FULL/LONG TITLE OF THE STUDY

Medication brand changes in hormone therapy for breast cancer. A community pharmacy intervention development to improve patients' adherence and quality of life. ENABLE

SHORT STUDY TITLE / ACRONYM

Medication brand changes in hormone therapy for breast cancer / ENABLE.

PROTOCOL VERSION NUMBER AND DATE

Version 1.0 (23/05/2024)

Version 1.1 (30/06/2024)

Version 1.2 (15/10/2024)

Version 1.3 (17/03/2025)

RESEARCH REFERENCE NUMBERS

IRAS Number:	327926
SPONSORS Number:	London Metropolitan University
FUNDERS Number:	NIHR 206589

This protocol has regard for the HRA guidance and order of content.

SIGNATURE PAGE

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the study in compliance with the approved protocol and will adhere to the principles outlined in the Declaration of Helsinki, the Sponsor's SOPs, and other regulatory requirement.

I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the investigation without the prior written consent of the Sponsor

I also confirm that I will make the findings of the study publicly available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the study will be given; and that any discrepancies from the study as planned in this protocol will be explained.

For and on behalf of the Study Sponsor:

Signature:
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Date:
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Name (please print):
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Position:
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Chief Investigator:

Signature:
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Date:
23/05/2024

Name: (please print): Prof Yolanda Eraso
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LIST of CONTENTS

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STUDY SUMMARY

Study Title	Medication brand changes in hormone therapy for breast cancer. A community pharmacy intervention development to improve patients' adherence and quality of life. ENABLE
Internal ref. no. (or short title)	Medication brand changes in hormone therapy for breast cancer / ENABLE.
Study Design	**WP 1**: Intervention development (O1&3) 1a. A rapid scoping review of the literature to identify the best available evidence on patient medication diary interventions for cancer patients. 1b. Two co-design Workshops:

	Co-production workshops with BC patients and pharmacists i. WS1: Develop content for a patient self-management diary; ii. WS2: Develop content for a medication consultation guide for pharmacists and training content. 1.c Qualitative interviews with pharmacists: We will explore the views of pharmacist representatives of professional bodies and owners of community pharmacies about the barriers and facilitators of implementing the intervention (O3). **WP 2**: Design of e-learning resource for pharmacists (O2) 2a. E-learning package design: A Web-developer specialist will collaborate in the design of an e-learning package based on the educational content of the prototype intervention. 2b. Qualitative interviews with pharmacists: Feedback will aim to establish the appropriateness of the educational intervention as a learning tool. **WP 3**: Testing and optimisation studies (O4&5) We will test the intervention to gather feedback from participants and optimise the different components as follows: 3a. Deliver of the e-learning package to 5 community pharmacists in North Central London ICS. Participants will access the e-learning for 1 month. 3b. The 5 trained pharmacists will recruit 20 (4 each) BC patients from their CPs. Eligible patients will receive a self-management diary and will attend a medication consultation with the pharmacist. Follow-up interviews with participants. 3.c Integration of feedback to produce ENABLE, and a protocol for a feasibility study (O5).
Study Participants	**WP 1**: Intervention development: BC patients; Community Pharmacists [co-production workshops]; pharmacist representatives of professional bodies; owners of community pharmacists [interviews]. **WP 2**: Design of e-learning resource for pharmacists: Community pharmacists to produce feedback **WP 3**: Testing and optimisation studies: Community pharmacists and BC patients
Planned Size of Sample	**WP1**: workshops [10 community pharmacists and 10 BC patients]; interviews [10 community pharmacists and pharmacists from professional bodies] **WP2**: Community pharmacists [8-10] **WP3**: 5 Community pharmacists; 20 BC patients

Follow up duration (if applicable)	N/A
Planned Study Period	20 months
Research Question/Aim(s)	Aim: The aim of the project is to co-produce with breast cancer patients and pharmacists an intervention to improve medication brand change consultations for women with breast cancer in community pharmacy settings. Achieving this will identify the communication and advice strategies that can be used by pharmacists in discussing HT medication brands and the delivery of a patient-centred approach that could improve adherence and QoL. We will assess the acceptability of the intervention to patients and pharmacists to inform the design of a future feasibility study. Objectives are to: 1. Co-develop intervention content using co-production workshops with patients and pharmacists. 2. Design and delivery of an e-learning resource targeting behaviour change components in pharmacy staff to improve HT medication-taking in women with breast cancer. 3. We will explore with pharmaceutical professional bodies and owners of community pharmacies (chain and independent) the barriers and facilitators of implementing the intervention in community pharmacies. 4. Assess patient and pharmacist's perceptions of the intervention and its acceptability. 5. Integrate feedback to refine the ENABLE intervention and the design of a feasibility study protocol.

FUNDING AND SUPPORT IN KIND

FUNDER(S) (Names and contact details of ALL organisations providing funding and/or support in kind for this study)	**FINANCIAL AND NON FINANCIALSUPPORT GIVEN**
National Institute for Health and Care Research (Research for Patient Benefit Programme)	Funding awarded for the development and testing of an intervention study to London Metropolitan University.

ROLE OF STUDY SPONSOR AND FUNDER

The sponsor of the study is London Metropolitan University. The University takes responsibility for ensuring that the design of the study meets appropriate standards and that arrangements are in place to ensure appropriate conduct and reporting. London Metropolitan University will ensure that all necessary approvals from an NHS research ethics committee are obtained before undertaking the study. Signed ethically approved informed consent and acknowledgement forms from any participants who will be involved in the project will be obtained.

The study is funded by the National Institute for Health Research – Research for Patient Benefit funding stream. The funder has not had any influence over the study design or analysis.

ROLES AND RESPONSIBILITIES OF STUDY MANAGEMENT COMMITEES/GROUPS & INDIVIDUALS

STUDY MANAGEMENT

The sponsor of the study is London Metropolitan University.

The Chief Investigator has overall responsibility for the study and shall oversee all study management.

Study Steering Committee. This panel will meet 4 times (virtually) throughout the duration of the project to assess progress against the defined milestones and deliverables, and provide advice and expertise.

Patient Advisory Group. The PAG will meet at different key instances in the development of the study, to ensure the study remains sensitive to patient and public preferences at all stages. They will provide feedback on all work packages of the intervention development and instruments of data collection, and will plan a dissemination strategy.

Project Management Group: will meet monthly (virtually) for the duration of the study to discuss progress and findings as they emerge. This group will be led by the by the CI and include co-investigators, and research support staff.

PROTOCOL CONTRIBUTORS

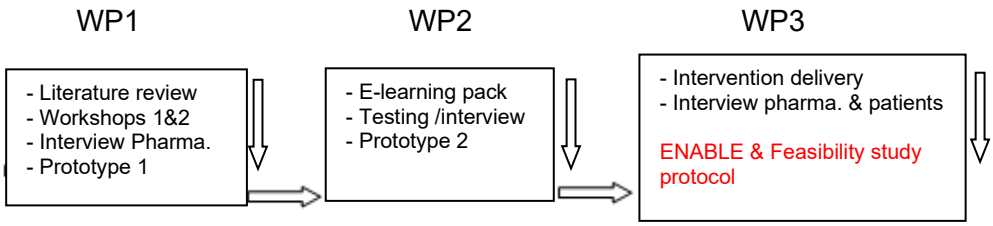
The protocol was designed by the CI, with contributions from all co-applicants.

A patient advisory group has provided feedback on an early design of the project and their views were incorporated into the protocol.

KEY WORDS: Breast cancer; adherence to hormone therapy; medication brand changes; community pharmacies; behaviour change; intervention co-development

STUDY FLOW CHART

The sequence of activities within each work page and among the work packages is illustrated below.



