

A population-based digital study offering people testing for cancer genes, to identify people at increased risk of cancer so they can take steps to prevent it or detect it early

Submission date 30/12/2025	Recruitment status Recruiting	☐ Prospectively registered ☐ Protocol
Registration date 31/12/2025	Overall study status Ongoing	☐ Statistical analysis plan ☐ Results
Last Edited 31/12/2025	Condition category Cancer	☐ Individual participant data ☒ Record updated in last year

Plain English summary of protocol

Background and study aims

PROTECT-C is a research study offering genetic testing to people to see whether they have a genetic change that increases their risk of breast, ovary, bowel, and/or womb cancer. This is regardless of whether they or their families have had cancer.

Breast, ovary, bowel, and womb cancers make up half of all cancers in women. Around 15-20% (15 to 20 in 100 cases) of ovary and 3-4% (3 to 4 in 100 cases) of breast, womb, and bowel cancers are linked to cancer genes and may be prevented. People with a genetic change that puts them at increased risk of any of these cancers have ways to help them manage their risk through the NHS. This may include screening to find cancers earlier when they are easier to treat, and surgery or medication to prevent cancers from developing. This can save lives.

Currently, genetic testing is only available on the NHS to people who meet certain criteria. For example, those who have had certain cancers, have a strong family history of cancer, or those with Jewish ancestry. But many people may not have a strong family history or meet NHS testing criteria. This means that this system of testing misses 50% to 80% of people (50 to 80 in 100 people) who have a genetic change. It is thought that only around 3 in 100 people overall who have a genetic change that increases their risk of cancer know about it. Given the effective screening and preventive options that are available, this represents a huge, missed opportunity to prevent cancers or find them earlier.

Overall, the PROTECT-C study aims to evaluate the option of offering genetic testing to everyone who may want it. This is regardless of whether they or their families have had cancer. We will offer genetic testing to 5000 people. The study will test for genetic changes in nine cancer genes associated with breast, ovary, womb and bowel cancer. These genes include: BRCA1, BRCA2, RAD51C, RAD51D, BRIP1, PALB2, MLH1, MSH2, and MSH6.

Additionally, the study will use a complex mathematical algorithm to provide women with their personal risk of breast cancer and ovarian cancer.

The study will look at how many people decide to have genetic testing and how many of them are found to have a genetic change. The study will evaluate how many people with the genetic change would have been missed by standard NHS criteria. The study will evaluate how many

women at increased risk are identified using a complex mathematical algorithm (called CANRISK).

It will evaluate their experience with using the study app and how this approach to genetic testing affects their quality-of-life, satisfaction, and mental well-being. This will give us a better understanding of how well the app works as a way of offering genetic testing to people.

The study is interested to see how people found to be at increased risk decide to manage their risk. We will assess the uptake of screening and prevention options.

Few participants will be invited to have 1:1 interviews by the study team. This will evaluate their experience of making a decision about genetic testing and taking part in the study. Taking part in these interviews is optional. The study will also assess if this way of offering genetic testing to people is affordable for the NHS.

Who can participate?

Participants may take part if they:

1. Are over the age of 18 years and
2. Are a woman, trans man, or non-binary person with female reproductive organs (ovaries, fallopian tubes, and/or a uterus) and
3. Have never had genetic testing for the cancer genes tested for in the study and
4. Do not have first-degree family members (e.g.: parent, sibling, child) or second-degree family members (e.g.: aunt, uncle, niece, nephew, grandchild, grandparent, half-sibling) with genetic changes in the cancer genes tested for in the study

What does the study involve?

PROTECT-C is a completely digital study. The study team will give participants access to an app developed specifically for this study. They can download this app using a smartphone or tablet or access it on any internet browser using a computer or laptop. Before they can access the app, participants will need to complete a consent form. They will also be asked to fill in a short questionnaire about themselves and their health.

The PROTECT-C app contains information including animation videos to help participants decide if they would like to have genetic testing (or not).

