the nurses' and surgeons' experiences related to acceptability, implementation, practicality, and proactive application of the PROM intervention in clinical practice.

Study III) To analyse baseline PROM data after 1 year, including outcomes and demographic variables for responders and non-responders.

The multimethod study includes the development of an ePROM intervention with repeated collection of ePROMs at timings (T) T1, T2, and T3 using the BREAST-Q tool and proactive use of ePROMs during follow-up visits at the department, and an evaluation of feasibility (Figure 1 and Figure 2). Studies I and II are qualitative ethnographic studies exploring the user perspectives of patients, nurses, and surgeons to gain insights into how the intervention can be refined. Additionally, Study II is complemented with a local anonymous survey study in collaboration with department nurses and surgeons to investigate user experiences, individual activities, perceived demand, preferences, and proactive application related to the ePROM intervention. Qualitative studies are guided by interpretive description (ID), an inductive methodology developed to explore clinical problems with the objective of generating insights that inform clinical practice [45]. ID draws upon recognised qualitative research techniques from ethnography, naturalistic inquiry, grounded theory, and phenomenology but focuses on explicit research logic and flexibility, permitting researchers to apply and combine the necessary pragmatic strategies to answer the research question [46]. The composition of an ID study is guided by distinctive features, including: scaffolding the study, framing the study, a credible study, entering the field, constructing data, making sense of data, and conceptualising findings[46]. The result is a coherent, conceptual description containing understandings and illuminations of clinical phenomena, characteristics, patterns, and structures in order to develop practice. The ID methodology will support understanding and knowledge related to the feasibility study outcomes.

Quantitative study III includes the PROM data from T1 to explore the patient population and their outcomes at baseline (Figure 2) [47]. This protocol describes a feasibility study

only. The evaluations of PROM data T2 and T3 will be reported elsewhere. Guidelines for Inclusion of Patient-Reported Outcomes in Clinical Trial Protocols: The SPIRIT-PRO Extension [48] were used to report the protocol (Supplementary Material 1).

Table 1 Key areas of focus for the feasibility study inspired by Bowen et al.(2009)

Feasibility outcomes/areas of focus	What is explored	Sample outcomes of interest	Explored in study		
			I	II	III
Acceptability	To what extent is the ePROM intervention suitable, satisfying, or attractive to programme deliverers? To programme recipients?	• Satisfaction • Intent to continue use • Perceived appropriateness • Completion rate	X	X	X
Demand	To what extent is the ePROM intervention likely to be used? When, how, and why do the nurses and surgeons actively review the patients' PROM answers during consultations, and how do they use the feedback from patients?	• Proactive use of ePROMs • Fit within organizational culture • Perceived positive or negative effects on organization • Actual use • Expressed interest or intention to use • Perceived demand	X	X	X
Implementation	To what extent can the ePROM intervention be successfully delivered to intended participants in some defined, but not fully controlled, context?	• Degree of execution • Success or failure of execution • Amount, type of resources needed to implement	X	X	
Practicality	To what extent can the ePROM intervention be carried out with intended participants using existing means, resources, and circumstances and without outside intervention?	• Factors affecting implementation ease or difficulty • Efficiency, speed, or quality of implementation • Positive/negative effects on target participants • Ability of participants to carry out intervention activities	X		X
Integration	To what extent can the ePROM intervention be integrated within the existing system/clinical practice?	• Perceived fit with infrastructure		X	X

		• Perceived sustainability			

Study participants

Patient participants are women with newly diagnosed breast cancer, who will be included in the multimethod study from September 2021 to September 2024, and the follow-up time will end in January 2028.

Inclusion criteria:

- Female patients age ≥18
- Newly diagnosed breast cancer that is treated with curative surgical therapy to remove breast cancer
- The ability to speak and understand Danish to comprehend the given information, complete the study questionnaires, and provide written informed consent.

Exclusion criteria:

- Treated with letrozol aromatase inhibitor hormone therapy as primary treatment (nonsurgical regime, therefore outcome measures of satisfaction with surgical result are not relevant)
- Not assigned digital information in the Danish Civil Registration System (Figure 2)
- Non-Danish speaking
- Any disability making ePROM follow-up impossible, such as blindness or mental disability, or a diagnosis of dementia.

Exclusion is assessed based on the medical record journal by a research assistant in collaboration with a breast surgeon at the department affiliated with the study. Approximately 600 women are newly diagnosed with breast cancer at the Department of

Plastic and Breast Surgery of Zealand University Hospital each year. Patients will be included continuously for 3 years. A minimum sample of 900 patients is expected to be included.

For qualitative studies I and II, patient participants are purposefully sampled from consenting to the ePROM intervention using the maximum variation concept [45]. Nurses and surgeons included for the qualitative studies are those whom the patients met during their visit on the day of observation by the present researcher. The patients' visits are pre-booked, and patients visit either a nurse, surgeon, or a surgeon and a nurse in one consultation. An anonymous survey will be distributed to all nurses and surgeons at the outpatient clinic as part of study II.

Recruitment procedures

Patients are recruited from the Department of Plastic and Breast Surgery at a large centre of plastic and breast surgery located at a tertiary Danish university hospital. The departments' research assistants are responsible for identifying and inviting patients who meet the inclusion criteria.

Patients eligible for inclusion are informed and invited through a digital postbox (e-Boks) to the ePROM intervention [49]. The invitation is supported by a four-minute video developed by the research assistant and a patient and public representative, which provides patient information about the aims of the ePROM-intervention. Furthermore, the patients receive a postcard at the outpatient clinic, which informs them about the ePROM intervention when they are diagnosed. Patients receive a link to the ePROM questionnaires in their digital postbox via the secure encrypted electronic system Research Electronic Data Capture (REDCap) [50]. Patients may consent or decline through invitation by mail. Patients may complete questionnaires on a PC, tablet, or

smartphone. The questionnaire is open for completion 14 days after invitation. After two days, a notification is automatically forwarded if no response is received. After 4 days, the research assistant calls and asks patients who have not responded to the invitation if they need assistance with the questionnaire. A research nurse assistant may assist with technical issues, if any. Patients included in the study can withdraw consent to participate without justification and without affecting the present or future treatment at any time. Patients withdrawing consent will be considered as 'lost to follow-up'. Patients who decline to participate are registered within an encrypted database as non-responders. Nurses and surgeons at outpatient clinics have access to patients' ePROM data through REDCap, including detailed responses and the total score of each questionnaire.

Strategies for the introduction of ePROMs

The introduction strategies related to this study aim to enable systematic and flexible implementation of ePROMs in an outpatient setting [15]. The strategy includes establishing an ePROM-intervention support group, a nurse education programme, and a surgeon education programme. As part of the strategy, ePROM intervention is described in detail within a clinical guideline developed with the ePROM-intervention support group. The guideline includes instructions for nurses, surgeons, and secretaries on their specific responsibilities related to the ePROM intervention. One part of the strategy is a steering group plus education programmes for the departments' nurses and surgeons.

Patient and public involvement

The study is supported by a patient and public representative from the Danish Cancer Society, who is an equal member of the study steering group. The representative was 'involved throughout the design phase, for instance, contributing to the formulation of

research questions and agreeing plans for dissemination of the study to participants. The representative continuously informed the study about patients' and public priorities, experiences and preferences and the representative will participate in the analysis of data.

The ePROM steering group

The ePROM intervention is delivered by a steering group of experts who assist in the implementation of ePROMs. The group consists of an outpatient nurse from the department, a breast surgeon, a secretary, the patient and public representative, a nurse research assistant, a leading head nurse, a leading chief surgeon, and a responsible nurse researcher. In addition, three external researchers are affiliated with the intervention study as supervisors and are experts in PROMs, statistics, qualitative methodology, and person-centred practice.

Nurse education programme

Before the PROM intervention, all nurses at the breast surgical outpatient clinic participated in face-to-face training on the use of ePROMs. The educational sessions were guided by person-centred care theory and included a brief lecture on person-centredness and person-centred communication, which supports previous departmental education for nurses, in which person-centred values have been inherent.

Training on the application of ePROMs during consultations was mandatory and provided by departments' clinical nurse specialist and research assistant and lasted for four hours. Nurses were expected to be the main users of PROM data for psychosocial support and conversations with patients, for example, on body image. Therefore, the nurses' education was planned to be more comprehensive 'than the surgeons' education,

and included skills training. The education programme included a broad introduction to PROMs and examples of proactive use of PROMs from other departments and research [51,52]. The educational programme was planned with didactical consideration for research-based teaching and teaching for learning, and with a focus on interaction and activation during sessions with case-based learning [53,54]. The training programmes included: how to access the timely and relevant individual patients' ePROMs linked to nurse consultations; how to respond to ePROMs in terms of caring for individuals with psychosocial support and symptom management; how to proactively engage in the discussion of PROM data with patients; and how to document nurses' application of PROMs in patient care. The intervention is associated with monthly 1-hour internal educational sessions that address issues related to the proactive use of ePROMs in clinical practice to improve outpatient nurses' knowledge and skills in relevant issues such as body image-related distress [55]. Nurses' use of ePROMs is evaluated every third month using a paper questionnaire and a 1-hour dialogue with the responsible researcher.