STUDY PROTOCOL

Medication brand changes in hormone therapy for breast cancer. A community pharmacy intervention development to improve patients' adherence and quality of life. ENABLE

1 BACKGROUND

Breast cancer (BC) is the most common cancer in the UK, with an estimated 55,900 new cases diagnosed in women every year [1]. Around 80% of BCs are oestrogen receptor positive, which means that for the great majority of BC survivors, treatment does not end with surgery, radiation and/or chemotherapy. Hormone therapy (HT) drugs (tamoxifen, letrozole, anastrozole, and exemestane) are prescribed for 5 to 10 years to reduce the risk of recurrence and mortality. These drugs are known to cause several side effects and have been consistently identified in the literature as a key factor of non-adherence [2] and poor quality of life (QoL) [3]. By the fifth year of treatment, adherence to HT is suboptimal, estimated between 41%-72% and treatment continuation between 31%-73% [4].
In the UK, it is common practice for community pharmacies (CPs) to dispense a different generic of the same drug when patients collect their prescriptions. Currently, the British National Formulary lists 10 generics for tamoxifen, 10 for letrozole, 17 for anastrozole and 13 for exemestane, in addition to their proprietary names [5]. Clinical studies on women's experiences with HT medications revealed that the use of generic drugs either to replace the proprietary name (generic substitution) or to switch amongst generic brands (generic switching) can have a negative impact on patients' side effects, attitudes and acceptance of certain generic brands [6-7]. In women switching tamoxifen generics, a small but significant number of patients (11-13%) attributed severe menopausal symptoms to brand switch, which stopped when taking a different brand. Authors considered that patients' perceived change in medication side effects was due to manufacturers' use of different excipient profiles [6-7]. Additionally, experimental studies have shown that patients often misattribute symptoms (emerging from everyday activities, disease or environmental factors) as medication side effects [8], raising the need to assist patients in recognising drug-related symptoms. Both experiences of new side effects (excipient-related or beliefs-induced) can hamper BC patients' QoL and treatment continuation.
Our previous study of medication brand changes (MBC) confirmed that a significant minority of BC patients have a negative experience when they receive a different generic drug, reporting new side effects, phycological impact, lack of information on generics, feeling unsupported, disbelief about symptoms from healthcare professionals, and concern about quality and effectiveness [9]. These medication concerns undermine patients' self-efficacy (skills and confidence) for medication-taking behaviours and have an impact on adherence and persistence [6-7,9-10].
A growing body of evidence points to the need for interventions to implement an enhanced form of support for BC patients to manage their medication better [11-13]. The Royal Pharmaceutical Society acknowledges a 'considerable scope' for pharmacist-led interventions in cancer care including medication dispensation [14]. However, to date no effective intervention exists in CPs to address patients' concerns with HT generic switching.
To address this gap in the provision of services, and in consultation with our patient advisory group (PAG) and stakeholders, we intend to co-develop and evaluate the acceptability of an intervention to improve patients' medication consultations about HT brand changes in community pharmacy settings, and to improve QoL and adherence.

1.2. Review of existing evidence

Existing evidence can be synthesise in the following areas:

HT generics: Research on patients' perspectives on generics (for conditions other than cancer) has consistently found that improving knowledge and information about generics, by physicians or pharmacists, can increase consumers' confidence and acceptability [15-17]. Patients' experiences with HT generic drugs have reported symptom changes associated with different brands [6,7,9], with

women more likely to consider discontinuing if they were unable to find a suitable generic [7,18]. Studies in the US have shown that the introduction of HT generic drugs resulted in an increase in adherence [19-22] due to a reduction in out-of-pocket costs. The study of Quin et al. [10], however, evidenced that an increase in adherence was because generic switching allowed patients a better management of drug-related side effects regardless of costs. Whilst there is a particular paucity of UK literature in this area, a wealth of discussion on MBC in patients' online forums, and in The Pharmaceutical Journal (RPS) have also maintained that patients can be 'brand sensitive' [23-25].

HT medication-taking behaviours: Systematic reviews have identified self-efficacy in medication taking as a potential predictor and modifiable factor for adherence and persistence with HT [13,26-27]. Higher self-efficacy for taking medication had a statistically significant association with greater adherence [28]. Medication concerns related to MBC undermine confidence (self-efficacy) in medication taking and can lead patients to intentionally discontinue treatment [7,9]. Additionally, lower self-efficacy could be a factor for non-adherence in ethnic minority patients which is 1.48 times higher compared to white British [29], thus evidencing the need for inclusive interventions, as proposed in our recruitment strategy.

CPs interventions: Many HT adherence studies have endorsed the development of interventions in the CPs setting [12,30-32], however, such interventions are non-existent in the UK and no trial is currently planned in the ISRCTN database. A recent study found that CPs are favourable to becoming more integral in supporting BC patients' care needs, including medication consultations and advice for managing side effects [33]. Our interviews with pharmacists and a review of the professional curriculum, however, revealed that no specific training on HT dispensing is available and the need for tailored guidance [34]. Thus, time is optimal for new interventions as CPs' role in cancer services is currently expanding (early cancer detection).

1.3. Preparatory work by the research team

Our team embarked on an intervention development process (Transformation Fund HEIF grant), following the Medical Research Council principles for complex interventions [35] and the Person-Based Approach [36].

Study1 explored the prevalence and needs of 281 women discussing MBC in the Breast Cancer Now forum (unpublished). *Study2* [9] interviewed BC patients with lived experience of MBC to identify patients' needs, preferences and concerns. Pharmacists emerged as patients' preferred professional to discuss MBC alongside the use of patients' diaries. *Study3* interviewed pharmacists about managing MBC consultations (unpublished).

Pharmacists identified raising awareness, mandatory training, and guidelines as consultation gaps. Based on our findings, we drafted the guiding principles of the intervention and identified barriers to behaviour change using the Theoretical Domains Framework [38] and the Mechanism of action (with evidence linked to Behaviour Change Techniques) for the initial behavioural mapping of intervention components [38]. Finally, in consultation with PAG, Breast Cancer Now nurses, and academic and community pharmacists we developed our initial intervention plan, described below.

2 RATIONALE

1.1.Why is this research important?

Annually, 55,900 women are diagnosed with invasive BC of whom around 44,720 (80%) are prescribed HT drugs [1]. Nonadherence is a significant problem, resulting in poorer breast cancer outcomes for women [39]. BC survivors are expected to grow from 840,000 in 2020, to over 1.2M in 2030 [40], and with an ageing population, support for medication management (polypharmacy) and self-management increases the challenges for community-based follow-up care. These developments make it increasingly important to support all women with BC to adhere to HT across the 5 /10 years of treatment. Additionally, changing a patient from low to high adherence was estimated at £33,897,

making interventions on adherence highly cost-effective due to improved health outcomes and savings in demand for services [41].
Studies on the recent NHS 'personalised stratified follow-up pathway' [42] evidence that more needs to be done to help patients self-manage their medication better [43,44]. Our own research [9] also confirms that the support women receive to self-manage their HT medication is inadequate, and even worse in regard to generic switching.
The proposed intervention addresses key priorities in cancer research identified by the National Cancer Research Institute and the James Lind Alliance urging new interventions to manage long-term side effects [45], and the NHS Long Term Plan cancer ambitions to improve QoL, patient's experience outcomes, and to reduce inequalities [46].

3 THEORETICAL FRAMEWORK

With our current knowledge, we don't know which interventions can be acceptable or can be realistically implemented to support patients' concerns with MBC. Therefore, before conducting a feasibility study, we need to ensure that the intervention is acceptable for patients and pharmacists, and practically adaptable in routine medical consultations.

