STUDY PROTOCOL

Feasibility study: EXpanding into communities to imProve physical activity sUpport foR womEn after breast cancer (PURE-EX)

FULL TITLE
EXpanding into communities to imProve physical activity sUpport foR womEn after breast cancer

SHORT TITLE (ACRONYM)
PURE-EX

PROTOCOL VERSION NUMBER AND DATE
Version 1.1 (03/09/25)

IRAS: 361493
REC Reference:
ISRCTN:

Sponsor: Newcastle University
Sponsor Ref: NU-01264

Funder: Breast Cancer Now
Grant Ref: 2022.11PR1567

Protocol 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 Sponsor:

Name (print):

Position:

Signature: **Date:**

Chief Investigator:

Name (print):

Position:

Signature: **Date:**

Principal Investigator:

I confirm that I have read and understood Protocol v1.1 dated 03/09/2025. I agree to comply with the study protocol, the principles of Good Clinical Practice and all required regulatory requirements.

Name (print): **Site:**

Position:

Signature: **Date:**

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1. STUDY CONTACTS

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2. STUDY SUMMARY

Study Title	EXpanding into communities to imProve lifestyle sUpport foR womEn after breast cancer
Short Title	PURE-EX
Study Design	Single-arm, non-randomised, feasibility study
Study Participants	Eligible participants are: • Women aged ≥18 years • Clinical diagnosis of early-stage or locally advanced breast cancer (stage I-III) • Have completed surgery for breast cancer • Have received clearance from a treating clinician to participate in the study • Willing and able to provide written informed consent
Planned Sample Size	45
Planned Start Date	05 January 2026
Planned Duration	15 months
Study Aims	This study will assess: i. The feasibility and acceptability of being offered referral to, and attending, a community-based physical activity programme in women who have completed surgery for breast cancer. ii. The feasibility and acceptability of breast cancer healthcare professionals (HCPs) offering physical activity referrals. iii. The feasibility, acceptability, and views of trained instructors delivering a community-based physical activity programme to women after breast cancer treatment. iv. The feasibility of data collection, measures of adherence and retention to the intervention v. potential signals of intervention efficacy

3. ABSTRACT

Background

Breast cancer and its treatment can have long-term adverse effects on physical and mental health. Evidence-based guidelines recommend that healthcare professionals

(HCPs) advise women with breast cancer to engage in physical activity to improve health outcomes. However, support to be active is not standard care. The PURE-EX (EXpanding into communities to imProve physical activity sUpport foR womEn after breast cancer) programme aims to address this knowledge-practice gap.

Through a programme of research, we have co-developed a programme that integrates physical activity referrals into standard care for women who have been treated for early-stage and locally-advanced breast cancer, and provides access to a supportive community-based physical activity programme which has been designed specifically for women who have been treated for breast cancer, and which can be tailored to their individual needs.

PURE-EX programme components include:

1. A referral pathway enabling HCPs to refer women to community-based physical activity programmes after they have completed primary treatment for breast cancer;
2. A one-to-one review with a trained exercise instructor;
3. A community-based physical activity programme for women after breast cancer treatment.

Aim

To conduct a feasibility trial in 45 women who have finished primary treatment for breast cancer to assess the feasibility and acceptability of the PURE-EX programme.

Discussion

The PURE-EX programme is an evidence-based, theory-informed, and person-centred intervention, with the potential to make physical activity support routinely available for women after breast cancer treatment. This study will assess the feasibility and acceptability of the PURE-EX programme.

4. PLAIN ENGLISH SUMMARY

Background

More women are surviving breast cancer than ever before. But women often experience low mood, reduced strength and fitness, and extreme tiredness. These issues can last for years after treatment.

Being active after breast cancer treatment can help. It can make women feel less tired, help them return to full strength, and improve their overall health and wellbeing. It may also lower the chances of cancer coming back.

Unfortunately, most women do not get support to be active after treatment. The main issue is that there aren't enough suitable physical activity classes for women to join.

There also are no easy ways for healthcare professionals (such as breast care doctors and nurses) to refer women to classes.

We have developed a programme that allows women to be referred to suitable and supportive physical activity classes after their treatment. This PURE-EX programme has three main parts:

1. A pathway which healthcare workers can refer women to local physical activity classes;
2. A one-to-one review with a trained exercise instructor;
3. A physical activity programme which, has been especially designed for women who have had breast cancer treatment, and which will be held in a location in the local community.

Aim

We will test the PURE-EX programme with 45 women who have completed surgery for breast cancer. We want to find out if they liked the programme, if it helped them, and how we can improve it. We also want to understand how the programme is viewed by the healthcare professionals and exercise instructors involved in delivering it.

5. FUNDING

Funder: Breast Cancer Now

Financial Support Given: £249,999 for the full research programme

Grant Holder: Dr Sam Orange, Newcastle University, sam.orange@newcastle.ac.uk

6. BACKGROUND

Survival from breast cancer has doubled in the last 40 years in the UK due to advances in screening, early detection, and treatment.[1] In 2020, the 5-year survival rates for early-stage and locally advanced breast cancer were 98% for stage I, 90% for stage II, and 72% for stage III.[2] This has led to a significant increase in the number of breast cancer survivors, with an estimated 600,000 women currently living in the UK after a breast cancer diagnosis. This number is predicted to rise by approximately 10% each year, reaching 1.7 million by 2040.[3]

Breast cancer and its treatment can have long-term adverse effects on both physical and mental wellbeing. Women diagnosed with breast cancer report lower quality of life (QoL) during treatment, and for at least 1-year afterwards, compared with women with no history of breast cancer.[4,5] Almost half (48%) of women diagnosed with early-stage breast cancer experience depression or anxiety in the year after diagnosis.[6] Cancer-related fatigue persists in around one-third of women for 5 to 10 years post-treatment,[7] which can contribute to difficulties in returning to work and living independently.[8] Cardiorespiratory fitness and muscle strength, which are strong predictors of all-cause and cancer-specific morbidity and mortality,[9–11] are 20-25% lower in women after breast cancer treatment compared with sedentary women with no history of cancer.[12] Breast cancer survivors also have increased risk of developing non-breast primary cancers[13] and other chronic health conditions, including type II diabetes[14] and cardiovascular disease.[15] Therefore, strategies are needed to address the physical and psychosocial sequelae of breast cancer and its treatment.