Surgeons' education programme

'Prior to commencing the PROM intervention, surgeons from the department participated in a 1-hour mandatory education programme about the ePROM-intervention, which provided information about its objectives, processes, and rationales, including how to proactively engage with ePROMS with patients. Once a month, surgeons participate in further follow-up training on PROMs, which is conducted by the responsible researcher and a clinical nurse specialist. The sessions include practical training on how to access the timely and relevant individual patients' ePROMs linked to surgeons' consultations as a comparison of the T1 and T2 questionnaires (Table 2); how to engage with and respond to ePROMs in terms of person-centred surgical follow-up in ePROMs with patients; and

how to document surgeons' application of PROMs in the medical record journal. Didactical considerations correspond to those mentioned in the nurses' education programmes.

Table 2. Study assessment times, measures and tasks

Data Collection		**Baseline (T1*)**	**Follow-up[1] (T2)**	**Endpoint (T3)**
All patient participants (ePROM group)	Informed consent	●		
	Demographic data[2]	●		
	Breast Cancer Core Scale (Pre- and postoperative): Satisfaction with Breasts[3]	●	❷❸	
	Breast Cancer Core Scale (Preoperative): Physical Well-Being: Chest[3]	●		
	Breast Cancer Core Scale (Pre- and Postoperative): Psychosocial Well-Being[3]	●	❶❷❸	●
	Breast Cancer Core Scale (Pre- and Postoperative): Sexual Well-Being[3]	●	❶❷❸	●
	Breast Conserving Therapy Module (Postoperative): Satisfaction with Breasts[3]		❶	
	Breast Conserving Therapy Module (Postoperative): Physical Well-Being: Chest[3]		❶	
	Breast Cancer Core Scale (Pre- and Postoperative): Physical Well-Being: Chest[3]		❷❸	●
	Reconstruction Module (Postoperative): Satisfaction with Breasts[3]			●
	[A]Reconstruction Module (Postoperative): Satisfaction with Nipple Reconstruction[3]			●
	[A]Reconstruction Module (Postoperative): Satisfaction with Implants[3]			●
	[A]Latissimus Dorsi Module (Postoperative): Satisfaction with Back[3]			●
Invited non-respondents	Reasoning for study dropout			
User perspectives	Participant observations during patient consultations	◊	◊	
	Individual interviews with patients	◊	◊	
	Individual interviews with nurses	◊	◊	
	Survey with nurses and surgeons		◊	

*Timing (T) and questionnaire distribution number, [1]Patients after surgical therapy: ❶ initial breast conserving therapy, ❷ initial mastectomy, ❸ initial immediate reconstruction; [1]Demographic data (identification-number, age, marital status, educational level, body mass index, zip code); [3]BREAST-Q™ version 2.0 Questionnaire scale; [a]Individual supplementary modules.

Intervention with ePROMs

The ePROM intervention includes patients' completion of ePROMs related to satisfaction with breasts, physical well-being, psychosocial well-being, and sexual well-being, which are to be proactively applied in patients' trajectory to monitor the individual patient's condition and accommodate individualised psychosocial and surgical follow-up based on patient preferences and values. Over a 3-year period, the patients receive two to three questionnaires, depending on their trajectory, with treatment arms surgical therapy upfront or neoadjuvant therapy before surgical therapy (Figure 2 and Table 2). The ePROMs are to be actively reviewed by departments' nurses before the patient's visit at the following times: first, prior to the patient's 4-day postoperative control with a nurse (T1, baseline data completed before surgery); second, for the 1-year follow-up (T2, follow-up completed 11 or 18 months after surgery, dependant on treatment regime), which is initially a nurse consultation. The rationale for using baseline PROMs completed before surgery for the 4-day postoperative is: 1) The patient's assessment of breasts before the surgery is recommended to be actively discussed with the patient in relation to the choice of breast prosthesis, bra, and life with a changed body after breast cancer; 2) The baseline measurement is essential to monitor patients' satisfaction with breasts over time, and surgical results are best evaluated at the earliest one year after surgery [56]. Patients in the low-risk recurrence regime have standardized 1-year postoperative follow-up with nurses, where ePROMs are to be applied. Patients in high-risk recurrence regimes are not offered as standard breast surgical follow-up, but this is offered to patients through the ePROM intervention. During the second follow-up, nurses are educated to proactively use patients' ePROMs for dialogue about patients' perception of body image issues related to their breasts. Based on patients' individual needs, the nurse may recommend the patient for further assessment with one of the department's plastic surgeons, who will

also have the ePROMs for comparison (Table 2). Patients who accept correction or reconstruction of the breasts after their 1-year follow-up, the T2, receive a third ePROM 18 months after T2, as patients are expected to have finished their breast surgical trajectory at this point (T3, endpoint).

Data collection and measurements

The outcomes of the multimethod study relate to feasibility parameters, including acceptability, proactive use of ePROMs, demand, implementation (degree of execution), practicality, and integration (perceived sustainability and fit with infrastructure), as described by Bowen et al. (2009) [44]. These will be conducted through multiple measurements and outcomes in Studies I to III. The data to be analysed in sub-studies I to III are collected as follows:

Ethnographic studies I and II

Feasibility data are collected qualitatively by exploring the user perspectives of patients, nurses, and surgeons to gain insights into how the intervention can be refined. Qualitative studies I and II investigate users' interests related to using ePROMs and practice interests that can drive or limit development. User experiences of patients, nurses, and surgeons will be qualitatively explored and guided by the interpretive description methodology for applied research [45].

For studies I and II, data collection includes participant observations during patient consultations with nurses and surgeons and individual interviews with patients, nurses, and surgeons to explore the application of ePROMs in clinical practice and the implications for practice. The time of the observations will follow the appointment times for the consultations (see Figure 2). An observation and interview guide is developed based on the researchers' experiences as a nurse at the department, which

also allows entry into department consultations [45]. The participant observations and interviews will be conducted by the first author with a focus on whether, when, how, by whom, why, or why not, the ePROMs are proactively used. This work calls for critical reflection and transparency on the researcher's positioning, degree of participation and ability to disregard the professional lens from one's practice discipline [45,57–59]. This will be reported with the results of the studies. For study II, the survey with nurses and surgeons is conducted as an online survey with questions developed specifically for this study to investigate perceptions, defined as the way in which the intervention is regarded, understood, and interpreted [60] as well as feasibility [47], based on the principles of applied research [45].

Study III on PROMs data

PROMs are collected electronically via REDCap at time points T1, T2, and T3 (Table 2). Additional baseline demographics for Study III data are collected electronically via REDCap within T1 (Figure 2 and Table 2) and include age, marital status, educational level, height, weight, body mass index, and municipality [50]. The PROM used for the intervention is BREAST-Q, as recommended by the International Consortium for Health Outcomes Measurement (ICHOM) standard order set for breast cancer patients to monitor PROMs following breast surgery [61]. BREAST-Q was developed according to recommended guidelines through patient interviews, focus groups, an expert panel, and a literature review and has undergone thorough validation with measures of high reliability which use both the paper and the electronic version [41,62–65]. BREAST-Q was designed specifically for breast surgery and has pre- and post-operative versions in modules for mastectomy, breast-conserving therapy, breast reconstruction, breast reduction, and breast augmentation [66]. All modules contain three subdomains,

including physical, psychosocial, and sexual well-being, and three sub-domains on patient satisfaction, comprising satisfaction with breasts, outcome, and care. No overall BREAST-Q scores are obtained. Each independent scale results in a score that is computed by adding the response items and then converting the raw sum scale score to a score from to 0–100 [67]. For all BREAST-Q scales, a higher score indicates greater satisfaction or better QOL (depending on the scale). If missing data are less than 50% of the scale's items, the mean of the completed items are inserted. Each set of questionnaires, for instance BREAST-Q questionnaire 1, takes 5–10 minutes to complete. Each scale is accompanied by a conversion table to calculate a total scale score of 0–100 [22,67].