Our theoretical approach will be informed by:

The Person-Based Approach, which is a method for optimising interventions that focuses on user-centre design to ensure that interventions are as acceptable, engaging, and feasible as possible, and ultimately effective in their implementation [36]. Its theoretical approach is grounded on behavioural analysis and qualitative research methods to collect data on user perspectives at different stages of the intervention development process. In its combination of evidence (barriers and facilitators to intervention success, users' needs), theory (behaviour change identification and target techniques), and person-centred (qualitative research, optimisation studies to gather user feedback) it aligns with the guidance for developing complex interventions recommended by the MRC [35]. Of greater importance is the stakeholder involvement (healthcare professionals and patients or service users) throughout the intervention planning, which has been emphasised by the MRC framework to ensure that an intervention is compatible within the local setting where it is implemented.

Co-production research will inform the intervention development process, thus extending the stakeholder involvement in our initial stages of the project. Co-production is defined as 'The interdependent work of users and professionals to design, create, develop, deliver, assess and improve the relationships and actions that contribute to the health of individuals and populations to create value' [47]. The GRIPP-2 guidelines for research reporting will support the co-production planning of the study [48].

Finally, we will draw on the Theoretical Domains Framework (TDF) for behavioural analysis, which was developed to analyse determinants of behaviours in health contexts where new evidence-based guidelines have been or are about to be implemented in practice [37]. In our study, we will apply the TDF to identify different components (i.e. reasons for suboptimal behaviour) as the starting point of intervention planning. Each TDF allows for identification of the behaviour change techniques, i.e. the active components of an intervention that bring about behavioural change in individuals. In addition, the Theory and Techniques Tool is an evidence-based resource that helps in selecting behaviour change techniques linked to their mechanism of action (TDF domains) in intervention development [38].

4 AIM

The aim of the project is to co-produce with breast cancer patients and pharmacists an intervention to improve medication brand change consultations for women with breast cancer in community pharmacy settings. Achieving this will identify the communication and advice strategies that can be used by pharmacists in discussing HT medication brands and the delivery of a patient-centred

approach that could improve adherence and QoL. We will assess the acceptability of the intervention to patients and pharmacists to inform the design of a future feasibility study.

4.1 Objectives

Objectives are to:

1. Co-develop intervention content using co-production workshops with patients and pharmacists.
2. Design and delivery of an e-learning resource targeting behaviour change components in pharmacy staff to improve HT medication-taking in women with breast cancer.
3. We will explore with pharmaceutical professional bodies and owners of community pharmacies (chain and independent) the barriers and facilitators of implementing the intervention in community pharmacies.
4. Assess patient and pharmacist's perceptions of the intervention and its acceptability.
5. Integrate feedback to refine the ENABLE intervention and the design of a feasibility study protocol.

4.2 Outcome

The main outcome of this study is the co-development of a two-component intervention, a self-management diary for patients; and a structured guide for pharmacists to elicit person-centred conversations with a solution-focused approach to MBC. Also, a key instrumental component of the intervention is an e-learning package to train pharmacists in the development of skills specifically needed to deliver a person-centred approach to HT medication consultations. Finally, we will produce a feasibility study protocol to further test the intervention.

5 STUDY DESIGN and METHODS of DATA COLLECTION AND DATA ANALYIS

Research plan/Methods

This multi-methods study consists of 3 work packages spanning 20 months. We will draw on co-production methods, the Person-Based Approach to intervention development and Normalization Process Theory (NPT) for the implementation process [49].

WP 1: Intervention development (O1&3)

This WP will use the findings from our previous studies to undertake a rapid scoping review, two co-design workshops, and interviews with pharmacists:

<u>1a. A rapid review of the literature;</u>

To identify the best available evidence on patient medication diary interventions for cancer patients. Rapid scoping reviews are most pertinent for intervention development studies due to their exploratory nature and 'broader scope' to determine what kind of evidence is available on a topic drawing on heterogeneous sources [50].

Findings will be used to inform discussions in subsequent workshops about the most suitable information-recording items for patients to monitor symptoms, enhance self-efficacy, and receive adequate counselling in medication consultations (O1). Additionally, findings will refine the preliminary guiding principles, behavioural analysis and logic model of the intervention development [36].

Research Question: What patient medication diary interventions are available for cancer survivors after primary treatment?

Search strategy
It will include reviews and primary studies of any design and searches of titles and abstracts in the following electronic databases: Cochrane Library, Ovid MEDLINE, CINAHL Database, PsycINFO and TRIP database. Due to time constraints searches will be limited to the past 20 years and English language. The search terms used for each database will be modified to derive the most meaningful search, using a combination of free text, MeSH and subject headings. Additional key papers will be identified from reference lists, targeted author searches, forward citation searching, and from author expertise.

Search terms:
• Cancer* or neoplasm* or carcinoma* or malignan* or tumor* or tumour* or oncolog*
• Survivor* or post-treatment or “after treatment” or “cancer survivor*” or “self-management” or “self management” or “self care” or “self-care” or “self-monitor*” or “self monitor*” or “self-report*” or “self report*”
• Review or synthesis or qualitative or grounded or interview or “focus group*” or ethnograph* or phenomenol* or perspective* or experienc* or “lived experience” or descript* or survey*
• Program* or intervention or trial* or pilot or feasibility or RCT or “process evaluation” or evaluation*
• Adher* or efficacy or use or usability or accept* or satisf* or barriers or facilitat* or preferen* or challeng* or engagement
• Diary or diaries or “cancer diary” or “cancer diaries” or “patient medication diary” or “medication diary” or “medication diaries” or “symptom diaries” or “symptom monitoring diary” or “patient diary” or “patient diaries”

Inclusion criteria

Types of participants: Adults who have completed primary treatment for cancer and participated in patient medication diaries interventions considered likely to be applicable or adapted to HT for BC. Articles excluded: studies of children, palliative care, and interventions during primary treatment.

Concept: the overarching concept of interest is patient medication diaries interventions designed for cancer survivors. Further elements of relevance to this review are intervention components and data on people's experiences, views, usability and acceptability. This review will also identify and map adherence and QoL outcomes.

Context: Studies published in English in the last 20 years, about interventions taking place after primary or acute cancer treatment.

Types of studies: Reviews, evaluation of interventions and primary research articles will be included. Also, randomised controlled trials, qualitative, quantitative and mixed-method studies. Grey literature will be excluded.

Review strategy: Citations generated from the search will be stored and managed in Endnote and duplicates will be removed. Initial screening of all titles and abstracts identified against the inclusion criteria will be conducted by the primary reviewer (Research Associate [RA]) with a second reviewer Yolanda Eraso (YE) screening 10%. Disagreements will be resolved through consensus with a third

reviewer. The primary reviewer will obtain and read the full text of selected articles and assess suitability for inclusion, with a second reviewer (YE) assessing a random 10% of studies. Unresolved disagreement will be subject to third party review. Reasons for exclusion of studies will be recorded.

Data Extraction: The primary reviewer will extract the data using a Microsoft Excel data extraction sheet. YE will check at least 10% of a random sample of extractions for accuracy. Extraction sheet will include title, author(s), date of publication, study design and methodology, number of participants, cancer type, country, intervention aim/type, potential barriers/facilitators, results summary.

Scoping review analysis: The purpose of this review is to identify evidence that can be shared and help discussion at the two co-design workshops. Analysis of extracted data will be descriptive, using tables with key sections of relevance for the study: findings on diary format; self-reporting components; behavioural theory used, barriers and facilitators experienced by patients; healthcare professionals perspectives; and summary of outcomes (QoL and adherence).

1b. Two co-design Workshops:

BC patients (10) and pharmacists (10) will be introduced to the two main components of the intervention alongside a synopsis of findings form the scoping review before the workshop, and with the aim to:

i. WS1: Develop content for a patient self-management diary: Identify preferred medium (paper or electronic version in OneDrive); type of symptoms recorded; frequency; behavioural action.

ii. WS2: Develop content for a medication consultation guide for pharmacists (steps to organise consultation about MBC): Pharmacists' skills identification for person-centred consultations, side-effect attributions; pharmacological and nonpharmacological factors; problem-solving; training content.