On the app, information is available about:

1. Genetic changes and cancer risk
2. Breast, ovary, bowel, and womb cancers
3. How genetic testing is performed
4. Possible advantages and disadvantages of testing
5. Other considerations of testing
6. Possible results of genetic testing
7. What the test results mean for them and their family
8. Ways to manage their risk
9. Cascade (family) testing

Participants can watch videos on the app that has been created to help them understand this information. These videos will also be translated into Bengali, Polish, Romanian, Punjabi and Urdu. When a participant feels ready to decide, they can make their decision about genetic testing on the app.

If they decide to have genetic testing, they will complete a consent form for genetic testing on the app. The study team will send them a saliva based test kit in the post. The study participant will return the saliva sample by freepost. Results will be returned to participants via the app and email, and by post if they wish.

Participants will be able to access support throughout the study by contacting a helpline (available via telephone, email, and an online booking system) staffed by specially trained counsellors experienced in cancer genetic counselling. Both technical and counselling support is available via the helpline.

If participants decide not to have genetic testing, they will not be sent a test kit in the post. They study team will ask participants to answer some questions about their experience with using the app and their reasons for not having testing. Participants will then exit the study, and no further action will be required.

Participants found to carry a genetic change or those with increased risk (positive) or VUS results will be given post-test counselling (virtual (e.g. via Teams) or telephone). This can be booked via an online booking system by the participants themselves, or the study counsellors will contact the participants directly and book an appointment. Participants at an increased risk will be referred to Clinical Genetics within the NHS and offered access to screening and prevention options in the NHS.

As part of the study, they study team will ask participants to fill in questionnaires about their health and lifestyle, history of cancer in their family, experience with using the app, and how genetic testing has affected them. The information they provide in these questionnaires is confidential.

Participants may be invited to have 1:1 interviews by the study team. This will evaluate their experience of making a decision about genetic testing and taking part in the study. Taking part in these interviews is optional.

Testing of family members or Cascade testing:

Participants who are found to have a genetic change in any one of the nine cancer genes tested for in the study can share this information with their family members. Family members too can be offered the opportunity through the study itself to find out if they have inherited this genetic change. This is called cascade testing.

What are the possible benefits and risks of participating?

If participants decide to take part, they will get the opportunity to learn more about genetic testing and cancer risk. They can also choose to have genetic testing to find out if they have a genetic change which increases their risk of breast, ovary, bowel, and/or womb cancer. They can provide the study team with a saliva (spit) sample in the comfort of their own home.

If a participant has genetic testing and find out that they are at increased risk of any of these cancers, they will be offered screening to find cancers earlier when they are easier to treat, and surgery or medication to prevent cancers from developing. This can save lives.

If a participant has genetic testing and find out that they have a genetic change in a cancer gene, their family members can be offered the opportunity to find out if they have a genetic change. This can be through the study itself or the NHS. Family member who are affected can also then opt for screening or prevention options to reduce their cancer risk.

By taking part, participants will be contributing to research for prevention and early detection of cancer. This may benefit other people in the future. The PROTECT-C study is looking to see if genetic testing for cancer genes can be offered to everyone in the population.

The PROTECT-C study team does not believe there are significant major risks of taking part in this study or receiving information about genetic testing. However, some people who are found to be at increased risk or carry an inheritable genetic change may feel emotionally upset, sad or guilty of passing this on to their children. They can discuss these issues with the study counsellor either before deciding to undergo testing should they wish. They will receive mandatory counselling support to help them following a positive result.

Where is the study run from?

PROTECT-C is a completely digital study centrally coordinated at Queen Mary University of London (UK)

When is the study starting and how long is it expected to run for?

The PROTECT-C study is projected to start recruitment in December 2025 and will run for approximately 11 years (including an 8-year follow-up period).

Who is funding the study and who is the main contact?

Yorkshire Cancer Research (UK)

Who is the main contact?

Prof. Ranjit Manchanda, protect.study@qmul.ac.uk

Contact information

Type(s)

Public, Scientific, Principal investigator

Contact name

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Additional identifiers

Integrated Research Application System (IRAS)

328404

Central Portfolio Management System (CPMS)

64677

Study information

Scientific Title

Population-based germline testing for early detection and prevention of cancer

Acronym

PROTECT-C

Study objectives

The overall objective is to evaluate the impact of population-based genetic testing on identification of high and moderate penetrance cancer susceptibility genes (CSGs), and the impact of testing common genetic variants on ascertainment of general population women at moderate/high risk of breast and ovarian cancer using personalised breast cancer (BC) and ovarian cancer (OC) risk prediction, along with the impact on health behaviour, psycho-social health, screening, prevention and cost-effectiveness.