Analysis

Qualitative studies I and II

The interviews and observations will be analysed in relation to user perspectives guided by ID. ID does not prescribe a straightforward data analysis process but relies on the pragmatic obligation of the researchers to work on data beyond initial descriptive claims towards interpretations that will enlighten the phenomenon investigated in a new and meaningful manner [68]. The ID analysis aims to make sense of what has been observed and heard through an explorative process in which questions are continuously posed about the data, and answers are sought to generate explanations supported by theory [46,68]. The analysis for studies I and II will be inspired by the theoretical framework of person-centred care to evaluate the feasibility of the proactive ePROM intervention by questioning whether the ePROM intervention supports the intentions on targeted, individual, psychosocial support and assessment of candidates for reconstructive and/or corrective breast surgical therapy. Specifically, the parameters of acceptability, demand, introduction, practicality, and integration will be elaborated throughout the analysis

(Table 1) [33,45]. These outcomes will be informed and further analysed from the observation and interview data that is expected to add rigorous information on priorities, mechanisms and practicalities in the outpatient clinic to answer the study aims [46,68].

Study III – Statistical analysis

Descriptive statistics and completion rate will be calculated for all demographic variables for both responders and non-responders to the BREAST-Q questionnaire, based on data from T1 (baseline). Depending on the normality of the numerical variables, means (SD) or medians (interquartile range) will be calculated, while categorical variables will be expressed as proportions. Differences will be analysed using t-tests, Mann-Whitney U tests, and chi-squared tests. Furthermore, among responders, linear regression models will be used to identify which demographic variables are associated with the subscale scores from the BREAST-Q questionnaire. All variables will be entered into univariate and multivariate regression models to identify demographic variables that were independently associated with the questionnaire scores. Data will be analysed using the Stata software package [69]. The significance level will be set at $p < .05$, and all tests will be two-tailed. If applicable, sensitivity analysis using multiple imputation will be conducted on item-wise missing responses if the rate of missing data exceeds 5%.

ETHICS AND DISSEMINATION

The patients provide informed consent, which they can withdraw at any time. Data will be stored in REDCap and on an encrypted regional team site for sensitive personal research data. The study is designed according to the General Data Protection Regulation (GDPR) and adheres to the principles defined by the World Medical Association in the Helsinki Declaration. The use of the BREAST-Q questionnaire, authored by Drs Klassen,

Pusic, and Cano, was licensed by the Memorial Sloan Kettering Cancer Center, New York, USA.

The findings of this study will be submitted to international peer-reviewed journals and presented at conferences.

CONCLUSIONS

The study will generate detailed information on the feasibility aspects of the ePROM intervention for person-centred follow-up. Details include the users' experiences related to the proactive use of ePROMs and the practical interests that can drive its development. Furthermore, the study will explore whether a systematic approach to the patients' experiences of satisfaction with breasts, physical well-being, psychosocial well-being, and sexual well-being in ePROMs with patients can function as enablers and triggers for the integration of person-centred care in follow-up consultations. This study will generate evidence-based knowledge on the feasibility and effects of a digital approach to assessing and integrating surgery-related well-being and aesthetic outcomes in patients with breast cancer. To our knowledge, this is the first study to investigate the proactive use of BREAST-Q as an ePROM in clinical practice for women diagnosed with breast cancer.

DECLARATIONS

Acknowledgements

KH Karlsen for representing patients and public into the study design. JH Prüsse for building the research database.

Competing interests

The authors do not have any conflicts to declare.

Patient consent for publication

Not applicable.

Authors' contributions

STH was responsible for the initial study design and the grant application, and is responsible for supervising as project leader. STH, VJS, KML and KP did the background research and were responsible for the protocol's in-depth development and drafting of this manuscript, including its figures and tables. LBH and BHH helped supervise. KP, LBH and BHH contributed with thorough revisions to the manuscript. All authors read and approved the final manuscript.

Funding

This work was supported by Region Zealand, National Cancer Plan IV [grant number 20-082, 2020]. The Region Zealand has not been part of designing the study, nor will the region be part of the analysis or interpretation of data. The Department of Plastic- and Breast Surgery, Zealand University Hospital and The University of Southern Denmark covers STH's salary. KP, BHH, KML, and VJS are currently not receiving a salary for this work.

Ethics Approval

The study is approved by the Danish Data Protection Agency (REG-104-2021) and the National Committee on Health Research Ethics (SJ-914, EMN-2021-01530).

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Supplemental material

Supplementary material 1 - SPIRIT 2013 and SPIRIT-PRO Extension Checklist

Legends

Figure 1. Illustration of the multimethod feasibility study, the intervention and sub-studies

Figure 2. Illustration of the ePROM-intervention flowchart. Dark boxes illustrate intervention features. T1, T2, and T3 refer to the timely specific questionnaires that are sent to the patients.

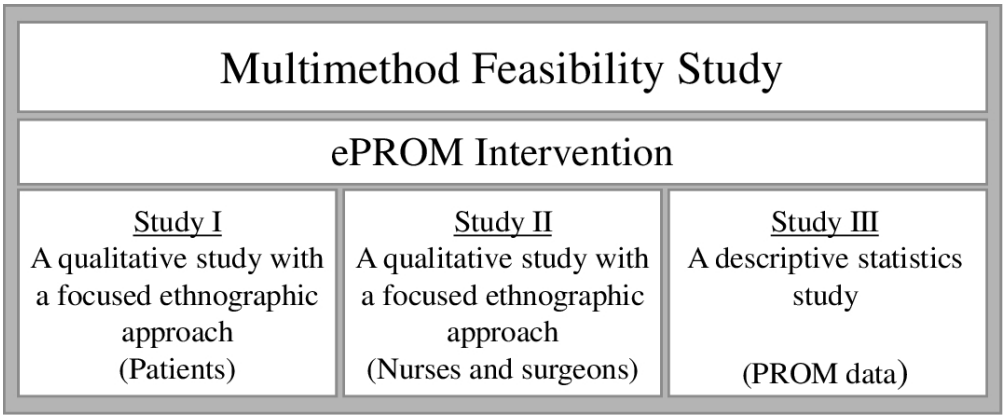

Figure 1. Illustration of the multimethod feasibility study, the intervention and sub-studies

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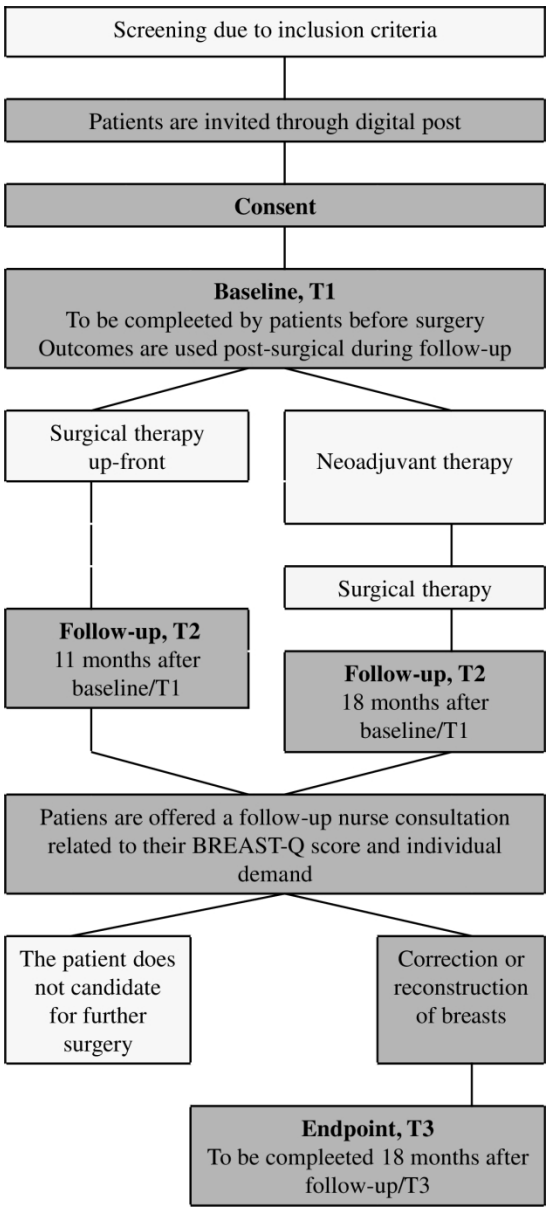

Figure 2. Illustration of the ePROM-intervention flowchart. Dark boxes illustrate intervention features. T1, T2, and T3 refer to the timely specific questionnaires that are sent to the patients.