Guidelines issued by several expert bodies, including the American Society of Clinical Oncology (ASCO),[16] National Comprehensive Cancer Network (NCCN),[17] and American College of Sports Medicine (ACSM),[18] recommend that healthcare professionals (HCPs) advise people diagnosed with cancer to engage in regular physical activity to mitigate the side effects of treatment. This recommendation is based on strong evidence from randomised controlled trials that physical activity interventions improve QoL, fatigue, cardiorespiratory fitness, muscular strength, and symptoms of anxiety and depression in people with cancer, including breast cancer.[16,18] Additionally, recent findings from the Global Cancer Update Programme showed that participating in the highest versus lowest amounts of leisure-time physical activity after a breast cancer diagnosis was associated with a 44% lower risk of all-cause mortality and 42% lower risk of breast cancer-specific mortality.[19]

Support from HCPs is crucial because physical activity levels decline during breast cancer treatment and do not return to pre-treatment levels.[20] Self-reported UK data show only 20% of breast cancer survivors are regularly physically active[21,22] and 28% are completely inactive.[21] Most women want to receive physical activity guidance from their

breast cancer care team,[22–24] and an oncologist's recommendation to exercise increases exercise levels in women during and after treatment.[25,26]

Despite evidence-based guidelines, support to be active is not standard care. Our UK-wide survey[22] showed one in five (20%) women with breast cancer recall receiving physical activity advice after completing treatment, and only 10% were referred to another source of information or physical activity specialist. These findings align with other UK-based data showing only 9% of cancer nurses report talking to patients about physical activity.[27] HCPs report many barriers to providing physical activity support, including organisational-level barriers such as limited resources (e.g., staff, funding), absence of a referral pathway, and a lack of suitable physical activity programmes to refer to.[28–31] HCPs also report individual barriers, such as having a lack of time, inadequate knowledge of physical activity, and not being the right person to give advice.[28,29,32]

7. RATIONALE

Efforts to make physical activity support standard practice in oncology have been proposed, most notably through the USA-based 'Moving Through Cancer'[33,34] initiative. This initiative draws on the 3A's approach (Ask, Advise, Act) - originally developed for smoking cessation[35] - to provide HCPs with a framework to ask patients about physical activity, advise them to be active, and offer referral to community-based programmes. This approach is appealing because it can be delivered by HCPs in less than 30-seconds[36] and leverages existing community resources, reducing burden on healthcare systems.

Exercise referral schemes are available in some UK regions through the National Health Service (NHS), allowing General Practitioners and allied health professionals (e.g., physiotherapists) to refer sedentary patients to physical activity programmes.[37] However, these schemes are not consistently available nationwide, and no referral pathway exists for breast cancer HCPs to offer women physical activity referrals.[31] Furthermore, most community-based physical activity programmes are not cancer-specific and are led by instructors who lack specialised training or knowledge about breast cancer. The National Institute for Health and Care Excellence (NICE) recommends that policymakers fund exercise referral schemes only if the programmes are tailored to meet individual needs.[37] For women with breast cancer, this requires adaptations to address or circumvent the physical and psychosocial sequelae of treatment, such as lymphoedema, arthralgia, upper-body pain and immobility, peripheral neuropathy symptoms, menopause symptoms, web axillary syndrome, and body image concerns. Having guidance from knowledgeable exercise instructors who understand issues regarding breast cancer treatment is important for encouraging physical activity participation in breast cancer survivors.[38]

While being active can benefit women during and after treatment,[18] most prefer to be active at home during treatment[39] and attend an exercise facility post-treatment.[40–42] Evidence suggests that breast cancer survivors are more likely to seek physical activity advice after completing treatment[40,43,44] with chemotherapy being negatively associated with wanting to receive advice,[40] likely due to treatment-related side effects.[45] These preferences are supported by findings from an exercise trial showing higher adherence to supervised facility-based exercise in women who had completed adjuvant treatment (83%) compared to those currently receiving chemotherapy (71%).[46] Additionally, patients who initiate a physical activity programme after chemotherapy may regain cardiorespiratory fitness to the same degree as those who were physically active during chemotherapy.[47] Thus, the post-treatment period may be the ideal time to offer women referral to community-based physical activity programmes.

The PURE-EX programme (EXpanding into communities to imProve physical activity sUpport foR womEn after breast cancer) aims to integrate physical activity referrals into standard care for women after breast cancer treatment through four interlinked work packages:

- Work package 1: A systematic scoping review to describe the characteristics of community-based physical activity programmes for women with breast cancer reported in the literature.
- Work package 2: Qualitative research with: (i) women with breast cancer, (ii) HCPs responsible for their care, and (ii) exercise professionals, to explore barriers and facilitators to incorporating physical activity into breast cancer care from different perspectives.
- Work package 3: co-development events to develop and refine components of the PURE-EX programme and gain insights as to how it could be operationalised in practice.
- Work package 4: A feasibility trial in 45 women who have finished primary treatment for breast cancer to assess the feasibility and acceptability of the PURE-EX programme.

Data collection for work packages 1, 2, and 3 are complete and have informed design of the PURE-EX programme and the feasibility study.

Therefore, this protocol and IRAS application describe work being undertaken for work package 4 only.

8. PATIENT AND PUBLIC INVOLVEMENT (PPI)

PPI has shaped this study and will remain central throughout. Feedback from women with breast cancer highlighted the lack of physical activity support. Many suggested that an end-of-treatment appointment could be an ideal time to offer physical activity referrals, as some feel a “sense of abandonment” after finishing primary treatment. Two patient representatives with lived experience of breast cancer are key members of our research team, having actively contributed to the study’s conception and design. These two representatives co-chair a PPI panel of 10 women with varied experiences of early-stage and locally advanced breast cancer. The panel provide ongoing PPI feedback into research team meetings as a dedicated rolling agenda item. Meeting every 3–4 months in a local café, the PPI panel have offered user perspectives across all work packages, and will continue to provide input regarding recruitment and trial materials in this feasibility study.

9. STUDY PROTOCOL

9.1. Study aim

Explore the feasibility and acceptability of the PURE-EX programme from different user perspectives.