Co-production methods will inform the workshops with the aim to develop an intervention 'with' relevant stakeholders, patients (with lived experience of MBC) and pharmacists (dispensing and setting knowledge) [51]. Such an approach can develop interventions that focus on changes that are relevant to stakeholders and practical to deliver [52].

Data collection:
Workshops will take place at London Metropolitan University (LMU), and online for those registered and unable to attend, and are scheduled for 4 hrs (in person) and 3 hrs (online) each. PPIE-lead Carrol Lamouline (CL), Breast Cancer Now nurse, YE and Duncan Stewart (DS) will facilitate the workshops. Participants will receive a summary of the scoping review findings (tables, synopsis) prior to the workshops. Detailed written instructions will be provided to facilitators including, the aim of each task, questions and printed material to discuss different scenarios, timing and resources (face-to-face: coloured voting dots, post-in notes, A5 sheets, audio-recording; online: voting and comments in chat box, videorecording).
Participants will be introduced to the NIHR key principles and features of co-production [53], adapted to the level engagement they will have in the life of the project.

WS1 will focus on developing the patient medication diary. The first part of the workshop, participants will be divided into homogeneous groups of up to 5 individuals (patients and pharmacists separately). Discussion on MBC; barriers/facilitators for using a diary; what helps in identifying side effects after drug changes. The second part will bring mixed groups of pharmacists and patients to identify key intervention ingredients for the diary. Thus, allowing consideration of both patients' preferences and

pharmacists' perspectives on feasibility of the intervention. The final part will be an all-group discussion of items selected by groups, exploring agreements and disagreements with the facilitators.

WS2 will focus on developing the medication consultation guide (steps) and key content of the e-learning package. It will adopt the same group organisation as developed for WS1 (homogeneous and blended) and tasks (exploration through guided hypothetical questions and case studies; and identification of key components). Discussion on communications with pharmacists; what needs to change; knowledge needed on MBC; key steps for a consultation guide.
All participants will receive a certificate of attendance, and will be asked to complete a feedback form.

Data Analysis:

A detailed qualitative analysis of transcripts from the workshops will not be conducted. Instead, recording transcripts and paper copies capturing suggestions, disagreement and consensus around the intervention components will be the main focus of analysis. The co-leads (YE & DS) will consider 'ingredients' agreed by participants to be included in the diary, medication consultation guide, and e-learning package, as well as reasons for exclusion. An Intervention Planning Table [36] will be developed to map the intervention components onto the behavioural analysis. PPIE-lead, PAG and Brest Cancer Now nurse will discuss findings from WS1 and WS2 with research team for refining the prototype intervention (O1). The latter will be shared with workshop participants.

1.c Qualitative interviews with pharmacists:

We will explore the views of pharmacist representatives of professional bodies and owners of community pharmacies about the barriers and facilitators of implementing the intervention (O3).

Data collection:
Guiding principles of the intervention and a synopsis of the prototype intervention will be circulated in advance of the interview. Semi-structured interviews will use a topic guide developed in collaboration with PPI and PAG to explore views about the intervention, barriers and facilitators for implementation (practical and service contract issues). RA and YE will conduct interviews via Microsoft Teams (videoconference or telephone), according to participant preference. Interviews will be audio-recorded and transcribed using a transcription company that is GDPR compliant. Pharmacists will be offered a £30 voucher as a thank you for their time.

Data analysis:
Interview analysis will adopt a Thematic Analysis approach [54] and coding (RA and YE) will be mapped onto the Intervention Planning Table where intervention components and behavioural analysis will be reviewed and discussed with the research team.

WP 2: Design of e-learning resource for pharmacists (O2)

2a. E-learning package design:

A Web-developer specialist (to be recruited) with WP2 lead Ruth Edwards (RE) will design the package based on the educational content of the prototype intervention. It is envisioned that this will include 3 (20 minutes) blocks including interactive sections on communication skills, knowledge, and problem-solving. Patient stories (lived experience) will be used to illustrate key issues around concerns and interactions with pharmacists. PAG will provide feedback on the content and interactive tools used.

2b. Qualitative interviews with pharmacists (8-10): Feedback will aim to establish the appropriateness of the educational intervention as a learning tool.

Data collection: Semi-structured interviews will be conducted by RA, via Microsoft Teams (telephone or videoconference) according to interviewee preference, and audio-recorded. Topic guide will include questions about content (accuracy, relevance, easy to understand); engagement (visuals, quizzes); and behavioural intention.

Data analysis: Transcripts (provided by a transcription company) will be analysed by RA, RE and YE onto a three-column table containing: Participant feedback; participant quote; and e-learning package modification [36].

WP 3: Testing and optimisation studies (O4&5)

We will test the intervention to gather feedback from participants and optimise the different components as follows:

3a. Deliver of the e-learning package to 5 community pharmacists in North Central London ICS. Participants will access the e-learning for 1 month, and will be encouraged to contact (online or telephone) a designated member of the research team to clarify any questions they may have about the content (skills and medication consultation guide).

3b. The 5 trained pharmacists will recruit 20 (4 each) BC patients from their CPs for two months. Pharmacists will collect a screening and enrolment log; and demographic data from patients enrolled in the study. Eligible patients will receive a self-management diary to record side effects and other relevant life-events/environmental details, with a separate sheet to keep notes about what they liked and disliked about using the diary. Patients will complete the diary for a minimum of 1 month and a maximum of 3 months. Patients will attend a medication consultation (10 minutes) with the pharmacist within a 3 month-period. Patients should contact the pharmacy to arrange an appointment. If no request to attend the appointment is made, the pharmacist will send an invitation to attend the consultation 1 week after the 3 months.
Each pharmacist will audio-record 1 consultation (O4) and keep feedback notes about all the consultations (*Appendix: WP3- Pharmacist Feedback Form*). Pharmacists will be able to contact the research team at any point for issues arising, and there will be monthly visits from the team for additional support or advice.

3.c Integration of feedback to produce ENABLE, and a protocol for a feasibility study (O5)

Data collection:

Informed by the Person-Based Approach, the qualitative optimisation studies (1&2) will address barriers to behaviour change, intervention engagement and implementation.

3b.1. A qualitative optimisation study (pharmacists):

Semi-structured, individual interviews with all participating pharmacists will be conducted by Microsoft Teams (phone or videoconference) 1-2 weeks after the 4th consultation by RA and YE. Topic guide will explore:

a. What educational components of the e-learning package and the consultation guide where useful, and what was missing to better support the medication consultation;

b. Perceived behavioural capability, opportunity and motivation to adopt the intervention (i.e. barriers and facilitators to acceptability, usability, practicality in the pharmacy setting).

3b.2. A qualitative optimisation study (patients):

Semi-structured, individual interviews with all participating patients will be conducted by Microsoft Teams (phone or videoconference) a week after the consultation by RA and YE. Topic guide will explore:

a. What recorded elements of the diary were useful and what was missing to better support medication consultations with pharmacists;

b. Perceived behavioural capability, opportunity and motivation to adopt the intervention (i.e. barriers and facilitators to acceptability, engagement, usability, practicality at home and in the pharmacy setting).

3b.3 Audio-recording:

Collected by pharmacists during medication consultation, one per pharmacist.

Data analysis: Interviews will be transcribed, analysed using Thematic Analysis, with codes derived (by RA and YE) both inductively from the participant's accounts and deductively from the target constructs of the TDF (barriers to behaviour change), and the NPT (barriers to intervention implementation). The potential benefit of the intervention to different demographic groups will also be explored. Interviews, alongside feedback recorded from patients' diaries and CPs notes, will identify areas of the intervention which might require modification, and we will record these on a 'Table of Changes' including decisions made by the research team based on the Must have, Should have, Could have, Would like criteria and the guiding principles [36].

The 5 audio-recorded sessions will inform further adjustments of the e-learning package, and segments highlighting best-practice will be incorporated as case studies (if participants consent).

