ISRCTN33767504 https://doi.org/10.1186/ISRCTN33767504

Does removing both ovaries prior to menopause reduce breast cancer risk in BRCA1 and BRCA2 mutation carriers?

Submission date
08/09/2025

Recruitment status
No longer recruiting

Registration date
01/10/2025

Overall study status
Ongoing

Last Edited
29/09/2025

Condition category
Cancer

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
It is unclear whether removing both ovaries and the fallopian tubes (bilateral salpingo-oophorectomy) before menopause reduces the risk of breast cancer in women who carry BRCA1 or BRCA2 gene mutations. There is no clear agreement in international guidelines either. Undertaking a randomised study is not practical because most women would not agree to be randomly assigned. Therefore, we propose an analysis of pooled individual data from established cohorts to better understand this.
The aims of this study are:
1. To estimate the effect of removing both ovaries and the fallopian tubes before menopause on breast cancer risk for (i) women with BRCA1 gene mutations and (ii) women with BRCA2 gene mutations.
2. To test whether any effect of ovary and fallopian tube removal is stronger when carried out at younger ages.

Who can participate?
Existing data will be included from cohort participants that meet the following criteria:
• carrier of pathogenic or likely pathogenic variant (class 4 or 5) in BRCA1 or BRCA2
• born after 1920
• aged at least 18 years at cohort entry
• no personal history of cancer (except cervix carcinoma in situ or non-melanoma skin cancer) at cohort entry
• no personal history of risk-reducing bilateral mastectomy at cohort entry
• follow-up information available (for at least invasive breast cancer, ductal carcinoma in situ and death)

What does the study involve?
This study will combine and analyse individual data from established cohorts to understand whether having both ovaries and the fallopian tubes removed before menopause lowers breast cancer risk for women with BRCA1 or BRCA2 mutation carriers. We will use an optimised analytical design to minimise bias and confounding.

Are There Any Benefits or Risks?
Since this study only looks at existing data, there are no direct benefits or risks to participants. However, results from this research may help influence future clinical care.

Where is the study run from?
Cancer Council Victoria, Australia

When is the study starting and how long is it expected to run for?
Data analysis will begin in Feb 2026 and take approximately 12 months to complete.

Who is funding the study?
The analyses will be conducted by researchers at Cancer Council Victoria, using local funds.

Who is the main contact?
Professor Roger Milne, Roger.Milne@cancervic.org.au

Contact information

Type(s)
Scientific, Principal investigator

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Type(s)
Public

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Protocol serial number
RGU/EX2202/20241031

Study information

Scientific Title
Pre-menopausal bilateral salpingo-oophorectomy and breast cancer risk for carriers of BRCA1 and BRCA2 pathogenic variants: A pooled cohort analysis

Study objectives
1. Pre-menopausal risk reducing bilateral salpingo-oophorectomy is associated with reduced risk of breast cancer for BRCA2, but not BRCA1, pathogenic mutation carriers
2. Pre-menopausal risk reducing bilateral salpingo-oophorectomy before age 40 years is associated with greater reduced risk of breast cancer than pre-menopausal risk reducing bilateral salpingo-oophorectomy after age 40 years

Ethics approval required
Ethics approval not required

Ethics approval(s)

Study design
Pooled analysis of multiple longitudinal observational cohort studies.

Primary study design
Observational

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Breast cancer

Interventions
This is an observational study that involves analysing pooled individual data that has already been collected within established cohorts. No interventions or treatments will be given and no further data collected from study participants.

Intervention Type
Other

Primary outcome(s)
Diagnosis of invasive breast cancer or ductal carcinoma in situ (DCIS) derived from self-report (in follow-up questionnaires), pathology reports, medical records and linkages to cancer registries at any time during follow-up.

Key secondary outcome(s))
There are no secondary outcome measures

Completion date
01/02/2027

Eligibility

Key inclusion criteria
1. Carrier of pathogenic or likely pathogenic variant (class 4 or 5) in BRCA1 or BRCA2
2. Born after 1920
3. Aged at least 18 years at cohort entry
4. No personal history of cancer (except cervix carcinoma in situ or non-melanoma skin cancer) at cohort entry
5. No personal history of risk-reducing bilateral mastectomy at cohort entry

Participant type(s)
Other

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
Female

Key exclusion criteria
No follow-up information available

Date of first enrolment
30/11/2025

Date of final enrolment
01/02/2026

Locations

Countries of recruitment
United Kingdom

England

Australia

Austria

Canada

Czech Republic

France

Germany

Hungary

Netherlands

New Zealand

Norway

Poland

Spain

Sweden

United States of America

Study participating centre
NRG Oncology
Four Penn Center, 1600 JFK Blvd, Suite 1020
Philadelphia
United States of America
19103

Study participating centre
Columbia University
116th and Broadway
New York
United States of America
10027

Study participating centre
Cancer Prevention Institute of California
2201 Walnut Ave
Fremont
United States of America
94538

Study participating centre
Cancer Care Ontario
620 University Ave
Toronto
Canada
ON M5G 2C1

Study participating centre
Fox Chase Cancer Centre
333 Cottman Ave
Philadelphia
United States of America
19111

Study participating centre
The University of Utah Health Sciences Centre
201 Presidents' Cir
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United States of America
84112

Study participating centre
The University of Melbourne
Grattan Street
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Study participating centre
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19104

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Marseille
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The Netherlands Cancer Institute
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1066 CX

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Medical University of Vienna
Spitalgasse 23
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1090

Study participating centre
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Study participating centre
University Medicine of Greifswald
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Study participating centre
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Study participating centre
The International Hereditary Cancer Center
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70-204

Study participating centre
Masaryk Memorial Cancer Institute
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Czech Republic
656 53

Study participating centre
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Madrid
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Study participating centre
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Melbourne
Australia
3000

Study participating centre
Auckland Hospital
2 Park Road
Auckland
New Zealand
1023

Sponsor information

Organisation
Cancer Council Victoria

ROR
https://ror.org/023m51b03

Funder(s)

Funder type
Charity

Funder Name
Cancer Council Victoria

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location

Australia

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study will not be made publicly available. Data may be available on reasonable request to the PIs of the component cohorts used in this study.

IPD sharing plan summary

Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 2	08/08/2025	29/09/2025	No	No