Original Article
ISSN (Online): 2350-0530
ISSN (Print): 2394-3629

International Journal of Research - GRANTHAALAYAH
March 2025 13(3), 202–210

# FERTILITY IN WOMEN WITH HEREDITARY BREAST AND OVARIAN CANCER

Boskhomdzhieva Mira Vladimirovna [1], Nikolaev Alexander Arkadyevich [2], Ploskonos Maria Vyacheslavovna [3]

[1] Deputy Chief Physician for Medical Work, Budgetary institution of the Republic of Kalmykia "Republican Oncology Dispensary named after Timoshkaeva E.S.", 358000 Russian Federation Elista st. A. Suseeva, 17, Russian Federation
[2] Doctor of Medical Sciences, Professor & Head of the Department of Fundamental Chemistry, Federal State Budgetary Educational Institution of Higher Education "Astrakhan State Medical University" of the Ministry of Health of the Russian Federation, 41400, Russian Federation Astrakhan, st. Bakinskaya 121, Russian Federation
[3] Doctor of Biological Sciences, Professor, Department of Fundamental Chemistry, Federal State Budgetary Educational Institution of Higher Education "Astrakhan State Medical University" of the Ministry of Health of the Russian Federation, 41400, Russian Federation Astrakhan, Bakinskaya 121, Russian Federation

**Received** 06 February 2024
**Accepted** 12 March 2025
**Published** 15 April 2025

**Corresponding Author**

Boskhomdzhieva Mira Vladimirovna,
miravladimirovna1450@gmail.com

**DOI**
10.29121/granthaalayah.v13.i3.2025.5993

**Funding:** This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

**Copyright:** © 2025 The Author(s). This work is licensed under a Creative Commons Attribution 4.0 International License.

With the license CC-BY, authors retain the copyright, allowing anyone to download, reuse, re-print, modify, distribute, and/or copy their contribution. The work must be properly attributed to its author.

OPEN ACCESS

## ABSTRACT

Among the causes of breast cancer and ovarian cancer in women, mutations of the BRCA1/2 genes have been characterized in detail. However, the effect of BRCA1/2 gene mutations on female fertility remains controversial. The purpose of this review is to assess the relationship between the BRCA1 and BRCA2 mutation status and female fertility in its various manifestations. A number of scientists consider mutations of the BRCA1/2 genes as a negative factor that reduces the reproductive abilities of women. A study of BRCA1/2 mutations in oocytes showed the possibility of spontaneous inactivation of the X chromosome, which can lead to infertility of female offspring, as well as a significantly reduced ovarian reserve and low oocyte yield. There are studies devoted to the assessment of gene expression in young and old oocytes, which showed a decrease in protein expression by DNA repair genes in parallel with age in rodents, cattle and humans. A series of studies confirm a significant decrease in the number of follicles in women carriers of BRCA1/2. There is an opinion that mutations of the BRCA1/2 genes do not affect the fertility of women carriers of these mutations. These studies are based on epidemiological and demographic data. A number of scientists attribute the presence of BRCA1\2 mutations to factors that increase fertility. They base their point of view on the longer telomeres in the reproductive cells of mutation carriers. In mutation carriers, the average telomere length is significantly longer than in their relatives who are not carriers (P = 0.0018), especially in families with BRCA2 mutations (P = 0.0016). The authors of the studies rely on such a well-known phenomenon as antagonistic pleiotropy. The mechanisms linking BRCA1 and BRCA2 mutations with female fertility remain a subject of debate and have not been fully studied. Animal model studies may reveal new mechanisms by which BRCA1/2 gene mutations affect female fertility.

**Keywords:** Female Fertility, Breast Cancer, Ovarian Cancer, BRCA1/2 Gene Mutations

## 1. INTRODUCTION

In 2022, more than 2.45 million women will be diagnosed with breast cancer (BC). BC in women has the highest proportion of all cancers, both in men and women. Schlottmann et al. (2024). In addition to being widespread, BC has a wide

range of molecular and histological characteristics Pianigiani et al. (2010). Among the causes that contribute to the development of cancer, including BC in women, mutations in the BRCA1 and BRCA2 genes have been characterized in detail. These mutations occupy a special place, since in women who carry these mutations, the probability of developing BC is 40-85%, and the probability of developing ovarian cancer is 16-64% Sung et al. (2021).