3.c Integration of feedback to produce ENABLE, and a protocol for a feasibility study (O5)

The analyses conducted following the testing and optimisation studies will identify the core materials and processes to be included in the intervention. These findings will be reviewed by the PPIE, PAG, Brest Cancer Now nurse and research team to produce the ENABLE intervention and a feasibility study protocol.
Sharing study progress: All participants (if they consent) will receive email briefings with a synopsis of changes introduced to the intervention based on their input at different stages of the development process. We will also share the full report.

6 STUDY SETTING

For WP3, testing and optimisation study, we will recruit 5 CPs from North Central London ICS. This area includes five boroughs: Barnet, Camden, Enfield, Haringey, and Islington. We will recruit 1 CP from each borough via Pharmacy champions from the Local Clinical Research Network, North Thames (NIHR) and in person, by a research team member, if needed.

Patients will be recruited by community pharmacists following the eligibility criteria protocol. CPs will seek consent from women and deliver the two intervention components: distribute a diary (for women to complete at home) and a medication consultation at the CP. The CI will seek the transfer of Consent Forms gathered by the CPs following the Data Sharing and Transfer protocol at LMU (GDPR compliant), and the transfer of screening & enrolment logs, and demographic data. The CI and RA will contact the pharmacists and patients for a follow-up interview at each site. This is a single site type study, each delivering the same activities (as described on p8-3b). There are no specific site requirements.

7 SAMPLE AND RECRUITMENT

7.1 Eligibility Criteria

a. WP1 – 1.b Two co-design workshops:

Eligibility:

Women diagnosed with breast cancer who are,

- living in London (and)
- currently taking Hormone Therapy drugs (e.g. tamoxifen, anastrozole, letrozole, or exemestane) or had taken these drugs in the last 12 months (and)
- has/had concerns about changing medication brands.

Community Pharmacists who are,

- A pharmacist or pharmacist technician, permanent or locum (and)
- Working in pharmacies located in London (and)
- Dispensing Hormone Therapy drugs (e.g. tamoxifen, anastrozole, letrozole, or exemestane)

b. WP1 - 1.c Qualitative interviews with pharmacists:

Eligibility:

- Pharmacists who are owner or manager of a community pharmacy, chain and independent;
- pharmacists with a representative role in professional pharmaceutical bodies, e.g. Local Pharmaceutical Committee, Community Pharmacy England, Royal Pharmaceutical Society.

Exclusion:

- locum, technician, assistants, pharmacist not owner or manager
- Pharmacists without a representative role in professional pharmaceutical bodies

c. WP2 - 2b. Qualitative interviews with pharmacists:

Eligibility:

- A pharmacist or pharmacist technician, permanent or locum (and)
- Working in community pharmacies located in London (and)
- Providing hormone therapy medication to clients

Exclusion:

- Accredited Checking Technician, assistants

d. WP3 – Testing and optimisation studies

Eligibility: Pharmacists

Inclusion

- Pharmacists and pharmacy technicians; from the London boroughs of Barnet, Camden, Enfield, Haringey, or Islington
- Providing Hormone Therapy medication to clients
- Agree to participate in online training

- Agree to recruit 4 patients from their pharmacy
- Agree to deliver a medication consultation with recruited participants and audio record 1 consultation (with patient consent), and provide feedback notes of the consultation.
- Agree to provide feedback in a study follow-up interview.
- Is willing to provide written (signed and dated) informed consent.

Exclusion:

- Locum, Accredited Checking Technician, pharmacy assistants.

Eligibility: Patients

Inclusion

- Women 18+ with early BC (stage 1-3);
- Talking oral HT medication (tamoxifen, anastrozole, or letrozole) and had/have concerns about changing HT brands;
- Not taking HT medication as neo-adjuvant or secondary metastatic BC;
- Is willing and able to record notes on side effects and medication taken (diary) and attend a medication consultation with the CP;
- Is willing and able to participate in a study follow-up interview (phone or video conference);
- Is willing to provide a copy of the diary;
- Is willing to be audio recorded during the pharmacy consultation;
- Is willing to provide written (signed and dated) informed consent.

Exclusion

- Male
- Currently or recently (last 6 months) involved in another research study where medication adherence is a primary outcome;
- Have had in the last 6 months a medication review about changing brands of HT drugs.

The target population will comprise women with greatest potential to benefit clinically from HT: women with early stage (1-3) ER-positive breast cancer. The evidence-base for this study, our primary research, and the PAG who provided feedback, consist of women with BC. Its suitability for men is not known, therefore, men will be excluded. Proficiency in English is not a requirement, we will facilitate translations and interpreters from our Language team (LMU) for common languages spoken in the boroughs. We will be guided by pharmacists' requests.

7.2 Sampling

a. WP1 – 1.b Two co-design workshops:

We will purposively sample 10 BC patients and 10 community pharmacists.

b. WP1 - 1.c Qualitative interviews with pharmacists:

A purposive stratified sample of 10 pharmacists: 6 from Community Pharmacies (3 chain; 3 independent) and 4 from professional pharmaceutical bodies. For the latter, snowball technique may also be used.

c. WP2 - 2b. Qualitative interviews with pharmacists:

Between 8-10 community pharmacists will be purposively sampled. We will seek their feedback after testing the e-learning package.

d. WP3 - Testing and optimisation studies

A purposive sample of 5 community pharmacists [2 located in the 20% IMD], and 20 patients.

Sample size: the overall approach to sample size for intervention development studies, following the Person-Based Approach [36], is to collect feedback from target users and stakeholders iteratively, at different stages in the development process. The development of intervention ingredients and content will include 2 workshops of 20 target users each (patients and pharmacists) involved as PPIE (public contributors). This will be followed by three instances of qualitative feedback from research participants in the samples provided above. This is a different form of sample size estimation to the one observed in stand- alone qualitative studies, in that the first intervention prototype is being modified by target users at different stages. Finally, for the testing stage, given the nature and organisational requirements of the intervention, it is not possible to recruit participants until reaching data saturation on its acceptability. This will be further explored in a future feasibility study, with a sample size calculation and sufficiently powered to analyse acceptability and feasibility.

7.3 Recruitment

a. WP1 – 1.b Two co-design workshops: Patients: We will recruit women in London with different sociodemographic characteristics (age, ethnicity, language and socioeconomic status). Evidence indicates that BC incidence rates are lower (7%) in non-White British women [55]. However, women's care experiences in minoritised ethnic groups are comparatively lower than Whites [56], whilst intentional non-adherence to HT drugs is higher than Whites [29]. There is also evidence that younger and older age, and deprivation are factors influencing non-adherence [29]. As these groups might benefit from the intervention, our recruitment approach will draw on two strategies; 1) inviting participants through organisations representing minoritised groups: Brest Cancer Now, Bric Centre, Race on the agenda [ROTA], Black Women Rising, South Asian Health Action, and others representing Turkish and Arabic communities prevalent in the study area, and 2) monitoring of recruitment to focus on particular characteristics not reflected in our criteria. The PIS form will be explicit about the need to capture a plurality of voices from people with different backgrounds, the limited numbers, and the selection process prior acceptance of participants. Our PPIE-lead will monitor this task.
Organisations will post invitations (English and translated) with a link to the PIS through a newsletter (email), social media (Tweeter, Instagram, Facebook), and/or webpage. We will also attend community venues of relevant local ethnic groups to promote the study and its benefits to patients, and seek their advice on the best form of communication. Contact with patient groups within GP practices and snowball technique will also be used as recruitment methods. The PIS will describe the nature of the study, details of the 2-day in-person workshop participation requirement, payment offered, a link to access the registration form (OneDrive) or printed copy, and an email to contact the research team for further information. Interested women will complete a registration form about their preferred way of contact, confirm their HT medication taking status, age, ethnicity, and post code (for IMD identification). Those registered will be notified on whether they have been selected or not based on recruitment criteria. Those who registered and could not attend in person, will be offered the opportunity to contribute online to the workshop they have missed. Selected patients will sign an informed consent form prior attendance via a 'simple' electronic signature, or by bringing a signed paper copy to the workshop.