9.2. Study objectives

To assess:

i. The feasibility and acceptability of being offered referral to, and attending, a community-based physical activity programme in women who have completed surgery for breast cancer.
ii. The feasibility and acceptability of breast cancer HCPs offering physical activity referrals.
iii. The feasibility, acceptability, and views of instructors delivering a community-based physical activity programme to women after breast cancer treatment.
iv. The feasibility of data collection, measures of adherence and retention to the intervention.
v. Potential signals of intervention efficacy.

9.3. Study design

This is a prospective, single-arm, pretest-posttest feasibility trial. Forty-five women with early-stage or locally advanced breast cancer will be offered referral by a HCP to a 12-week community-based group exercise programme. The preliminary trial protocol has been published.[48] Trial findings will be reported in line with the Consolidated Standards of Reporting Trials (CONSORT) extension to randomised pilot and feasibility trials.[49]

9.4. Study setting

Participants will be recruited from outpatient breast cancer clinics at Newcastle Hospitals NHS Foundation Trust and Gateshead Health NHS Foundation Trust, UK. Newcastle University will sponsor the trial. We will seek Health Research Authority (HRA) approval, including ethical approval from an independent NHS Research Ethics Committee. Written informed consent will be obtained from all participants before data collection.

9.5. Participant eligibility

9.5.1. Inclusion criteria

- Women aged ≥18 years
- Clinical diagnosis of early-stage or locally advanced breast cancer (stage I-III)
- Have completed surgery for breast cancer
- Have received clearance from a treating clinician to participate in the study
- Willing and able to provide written informed consent

9.5.2. Exclusion criteria

- Diagnosis of metastatic breast cancer (stage IV)
- Currently undergoing chemotherapy or scheduled to start chemotherapy during the study period
- Not sufficiently recovered from surgery in a manner that would contraindicate exercise, as determined by the treating clinician (e.g. inadequate wound healing, reduced range of motion, or other clinical concerns)
- Musculoskeletal, neurological, or rheumatological condition that could be exacerbated by exercise, as determined by the treating clinician
- Uncontrolled cardiovascular or metabolic disease
- Pregnant or planning pregnancy during the study period

9.6. Sample size

There are no clear guidelines on sample size requirements for non-randomised feasibility trials. Our aim is to recruit 45 women into the study. Assuming a conservative loss to follow-up of 20%,[50] the research team considers this number of participants sufficient to achieve the study objectives and evidence suggests it is likely to achieve adequate qualitative data in post-study interviews.[51]

9.7. Participant identification

A research nurse, member of the clinical care team, or clinical trials officer will identify potential participants via reviewing their medical records against the eligibility criteria ahead of a routine follow-up appointment at the breast cancer clinic.

9.8. Participant recruitment and consent

In our co-design workshops, women with breast cancer and HCPs recommended recruitment procedures were kept flexible to maximise the opportunity for women to participate. Discussions with site R&D Departments also suggested that maintaining a degree of flexibility in the way women were approached and consented would be advantageous from a site operational perspective. Therefore, four options for recruitment will be implemented:

Option A: Approached at pre-assessment clinic

- A research nurse, member of the clinical care team, or clinical trials officer will approach eligible women at the pre-assessment clinic (which occurs about a week before the woman's surgery) and provide brief verbal information about the study and a Patient Information Sheet for the full study (covering both the offer of a referral from their HCP and an invitation to participate in the PURE-EX programme).

- Prior to the woman's attendance at a follow-up appointment *post-surgery*, the clinical care team will once again review the woman's medical records to confirm eligibility.
- Either by telephone prior to one of their follow-up appointments, or in-person at the clinic, a research nurse, member of the care team, or clinical trials officer will provide the potential participant with the opportunity to ask any questions and request more information.
- If after this the woman would like to take part, informed consent will be obtained either by verbal consent over the phone (using the relevant verbal consent form), or written consent in-person at the clinic (using the relevant written consent form).
- After which the participant will then attend their follow-up appointment with a member of their clinical care team (e.g., surgeon/breast care nurse), during which they will be offered a referral to the PURE-EX programme, and if accepted by the participant, the referral will then be enacted by a member of the clinical team.

Option B: Information (for full study) sent ahead of follow-up appointment post-surgery

- A research nurse, member of the clinical care team, or clinical trials officer will send eligible women a Study Invitation Letter and a Patient Information Sheet for the full study (covering both the offer of a referral from their HCP and an invitation to participate in the PURE-EX programme). This will be sent via email or post before a routine *post-surgery* follow-up appointment at the breast cancer clinic.
- Either by telephone prior to their follow-up appointment, or in-person at the clinic, a research nurse, member of the care team, or clinical trials officer will provide the potential participant with the opportunity to ask any questions and request more information. If the woman would like to take part in the study, informed consent will be obtained either by verbal consent over the phone (using the relevant verbal consent form), or written consent in-person at the clinic (using the relevant written consent form).
- After which the participant will then attend their follow-up appointment with a member of their clinical care team (e.g., surgeon/breast care nurse), during which they will be offered a referral to the PURE-EX programme, and if accepted by the participant, the referral will then be enacted by a member of the clinical team.

Option C: Information (for offer of referral) sent ahead of follow-up appointment post-surgery

- A research nurse, member of the clinical care team, or clinical trials officer will send eligible women a Study Invitation Letter and a Patient Information Sheet for the study (covering only the offer of a referral from their HCP). This will be sent via email or post before a routine *post-surgery* follow-up appointment at the breast cancer clinic.
- Either by telephone prior to their follow-up appointment, or in-person at the clinic, a research nurse, member of the care team, or clinical trials officer will provide the potential participant with the opportunity to ask any questions and request more information. If the woman would like to take part in an offer of a referral, informed consent will be obtained either by verbal consent over the phone (using the relevant verbal consent form), or written consent in-person at the clinic (using the relevant written consent form).
- After which the participant will then attend their follow-up appointment with a member of their clinical care team (e.g., surgeon/breast care nurse), during which a member of the clinical team (e.g., surgeon/breast care nurse) will carry out the referral offer.
- If the patient accepts the referral to the PURE-EX programme, the referral will then be enacted by providing further information about PURE-EX, including the Patient Information Sheet for participation in the PURE-EX programme.
- If after this, the woman decides she would like to take part in the PURE-EX programme, written informed consent will be obtained at clinic (using the relevant written consent form).