97x215mm (300 x 300 DPI)

SPIRIT 2013 AND SPIRIT-PRO EXTENSION CHECKLIST: RECOMMENDED ITEMS TO ADDRESS IN A CLINICAL TRIAL PROTOCOL AND RELATED DOCUMENTS*

SPIRIT Section/item	SPIRIT Item No	SPIRIT Item Description	SPIRIT-PRO Item No	SPIRIT-PRO Extension or Elaboration Item Description	Page **
Administrative information					
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym			p.1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry			-
	2b	All items from the World Health Organization Trial Registration Data Set			-
Protocol version	3	Date and version identifier			p.6
Funding	4	Sources and types of financial, material, and other support			p.19
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	SPIRIT-5a-PRO elaboration	Specify the individual(s) responsible for the PRO content of the protocol	p.19
	5b	Name and contact information for the trial sponsor			-

	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities			-
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)			-
Introduction					
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	SPIRIT-6a-PRO Extension	Describe the PRO-specific research question and rationale for PRO assessment and summarize PRO findings in relevant studies.	p.6
	6b	Explanation for choice of comparators			-
Objectives	7	Specific objectives or hypotheses	SPIRIT-7-PRO Extension	State the specific PRO objectives or hypothesis (including relevant PRO concepts/domains).	p.16
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)			p.2
Methods: Participants, interventions, and outcomes					

Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained			p.6
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	SPIRIT-10-PRO Extension	Specify any PRO-specific eligbility citeria (eg, language/reading requirements or prerandomization completion of PRO). If PROs will not be collected from the entire study sample, provide a rationale and describe the method for obtaining the PRO subsample	p.8
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered			p.14
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)			-
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)			p.10
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial			-
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	SPIRIT-12-PRO Extension	Specify the PRO concepts/domains used to evaluate the intervention (eg, overall health-related quality of life, specific domain, specific symptom) and, for each one, the analysis metric (eg, change from baseline, final value, time to event) and the principal time point or period of interest.	p.15

Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	SPIRIT-13-PRO Extension	Include a schedule of PRO assessments, providing a rationale for the time points, and justifying if the initial assessment is not prerandomization. Specify time windows, whether PRO collection is prior to clinical assessments, and, if using multiple questionnaires, whether order of administration will be standardized.	Fig. 2
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	SPIRIT-14-PRO Elaboration	When a PRO is the primary end point, state the required sample size (and how it was determined) and recruitment target (accounting for expected loss to follow-up). If sample size is not established based on the PRO end point, then discuss the power of the principal PRO analyses.	p.9
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size			p.9
Methods: Assignment of interventions (for controlled trials)					
Allocation:					
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions			-
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned			-

Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions			-
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how			-
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial			-
Methods: Data collection, management, and analysis					p.15
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	SPIRIT-18a (i)-PRO Extension	Justify the PRO instrument to be used and describe domains, number of items, recall period, and instrument scaling and scoring (eg, range and direction of scores indicating a good or poor outcome). Evidence of PRO instrument measurement properties, interpretation guidelines, and patient acceptability and burden should be provided or cited if available, ideally in the population of interest. State whether the measure will be used in accordance with any user manual and specify and justify deviations if planned.	
			SPIRIT-18a (ii)-PRO Extension	Include a data collection plan outlining the permitted mode(s) of administration (eg, paper, telephone, electronic, other) and setting (eg, clinic, home, other).	p.15

			SPIRIT-18a (iii)-PRO Extension	Specify whether more than 1 language version will be used and state whether translated versions have been developed using currently recommended methods.	p.8
			SPIRIT-18a (iv)-PRO Extension	When the trial context requires someone other than the trial participant to answer on his or her behalf (a proxy-reported outcome), state and justify the use of a proxy respondent. Provide or cite evidence of the validity of proxy assessment if available.	-
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	SPIRIT-18b (i)-PRO Extension	Specify PRO data collection and management strategies for minimizing avoidable missing data.	p.10
			SPIRIT-18b (ii)-PRO Elaboration	Describe the process of PRO assessment for participants who discontinue or deviate from the assigned intervention protocol.	p.10
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol			p.10, 17
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	SPIRIT-20a-PRO Elaboration	State PRO analysis methods, including any plans for addressing multiplicity/type I (α) error.	p.17

	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)			
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	SPIRIT-20c-PRO Elaboration	State how missing data will be described and outline the methods for handling missing item or entire assessments (eg, approach to imputation and sensitivity analyses)	p.17
Methods: Monitoring					
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed			p.11
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial			-
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	SPIRIT-22-PRO Extension	State whether or not PRO data will be monitored during the study to inform the clinical care of individual trial participants and, if so, how this will be managed in a standardized way. Describe how this process will be explained to participants; eg, in the participant information sheet and consent form.	p.12
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor			-

Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	p.19
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	p.11
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	p.17
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	-
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	p.3
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	p.18
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	p.6
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	-

Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	p.18
	31b	Authorship eligibility guidelines and any intended use of professional writers	-
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	-
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	-
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	-

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

**page numbers refers to protocol paper

BMJ Open

Electronic Patient-Reported Outcome Measures to enable systematic follow-up in treatment and care of women diagnosed with Breast Cancer: A Feasibility Study Protocol

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2022-065110.R2
Article Type:	Protocol
Date Submitted by the Author:	26-Oct-2022
Complete List of Authors:	Thestrup Hansen, Stine; Zealand University Hospital Roskilde, Department of Plastic & Breast Surgery; University of Southern Denmark Faculty of Health Sciences, Department of Regional Health Research Piil, Karin; Copenhagen University Hospital Centre for Cancer and Organ Diseases, Department of Oncology; Aarhus Universitet Sundhedsvidenskabelige Fakultet, Department of Public Health Bak Hansen, Lone; Zealand University Hospital Roskilde, Department of Plastic & Breast Surgery; University of Copenhagen Faculty of Health and Medical Sciences, Department of Clinical Medicine Ledertoug, Karen Marie; Zealand University Hospital Roskilde, Department of Plastic & Breast Surgery; Capital Region of Denmark, Copenhagen Emergency Medical Services Hølge-Hazelton, Bibi; Zealand University Hospital Roskilde, Research Support Unit; University of Southern Denmark, Department of Regional Health Research Schmidt, Volker ; Zealand University Hospital Roskilde, Department of Plastic & Breast Surgery; University of Copenhagen Faculty of Health and Medical Sciences, Department of Clinical Medicine
Primary Subject Heading:	Surgery
Secondary Subject Heading:	Nursing, Surgery, Health services research, Qualitative research
Keywords:	Breast surgery < SURGERY, Breast tumours < ONCOLOGY, Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT

TITLE: Electronic Patient-Reported Outcome Measures to enable systematic follow-up in treatment and care of women diagnosed with Breast Cancer: A Feasibility Study Protocol

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Word count: 4430

ABSTRACT

Introduction

The use of patient-reported outcome measures (PROMs) in clinical practice has the potential to promote person-centred care and improve patients' health-related quality of life. We aimed to develop an intervention centred around electronic PROMs (ePROMs) for systematic follow-up in patients diagnosed with breast cancer and to evaluate its feasibility.

Methods and analysis

We developed a nurse- and surgeon-oriented intervention in PROMs, including 1) an education programme for nurses and surgeons; 2) administration of BREAST-Q as proactive ePROMs during follow-up in patients diagnosed with breast cancer; and 3) feedback to nurses and surgeons on PROM scores and a guidance manual for healthcare practitioners. Subsequently, we designed a non-controlled feasibility evaluation on the outcomes acceptability, demand, implementation, practicality and integration. The feasibility evaluation includes qualitative ethnographic studies exploring the user perspectives of patients, nurses and surgeons, and quantitative studies to explore the characteristics of the patient population regarding demographic background, response rates and response patterns. The feasibility study was initiated in September 2021, will continue until 2024, and will include approximately 900 patients. EPROMs are collected at the following assessment time points: baseline (after diagnosis, before surgery), 1-year follow-up, and 3-year endpoint.

Ethics and dissemination

The study will be conducted according to the General Data Protection Regulation and the 5th version of the Helsinki Declaration. The National Committee on Health

Research Ethics approved the study according to the law of the Committee § 1, part 4. All data will be anonymised before its publication. The results of the feasibility study will be published in peer-reviewed, international journals.

Keywords: breast cancer, person-centred care, BREAST-Q, breast surgery, Patient-Reported Outcome Measures

- **Strengths and limitations of this study**Patient-reported outcome measures may support a systematic approach for improved person-centred care, including targeted, individual, psychosocial support and assessment of candidates for reconstructive and/or corrective breast surgical therapy.
- This study will generate detailed information on the feasibility aspects of the ePROM intervention for person-centred follow-up in women diagnosed with breast cancer.
- This multi-method study will result in both detailed, contextualized insights of qualitative data and the generalizable, externally valid insights of quantitative data.
- To our knowledge, this is the first study to investigate the proactive use of BREAST-Q as ePROMs in clinical practice for women diagnosed with breast cancer undergoing different types of reconstructive breast cancer surgeries.

INTRODUCTION

Breast cancer is one of the most common cancers, with 2.3 million women globally diagnosed with breast cancer in 2020 [1]. The survival rate of these women is 75% in most developed countries [2] and 90% in Denmark [3]. In Denmark, national screening programmes and improvements in breast cancer treatment have high priority in the healthcare system, and patients have several options for treatment [4]. The treatment of breast cancer is complex, multidisciplinary, and refers to standardised national guidelines by the Danish Breast Cancer Group to guarantee the highest standard of treatment and care [5].