Community Pharmacists: Recruitment will take place via newsletter (email or website) distributed by Local Pharmaceutical Committee networks in London. PIS will describe the nature of the study, details of the 2-day workshop participation requirement, a certificate (for use as CPD portfolio), payment

offered, a link to access the registration form (OneDrive), and an email to contact the research team for further information. At registration, interested pharmacists will be asked about their preferred way of contact, job title, years of work experience, and CP post code (IMD). The latter will ensure we include representatives from different boroughs, occupations, work experience, and different SE areas. Similarly to our patients' PIS, those registered will be notified on whether they have been selected or not. Those who registered and could not attend in person, will be offered the opportunity to contribute online to the workshop they have missed. Selected pharmacists will sign an informed consent form prior attendance via 'simple' electronic signature.

All workshop participants will be offered a £75 voucher p/workshop, travel expenses and lunch. Pharmacists attending in person will be offered a reimburse for locum backfill for 4 hrs.

b. WP1 - 1.c Qualitative interviews with pharmacists: To ensure representation from deprived communities, we will recruit 3 community pharmacists servicing these areas. We will use our existing contacts with Local Pharmaceutical Committee networks and Pharmacy champions from the Local Clinical Research Network, North Thames (LCRN) to advertise via website, newsletter or social media (*Appendix: WP1- Leaflet Pharmacy interviews [owners or managers]*); and professional bodies (Local Pharmaceutical Committee, Community Pharmacy England, Royal Pharmaceutical Society) to obtain a list of potential participants. PIS and consent forms will be available and stored in our OneDrive study folder (*Appendix: WP1- Pharmacist staff & Professional bodies – PIS and Consent forms*). A 'simple' electronic signature will be required prior to the interview. Pharmacists will be offered a £30 voucher for their interview time with the research team.

c. WP2 - 2b. Qualitative interviews with pharmacists: Pharmacists participating in workshops [point a.] will be invited to test the e-learning package and provide feedback. If more participants are needed, they will be recruited in the same way as described for the workshops, via leaflet (email or website) distributed by Local Pharmaceutical Committee networks in London, and in person visits to CPs by our research team (*Appendix: WP2- Leaflet Pharmacy feedback*). PIS and consent forms will be available in our OneDrive study folder, and a 'simple' electronic signature will be required prior to the interview (*WP2-Pharmacist feedback PIS and Consent form*). Pharmacists who take part in testing and interviews will be offered a certificate (CPD) and a £75 voucher as a thank you for their time.

d. WP3 - Testing and optimisation studies: <u>Pharmacists</u>: We will recruit 5 CPs, one for each borough, and from different socio-economic areas, including 2 in the bottom 20% by IMD, serving diverse ethnic minority groups to maximize intersectional contrasts in our analysis. We will send invitations to participate through Pharmacy champions LCRN and in person (if needed) to meet our recruitment criteria (*Appendix: WP3 - Leaflet invitation Community Pharmacies*). We will seek permission from the pharmacy's Head office or owner before approaching a pharmacy. Once permission is granted, we will invite the pharmacy staff to the study with the PIS, explaining all its components (training, recruitment, medication consultation, feedback forms, and interview) (*Appendix: WP3 – Pharmacist PIS & Consent form*). Pharmacists interested in taking part will have at least 24 hours to decide whether or not to take part, and will hand in their written Consent forms to the CI. Pharmacy organisations will receive a small expenses fee for participating in the study of £1,100 (time incurred in online training, recruitment, medication consultation). Pharmacists will be offered a £30 voucher for their follow-up interview time with the research team.

<u>Patients:</u> Trained pharmacists will recruit 4 BC patients each, from their CPs, during a 2 month-period. Women will be approached opportunistically, when collecting their HT prescription. If pharmacies consider it necessary to facilitate recruitment, they will be able to put a poster about the study, visible to the public, inviting interested women to approach the pharmacy staff for information (*Appendix: WP3- Poster Community Pharmacy 1&2*). This will target patients who might be willing to participate but are not collecting a HT prescription within the recruitment time frame.

Pharmacists will ask potential participants if they would be interested in taking part in a study about discussing with pharmacists concerns with HT medication brand changes. If patients accepted, the pharmacist will ask each patient to answer a few questions (*Appendix: Participant Screening and Enrolment log*). Eligible patients will be provided with a PIS and the informed consent form (*Appendix: WP3- Patient PIS & Consent Form*). At least 24 hours after the receipt of the PIS, the pharmacy will telephone the woman, answer any questions and, if she wishes to take part, ask her to bring the signed consent form to the pharmacy. It should be noted that if a woman is happy to be consented immediately, and the pharmacist is satisfied the woman has fully comprehended what is being asked of her, then consent can be taken immediately. Mental capacity will be assumed unless proven otherwise. When women return their consent form, they will receive a diary from the pharmacist, who will also collect simple demographic data [post code, age, ethnicity, medication taken, education, living alone or with family, work status and email or prefer contact for arranging medical consultation] (*Appendix: WP3-Participant demographic information*). Each patient will be assigned an ID number by the pharmacist.

Pharmacists will be able to recruit women who are not fluent in English, and with whom they communicate in another language. The most common languages used in the area are Turkish, Arabic and Bengali. If the pharmacist consider that such women might be able to participate, we will provide translated PIS and consent forms. If the woman accepts to take part in the study, we will provide a translated copy of the diary for her to complete.

To this aim, we will first contact LMU Translation Department staff to identify a translator with a Diploma in Public Service Interpreting – Health (DiPS-H) – as recommended by the NIHR. If need be, we will engage with our host organisation (NCL ICB) to put us in contact with specific translators.

For the interviews, a female DiPS-H translator and interpreter will help us communicate as follows:

- translate the diary entries

- translate our email correspondence to arrange an interview.

- translate the key questions we are interested in asking for the interview – so patient and interpreter know content in advance.

- attend the interview to simultaneously interpret for the participant and interviewer.

To protect the participant's privacy in our correspondence with the translator, we will copy the participant using a blind copy.

Patients will be offered a £30 voucher for their follow-up interview time with the research team.

<u>Patient Advisory Group (PAG):</u>

It will comprise a group of 5 women with BC, taking HT, who have experienced concerns about changing medication brands. Three members of this group provided feedback on early stages of this study and have expressed willingness to continue. Recruitment: 2 members will be recruited from minoritised ethnic groups living in London. This is to ensure representativeness as the existing members are White British, age range (35-72) based in England.

We will advertise the PAG role in the patient organisations already mentioned, using the Cancer Research UK patient involvement registration form, whereby interested applicants are invited to an interview. This is to explain the work involved and the importance of commitment for 20 months. Meetings will take place online to facilitate issues with time, patients' mobility, and costs. PAG members will receive payment for their time in line with NIHR INVOLVE recommendations.

7.3.2 Consent

Participation in all work packages will be contingent on informed consent being obtained. Prior to expressing their interest in participating, all potential participants will be provided with the appropriate participant information sheet detailing the study aims and what taking part will involve.

All potential participants will have the opportunity to ask questions using contact details provided and will be given at least 24 hours between being provided with the information about the study and being asked to provide consent (if participant is happy to be consented immediately, and the study team feel they fully understand what is being asked of them, then consent can be taken without a 24 hour wait period).

Participants will be informed that participation is voluntary and that they can withdraw from the study at any point, without affecting their medical care or legal rights. The form will make clear that any information arising from the study will be anonymised so participants will not be identifiable in any publications or reports. Participants will be asked to indicate their understanding that this anonymous information may be used in future related research or may be shared with other researchers after data is deposited and made available.

WP1: Workshop participants will be able to consent by ‘simple’ electronic signature or by singing a paper copy (according to their preference).