Option D: Approached at follow-up clinic post-surgery

- A research nurse, member of the clinical care team, or clinical trials officer will approach eligible women at the follow-up clinic and provide brief verbal information and a Patient Information Sheet (covering the offer of a referral from HCP only).
- If the woman is willing to take part, they will provide written informed consent (using the relevant written consent form) whilst waiting for their appointment.
- During the appointment, a member of the clinical team (e.g., surgeon/breast care nurse) will carry out the referral offer.
- If the patient accepts the referral to the PURE-EX programme, the referral will then be enacted by providing further information about PURE-EX, including the Patient Information Sheet for participation in the PURE-EX programme.
- If after this, the woman decides she would like to take part in the PURE-EX programme, written informed consent (using the relevant written consent form) will be obtained at clinic.

For all options, if the women would like longer to consider her participation, the member of the clinical team will offer to contact the women in a day or two by phone, and if at that point the woman wishes to take part, informed consent will be obtained verbally over the phone (using the relevant verbal consent form).

Our PPI and co-design work also stressed that the offer of the referral/invitation to participate in the PURE-EX programme was not 'just a one off and then forgotten', but rather that that the offer of the referral/participation in PURE-EX could be revisited at a later follow-up appointment, if the woman wished. This was in recognition that some women may require more time before deciding/feeling able to take part in activity.

Throughout the eligibility and recruitment process, the research nurse, other member of the clinical care team, or clinical trials officer will complete **screening logs** documenting each potentially eligible participant, including whether the relevant clinical data could be found to determine her eligibility (e.g. early-stage or locally advanced breast cancer), whether she was eligible and, if so, whether she was approached (including how and by whom) and consented (and, if not, reasons why will be recorded). Prior to being approached, each eligible participant will need to have received clearance from a treating clinician to participate in the study (this will also be recorded on the screening log).

9.9. The PURE-EX intervention

The intervention was developed in collaboration with stakeholders and end-users. We conducted focus groups and interviews with 35 breast cancer survivors, 23 healthcare professionals (including breast nurses, surgeons, oncologists, and physiotherapists), and 7 exercise professionals to understand the barriers and facilitators to physical activity in breast cancer care from multiple perspectives. Building on this qualitative research, we co-designed the intervention through several iterative workshops. Specifically, we held three in-person workshops with 28 women, two online workshops with 6 breast nurses, and four 1-to-1 consultations with 4 consultants (2 oncologists and 2 surgeons). Our aim was to ensure the intervention is both highly acceptable to women and practically implementable within the NHS.

The intervention consists of three main components:

[1] An offer of exercise referral from a healthcare professional
[2] A one-to-one review with an exercise instructor
[2] A 12-week community-based group exercise programme

[1] Exercise referral offer

Healthcare professionals will be trained to **ASK** about physical activity, **ADVISE** women to be active, and **ASSIST** by offering a referral into a 12-week, community-based group exercise programme. This intervention draws on the "3As" approach – originally developed for smoking cessation[36] – to provide HCPs with a framework to ask patients about physical activity, advise them to be active, and offer referral to community-based programmes to give healthcare professionals a structured yet brief way to raise the topic of physical activity. The referral offer is designed to be concise (30–60 seconds), addressing concerns about limited time and competing priorities.[32] We envisage that the referral will most commonly be delivered by the treating surgeon in breast cancer clinics, as >90% of women diagnosed with early-stage or locally advanced breast cancer undergo surgery.[52] At participating study sites, all women have routine follow-up appointments with their surgeon at approximately 2 weeks and 6 months post-surgery. Additional appointments may occur depending on complications or multiple surgeries. These predictable "touchpoints" provide ideal opportunities to introduce the exercise referral. However, depending on operational circumstances, another member of the clinical care team may be better placed to offer the referral.

At the breast cancer clinic, the HCP will:

- **ASK** about previous and current physical activity levels
- **ADVISE** that being active after breast cancer surgery can reduce fatigue and other side effects (e.g., nerve pain), support physical and mental recovery, improve fitness for any planned treatments, and reduce recurrence risk by ~35%
- **ASSIST** by:
    - Providing a brief information booklet on exercise after breast cancer (https://breastcancernow.org/download-and-order-publications/exercises-after-breast-cancer-surgery-bcc6)
    - Recommending joining a local exercise class as one of the best ways to support recovery
    - Asking whether the woman would like a free referral into a 12-week group exercise class with other women recovering from breast cancer surgery

If the woman agrees to the referral and for her contact details to be shared, a research nurse, clinical team member, or clinical trials officer will complete a referral proforma including the woman's contact details, preferred method of contact, and brief medical history (e.g., type of surgery, other treatments). The completed proforma will be securely sent (via post or secure email, depending on site preference) to a qualified exercise instructor at Healthworks, a community health charity in North East England (see below). The instructor will then contact the woman to arrange a one-to-one review before she joins the group class. If the woman declines the referral, the reason will be recorded on the screening log.

Healthworks (https://www.healthworksne.org.uk/) is a community health charity supporting disadvantaged communities to reduce health inequalities. Commissioned and funded by NHS Trusts and local healthcare partners, Healthworks delivers a range of services, including:

- Personalised physical activity and mobility programmes
- Prehabilitation and rehabilitation for stroke and cancer
- Pain management (e.g., hip, knee, back)
- Smoking cessation, diabetes prevention and management
- Nutritional support and "waiting well" services
- Cancer screening promotion and breastfeeding advocacy

Current exercise services provided by Healthworks are outlined on their website: https://www.healthworksne.org.uk/service/getting-active/.

All exercise instructors at Healthworks hold a recognised qualification (Level 3, Register of Exercise Professionals) and have extensive experience delivering exercise programmes for individuals with a range of health conditions (including cancer). Bespoke training for PURE-EX will be delivered by expert members of the research team (Dr Sam Orange, Dr Morven Brown) via a PDF training resource, covering: (i) Types of breast cancer; (ii) Types of surgery, treatments, and medications; (iii) Recovery considerations after surgery; (iv) Common treatment side effects; (v) Basic and advanced arm exercises; (vi) Assessing energy levels; (vii) Exercise adaptations for individual ability; (viii) Guidance on sports bras; (ix) Behaviour change techniques to support sustained activity. These training areas were co-developed with our PPI group and through the co-design workshops.