Primary Objective:

To evaluate detection of pathogenic and likely pathogenic variants (here forth called PVs) in moderate to high penetrance Cancer Susceptibility Genes (CSGs) (BRCA1, BRCA2, RAD51C, RAD51D, BRIP1, PALB2, MLH1, MSH2, MSH6) in women from unselected population-based genetic testing compared with family history based criteria for genetic testing.

Secondary & Other Objectives:

1. To evaluate satisfaction and regret with population-based genetic testing.
2. To evaluate the impact of genetic testing on quality-of-life and psychological well-being
3. To determine uptake of risk management options in CSG specific PV carriers and women at moderate to high risk of BC and OC
4. To determine uptake of cascade testing in PV carriers identified
5. To evaluate variants of uncertain significance (VUS) carrier frequency
6. To determine the cost-effectiveness of population-based genetic testing in general population women
7. To determine the uptake of population-based genetic testing
8. To determine the proportion of women categorised as moderate and high risk of BC and moderate and high risk of OC
9. To evaluate the experience with using and usability of the PROTECT-C app
10. To evaluate the use of a helpline in population testing.
11. To evaluate the impact of genetic testing on health behaviours
12. To explore women's motivations and experiences of panel genetic testing and personalised BC and OC risk estimation for cancer screening and prevention
13. To explore the impact of return of VUSs
14. To evaluate the feasibility of running a study within a trial (SWAT)
15. To evaluate the effectiveness of different letters on registration interest in the trial
16. To evaluate sociodemographic factors

Ethics approval required

Ethics approval required

Ethics approval(s)

Approved 11/10/2024, North West Preston Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)2071048364, +44 (0)2071048037, +44 (0)2071048181; preston.rec@hra.nhs.uk), ref: 24/NW/0294

Primary study design

Interventional

Study design

National digital app-enabled population based genetic testing cohort study

Study type(s)

Efficacy, Prevention, Quality of life, Screening

Health condition(s) or problem(s) studied

Cancer

Interventions

PROTECT-C offers Direct to Participant saliva based genetic testing for cancer susceptibility genes BRCA1, BRCA2, RAD51C, RAD51D, BRIP1, PALB2, MLH1, MSH2, MSH6, along with testing for common genetic variants and personalised breast and ovarian cancer risk prediction.

PROTECT-C is a completely digital study. The study team will give participants access to an app developed specifically for this study. They can download this app using a smartphone or tablet or access it on any internet browser using a computer or laptop (iOS and Android).

The app will include a consent form, where participants can accept or decline genetic testing electronically.

Participants will be provided with information about the study, the participant pathway, genes and cancer, possible results from genetic testing, advantages and disadvantages of genetic testing, and ways to manage their risk on an app (digital decision aid).

Participants consenting to genetic testing will receive a saliva collection kit through the post, provide their sample at home by following the instructions found on the kit-insert, and post it back to the genetic testing laboratory to perform the genetic testing.

Results will be returned via the app and email, and by post if they wish.

Participants will be able to access support throughout the study by contacting a helpline (available via telephone, email, and an online booking system) staffed by specially trained counsellors experienced in cancer genetic counselling. Pre-test counselling is optional but available.

Participants with increased risk (positive) or VUS results will be given post-test counselling (virtual (e.g. Teams) or telephone). This can be booked via an online booking system by the participants themselves, or the study counsellors will contact the participants directly and book an appointment.

Participants at an increased risk will be referred to Clinical Genetics within the NHS and access relevant enhanced surveillance and medical or surgical prevention options.

Participants fill in questionnaires at baseline and throughout the study at 21 days, 6 months and annually post test results. Data are collected via the study App.

A small number of participants will undergo 1:1 Qualitative interviews to explore women's motivations and experiences of panel genetic testing and personalised BC and OC risk estimation for cancer screening and prevention.