WP1 and WP2: Pharmacists participating in interviews by phone or videoconference, a ‘simple’ electronic signature will be required in accordance with the joint HRA and MHRA statement on seeking consent by electronic methods.

WP3: Written informed consent will be obtained from pharmacists and patients.

Pharmacists will provide their consent to participate in the study to the CI.

Pharmacists will seek informed consent from patients. They will provide at least 24 hours, after the receipt of the PIS, before phoning the patient, answer any questions they may have about the study, and, if the patient wishes to take part, the pharmacy will ask her to bring the signed consent form to the pharmacy. It should be noted that if a woman is happy to be consented immediately, and the pharmacist is satisfied the woman has fully comprehended what is being asked of her, then consent can be taken immediately. Mental capacity will be assumed unless proven otherwise.

Pharmacists will store participants’ consent forms in a lockable document box1 provided by the CI, and after recruitment is completed, box1 will be transferred to LMU following a Data Transfer protocol. Patients consent forms will inform about this data transfer process; and patients will be provided with CI contact details should they have further questions about the study.

Obtaining participant informed consent will be in accordance with the REC guidance, and UK Policy Framework for Health and Social Care Research. The pharmacist or the researcher, and the participant shall both sign and date the Informed Consent Form before the person can participate in the study. One copy of the form will be kept by the participant, one will be kept by the CI. Should there be any subsequent amendment to the final protocol, which might affect a participant’s participation in the study, continuing consent will be obtained using an amended consent form which will be signed by the participant.

7.3.3 End of Study

For an individual participant, completion of an interview will be the end of their participation in the study. For the research team, the end of the study will be when the ENABLE intervention is developed alongside a feasibility study protocol.

8 ETHICAL AND REGULATORY CONSIDERATIONS

8.1 Assessment and management of risk

Workshops: Patients might be revisiting distressing feelings in relation to their breast cancer medication-taking experience. They will understand they can withdraw from the workshop at any time should they become upset. In situations where participants feel upset because of the discussion generated in the group, the facilitator will offer initial emotional support and refer the participant to the support of a Breast Cancer Now nurse who will be acting as facilitator (for in person workshops) or the MacMillian support line (if participating online). Should they wish, the participant will be invited to leave the discussion / room as long as is needed. They may either withdraw or come back to the group depending on their preferences. Also, facilitators will be instructed to consider issues of participants' distress and breaches of confidentiality (e.g. identifying a pharmacist in the area), and to manage/redirect the conversation into an appropriate course. Participants and facilitators will be respectful of everyone taking part, their views and rights. Facilitators will ensure that everybody has the chance to speak.

YE has experience in interviewing and running patient advisory groups for breast cancer patients; DS and CL (patient and public engagement) have both experience of co-production and workshop facilitation; and a BCN nurse will also facilitate the workshops.

WP3 – testing the intervention. Patients: The risk of taking part is minimal. The intervention will be developed alongside patients, pharmacists and a breast cancer nurse and therefore should not cause any harm.

During follow-up interviews, there might be cases when women feel upset when discussing their previous experiences and decisions made regarding therapy, whereby changing medications brands, describing new side effects or troubles in accessing a preferred brand could be upsetting. The CI (Prof Eraso) is experienced in interviewing BC patients and the RA will receive support if she lacks experience of interviewing vulnerable groups. In situations where a participant feels upset, the interviewer will ask the participant if she'd like to continue, stop temporally or stop completely the interview. After offering initial emotional support, the interviewer will offer to contact a family member, a specific person or the GP on their behalf. Our PIS will also contain information on support offered by charities, Breast Cancer Now and Macmillan.

If patients would like to discuss issues in relation to their experience as participants in the study, we will offer contact details from the CI, and suggest contacting their GP, or the BC hospital team responsible for their care.

Pharmacists: Delivering the intervention to patients and all interviews with pharmacists, are not expected to raise any significant ethical issues, cause distress or make the participant upset. We will make explicit at the start of the recording that video is not necessary, and that participants can decide if they have their camera on/off. Data storage: we will first download the recording from Microsoft Teams and delete it from the site. We will then upload the recording in OneDrive study folder (password protected). The same procedure will be followed by telephone interviews which will be conducted via Microsoft Teams.

Finally, if the researchers come across a participant (workshops or interviews) becoming abusive to others, in danger of self-harm or a threat to others, we will report it to the police. If a participant discloses sensitive information about abuse or neglect, we will report this to the local authority safeguarding team.

8.2 Research Ethics Committee (REC) and other Regulatory review & reports

Ethical approval will be obtained from the NHS HRA's Research Ethics Committee (REC) for the study protocol, informed consent forms, participant information sheets and leaflets. Before any CP can enrol patients, the CI will ensure that appropriate approvals from participating sites are in place.
The sponsor will be responsible for deciding whether amendments are substantial and non-substantial in collaboration with the CI.
Where an amendment is required to study documentation that required REC approval, changes will not be implemented until REC approval and HRA categorisation is received. Where an amendment requires local approval, this shall be sought prior to the amendment be implemented at each site in accordance with the categorisation given on the HRA approval letter.
Minor amendments for logistical or administrative purposes may be implemented immediately
Amendments will be logged on the Sponsor's Study Amendment Log and stored with the study files.
Annual Progress Reports shall be submitted to the REC within 30 days of the anniversary date on which the favourable opinion was given – until the end of the study.
A final report shall (where possible) be submitted to the REC within one year after the end of the study.
If the study is terminated prematurely the CI will notify the REC, including the reasons for premature termination.

8.3 Peer review

The project has received external peer reviewed and has received funding by the NIHR (Research for Patient Benefit programme).

8.4 Patient & Public Involvement

The initial idea for this project emerged from Eraso's previous study on women's perspectives about extending HT to 10 years conducted on data from the Brest Cancer Now online forum. MBC emerged as a relevant factor underpinning continuation and discontinuation with treatment. A further study focused on MBC with data collected from 10 interviews with patients and 8 interviews with pharmacists. Patients' views on engaging pharmacists were overwhelmingly positive as they deemed pharmacy staff are trusted professionals for managing drugs and more accessible than other health professionals.
Preliminary findings on MBC were presented to 20 BCN nurses at a training event, and a feedback survey on this session revealed that 67% of nurses knew 'something about this topic' and 33% knew 'a lot'; and on the usefulness of having guidelines to support patients, 67% responded it would be 'very useful' and 33% 'useful'.
Continued engagement with BCN research nurses, academic pharmacists and the Chief Scientist of the Royal Pharmaceutical Society (who has also researched in breast cancer adherence) was very productive and their views have influenced our proposal design in terms of the format of the medication consultation guide i.e. brief, clear steps and easy to follow in busy pharmacy settings.
Our Patient Advisory Group (PAG) composed by 5 BC patients and 2 members of LMU PPIE group, provided feedback on early stages of the proposal. The idea of asking patients to think carefully about their side effects, monitor and report on them had a very positive response. The PAG have also shaped and extended our project by emphasising the importance of developing a problem-solving approach in CPs, including skill development plans for pharmacists, and the importance of inclusivity e.g. providing choice for a patient diary (online or paper).
We consulted the PAG members again as the project progressed in its request for funding. We are planning to recruit 2 more members as explained in the recruitment section of this protocol. We

created a fully-costed programme of PPIE activities in response to members expressed needs, including induction and providing future study materials in easy read format.

The input from patients and the public will remain central throughout the study and will continue through 4 main routes.

1. Patients and pharmacists are directly involved as public contributors in 2 co-production workshops (WP1).
2. The PAG, which will meet regularly during the study, will provide feedback on all WPs and instruments of data collection, and plan dissemination strategies.
3. Carrol Lamouline is our PPIE-lead and co-applicant. She will contribute in all stages of intervention design (recruitment, facilitating workshops) and reporting on patients' ideas in team meetings, will manage the PAG including their induction, and sit monthly on the Project Management Group.
4. A BC patient will sit in the Steering Committee group.

