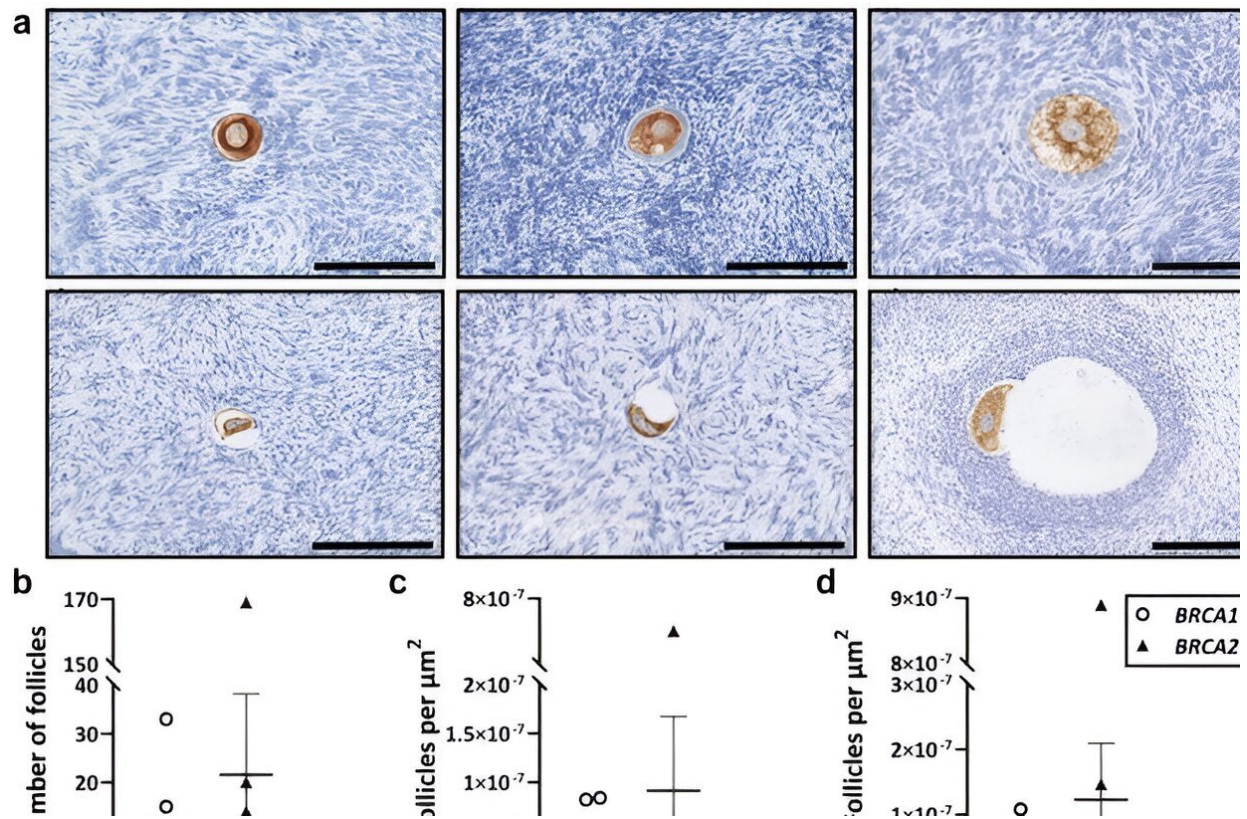


BRCA1 gene mutation may increase the risk of impaired fertility, study shows

July 31 2024



(a) Human cortical ovarian tissues from BRCA1 (n = 8) and BRCA2 (n = 10) mutation carriers (mc) were immunohistochemically stained for DDX4 as a marker of oocytes. Photomicrographs are representative of the classifications used to identify i. primordial follicles; bar = 100 μm , ii. primary follicles; bar = 100 μm , iii. secondary follicles; bar = 100 μm iv-v. abnormal follicles; bar = 100 μm vi. abnormal follicles; bar = 200 μm . (b) Total primordial follicle number, (c) primordial follicle density per tissue area (μm^2) and (d) total healthy follicle density per tissue area (μm^2) were enumerated. (e) Total abnormal

follicle number and (f) abnormal follicle rate (%) were quantified. (g) Serum AMH levels were quantified by ELISA. Data are mean \pm SEM; unpaired t-test. Credit: *eBioMedicine* (2024). DOI: 10.1016/j.ebiom.2024.105262

People with a BRCA1 gene mutation, which increases breast and ovarian cancer risk, are also at increased risk of impaired fertility, Monash University-led research has confirmed in preclinical models and human tissue samples.