Cascade genetic testing via the App is offered to family members of those found to carry PVs.

Intervention Type

Mixed

Primary outcome(s)

The number of pathogenic and likely pathogenic variants (here forth called PVs) in moderate to high penetrance Cancer Susceptibility Genes (CSGs) (BRCA1, BRCA2, RAD51C, RAD51D, BRIP1, PALB2, MLH1, MSH2, MSH6) in women from unselected population-based genetic testing. CSG patients who fulfil the family history-based NHS testing criteria (~10% carrier probability for high risk breast/ovarian CSGs or Amsterdam-2 criteria for Lynch Syndrome) (FH positive).

The primary outcome measure is the proportion of women with one or more CSGs who have undergone genetic testing and received a valid result. Proportion of CSG positive women identified as FH positive. Analysed 6 months after return of last genetic test result.

Key secondary outcome(s)

1. Satisfaction and regret:

1.1. Satisfaction is measured using 1-item ("I am satisfied with the decision I have made") on a 5-point Likert scale. The proportion of positive responses: "very satisfied and satisfied" .

1.2. Regret is measured using the Decision Regret Scale questionnaire

Measured at acceptance, 21 days, 6 months and 12 months

2. Quality of life measured using the EORTC EQ5D-5L instrument pre-genetic testing and at 21 days, 6 months and 12 months

3. Psychosocial wellbeing measured pre-genetic testing and at 21 days, 6 months and 12 months:

3.1. Cancer worry is measured using the Cancer Worry Scale questionnaire. (4-item Cancer Worry Scale questionnaire on a 4-point Likert scale)

3.2. Risk perception is measured as the proportion responding as at "high or much higher" chance of cancer to the 1-item question ("compared with other people of your age, do you think your chances of getting cancer at some point in your life are..." on a 5-point Likert scale

3.3. Anxiety is measured using the Hospital Anxiety and Depression Scale (HADS) anxiety questionnaire (7-item questionnaire on a 4-point Likert scale)

3.4. Depression is measured using the HADS depression questionnaire (7-item questionnaire on a 4-point Likert scale)

3.5. Distress is measured using the Impact of Events (IES) questionnaire (22-item IES questionnaire on a 5-point Likert scale): Mean score IES Intrusive scale (range 0-35) and IES Avoidance scale (range 0-38); where higher scores indicate greater distress

3.6. Impact of genetic testing is measured using the Multidimensional Impact of Cancer (MICRA) questionnaire (21 item questionnaire on a 4-point Likert scale)

4. Uptake of risk management options (for breast, ovarian, endometrial and bowel cancers) measured using self-reported and/or clinical or registry data annually till year 8:

4.1. Breast: uptake of self-examination, mammography, MRI, risk reducing mastectomy, medical prevention

4.2. Ovary: uptake of surveillance, or surgical prevention (risk reducing salpingo-oophorectomy or risk reducing early salpingectomy)

4.3. Endometrial: uptake of risk reducing hysterectomy (with bilateral salpingo-oophorectomy in women with Lynch Syndrome); endometrial cancer surveillance

4.4. Bowel: uptake of FIT test, colonoscopy, aspirin

4.5. Pre-implantation genetic testing in individuals planning a family

5. Uptake of cascade testing measured as the total number of people who undergo cascade testing per family in an individual with a PV in a CSG at 2 years after the return of the last test result

6. VUS carrier frequency measured as the proportion of VUS carriers in women who have undergone testing at 6 months after return of the last test result

7. Cost-effectiveness of genetic testing measured by:

7.1. ICER per QALY of population based genetic testing compared to family history based genetic testing. This is compared to the NICE established willingness to pay threshold of £30,000

/QALY.

7.2. Incremental costs

7.3. Incremental QALYs

7.4. Number of cancers/deaths prevented

Undertaken initially at 12 months after the return of the last test result and then at 8 years after study end.

8. Women's motivations and experiences of panel genetic testing and personalised BC and OC risk estimation for cancer screening and prevention . Qualitative interview transcripts. Nvivo will be used to identify themes, index, chart, map, synthesize and interpret data, including comparison between relevant groups.