Standard treatments in the curative setting of breast cancer include surgery and medical treatment as key components. The spectrum of surgical approaches for treating breast tumours includes breast-conserving therapy with or without the use of oncoplastic techniques, or mastectomy alone, or with primary or delayed reconstruction. Treatments may further include chemotherapy, radiation therapy, and hormone therapy [6–8]. Furthermore, follow-up with reconstructive corrective plastic surgery may support an increased self-rated quality of life [9,10]. Irrespective of the treatment intensity, patients are often long-term impaired by multiple side effects, including fatigue, sleep problems, pain, reduced mobility in the shoulder, and lymphedema in the arm [11]. Psychosocially, breast loss or changes in the appearance of the breast influence individual patients [12] who may experience negative psychological impacts, such as body image and sexuality concerns, worry, anxiety, depression, and stress [13–18]. Put together, these circumstances negatively affect the patients' self-rated Health-Related Quality Of Life (HRQOL) [19]. Hence, the assessment and monitoring of individual patient experiences are important in breast cancer surgery because the success of aesthetic breast surgery is

measured by the extent to which patients' physical, psychological, and social well-being are enhanced [7,18,20].

There is strong evidence that different forms of breast surgery and reconstruction positively affect patients' quality of life [21]. Previous research has identified that evaluating patients' outcomes of breast surgery and related psychosocial aspects through patient-reported outcome measurements (PROMs) might provide useful information for nurses, surgeons, and patients [22,23]. PROMs are defined as "any report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else [24]". Previous PROM research has found that proactive PROMs, meaning that the clinicians actively review the patients' PRO answers during therapy and use the feedback from patients to optimise the treatment and care [25,26], enable 1) earlier detection of symptoms; 2) improve communication between clinicians and patients about symptoms and HRQOL; and 3) increase the person-centredness of consultation processes [27–32]. A person-centred approach focuses on the care and treatment of the needs of individuals and ensures that individual preferences, needs, and values guide clinical decisions and that clinicians provide care that is respectful and responsive to patients [33]. Previous research in palliative care settings found that information on patients' perception of their state through PROMs may enable clinicians to enhance person-centred care and treatment if the perspectives and experiences of patients are revealed and integrated [34].

Research in PROMs has also identified several barriers to the implementation of PROMs in clinical practice [35–39]. Those barriers include limited time, lack of specification of use, insufficient knowledge of clinicians on how to use PROMs, lack of capacity, and electronic barriers from both patients and clinicians [35–38].

The Danish government and regions have agreed to initiate a nationwide extension of PROM use in breast cancer hospitals [4]. Accordingly, the Danish Breast Cancer Cooperative Group initiated a single-region PROM study on late effects in women diagnosed with breast cancer [40]. This initiative is expected to become national by around 2023. However, this initiative does not include the assessment of breast surgical outcomes or systematic follow-up at the hospital, which are the core elements of this study.

PROMs in the field of breast cancer surgery have the potential to involve patients by inviting them to contribute with their pre- and postoperative expert knowledge on their own experiences, values, and concerns. PROMs may be used for systematic and person-centred follow-ups related to surgical outcomes. This has yet to be demonstrated in clinical trials [41,42].

This protocol, version 1.2, 22 February 2022, describes the organisation and methodology behind a feasibility study on electronic patient-reported outcome measures (ePROMs) that are integrated in the treatment and care of women diagnosed with breast cancer in a plastic surgery and breast surgical outpatient setting of a tertiary university hospital. Given the emphasis on person-centred care in the organisation in which the study takes place, person-centred care is an underpinning theoretical perspective that aims to be incorporated into clinical practice; thus, the hypothesis in this multimethod study is that proactive use of ePROMs (including dialogue on satisfaction and HRQOL outcomes), promotes mutual understanding of patients' preferences during patient trajectories at the outpatient clinic and improves patient care and communication by 1) focusing person-centred care on individual values and concerns related to surgical outcomes and psychosocial care during surgical follow-up and 2) systematic assessment of patients' potential need for supplemental breast surgery, including reconstruction or

correction, to improve patients' well-being related to breast and body image after breast cancer. Hence, the overall aim of this study is to develop knowledge on the proactive application of ePROMs in breast surgical and breast reconstructive clinical practice.

METHODOLOGY

Study Design

This is a multimethod, non-controlled feasibility study [43,44] to investigate whether an intervention with ePROMs can be shaped to be relevant and sustainable in clinical practice. In this study, the term feasibility was inspired by Bowen et al. (2009) who introduce the term *feasibility study* for a more broad use to encompass any sort of study that can help investigators prepare for full-scale research leading to intervention study [44]. We investigated and evaluated feasibility outcome variables including acceptability, demand, implementation, practicality, and integration as described by Bowen and colleagues throughout three sub-studies (Figure 1 and Table 1) with the following aims:

Study I) To explore patients' experiences related to acceptability, practicality, and demands on completion of PROMs following physical meetings at the department with nurses and surgeons.

Study II) To investigate the nurses' and surgeons' experiences related to acceptability, implementation, practicality, and proactive application of the PROM intervention in clinical practice.

Study III) To analyse baseline PROM data after 1 year, including outcomes and demographic variables for responders and non-responders.

The multimethod study includes the development of an ePROM intervention with repeated collection of ePROMs at timings (T) T1, T2, and T3 using the BREAST-Q tool and proactive use of ePROMs during follow-up visits at the department, and an evaluation of feasibility (Figure 1 and Figure 2). Studies I and II are qualitative ethnographic studies exploring the user perspectives of patients, nurses, and surgeons to gain insights into how the intervention can be refined. Additionally, Study II is complemented with a local anonymous survey study in collaboration with department nurses and surgeons to investigate user experiences, individual activities, perceived demand, preferences, and proactive application related to the ePROM intervention. Qualitative studies are guided by interpretive description (ID), an inductive methodology developed to explore clinical problems with the objective of generating insights that inform clinical practice [45]. ID draws upon recognised qualitative research techniques from ethnography, naturalistic inquiry, grounded theory, and phenomenology but focuses on explicit research logic and flexibility, permitting researchers to apply and combine the necessary pragmatic strategies to answer the research question [46]. The composition of an ID study is guided by distinctive features, including: scaffolding the study, framing the study, a credible study, entering the field, constructing data, making sense of data, and conceptualising findings[46]. The result is a coherent, conceptual description containing understandings and illuminations of clinical phenomena, characteristics, patterns, and structures in order to develop practice. The ID methodology will support understanding and knowledge related to the feasibility study outcomes.

Quantitative study III includes the PROM data from T1 to explore the patient population and their outcomes at baseline (Figure 2) [47]. PROM data from T2 and T3 will be

reported elsewhere. This protocol describes a feasibility study only. The evaluations of PROM data T2 and T3 will be reported elsewhere. Guidelines for Inclusion of Patient-Reported Outcomes in Clinical Trial Protocols: The SPIRIT-PRO Extension [48] were used to report the protocol (Supplementary Material 1).

Table 1 Key areas of focus for the feasibility study inspired by Bowen et al.(2009)

Feasibility outcomes/areas of focus	What is explored	Sample outcomes of interest	Explored in study		
			I	II	III
Acceptability	To what extent is the ePROM intervention suitable, satisfying, or attractive to programme deliverers? To programme recipients?	• Satisfaction • Intent to continue use • Perceived appropriateness • Completion rate	X	X	X
Demand	To what extent is the ePROM intervention likely to be used? When, how, and why do the nurses and surgeons actively review the patients' PROM answers during consultations, and how do they use the feedback from patients?	• Proactive use of ePROMs • Fit within organizational culture • Perceived positive or negative effects on organization • Actual use • Expressed interest or intention to use • Perceived demand	X	X	X
Implementation	To what extent can the ePROM intervention be successfully delivered to intended participants in some defined, but not fully controlled, context?	• Degree of execution • Success or failure of execution • Amount, type of resources needed to implement	X	X	
Practicality	To what extent can the ePROM intervention be carried out with intended participants using existing means, resources, and circumstances and without outside intervention?	• Factors affecting implementation ease or difficulty • Efficiency, speed, or quality of implementation • Positive/negative effects on target participants • Ability of participants to carry out intervention activities	X		X

Integration	To what extent can the ePROM intervention be integrated within the existing system/clinical practice?	• Perceived fit with infrastructure • Perceived sustainability		X	X

Study participants

Patient participants are women with newly diagnosed breast cancer, who will be included in the multimethod study from September 2021 to September 2024, and the follow-up time will end in January 2028.