[2] One-to-one review

The one-to-one review will take place at the same location as the exercise class (Health Resource Centre, Adelaide Terrace, Newcastle upon Tyne, NE4 8BE). The instructor will collect background information using a Case Report Form (CRF), including:

- Sociodemographics (e.g., age, ethnicity, postcode)
- Other medical conditions (e.g., asthma, cardiovascular disease)
- Recovery after surgery (e.g., range of motion, pain, wound healing, lymphedema, cording, frozen shoulder)
- Previous and current physical activity levels
- Height, weight, and resting blood pressure
- Muscle or joint issues
- Personal goals for being active
- Interest in the "Buddy Up" system – with permission, the woman's contact details will be shared with another participant to encourage social support and class attendance. This was a key preference raised during co-design workshops.

The exercise instructor will then collect baseline data, including questionnaires and basic tests of strength and physical function (outlined in Section 9.10).

[3] A community-based group exercise programme

The group exercise programme will be delivered by the same Healthworks-employed instructor who conducted the one-to-one review. Participants will be invited to attend one class per week for 12 weeks. Women will be given a 16-week window to complete this to allow flexibility should there be weeks that they cannot/do not feel able to attend. This approach was encouraged by our PPI group and through our co-design workshops. Classes will take place in a private room at the Health Resource Centre (Adelaide Terrace, Newcastle upon Tyne, NE4 8BE) and will be exclusively for study participants.

Each class will last 50 minutes and include up to 12 women, consisting of:

1. A brief welcome/introduction to any attendees
2. A 15-minute warm-up (pulse-raising activities, full-body stretches, arm/shoulder movements)
3. A 25-minute main session (aerobic, strength, and balance exercises)
4. A 10-minute cool-down (static stretches held for ~20 seconds at the point of slight discomfort)

The main session will focus on multi-joint exercises that target major muscle groups in the upper and lower body. Exercises will be delivered in a circuit format: each movement performed for 60 seconds with ~15-second rest intervals, allowing participants to ready themselves for the next exercise in the sequence. Equipment will include dumbbells and resistance bands, and chair-based options will be available for those who need them. Exercise selection and sequencing will vary across sessions to accommodate preferences for variety, as indicated in PPI feedback and co-design workshops. A designated "time out" space will allow participants to rest as needed.

The intensity of exercise will be performed at 3–6 on a 10-point rating of perceived exertion scale (RPE) scale (Appendix A),[53] which corresponds to moderate intensity from a physiological perspective[54] and qualitative descriptions of 'moderate' to 'hard'.[53] Moderate-intensity exercise is effective for improving quality of life among cancer survivors[18] and poses less risk of adverse events than vigorous exercise.[55] Using RPE ensures that intensity is tailored to individual capacity and progresses over time. An example exercise class is presented below in Appendix B.

Throughout the 12-week programme, each participant will be provided with personalised recommendations and support for engaging in additional suitable physical activity (e.g., through local physical activity/exercise classes and groups; home-based exercises). This will have the aim of providing women with the support to explore and engage with

other opportunities for physical activity and exercise and help them build a routine which can continue past the duration of the intervention.

9.10. Data collection

The primary outcome of this study is the feasibility of the PURE-EX intervention. Cardiorespiratory fitness, physical function, and muscle strength will be assessed by the exercise instructor before and after the 12-week exercise programme. Paper copies of study questionnaires will be given to participants to complete in-person, to take home and return by post in pre-paid envelopes, or to complete online (Microsoft Forms), depending on preference. A wrist-worn accelerometer (for measurement of physical activity) to take home and return by post in a pre-paid envelope. Clinical information will be extracted from medical records onto an electronic CRF by a research nurse. A detailed study schedule is presented in Table 1.

9.10.1. Feasibility

A research nurse, other member of the clinical care team, or clinical trials officer will complete screening logs documenting each woman who was approached and consented (and, if not consented, reasons why will be recorded where possible to enable identification of issues regarding feasibility/acceptability in those who decline). This information will be used to calculate the recruitment rate (the number of consenting participants divided by the number of women approached). The HCP who offers the exercise referral will document whether participants accept the physical activity referral (defined as whether the woman agrees for their contact details to be shared with the intervention provider). The exercise instructor will record attendance at the community-based exercise programme and any adverse events. Reporting of adverse events will be conducted in line with the study sponsor's policy on adverse event reporting for non-clinical trials of investigational medicinal products; we will record all serious adverse events, as well as all non-serious adverse events that are deemed to be related to study participation. A research team member attending a random sample (≈20%) of physical activity sessions will assess fidelity to the delivery of the physical activity programme using a standardised checklist, informed by the Template for Intervention Description and Replication (TIDieR).[56]

9.10.2. Acceptability

Acceptability of PURE-EX programme components will be assessed using a validated acceptability questionnaire based on the theoretical framework of acceptability (TFA).[57] The questionnaire consists of 9 items: one item reflecting each of the TFA constructs of affective attitude, burden, perceived effectiveness, intervention coherence, self-efficacy, and opportunity costs, two items reflecting ethicality, and one general acceptability item.

9.10.3. Study questionnaires

The Functional Assessment of Cancer Therapy-Breast (FACT-B) total score will be used to measure disease-specific QoL.[58] Fatigue will be measured with the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) total score.[59] Anxiety and depression symptoms will be assessed via the Depression, Anxiety and Stress Scale - 21 Items (DASS-21) total subscale scores.[60] We will assess self-reported physical activity using the International Physical Activity Questionnaire – Short Form (IPAQ-SF),[61] which provides data on time spent sitting and MET-minutes per week of walking and doing moderate and vigorous activity. The Health-Promoting Lifestyle Profile-II (HPLP-II) total score will be used to assess the extent to which participants engage in health-promoting behaviours. The HPLP-II comprises 52 items that measure six dimensions of a health-promoting lifestyle: health responsibility, physical activity, nutrition, spiritual growth, interpersonal relations, and stress management.