Undertaken:

8.1. For decliners – post decision

8.2. For those with a PV or moderate or high risk result – 9-12 months

8.3. For VUS: 12-18 months

ADDITIONAL OUTCOMES, OUTCOME MEASURES:

9. Uptake of population-based genetic testing: Women who consent to genetic testing.

Proportion of women who consent to undergo genetic testing (amongst those consenting to the study). Undertaken 6 months after return of the last test result.

10. Proportion of women categorised as moderate and high risk of BC and moderate and high risk of OC. Women categorised as moderate or high risk for BC or moderate or high risk for OC using the CAN-RISK model. Women categorised as moderate or high risk for breast cancer using the Tyrer-Cuzick model, and difference compared with use of the CAN-RISK model.

Measured 6 months after return of the last test result.

11. Proportion of women who have undergone genetic testing and found to have a specific individual CSG: BRCA1, BRCA2, RAD51C, RAD51D, BRIP1, PALB2, MLH1, MSH2 or MSH6. Women with each individual CSG who fulfil the NHS testing criteria (FH positive) (10% carrier probability for HBOC or Amsterdam-2 criteria positive for Lynch Syndrome).

12. Satisfaction and regret with population-based testing longer term, measured 2 years, 3 years post-test result.

12.1. Satisfaction is measured as the proportion of positive responses to the statement "I am satisfied with the decision I have made"

12.2. Regret is measured using the Decision Regret Scale questionnaire

13. Experience of using and usability of the PROTECT-C app, evaluated separately for women who accept genetic testing (at 6-month post-test result) and decline genetic testing (post decision). Measured using a customised questionnaire:

13.1. App usage (y/n) - Proportion of women who used the app

13.2. Use of written information (y/n)- Proportion of women who accessed written information

13.3. Written information sections viewed - Proportion of women who accessed each section

13.4. 1-item usefulness of written information statement ("Looking at this information after receiving my results was helpful") on 5-point Likert scale) - Proportion of women who "strongly and very strongly agree" with the statement

13.5. Videos watched (y/n) - Proportion of women who accessed videos

13.6. Video topics viewed- Proportion of women who accessed videos, by topic

13.7. 1-item usefulness of video information statement ("Watching these videos after receiving my results was helpful") on 5-point Likert scale - Proportion of women who "strongly and very strongly agree" with the statement

13.8. Suggestions for improvement (free text) - Analysis of free text, coding of categories

13.9. Unhelpful features of app (y/n and free text) - Proportion of women who found elements of the app unhelpful and categorisation of features