The BRCA1 and BRCA2 genes protect against breast and [ovarian cancer](#), and a mutation of either gene increases the risk of developing cancer. An estimated 1 in 350 women have a BRCA1 or BRCA2 mutation.

Published in *EBioMedicine*, [the study](#) found that having no BRCA1 gene in mice reduced litter size and quality of their eggs, particularly with advancing age. Egg maturation rates were decreased by 45% in reproductively aged mice lacking BRCA1.

The study also analyzed [hormone levels](#) in the blood and estimated egg numbers in the ovarian tissue of women with BRCA mutations.

Senior author Professor Karla Hutt, head of the Monash Biomedicine Discovery Institute's (BDI) Hutt Laboratory, said that previous [preclinical models](#) indicated that partial loss of BRCA1 function may reduce egg numbers in the ovary.

"The potential impacts of complete loss of BRCA1 function on egg number and fertility had never been studied," she said. "Using a unique mouse model with targeted loss of the BRCA1 gene specifically in eggs, this study also comprehensively assessed fertility across the entire reproductive lifespan. The data show that BRCA1 is important for

maintaining egg number, quality, and fertility."

The mice were bred with no BRCA1 gene in their eggs, which models a BRCA1 [gene mutation](#) causing complete loss of BRCA1 function. While their fertile lifespan length was not altered, the mutation led to reduced litter sizes and egg numbers. Egg maturation was also impaired compared to mice without the mutation.

In women, measuring anti-Müllerian hormone (AMH) levels in blood is considered the gold-standard indirect marker of the number of eggs they may have. However, AMH levels and estimated egg numbers from ovarian tissues of a small number of women with a BRCA mutation showed no correlation between these measures.

This suggests that more studies are needed to better understand if AMH is a good predictor of egg number in women with a BRCA mutation.

Co-first author Dr. Amy Winship, from the Hutt Laboratory, said the study extended knowledge of BRCA1's critical role in maintaining fertility.

"This has implications for women who carry BRCA mutations to make considered family planning and possibly fertility preservation decisions, like egg freezing," Dr. Winship said. "Additionally, since these women are already at higher risk of developing breast and ovarian cancer during their lifetime, they are more likely to receive fertility-damaging cancer treatments."

Co-first author Dr. Lauren Alesi, from the Hutt Laboratory, said future studies were needed to understand the impacts of cancer treatments on fertility in the context of BRCA mutations.

"Because fertility may already be reduced, having a BRCA mutation and

receiving cancer treatments could worsen the fertility-damaging effects of these treatments," Dr. Alesi said. "Further research in our preclinical models and patient samples will help us to determine this."

Breast cancer survivor Leslie Gilham, who is a Breast Cancer Network Australia and Breast Cancer Trials Australia consumer advocate, co-authored the paper.

"Young women are often distressed when told they either have a BRCA1 mutation or have breast cancer," Ms. Gilham said. "A million things are swirling in their heads, one of them being 'Will I be able to have children?' This research provides the evidence needed to support these women when they are making decisions on their fertility. It has the potential to be practice changing and address one of the significant unmet needs in this young group of patients."

This study also involved the Royal Women's Hospital's Gynaecology Research Centre, and the University of Melbourne Department of Obstetrics and Gynaecology.

More information: Amy L. Winship et al, Conditional loss of Brca1 in oocytes causes reduced litter size, ovarian reserve depletion and impaired oocyte in vitro maturation with advanced reproductive age in mice, *eBioMedicine* (2024). [DOI: 10.1016/j.ebiom.2024.105262](https://doi.org/10.1016/j.ebiom.2024.105262)

Provided by Monash University

Citation: BRCA1 gene mutation may increase the risk of impaired fertility, study shows (2024, July 31) retrieved 31 July 2024 from <https://medicalxpress.com/news/2024-07-brca1-gene-mutation-impaired-fertility.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.