9.10.4. Cardiorespiratory fitness

The six-minute walk test (6MWT) is reliable (intraclass correlation coefficient = 0.93) and correlates well (r = 0.67) with peak oxygen consumption achieved during a cardiopulmonary exercise test.[62] Participants will be instructed to walk at a self-selected maximal pace back and forth along a flat surface, covering as much distance as they can in six minutes. All instructions, encouragement, and monitoring will adhere to American Thoracic Society Guidelines.[63] At the end of the test, participants will be asked to stop where they are and the total distance covered will be measured in meters.

9.10.5. Physical function

The Short Physical Performance Battery (SPPB), a composite measure of standing balance, five chair stands, and 4-meter gait speed, will be used to assess physical function. Each test is assigned a categorical score from 0 (worst performance) to 4 (best performance) according to standardised criteria. A total score from 0 to 12 is obtained by summing the scores from the three tests.

- **Five chair stands.** Participants will sit in a firm, armless chair with their arms crossed over their chest. They will position themselves at the edge of the seat to reduce trunk flexion[64] and be instructed to stand fully upright (legs straight) and then return to a seated position (full weight on the chair) five times as quickly as possible, while maintaining proper form. A practice repetition will ensure correct technique, followed by one timed trial. The completion time for five sit-to-stands will be recorded in seconds.
- **Standing balance.** Participants will stand unassisted with their feet placed in three different positions: side by side, semi-tandem, and tandem, each for up to 10 seconds. Timing will stop either at 10 seconds or when the participant loses balance (e.g., stepping out of position or grabbing support). One trial will be conducted for each stance, and the duration will be recorded in seconds.

- **4-meter gait speed.** Participants will walk 4 meters at their usual pace, with the time recorded in seconds. Walking aids will be allowed if required.

9.10.6. *Hand grip strength*

Participants will use their dominant hand to squeeze a hand-held digital grip dynamometer as hard as possible for 3 seconds. They will remain seated with their arm fully extended by their side during the test. The maximum score from three trials will be recorded in kilograms.

9.10.7. Device-measured physical activity

Device-based physical activity will be measured using a tri-axial accelerometer (Axivity AX3, Axivity Ltd, Newcastle upon Tyne, UK)[65] worn on the non-dominant wrist for 7 consecutive days, which is a well-established proxy for habitual physical activity.[66] Data will be considered valid if participants wear the accelerometer for at least 8 hours on at least 4 days.[67] From the raw accelerometer data, we use the GGIR package[68] in the latest version of R (R Foundation for Statistical Computing, Vienna, Austria; https://www.r-project.org/) to derive time spent sedentary and time spent in light, moderate, and vigorous activity. Published cut-points based on metabolic equivalents (METs) will be used to demarcate the intensity of physical activity.[69]

9.10.8. Clinical information

Clinical information extracted from medical records will include date of cancer diagnosis, tumour grade, stage and receptor status, and treatment received.

9.11. Interviews

We will invite participants to take part in semi-structured interviews at two timepoints: (i) 1-2 weeks after receiving the referral; and (ii) 1-2 weeks after completing the physical activity programme. Interviews conducted after the referral will explore experiences of interactions with HCPs, the referral pathway, and barriers and facilitators to accepting the referral and accessing the physical activity programme. Interviews held after programme completion will explore experiences of the physical activity programme and barriers and facilitators to sustained adherence to the 12-week programme. The interview topic guide will be informed by COM-B and our findings from the qualitative research in WP2. We will interview HCPs to explore experiences of the carrying out the referral and how it fitted into routine care, with the topic guide structured around COM-B and the constructs of NPT. Additionally, we will interview instructors to explore views of the online training course and barriers and facilitators to delivering the physical activity programme. Interviews will last approximately 60-minutes and be conducted in-person or remotely via telephone or videoconferencing (depending on interviewee preference), audio-recorded, and transcribed verbatim.

9.12. Qualitative analysis

Anonymised transcripts will be analysed, concurrently with data collection,[70] with thematic analysis using a combined deductive and inductive approach.[71] Transcripts will be coded deductively line by line using a pre-established coding scheme that aligns with the research questions and is guided by process evaluation recommendations.[72] Following coding completion, each section of the coding scheme will be subject to an inductive thematic analysis, in which salient themes and recurrent patterns within the data will be identified and sub-themes created within each section.[73] Data will be mapped onto the COM-B model and TDF to identify mechanisms through which the intervention brought about change (or otherwise) in: 1) the HCPs practice of offering brief physical activity advice and the referral; 2) the exercise instructors practice of delivering sessions; and 3) the women's physical activity behaviours and attendance/adherence to the PURE-EX programme.[74,75] NPT will also be used to structure the coding framework to identify how new behaviours and practices can be integrated within routine clinical care.[76] Analysis will be facilitated by NVivo software.[77]

9.13. Quantitative analysis

The flow of patients throughout the trial will be reported in a CONSORT flowchart.[49] Descriptive statistics will be used to present baseline characteristics and feasibility outcomes. A paired t-test or Wilcoxon signed-rank test (depending on data distribution, assessed via visual inspection of histograms and Q-Q plots) will be used to evaluate changes in outcomes from baseline to post-intervention, with the mean change and 95% confidence interval presented.[78] Participants with missing data will be excluded from the analysis. The analysis will be performed in the latest version of R.

Table 1. Study schedule						
	Screening	**Enrolment**	**Outpatient breast clinic**	**Baseline**	**Intervention**	**Post-intervention**
Eligibility screen	x					
Study invitation	x					
Informed consent		x				
Clinical data extraction		x				
Exercise referral			x			
Sociodemographics				x		
Medical history				x		
Height				x		
Weight				x		x
Blood pressure				x		x
FACT-B				x		x
FACIT-Fatigue				x		x
DASS21				x		x
IPAQ-SF				x		x
HPLP-II				x		x
Five chair stands				x		x
Standing balance				x		x
4-meter walk				x		x
6MWT				x		x
Grip strength				x		x
7-day accelerometery				x		x
Exercise programme					x	
Acceptability questionnaire						x
Fidelity assessments					x	
Qualitative interviews					x	x

6MWT = Six-minute walk test; AE = adverse events; FACIT-Fatigue = Functional Assessment of Chronic Illness Therapy – Fatigue; FACT-B = Functional Assessment of Cancer Therapy-Breast; DASS21 = Depression, Anxiety and Stress Scale - 21 Items; HPLP-II = Health-Promoting Lifestyle Profile II; IPAQ-SF = International Physical Activity Questionnaire - Short Form.