14. Use of a helpline in population testing. Measured for Accept/decline, 21-days and 6-month post-test questionnaire

- 14.1. Frequency of use of helpline - Total number of calls and proportion of consented women who contacted the helpline
- 14.2. Reasons for helpline use - Proportion of consented women who called by reason
- 14.3. Mode of helpline use - Proportion of calls by mode of use
- 14.4. Ease of access - Proportion who found the helpline “very easy or easy” to use in those who used the helpline
- 14.5. Satisfaction - Proportion who were “very satisfied or satisfied” with the helpline in those who used the helpline
- 14.6. Frequency of use of booking system - Total number of people who used the online booking system
15. Impact of return of VUSs. VUS reclassification is recorded on the study database and updated /returned every 6 months.
 - 15.1. VUS reclassification rate: proportion of VUS reclassified in women with at least one VUS
 - 15.2. Timepoint at which most VUS’s get reclassified
 - 15.3. Quality of life and psychosocial outcomes in individuals with VUS, over time (baseline, 6 months, 1-3 years)
16. Feasibility of running a study within a trial (SWAT), measured by the proportion of individuals who registered on the study website and indicated they received an invitation letter, (can later be linked to which type of letter). To be reported at 6 months.
17. Effectiveness of different letters on registration interest in the trial, measured by difference in proportions of those who received each (one of two types) letter and registered from those invited, by letter type. To be reported at 6 months
18. Association of sociodemographic factors, measured by differences in sociodemographic factors between accepters and decliners.
 - 18.1. Marital status (5 categories)
 - 18.2. Education status (9 categories)
 - 18.3. Income (6 categories)
 - 18.4. Race/ethnicity (5 broad categories)
 - 18.5. Religion (8 categories)This is evaluated at 6 months.
19. Impact of genetic testing on health behaviours. Measures on the Lifestyle and Behaviours include:
 - 19.1. Diet: Meat/Vegetable/Fruit consumption (7-point Likert scale for each)
 - 19.2. Vitamin supplement use (y/n)
 - 19.3. Alcohol consumption (y/n) and frequency/quantity
 - 19.4. Physical activity (y/n)
 - 19.5. Smoking frequency (current/former/never) and quantityMeasured by average change in proportions/scores between the baseline questionnaire and 6-month post-test questionnaire, as well as 1-3 year questionnaire in women who consent to genetic testing.
20. Quality of life longer term measured using the EORTC EQ5D-5L instrument. Measured by change in average scores between pre-genetic testing questionnaires, 6-months and 1-3 years post-test result.
21. Psychosocial wellbeing longer term measured by change in proportions/average scores between pre-genetic testing questionnaires, 6-months and 1-3 years post-test result.
 - 21.1. Cancer worry score is measured using the Cancer Worry Scale questionnaire. (4-item Cancer Worry Scale questionnaire on a 4-point Likert scale)
 - 21.2. Risk perception is measured as the proportion responding as at “high or much higher” chance of cancer to the 1-item question (“compared with other people of your age, do you think your chances of getting cancer at some point in your life are...” on a 5-point Likert scale)
 - 21.3. Anxiety is measured using the Hospital Anxiety and Depression Scale (HADS) anxiety questionnaire (7-item questionnaire on a 4-point Likert scale)

21.4. Depression is measured using the HADS depression questionnaire (7-item questionnaire on a 4-point Likert scale)

21.5. Impact is measured using the Impact of Events (IES) questionnaire (22-item IES questionnaire on a 5-point Likert scale): Mean score IES Intrusive scale (range 0-35) and IES Avoidance scale (range 0-38); where higher scores indicate greater distress

21.6. Distress is measured using the Multidimensional Impact of Cancer (MICRA) questionnaire (21 item questionnaire on a 4-point Likert scale)

Completion date

01/12/2037

Eligibility

Key inclusion criteria

Women, trans men, and non-binary people with female reproductive organs (ovaries, fallopian tubes, and/or a uterus) who are aged ≥ 18 years

Participant type(s)

Population

Healthy volunteers allowed

No

Age group

Mixed

Lower age limit

18 Years

Upper age limit

100 Years

Sex

Female

Total final enrolment

0

Key exclusion criteria

1. Individuals who have undergone genetic testing for one or more of the following CSGs: BRCA1, BRCA2, PALB2, RAD51C, RAD51D, BRIP1, MLH1, MSH2, MSH6
2. First-degree relative (FDR) or second-degree relative (SDR) with a pathogenic or likely pathogenic variant (PV) in any of above CSGs
3. Inability to provide informed consent

Date of first enrolment

18/12/2025

Date of final enrolment

31/12/2029

Locations

Countries of recruitment

United Kingdom

England

Northern Ireland

Scotland

Wales

Study participating centre

Queen Mary University of London

Wolfson Institute of Population Health Queen Mary University of London, Charterhouse Square
London

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EC1M 6BQ

Sponsor information

Organisation

Queen Mary University of London

ROR

<https://ror.org/026zzn846>

Funder(s)

Funder type

Not defined

Funder Name

Yorkshire Cancer Research

Alternative Name(s)

YCR

Funding Body Type

Government organisation

Funding Body Subtype

Trusts, charities, foundations (both public and private)

Location

United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated and/or analysed during the study may be available after study data publication, upon reasonable request from Prof. Ranjit Manchanda (protectc.study@qmul.ac.uk)

The results of this study will be presented at national and international conferences, and published in scientific peer reviewed journals. Participants will not be personally identified in any such publications. Information will also be disseminated via digital and non-digital media in collaboration with supporting charities, support groups, and all relevant stakeholders.

IPD sharing plan summary

Available on request