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Assessing the impact of personalised risk estimates on the uptake and timing of risk management options in women who have inherited a change in genes associated with an increased risk of breast and ovarian cancer

Submission date	**Recruitment status**	[_] Prospectively registered
18/03/2022	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
21/06/2022	Ongoing	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
04/09/2025	Cancer	[X] Record updated in last year

Plain English summary of protocol

Background and study aims

Women with disease-causing gene changes (faults/mutations) in BRCA1, BRCA2, PALB2, CHEK2 and ATM are at an increased risk of developing certain types of cancer - specifically breast (all genes) and epithelial ovarian cancer (BRCA1, BRCA2, PALB2 only). At present, the risk estimates given by most health practitioners to women are broad (e.g. 35-85% lifetime risk of breast cancer for BRCA1 and BRCA2) and are not personalised. This can make it difficult for women to make informed decisions regarding risk management options available to them. By combining information about genetic, lifestyle and hormonal risk factors, we can produce a narrower, more personalised risk estimate (e.g. 44% lifetime risk of breast cancer). In this study we aim to test whether offering personalised risk estimates to women undergoing predictive testing in genetics centres in the UK and USA better supports women's mental health and choices about their clinical care, relative to standard care. In addition, we will explore the experiences of both staff and women taking part in the study to understand whether personalised risk estimates are acceptable, feasible and cost-effective for use in clinical care.

Who can participate?

Women who are referred to the Genetics department to discuss "predictive" genetic testing are eligible for this study. Predictive genetic testing is when a relative has been found to have a gene fault, and a family member wishes to see if they also carry the same gene change. To participate, women must be over the age of 18 and able to give informed consent. A woman is not able to take part in this study if she has had a previous diagnosis of breast or ovarian cancer.

What does the study involve?

Genetic testing will be performed in the usual way. If the test shows that the participant has inherited the gene change, they will be randomly allocated to have a standard risk estimate or the "personalised" risk estimate, using a risk prediction tool called CanRisk. If they are allocated

to the “personalised” arm, we will do some additional genetic testing on the blood sample the patient gave to look at the hundreds of small genetic alterations and provide them with a combined risk estimate, called a Polygenic Risk Score (PRS). Both groups will be asked to complete some questionnaires. This would include one questionnaire before their clinical genetics appointment, followed by three more “follow-up” questionnaires after they receive their genetics result. Participants may be invited to give an interview with one of the research team. In this research study we will use information from the participant, their medical records, their GP and from NHS Digital. We will only use information that we need for the research study. Everyone involved in this study will keep participant data safe and secure following all privacy rules.

What are the possible benefits and risks of participating?
The participant will receive a different risk estimate depending on which group of the study they are randomised to. This could involve additional analysis than the standard genetic test (the analysis will be done on the same blood sample they gave for genetic testing). Our aim is to study how these differences affect the participant’s subsequent decisions regarding their medical management. There is no direct benefit to the participant. However, by taking part in our research study participants will potentially be helping future generations of women with these gene changes. We will publish our findings on our website and/or in a newsletter.

We will use the sample blood sample as the one given for the clinical genetic test. No additional blood test will be required. There are no medical risks in taking part.

Where is the study run from?
Cambridge University Hospitals NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
June 2021 to December 2026

Who is funding the study?
Cancer Research UK

Who is the main contact?
Dr Marc Tischkowitz, mdt33@cam.ac.uk

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
291629

Protocol serial number
CPMS 48658, CRUK C22770/A31523, IRAS 291629

Study information

Scientific Title
Stratifying risk for early detection in hereditary breast and ovarian cancer

Acronym
Precision-HBOC

Study objectives
The timing and uptake of risk management options will be different between women who receive the personalised risk estimates compared to women who receive the broad-range risk estimates, as per current clinical practice.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 21/05/2021, East of England - Cambridgeshire and Hertfordshire Research Ethics Committee (Temple Quay House, 2 The Square, Bristol Research Ethics Committee Centre, BS1 6PN, UK; +44 2071048278; cambsandherts.rec@hra.nhs.uk), ref: 21/EE/0062

Study design
Interventional randomized controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Hereditary breast and ovarian cancer

Interventions
Women who agree to take part in the study will be asked to complete a short questionnaire which will include basic demographics along with details regarding relevant risk factors (family history of cancer, height, body mass index, parity, age at first birth, age at menarche, age at menopause, use of oral contraception, use of hormone replacement therapy, alcohol intake). They will have a standard predictive test performed in the local clinical laboratory in the study and, if the result shows that they have inherited the mutation, a DNA aliquot (from the original blood sample taken for genetic testing) will be sent to Cambridge for the 313-SNP PRS. The PRS result, together with the other factors collected in the questionnaire, will be inputted into the CanRisk risk prediction tool to generate personalised risks.