10. ETHICAL AND REGULATORY CONSIDERATIONS

10.1. Consent

Participation will be contingent on informed consent being obtained. Prior to expressing their interest in participating, all potential participants will be provided with brief verbal information about the study and with a participant information sheet from a member of the healthcare team (e.g., breast surgeon, breast care nurse, research nurse) detailing the study objectives and what taking part will involve. They will be given the opportunity to ask any questions, and if are happy to proceed, will be asked to provide informed consent.

If the potential participant requests that they would like to take time to consider their participation, the member of the healthcare team will ask for permission to call them at a later point (ensuring at least 24 hours is given for them to consider).

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. It will be made clear that any information arising from the study will be anonymised so they will not be identifiable in any publications or report. 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 working in collaboration with the research team, including students.

10.2. Participant withdrawal

Participants may withdraw from the study at any time with no obligation to provide a reason or explanation. In the event of withdrawal, the participant's personal identifying data will be destroyed but any other data collected (e.g. interview transcript, completed questionnaires,) will be retained, as will any screening information that was used to inform their eligibility for the study. Consent forms will be retained but will be marked as a withdrawn participant.

10.3. END of study

For an individual participant, completion of the follow-up questionnaire or participation in the interview (whichever is the later) will constitute the end of their participation in the study. Overall, the end of the study will be defined as the point when questionnaires and interviews have been completed, all data analysed, and any changes required before the full trial have been made.

10.4. Assessment and Management of Risk:

Just like all forms of exercise, there is a small risk of tripping/falling or an adverse cardiovascular event during the exercise sessions. However, this type of exercise is considered extremely low risk and the exercise programme has been designed by a clinical exercise physiologist and a senior physiotherapist who have extensive experience of delivering safe exercise to cancer patients. All patients will be medically

cleared to participate by their breast cancer team and will undergo a thorough screening process in line with American College of Sports Medicine (ACSM) guidelines. Healthworks instructors, who will be delivering the exercise sessions, are also experienced in carrying out exercise sessions with clinical populations, including cancer, cardiovascular disease, and multiple long-term conditions. Healthworks are also a a National Institute for Health and Care Research (NIHR) recognised research site (see: https://www.healthworksne.org.uk/service/research-projects-copy/).

It is possible that participation, particularly the qualitative interviews, may have emotional consequences for women with breast cancer and may involve them considering and discussing potentially upsetting issues related to their own experiences.

The researcher (Brown) is experienced in interviewing individuals who have had cancer and/or other potentially vulnerable patient groups. If an interviewee does not wish to answer any question during the interview, this will be respected. If the interviewee becomes upset, the researcher will ask them if they wish to stop the interview, either temporarily or permanently. Moreover, if an interviewee becomes very distressed, the researcher will ask whether they would like them to contact someone (e.g. a family member, friend, GP, or clinician) on their behalf. A similar process will be followed in the event that a participant becomes distressed during the referral or the exercise sessions.

The participant information sheets will contain information about who (patient) participants might contact if they feel they want to discuss any issues arising from taking part in the study. For example, this will suggest that they contact the research team, their GP, their clinical team in the hospital, and will direct interviewees to information and helplines such as those offered by Breast Cancer Now and Mind.

10.5. Research Ethics Committee Reporting

Ethical approval will be obtained from a UK Health Department's Research Ethics Service NHS Research Ethics Committee (REC) for the study protocol, informed consent forms, participant information sheets and other study materials.

Substantial amendments that require review by NHS REC will not be implemented until that review is in place and other mechanisms are in place to implement at site. All correspondence with the REC will be retained. The chief investigator will organise the production of research reports as required and notify the REC of the end of the study. An annual progress report will be submitted to the REC within 30 days of the anniversary date on which the favourable opinion was given, and annually until the study is declared ended. If the study is ended prematurely, the Chief Investigator will notify the REC, including the reasons for the premature termination. Within one year after the end of the study, the Chief Investigator will submit a final report with the results, including any publications/abstracts, to the REC.

10.6. Regulatory Review and Compliance

Before any site can enrol patients, the Chief Investigator or a designee will ensure that appropriate approvals from participating organisations are in place.

For any amendment to the study, the Chief Investigator or designee, in agreement with the sponsor, will submit information to the appropriate body for them to issue approval for the amendment. The Chief Investigator or designee will work with sites (R&D departments at NHS sites) so they can put the necessary arrangements in place to implement the amendment and to confirm their support for the study as amended.

10.7. Amendments

If a substantial amendment to the REC application or the supporting documents is required, approval will be sought from the sponsor before submitting a notice of amendment to the REC for consideration. The sponsor will categorise the amendment as substantial or non-substantial. The Health Research Authority will be informed.

Substantial and non-substantial amendments will be communicated to the participating organisations (R&D office and local research team) departments of participating sites to assess whether the amendment affects the NHS permission for that site. Some amendments that may be considered to be non-substantial for the purposes of REC may still need to be notified to NHS R&D (e.g. a change to the funding arrangements).

The Chief Investigator will be responsible for the decision to amend the protocol and any supporting documents. The amendment history will be logged in the site-files. The protocol and all supporting documents will be version tracked, so that the most recent versions can be identified easily.

10.8. Peer Review

The project has been funded by Breast Cancer Now. The funding application for this project was independently peer reviewed by several independent experts and by the Breast Cancer Now funding panel.

10.9. Data Protection and Patient Confidentiality

Data controllers and regulatory compliance: Newcastle University is Sponsor for the study and will act as data controller. All investigators, researchers and study site staff will comply with the requirements of the Data Protection Act 2018, with regards to the collection, storage, processing and disclosure of personal information and will uphold the Act's core principles and General Data Protection Regulation (GDPR).

Recruitment of patient participants: The local clinical team will act as 'gate keepers' and eligible patients will be initially informed of the study via their healthcare

professionals. The exercise instructors and research team will not have access to contact details for any patient participants, until they themselves give their permission to a member of the clinical team that they are happy to take part in the study and for their details to be passed onto the instructor and research team. Participant data transferred between the NHS, Healthworks and the research team will be done so via NHS.net email.