Inclusion criteria:

- Female patients age ≥18
- Newly diagnosed breast cancer that is treated with curative surgical therapy to remove breast cancer
- The ability to speak and understand Danish to comprehend the given information, complete the study questionnaires, and provide written informed consent.

Exclusion criteria:

- Treated with letrozol aromatase inhibitor hormone therapy as primary treatment (nonsurgical regime, therefore outcome measures of satisfaction with surgical result are not relevant)
- Not assigned digital information in the Danish Civil Registration System (Figure 2)
- Non-Danish speaking
- Any disability making ePROM follow-up impossible, such as blindness or mental disability, or a diagnosis of dementia.

Exclusion is assessed based on the medical record journal by a research assistant in collaboration with a breast surgeon at the department affiliated with the study.

Approximately 600 women are newly diagnosed with breast cancer at the Department of Plastic and Breast Surgery of Zealand University Hospital each year. Patients will be included continuously for 3 years. A minimum sample of 900 patients is expected to be included.

For qualitative studies I and II, patient participants are purposefully sampled from consenting to the ePROM intervention using the maximum variation concept [45]. Nurses and surgeons included for the qualitative studies are those whom the patients met during their visit on the day of observation by the present researcher. The patients' visits are pre-booked, and patients visit either a nurse, surgeon, or a surgeon and a nurse in one consultation. An anonymous survey will be distributed to all nurses and surgeons at the outpatient clinic as part of study II.

Recruitment procedures

Patients are recruited from the Department of Plastic and Breast Surgery at a large centre of plastic and breast surgery located at a tertiary Danish university hospital. The departments' research assistants are responsible for identifying and inviting patients who meet the inclusion criteria.

Patients eligible for inclusion are informed and invited through a digital postbox (e-Boks) to the ePROM intervention [49]. The invitation is supported by a four-minute video developed by the research assistant and a patient and public representative, which provides patient information about the aims of the ePROM-intervention. Furthermore, the patients receive a postcard at the outpatient clinic, which informs them about the ePROM intervention when they are diagnosed. Patients receive a link to the ePROM questionnaires in their digital postbox via the secure encrypted electronic system Research Electronic Data Capture (REDCap) [50]. Patients may consent or decline

through invitation by mail. Patients may complete questionnaires on a PC, tablet, or smartphone. The questionnaire is open for completion 14 days after invitation. After two days, a notification is automatically forwarded if no response is received. After 4 days, the research assistant calls and asks patients who have not responded to the invitation if they need assistance with the questionnaire. A research nurse assistant may assist with technical issues, if any. Patients included in the study can withdraw consent to participate without justification and without affecting the present or future treatment at any time. Patients withdrawing consent will be considered as 'lost to follow-up'. Patients who decline to participate are registered within an encrypted database as non-responders. Nurses and surgeons at outpatient clinics have access to patients' ePROM data through REDCap, including detailed responses and the total score of each questionnaire.

Strategies for the introduction of ePROMs

The introduction strategies related to this study aim to enable systematic and flexible implementation of ePROMs in an outpatient setting [15]. The strategy includes establishing an ePROM-intervention support group, a nurse education programme, and a surgeon education programme. As part of the strategy, ePROM intervention is described in detail within a clinical guideline developed with the ePROM-intervention support group. The guideline includes instructions for nurses, surgeons, and secretaries on their specific responsibilities related to the ePROM intervention. One part of the strategy is a steering group plus education programmes for the departments' nurses and surgeons.

Patient and public involvement

The study is supported by a patient and public representative from the Danish Cancer Society, who is an equal member of the study steering group. The representative was

'involved throughout the design phase, for instance, contributing to the formulation of research questions and agreeing plans for dissemination of the study to participants. The representative continuously informed the study about patients' and public priorities, experiences and preferences and the representative will participate in the analysis of data.

The ePROM steering group

The ePROM intervention is delivered by a steering group of experts who assist in the implementation of ePROMs. The group consists of an outpatient nurse from the department, a breast surgeon, a secretary, the patient and public representative, a nurse research assistant, a leading head nurse, a leading chief surgeon, and a responsible nurse researcher. In addition, three external researchers are affiliated with the intervention study as supervisors and are experts in PROMs, statistics, qualitative methodology, and person-centred practice.

Nurse education programme

Before the PROM intervention, all nurses at the breast surgical outpatient clinic participated in face-to-face training on the use of ePROMs. The educational sessions were guided by person-centred care theory and included a brief lecture on person-centredness and person-centred communication, which supports previous departmental education for nurses, in which person-centred values have been inherent.

Training on the application of ePROMs during consultations was mandatory and provided by departments' clinical nurse specialist and research assistant and lasted for four hours. Nurses were expected to be the main users of PROM data for psychosocial support and conversations with patients, for example, on body image. Therefore, the

nurses' education was planned to be more comprehensive 'than the surgeons' education, and included skills training. The education programme included a broad introduction to PROMs and examples of proactive use of PROMs from other departments and research [51,52]. The educational programme was planned with didactical consideration for research-based teaching and teaching for learning, and with a focus on interaction and activation during sessions with case-based learning [53,54]. The training programmes included: how to access the timely and relevant individual patients' ePROMs linked to nurse consultations; how to respond to ePROMs in terms of caring for individuals with psychosocial support and symptom management; how to proactively engage in the discussion of PROM data with patients; and how to document nurses' application of PROMs in patient care. The intervention is associated with monthly 1-hour internal educational sessions that address issues related to the proactive use of ePROMs in clinical practice to improve outpatient nurses' knowledge and skills in relevant issues such as body image-related distress [55]. Nurses' use of ePROMs is evaluated every third month using a paper questionnaire and a 1-hour dialogue with the responsible researcher.

Surgeons' education programme

'Prior to commencing the PROM intervention, surgeons from the department participated in a 1-hour mandatory education programme about the ePROM-intervention, aiming to inform about its objectives, processes rationales including how to proactively engage with ePROMS with patients. Once a month, surgeons participate in further follow-up training on PROMs, which is conducted by the responsible researcher and a clinical nurse specialist. The sessions include practical training on how to access the timely and relevant individual patients' ePROMs linked to surgeons' consultations as a comparison of the T1 and T2 questionnaires (Table 2); how to engage with and respond to ePROMs

in terms of person-centred surgical follow-up in ePROMs with patients; and how to document surgeons' application of PROMs in the medical record journal. Didactical considerations correspond to those mentioned in the nurses' education programmes.

Table 2. Study assessment times, measures and tasks

Data Collection		**Baseline (T1*)**	**Follow-up[1] (T2)**	**Endpoint (T3)**
All patient participants (ePROM group)	Informed consent	●		
	Demographic data[2]	●		
	Breast Cancer Core Scale (Pre- and postoperative): Satisfaction with Breasts[3]	●	❷❸	
	Breast Cancer Core Scale (Preoperative): Physical Well-Being: Chest[3]	●		
	Breast Cancer Core Scale (Pre- and Postoperative): Psychosocial Well-Being[3]	●	❶❷❸	●
	Breast Cancer Core Scale (Pre- and Postoperative): Sexual Well-Being[3]	●	❶❷❸	●
	Breast Conserving Therapy Module (Postoperative): Satisfaction with Breasts[3]		❶	
	Breast Conserving Therapy Module (Postoperative): Physical Well-Being: Chest[3]		❶	
	Breast Cancer Core Scale (Pre- and Postoperative): Physical Well-Being: Chest[3]		❷❸	●
	Reconstruction Module (Postoperative): Satisfaction with Breasts[3]			●
	[A]Reconstruction Module (Postoperative): Satisfaction with Nipple Reconstruction[3]			●
	[A]Reconstruction Module (Postoperative): Satisfaction with Implants[3]			●
	[A]Latissimus Dorsi Module (Postoperative): Satisfaction with Back[3]			●
Invited non-respondents	Reasoning for study dropout			
User perspectives	Participant observations during patient consultations	◊	◊	
	Individual interviews with patients	◊	◊	
	Individual interviews with nurses	◊	◊	
	Survey with nurses and surgeons		◊	

*Timing (T) and questionnaire distribution number, [1]Patients after surgical therapy: ❶ initial breast conserving therapy, ❷ initial mastectomy, ❸ initial immediate reconstruction; [1]Demographic data (identification-number, age, marital status, educational level, body mass index, zip code); [3]BREAST-Q™ version 2.0 Questionnaire scale; [a]Individual supplementary modules.

