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

Submission date	Recruitment status	[X] Prospectively registered			
08/09/2025	Not yet recruiting	[X] Protocol			
Registration date	Overall study status Ongoing Condition category	Statistical analysis plan			
01/10/2025		Results			
Last Edited		Individual participant data			
29/09/2025	Cancer	[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

Contact name

Prof Roger Milne

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Type(s)

Public

Contact name

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Additional identifiers

Clinical Trials Information System (CTIS)

Nil known

ClinicalTrials.gov (NCT)

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

Adstria	
Canada	
Czech Republic	
France	
Germany	
Hungary	
Netherlands	
New Zealand	
Norway	
Poland	
Spain	
Sweden	
United States of America	

Australia

Austria

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 Salt Lake City United States of America 84112

Study participating centre The University of Melbourne

Grattan Street Parkville Australia 3010

Study participating centre University of Pennsylvania

3451 Walnut Street Philadelphia United States of America 19104

Study participating centre Vall d'Hebron University Hospital

Pg. de la Vall d'Hebron, 119, Horta-Guinardó Barcelona Spain 08035

Study participating centre University of Cambridge

The Old School
Trinity Lane
Cambridge
United Kingdom
CB2 1TN

Study participating centre Institute Paoli-Calmettes

232 Bd de Sainte-Marguerite Marseille France 13009

Study participating centre The Netherlands Cancer Institute

Plesmanlaan 121 Amsterdam Netherlands 1066 CX

Study participating centre Medical University of Vienna

Spitalgasse 23 Wien Austria 1090

Study participating centre Oslo University Hospital

Sognsvannsveien 20

Oslo Norway 0372

Study participating centre University Medicine of Greifswald

Fleischmannstraße 8 Greifswald Germany 17475

Study participating centre National Institute of Oncology

Ráth György u. 7-9 Budapest Hungary 1122

Study participating centre Lund University

Box 188 Lund Sweden SE-221 00

Study participating centre The International Hereditary Cancer Center

ul. Rybacka 1 Szczecin Poland 70-204

Study participating centre Masaryk Memorial Cancer Institute

Žlutý kopec 7 Brno Czech Republic 656 53

Study participating centre Spanish National Cancer Research

C. de Melchor Fernández Almagro, 3, Fuencarral-El Pardo Madrid Spain 28029

Study participating centre Peter MacCallum Cancer Centre

305 Grattan St 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

Other non-profit organizations

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?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Protocol file	version 2	08/08/2025	29/09/2025	No	No