Identifiable data, consents: Any identifiable data will be stored securely on a Newcastle University network. A small number of designated members of the research team will be able to access identifiable and contact information on all women recruited as required for specific purposes (e.g. delivering the intervention, sending questionnaires, arranging interviews, sending summary of findings).

Paper records of consent, which contain names or study IDs, will be kept at site for five years following the end of the study in order to allow for audit of the research process if required. No other personal data such as contact details will be kept longer than is necessary and any identifying information will be anonymised in the data for analysis.

Interviews: The audio-recordings of any interviews will be stored on a secure part of the Newcastle University network with password protection and access restricted to designated members of the research team (unless NHS sites stipulate that recordings of patient interviews be kept on NHS systems). Transcription of the interviews will be undertaken by a member of the research team or by an external company approved by Newcastle University. Those who transcribe interviews will sign a confidentiality agreement.

Recordings will be retained until the end the study to allow researchers to return to the data as needed. Following this they will be permanently deleted.

Interview transcripts will be anonymised (e.g. removing places, names) and stored on a secure part of the Newcastle University network. Each transcript will be saved with the individual's unique study ID number.

Site files will be held by the Principal Investigator for each clinical site in a lockable office. This folder will contain essential documents as well as recruitment and screening logs for the study site (who has been approached/written to about the study) and consent forms.

Archiving: After each study has ended, anonymised data will be archived in line with Sponsor policy once the final report and publication are complete. Research data will remain available for 10 years following any publication, after which retention will be reviewed.

Data sharing: The consent procedures include informing participants about the sharing of data and make clear that only their fully anonymised information will be used in future relevant research or shared with other researchers outside of the immediate research team.

10.10. Access to the Final Study Dataset

The final data set will be accessible by the research team; anonymized data may be made available to other researchers, including students, for secondary analysis. The consent procedures include consent for the sharing of data. It will be explained to participants verbally and in writing, that anonymised data may be shared in future for relevant research by other researchers working in collaboration with the research team.

10.11. Dissemination and outputs

Our dissemination strategy includes conference presentations, scientific papers, regular social media and lay communications, and briefings (paper, digital and events) for clinical teams, patient groups and commissioners.

Participants will be given the option of receiving a lay summary of the results once the final study report has been compiled. A lay summary will be prepared for dissemination on the Breast Cancer Now website, support groups and social media. In addition, we will engage with PPI members throughout the project to gain views on dissemination activities with patients and public.

11. Appendices

Appendix A. RATING OF PERCEIVED EXERTION (RPE) SCALE

Appendix B. EXAMPLE EXERCISE SESSION

10.1. APPENDIX A. RATING OF PERCEIVED EXERTION (RPE) SCALE

Rating	Descriptor
0	Rest
1	Very, Very Easy
2	Easy
3	Moderate
4	Somewhat Hard
5	Hard
6	.
7	Very Hard
8	.
9	.
10	Maximal

10.2. APPENDIX B. EXAMPLE EXERCISE SESSION

Component	Duration	Exercises	Reps / Time	Intensity (Borg / HR%)	Progression	Adaptation
Warm Up • Mobilisation • Pulse Raises • Dynamic Stretches • Arm exercises	15mins	This component incorporates dynamic movements to warm up major muscle groups and exercises which move the body through all 3 planes of movement (sagittal, frontal and transverse): • Marching • Toes aps / Heel taps all directions • Shoulder rolls • Trunk twitches • Walking • Side steps • Side Bends It also includes arm exercises for post-surgical shoulder rehabilitation: • Shoulder shrugs • Shoulder circling • Bent arm forwards • Bent arm sideways • Back scratching • Wall climbing • Arm lifts • Elbow pushes	5mins segments and increasing intensity every 5min until 15mins is completed.	Gradually building up to 3-6 RPE, corresponding to 64-79% maximum heart rate or descriptions of “moderate” to “hard”		
Component	**Duration**	**Exercises**	**Reps / Time**	**Intensity (Borg / HR%)**	**Progression**	**Adaptation**

Main session Each exercise station split into 3 levels of intensities to accommodate difference ability levels: -Red (Higher) -Amber (Medium) -Green (Low).	25mins 7 circuit stations. 3 rounds of 1 min activity per station	Mixture of cardiovascular exercises, muscular strength and endurance and balance exercises. Exercises such as: • Wall Press Ups • Step Ups • Tandem Walking • Calf Raises • Lunge • Curl To Press • Upright Row • Single arm shopping Carry • Farmer Carry • Shuttle Walking • Get Up and Go • Band Row • Flamingo Swing • Hip Abduction • Hamstring Curl	1min each station, 15s rest in between	Gradually building up to 3-6 RPE, corresponding to 64-79% maximum heart rate or descriptions of “moderate” to “hard”	Increased ROM Increased step Height Unsupported Single leg or added resistance Increased ROM Increase Weight Increase Weight Increase Weight / Tandem Walking Increased weight Increased Speed Increased Speed Purple Band Slow Increased ROM Slow Increased ROM Increased Speed	Decreased ROM Toe Taps Semi Tandem Wall supported Chair Supported No weight No Weight Decreased Weight Decreased Weight Decreased Speed Decreased Speed Pink Band Decreased ROM Decreased ROM Wall Supported

		• Knee Raises • Trunk Twists • Wood Chops • Double Side Step • Backward Walking • Sit To Stand • Side Bend • Tandem Stand • Semi Tandem Stand • Single Leg Standing • Pick up and Press • Front Carry			Increased Speed Added Weight Added Weight Increased Speed Unsupported Air Squat Added Weight Unsupported Unsupported Unsupported Increased Weight Increased Weight	Wall Supported No weight Reduced ROM No weight Reduced ROM Single Step Wall / Partner Supported Double Chair No Weight Reduced ROM Wall Supported Wall Supported Wall Supported No Weight Reduced ROM Reduced Weight
Cool Down	10 mins	The component involves dynamic movement and exercises similar to the warm up which reduced in intensity throughout the duration. This also involves static stretches targeting major muscle groups	Static stretches holding for ~20s	Reducing down from 6-3 RPE, corresponding to 64-79% maximum		

		incorporated in the last few mins of the session followed by some adapted Thai Chi. Stretching the following muscle groups: • Chest / Shoulders • Upper Back • Hamstring • Calf • Inner thigh • Glutes		heart rate or descriptions of “moderate” to “hard”		

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