Intervention with ePROMs

The ePROM intervention includes patients' completion of ePROMs related to satisfaction with breasts, physical well-being, psychosocial well-being, and sexual well-being, which are to be proactively applied in patients' trajectory to monitor the individual patient's condition and accommodate individualised psychosocial and surgical follow-up based on patient preferences and values. Over a 3-year period, the patients receive two to three questionnaires, depending on their trajectory, with treatment arms surgical therapy upfront or neoadjuvant therapy before surgical therapy (Figure 2 and Table 2). The ePROMs are to be actively reviewed by departments' nurses before the patient's visit at the following times: first, prior to the patient's 4-day postoperative control with a nurse (T1, baseline data completed before surgery); second, for the 1-year follow-up (T2, follow-up completed 11 or 18 months after surgery, dependant on treatment regime), which is initially a nurse consultation. The rationale for using baseline PROMs completed before surgery for the 4-day postoperative is: 1) The patient's assessment of breasts before the surgery is recommended to be actively discussed with the patient in relation to the choice of breast prosthesis, bra, and life with a changed body after breast cancer; 2) The baseline measurement is essential to monitor patients' satisfaction with breasts over time, and surgical results are best evaluated at the earliest one year after surgery [56]. Patients in the low-risk recurrence regime have standardized 1-year postoperative follow-up with nurses, where ePROMs are to be applied. Patients in high-risk recurrence regimes are not offered as standard breast surgical follow-up, but this is offered to patients through the ePROM intervention. During the second follow-up, nurses are educated to proactively use patients' ePROMs for dialogue about patients' perception of body image issues related to their breasts. Based on patients' individual needs, the nurse may recommend the patient for further assessment with one of the department's plastic surgeons, who will

also have the ePROMs for comparison (Table 2). Patients who accept correction or reconstruction of the breasts after their 1-year follow-up, the T2, receive a third ePROM 18 months after T2, as patients are expected to have finished their breast surgical trajectory at this point (T3, endpoint).

Data collection and measurements

The outcomes of the multimethod study relate to feasibility parameters, including acceptability, proactive use of ePROMs, demand, implementation (degree of execution), practicality, and integration (perceived sustainability and fit with infrastructure), as described by Bowen et al. (2009) [44]. These will be conducted through multiple measurements and outcomes in Studies I to III. The data to be analysed in sub-studies I to III are collected as follows:

Ethnographic studies I and II

Feasibility data are collected qualitatively by exploring the user perspectives of patients, nurses, and surgeons to gain insights into how the intervention can be refined. Qualitative studies I and II investigate users' interests related to using ePROMs and practice interests that can drive or limit development. User experiences of patients, nurses, and surgeons will be qualitatively explored and guided by the interpretive description methodology for applied research [45].

For studies I and II, data collection includes participant observations during patient consultations with nurses and surgeons and individual interviews with patients, nurses, and surgeons to explore the application of ePROMs in clinical practice and the implications for practice. The time of the observations will follow the appointment times for the consultations (see Figure 2). An observation and interview guide is developed based on the researchers' experiences as a nurse at the department, which

also allows entry into department consultations [45]. The participant observations and interviews will be conducted by the first author with a focus on whether, when, how, by whom, why, or why not, the ePROMs are proactively used. This work calls for critical reflection and transparency on the researcher's positioning, degree of participation and ability to disregard the professional lens from one's practice discipline [45,57–59]. This will be reported with the results of the studies. For study II, the survey with nurses and surgeons is conducted as an online survey with questions developed specifically for this study to investigate perceptions, defined as the way in which the intervention is regarded, understood, and interpreted [60] as well as feasibility [47], based on the principles of applied research [45].

Study III on PROMs data

PROMs are collected electronically via REDCap at time points T1, T2, and T3 (Table 2). Additional baseline demographics for Study III data are collected electronically via REDCap within T1 (Figure 2 and Table 2) and include age, marital status, educational level, height, weight, body mass index, and municipality [50]. The PROM used for the intervention is BREAST-Q, as recommended by the International Consortium for Health Outcomes Measurement (ICHOM) standard order set for breast cancer patients to monitor PROMs following breast surgery [61]. BREAST-Q was developed according to recommended guidelines through patient interviews, focus groups, an expert panel, and a literature review and has undergone thorough validation with measures of high reliability which use both the paper and the electronic version [41,62–65]. BREAST-Q was designed specifically for breast surgery and has pre- and post-operative versions in modules for mastectomy, breast-conserving therapy, breast reconstruction, breast reduction, and breast augmentation [66]. All modules contain three subdomains,

including physical, psychosocial, and sexual well-being, and three sub-domains on patient satisfaction, comprising satisfaction with breasts, outcome, and care. No overall BREAST-Q scores are obtained. Each independent scale results in a score that is computed by adding the response items and then converting the raw sum scale score to a score from to 0–100 [67]. For all BREAST-Q scales, a higher score indicates greater satisfaction or better QOL (depending on the scale). If missing data are less than 50% of the scale's items, the mean of the completed items are inserted. Each set of questionnaires, for instance BREAST-Q questionnaire 1, takes 5–10 minutes to complete. Each scale is accompanied by a conversion table to calculate a total scale score of 0–100 [22,67].

Analysis

Qualitative studies I and II

The interviews and observations will be analysed in relation to user perspectives guided by ID. ID does not prescribe a straightforward data analysis process but relies on the pragmatic obligation of the researchers to work on data beyond initial descriptive claims towards interpretations that will enlighten the phenomenon investigated in a new and meaningful manner [68]. The ID analysis aims to make sense of what has been observed and heard through an explorative process in which questions are continuously posed about the data, and answers are sought to generate explanations supported by theory [46,68]. The analysis for studies I and II will be inspired by the theoretical framework of person-centred care to evaluate the feasibility of the proactive ePROM intervention by questioning whether the ePROM intervention supports the intentions on targeted, individual, psychosocial support and assessment of candidates for reconstructive and/or corrective breast surgical therapy. Specifically, the parameters of acceptability, demand, introduction, practicality, and integration will be elaborated throughout the analysis

(Table 1) [33,45]. These outcomes will be informed and further analysed from the observation and interview data that is expected to add rigorous information on priorities, mechanisms and practicalities in the outpatient clinic to answer the study aims [46,68].

Study III – Statistical analysis

Descriptive statistics and completion rate will be calculated for all demographic variables for both responders and non-responders to the BREAST-Q questionnaire, based on data from T1 (baseline). Depending on the normality of the numerical variables, means (SD) or medians (interquartile range) will be calculated, while categorical variables will be expressed as proportions. Differences will be analysed using t-tests, Mann-Whitney U tests, and chi-squared tests. Furthermore, among responders, linear regression models will be used to identify which demographic variables are associated with the subscale scores from the BREAST-Q questionnaire. All variables will be entered into univariate and multivariate regression models to identify demographic variables that were independently associated with the questionnaire scores. Data will be analysed using the Stata software package [69]. The significance level will be set at $p < .05$, and all tests will be two-tailed. If applicable, sensitivity analysis using multiple imputation will be conducted on item-wise missing responses if the rate of missing data exceeds 5%.

ETHICS AND DISSEMINATION

The patients provide informed consent, which they can withdraw at any time. Data will be stored in REDCap and on an encrypted regional team site for sensitive personal research data. The study is designed according to the General Data Protection Regulation (GDPR) and adheres to the principles defined by the World Medical Association in the Helsinki Declaration. The use of the BREAST-Q questionnaire, authored by Drs Klassen,

Pusic, and Cano, was licensed by the Memorial Sloan Kettering Cancer Center, New York, USA.

The findings of this study will be submitted to international peer-reviewed journals and presented at conferences.

DECLARATIONS

Acknowledgements

KH Karlsen for representing patients and public into the study design. JH Prüsse for building the research database.

Competing interests

The authors do not have any conflicts to declare.

Patient consent for publication

Not applicable.

Contributorship

STH was responsible for the initial study design and the grant application, and is responsible for supervising as project leader. STH, VJS, KML and KP did the background research and were responsible for the protocol's in-depth development and drafting of this manuscript, including its figures and tables. LBH and BHH helped supervise. KP, LBH and BHH contributed with thorough revisions to the manuscript. All authors read and approved the final manuscript. STH is the guarantor.

Funding

This work was supported by Region Zealand, National Cancer Plan IV [grant number 20-082, 2020]. The Region Zealand has not been part of designing the study, nor will the region be part of the analysis or interpretation of data. The Department of Plastic- and Breast Surgery, Zealand University Hospital and The University of Southern Denmark covers STH's salary. KP, BHH, KML, and VJS are currently not receiving a salary for this work.

Ethics Approval

The study is approved by the Danish Data Protection Agency (REG-104-2021) and the National Committee on Health Research Ethics (SJ-914, EMN-2021-01530).

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Supplemental material

Supplementary material 1 - SPIRIT 2013 and SPIRIT-PRO Extension Checklist

Legends

Figure 1. Illustration of the multimethod feasibility study, the intervention and sub-studies

Figure 2. Illustration of the ePROM-intervention flowchart. Dark boxes illustrate intervention features. T1, T2, and T3 refer to the timely specific questionnaires that are sent to the patients.