The engagement with the public will be accompanied by continued and extended engagement with professionals and relevant organisations.

1. Pharmacists will participate as public contributors in providing feedback on e-learning package.
2. Representatives of pharmacy professional organisations and CPs owners/managers will provide feedback on issues of implementation of the intervention
3. There will be continued regular contact with the LPCs, Brest Cancer Now nurses and other relevant organisations.

Support for patients and stakeholders in workshops will be provided through sending relevant information in advance, using easy read, brief and graphic formats (accounting for time and comprehension).
Induction session for PAG will offer them a presentation and brief materials on their role for the project, and meeting with the research team.
Two existing PAG members also expressed an interest in ways of capturing feedback from/to PAG, for which we agreed to use the 'you said we did' format. Also, suggested by our PPIE-lead, we agreed to use the GRIPP2 checklist for reporting of public engagement.

8.5 Protocol compliance

This study will be conducted in accordance with this protocol. Accidental protocol deviations may occur at any time. Accidental protocol deviations will be adequately documented on the relevant forms and reported to the Chief Investigator and Sponsor immediately.

8.6 Data protection and patient confidentiality

All study staff and researchers will comply with the principles of the Data Protection Act (2018) in protecting the rights of study participants with regards to the collection, storage, processing and disclosure of personal information and will uphold the Act's/Regulations core principles. The data controller for this project will be LMU.

Consent forms obtained by pharmacists will be stored in a lockable document box1 provided by the research team. Once the 5 pharmacists complete the patient recruitment process, box1 with consent forms will be transferred to LMU following the Data Sharing and Transfer policy protocol which is GDPR compliant. Once at the university, all written consent forms obtained for the study alongside

printed copies of electronic signed forms (downloaded and deleted from the only site) will be stored in a locked filling cabinet for 10 years after the end of the study, following the LMU data retention policy. Only the CI will have access to consent forms.

Registration forms for workshop participation (WP1) and pharmacist interviews (WP1 & WP2) with personal data and contact details won't be kept longer than is necessary (to arrange a workshop participation and interviews), and will be securely deleted. This will be shared with co-applicants members of the team. Only if participants consent, we will keep emails to update them on the study.

Each patient in WP3 will be assigned a study identification number in their consent form. Personal data and research data collected by the pharmacist and stored in a lockable document box2 [screening log; demographic information and contact details, diary and feedback notes] will be transferred to LMU (following the above protocol) after the medication consultation for each patient is completed. This data will be stored at LMU in a separate locked filling cabinet, i.e. different location from ID and consent forms. Co-applicants members of the team will have access to this data and only for specific purposes (e.g. data analysis, arranging interviews, sending summary of findings).

All collected research data stored electronically will use a password protected folder in LMU OneDrive (study folder). Only the researchers in this project will have access to the project files stored at LMU secure cloud. All recordings will be retained until the end of the study to allow researchers to return to the data as needed. After this, recordings will be permanently deleted.

Transcription of the interviews will be undertaken by a member of the research team or an external company, Transcribe it, with whom we will sign a Non-Disclosure Agreement. Sending interview recordings to Transcribe it will be as follows: Files to be transcribed will be saved in a password-protected, encrypted zip folder and immediately uploaded to Transcribe it using their file upload service. The password will be provided to the service separately by email.

Interview transcripts, copy of diaries, and materials and recordings from workshops will be de-identified and anonymised. Similarly, only anonymised extracts of recorded medication consultations will be used to improve our online training package with the aim of demonstrating good practice examples to pharmacists.

Anonymised and deidentified data will be deposited in the University's Research Data Repository for future re-use and access to other researchers following the University and NIHR's share data policy.

Data generated as a result of this study will be available for inspection on request by LMU representatives, the REC, local R&D Departments and the regulatory authorities.

8.7 Indemnity

Insurance and indemnity for patients and pharmacists or pharmacist technicians at community pharmacies sites is covered within the article 32 of the Pharmacy Order 2010, which makes compulsory for pharmacists to have appropriate indemnity cover to be register with General Pharmaceutical Council. London Metropolitan University as research Sponsor indemnifies its staff, research participants and research protocols with public liability insurance.

8.8 Access to the final study dataset

The final data set will be accessible by the research team; anonymised data will be made available to other researchers for secondary analysis. The consent procedures include consent for the sharing of data. It will be explained to participants that anonymised data will be shared and maybe accessed in future for relevant research by other researchers.

9 DISSEMINIATION POLICY

9.1 Dissemination policy

The data custodian will be the Chief Investigator on behalf of London Metropolitan University.
PPIE and PAG will support dissemination of our findings. A Knowledge Exchange workshop with NHS cancer communities in London, Pharmacy professional bodies, charity organisations and patient groups will meet to discuss findings and potential practice implications.

We are planning to use a range of communications channels to maximise reach to all the stakeholders, scientific and lay audiences: A project dedicated page within the Health and Behaviour Research Centre website; LMU 'news items', shared through Twitter, Instagram, LinkedIn, and distributed to key stakeholders; Email newsletters to key stakeholders with research up-dates; Research briefings for study participants (if they consent) and PPIE, with key intervention changes.

The wider clinical and academic audiences will be reached via presentations at Breast Cancer Now, the UK Society of Behavioural Medicine, UK Interdisciplinary Breast Cancer Symposium. Three papers will be submitted for publication in peer review journals (e.g. J. Cancer Survivorship; British J. of Health Psychology; and J. of Pharmaceutical Policy & Practice). Papers and conference presentations will be publicised on the project website, including the study protocol and Final study report.

9.2 Authorship eligibility guidelines and any intended use of professional writers

We will be guided by the International Committee of Medical Journal Editors (ICMJE) who have defined authorship criteria for manuscripts submitted for publication.
The ICMJE recommends that authorship be based on the following 4 criteria:

- Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND
- Drafting the work or reviewing it critically for important intellectual content; AND
- Final approval of the version to be published; AND
- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

10 REFERENCES

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11. APPENDICIES

11.1 Appendix 1- Required documentation

- WP1 – Pharmacist staff & professional bodies – PIS & Consent Form V1.1
- WP1 – Leaflet pharmacist interviews [owners & managers] V 1.0

- WP2 – Pharmacist feedback PIS and Consent form V1.1
- WP2 – Leaflet pharmacist feedback V1.0

- WP3 – Patient PIS & Consent Form V1.1
- WP3 – Pharmacist PIS & Consent Form V1.1
- WP3 – Poster Community Pharmacy 1 & 2 – V1.0
- WP3 – Participant demographic information – V1.0
- WP3 – Participant Screening & enrolment log V1.0
- WP3 – Pharmacist feedback notes V1.0

11.2 Appendix 2 – Schedule of Procedures

Procedures	**Screening**	**Baseline**	**1-3 months**	**Post intervention**
Community Pharmacies				
Patients				
Patients assessment for eligibility	x			
Informed consent	x			
Demographics		x		
Diary		x		
Medication consultation and diary completion			x	
Interview				x
Pharmacy staff				
Recruitment, informed consent and training	x			
Recruitment of participants, consent	x			
Demographic data and diary distribution		x		
Medication consultation recording & feedback form			x	
Interview				x

13.3 Appendix 3 – Amendment History

Amendment No.	Protocol version no.	Date issued	Author(s) of changes	Details of changes made
1	V1.2	15.10.2024	Yolanda Eraso	Offer a separate online group participation for patients and pharmacists registered for the workshops who were unable to attend in person.
2	V1.3	17.03.2025	Yolanda Eraso	Changes in the payment offered to community pharmacies participating in the study; change of PPIE co-applicant

List details of all protocol amendments here whenever a new version of the protocol is produced.

Protocol amendments must be submitted to the Sponsor for approval prior to submission to the REC.