Intervention Type
Other

Primary outcome(s)
The type and the timing of risk management options (surveillance, chemoprevention, surgery) taken up over the course of the study (i.e. 12 months) measured via 4 questionnaires (baseline, then 1, 3 and 12 months post-results)

Key secondary outcome(s))
1. The type of risk management options planned to be taken up in the future (i.e. beyond the end of the study). measured via questionnaires at 1, 3 and 12 months post-results).
2. Informed decision-making about risk management options (measured by combining objective knowledge, attitude and behaviour) measured via questionnaires at 1, 3 and 12 months post-results).
3. Women's understanding of the test result measured via questionnaires at 1, 3 and 12 months post-results).
4. Psycho-social impact (including cancer worry, anxiety and quality of life), measured via 4 questionnaires (baseline, then at 1, 3 and 12 months post-results).
5. Information on women's use of health services will also be captured in order to perform a cost-utility analysis measured via 4 questionnaires (baseline, then at 1, 3 and 12 months post-results).
6. Exploring the acceptability and implementation of personalised risk calculations in clinical genetics services measured by semi-structured interviews with patients and staff at 12 months.

Completion date
31/12/2026

Eligibility

Key inclusion criteria
1. Female
2. Age >18 years
3. Undergoing predictive testing for a PV in BRCA1, BRCA2, PALB2, ATM or CHEK2
4. Able to give informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
Female

Key exclusion criteria
Previous history of breast cancer or ovarian cancer

Date of first enrolment
01/05/2022

Date of final enrolment
31/07/2025

Locations

Countries of recruitment
United Kingdom

England

United States of America

Study participating centre
Cambridge University Hospitals NHS Foundation Trust
Cambridge Biomedical Campus
Hills Road

Cambridge
United Kingdom
CB2 0QQ

Study participating centre
Manchester University NHS Foundation Trust
Cobbett House
Oxford Road
Manchester
United Kingdom
M13 9WL

Study participating centre
Canary Center at Stanford for Early Cancer Detection
3155 Porter Drive
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United States of America
94305

Study participating centre
Addenbrookes
Addenbrookes Hospital
Hills Road
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Study participating centre
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Tremona Road
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SO16 6YD

Study participating centre
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M13 9WL

Study participating centre
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Infirmary Square
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LE1 5WW

Study participating centre
Guy's and St Thomas' NHS Foundation Trust
St Thomas' Hospital
Westminster Bridge Road
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United Kingdom
SE1 7EH

Study participating centre
Oxford University Hospitals
John Radcliffe Hospital
Headley Way
Headington
Oxford
United Kingdom
OX3 9DU

Study participating centre
Nottingham University Hospitals NHS Trust
Trust Headquarters
Queens Medical Centre
Derby Road
Nottingham
United Kingdom
NG7 2UH

Study participating centre
Leeds Teaching Hospitals NHS Trust
St. James's University Hospital

Beckett Street
Leeds
United Kingdom
LS9 7TF

Study participating centre
Liverpool Women's NHS Foundation Trust
Liverpool Womens Hospital
Crown Street
Liverpool
United Kingdom
L8 7SS

Study participating centre
St George's University Hospitals NHS Foundation Trust
Blackshaw Rd
London
United Kingdom
SW17 0QT

Study participating centre
Birmingham Women's NHS Foundation Trust
Birmingham Womens Hospital
Metchley Park Road
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Study participating centre
Royal Devon and Exeter Hospital
Royal Devon & Exeter Hospital
Barrack Road
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EX2 5DW

Study participating centre
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Sponsor information

Organisation
Cambridge University Hospitals NHS Foundation Trust

ROR
https://ror.org/04v54gj93

Organisation
University of Cambridge

ROR
https://ror.org/013meh722

Funder(s)

Funder type
Charity

Funder Name
Cancer Research UK

Alternative Name(s)
CR_UK, Cancer Research UK - London, Cancer Research UK (CRUK), CRUK

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are not expected to be made available due to ethical approval not being granted to share data

IPD sharing plan summary

Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		31/05/2022	21/06/2022	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	version 2.0	18/11/2021	07/04/2022	No	Yes