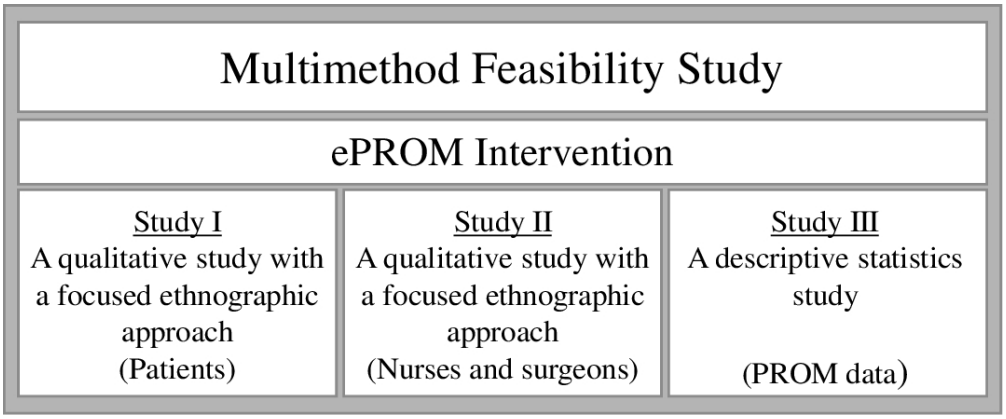

Figure 1. Illustration of the multimethod feasibility study, the intervention and sub-studies

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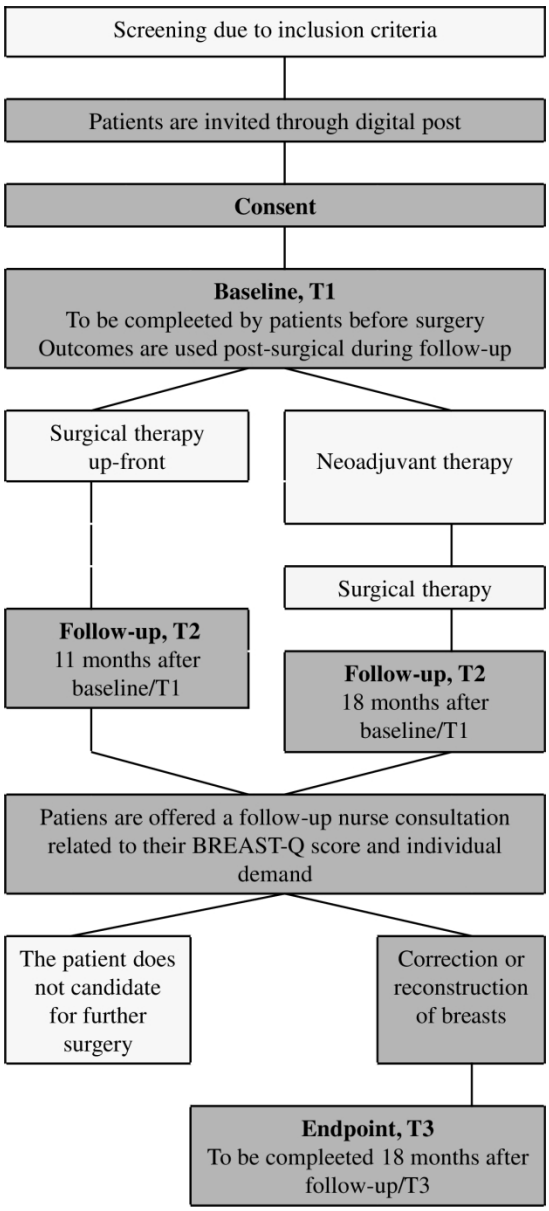

Figure 2. Illustration of the ePROM-intervention flowchart. Dark boxes illustrate intervention features. T1, T2, and T3 refer to the timely specific questionnaires that are sent to the patients.

97x215mm (300 x 300 DPI)

SPIRIT 2013 AND SPIRIT-PRO EXTENSION CHECKLIST: RECOMMENDED ITEMS TO ADDRESS IN A CLINICAL TRIAL PROTOCOL AND RELATED DOCUMENTS*

SPIRIT Section/item	SPIRIT Item No	SPIRIT Item Description	SPIRIT-PRO Item No	SPIRIT-PRO Extension or Elaboration Item Description	Page **
Administrative information					
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym			p.1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry			-
	2b	All items from the World Health Organization Trial Registration Data Set			-
Protocol version	3	Date and version identifier			p.6
Funding	4	Sources and types of financial, material, and other support			p.19
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	SPIRIT-5a-PRO elaboration	Specify the individual(s) responsible for the PRO content of the protocol	p.19
	5b	Name and contact information for the trial sponsor			-

	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities			-
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)			-
Introduction					
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	SPIRIT-6a-PRO Extension	Describe the PRO-specific research question and rationale for PRO assessment and summarize PRO findings in relevant studies.	p.6
	6b	Explanation for choice of comparators			-
Objectives	7	Specific objectives or hypotheses	SPIRIT-7-PRO Extension	State the specific PRO objectives or hypothesis (including relevant PRO concepts/domains).	p.16
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)			p.2
Methods: Participants, interventions, and outcomes					

Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained			p.6
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	SPIRIT-10-PRO Extension	Specify any PRO-specific eligbility citeria (eg, language/reading requirements or prerandomization completion of PRO). If PROs will not be collected from the entire study sample, provide a rationale and describe the method for obtaining the PRO subsample	p.8
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered			p.14
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)			-
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)			p.10
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial			-
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	SPIRIT-12-PRO Extension	Specify the PRO concepts/domains used to evaluate the intervention (eg, overall health-related quality of life, specific domain, specific symptom) and, for each one, the analysis metric (eg, change from baseline, final value, time to event) and the principal time point or period of interest.	p.15

Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	SPIRIT-13-PRO Extension	Include a schedule of PRO assessments, providing a rationale for the time points, and justifying if the initial assessment is not prerandomization. Specify time windows, whether PRO collection is prior to clinical assessments, and, if using multiple questionnaires, whether order of administration will be standardized.	Fig. 2
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	SPIRIT-14-PRO Elaboration	When a PRO is the primary end point, state the required sample size (and how it was determined) and recruitment target (accounting for expected loss to follow-up). If sample size is not established based on the PRO end point, then discuss the power of the principal PRO analyses.	p.9
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size			p.9
Methods: Assignment of interventions (for controlled trials)					
Allocation:					
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions			-
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned			-

Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions			-
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how			-
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial			-
Methods: Data collection, management, and analysis					p.15
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	SPIRIT-18a (i)-PRO Extension	Justify the PRO instrument to be used and describe domains, number of items, recall period, and instrument scaling and scoring (eg, range and direction of scores indicating a good or poor outcome). Evidence of PRO instrument measurement properties, interpretation guidelines, and patient acceptability and burden should be provided or cited if available, ideally in the population of interest. State whether the measure will be used in accordance with any user manual and specify and justify deviations if planned.	
			SPIRIT-18a (ii)-PRO Extension	Include a data collection plan outlining the permitted mode(s) of administration (eg, paper, telephone, electronic, other) and setting (eg, clinic, home, other).	p.15

			SPIRIT-18a (iii)-PRO Extension	Specify whether more than 1 language version will be used and state whether translated versions have been developed using currently recommended methods.	p.8
			SPIRIT-18a (iv)-PRO Extension	When the trial context requires someone other than the trial participant to answer on his or her behalf (a proxy-reported outcome), state and justify the use of a proxy respondent. Provide or cite evidence of the validity of proxy assessment if available.	-
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	SPIRIT-18b (i)-PRO Extension	Specify PRO data collection and management strategies for minimizing avoidable missing data.	p.10
			SPIRIT-18b (ii)-PRO Elaboration	Describe the process of PRO assessment for participants who discontinue or deviate from the assigned intervention protocol.	p.10
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol			p.10, 17
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	SPIRIT-20a-PRO Elaboration	State PRO analysis methods, including any plans for addressing multiplicity/type I (α) error.	p.17

	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)			
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	SPIRIT-20c-PRO Elaboration	State how missing data will be described and outline the methods for handling missing item or entire assessments (eg, approach to imputation and sensitivity analyses)	p.17
Methods: Monitoring					
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed			p.11
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial			-
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	SPIRIT-22-PRO Extension	State whether or not PRO data will be monitored during the study to inform the clinical care of individual trial participants and, if so, how this will be managed in a standardized way. Describe how this process will be explained to participants; eg, in the participant information sheet and consent form.	p.12
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor			-

Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	p.19
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	p.11
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	p.17
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	-
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	p.3
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	p.18
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	p.6
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	-

Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	p.18
	31b	Authorship eligibility guidelines and any intended use of professional writers	-
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	-
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	-
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	-

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

**page numbers refers to protocol paper