Currently, new genetic variants of human diseases are constantly being reported, and questions about the reasons for the preservation of some pathological mutations in the population, in contrast to others that are rejected by evolution, are becoming relevant Harbeck et al. (2019). There is a hypothesis Dyba et al. (2021) according to which some pathological mutations give their carrier advantages in unusual biological situations.

## 2. RESEARCH PURPOSE

The objective of this review is to assess the relationship between BRCA1 and BRCA2 mutation status and female fertility in its various manifestations.

## 3. MATERIALS AND METHODS

The work used review and original publications indexed in MedLine, Cochrane Library, PubMed until 2024.

## 4. RESULTS

There is no consensus in the literature on the effect of BRCA1/2 mutations on female fertility. A number of scientists consider BRCA1/2 gene mutations to be a negative factor that reduces female reproductive capacity. A study of BRCA1/2 gene mutations in oocytes has shown Zheng et al. (2024) the possibility of spontaneous inactivation of the X chromosome, which can lead to infertility in female offspring. Data obtained in a study of BRCA2 null gene mice carrying human BAC with the BRCA2 gene are consistent with these studies Polizio et al. (2023). It has been shown that the percentage of oocytes with a BRCA2 gene mutation that have passed meiotic prophase I is sharply reduced. And adult females have a low ovarian reserve. The functions of the proteins encoded by the BRCA1/2 genes are aimed at DNA reparation and are responsible mainly for the accurate restoration of double-strand breaks. On this basis Li et al. (2021), it is believed that multiple divisions during the cell cycle of germ cells, in the absence of effective DNA reparation in carriers of BRCA1/2 gene mutations, will contribute to a decrease in fertility. In another study, hormonal stimulation of the ovaries was carried out for the purpose of subsequent cryopreservation of oocytes and, in parallel, BRCA gene mutations were assessed Sengodan et al. (2024) and an unambiguous conclusion was reached that in the presence of a BRCA1 gene mutation, the ovarian reserve and low oocyte yield are significantly reduced. According to the authors, in carriers of the BRCA2 gene mutation, the stimulation indices did not differ from the control group.

The reproductive potential of women is ensured at different stages of development in the ovary. The supply of germ cells in women is limited and is determined at birth Liu et al. (2022). During embryogenesis in women, primary germ cells differentiate into oogonia, and by the 20th week, about 7 million of them are formed. The oogonia then develop into a primordial follicle. At birth, a healthy woman's body contains about 2 million primordial follicles. The ovarian pool during puberty is about 400,000 primordial follicles, decreasing to 1000 by menopause

Oktay et al. (2024). There are several factors that regulate ovarian aging Melnick (2023). These include genomic abnormalities, meiotic errors, and activation of regulated cell death mechanisms (apoptosis, ferroptosis) Zhu et al. (2022). Among the factors of DNA damage are genetic factors, including mutations in genes involved in DNA repair pathways, such as mutations in the BRCA genes, which can lead to premature ovarian failure Wang et al. (2023). Quite a few studies have been devoted to assessing gene expression in young and old oocytes, showing a decrease in expression of proteins by DNA repair genes in parallel with age in rodents Yuan et al. (2021), cattle Turan and Oktay (2020), and humans Horta et al. (2021). The general conclusion from the cited studies is a decrease in BRCA1 expression and accumulation of double-stranded DNA breaks in oocytes from old individuals compared to oocytes from young individuals. Consequently, DNA damage accumulates in the oocyte during life, and the expression of genes involved in DNA repair mechanisms decreases. In general, these events lead to higher levels of apoptosis in old oocytes. The presence of mutations in the BRCA1/2 genes provokes accelerated aging of oocytes, a decrease in the ovarian reserve and, as a consequence, a decrease in fertility Horta et al. (2021). These data echo the studies on premature ovarian failure (POF) Bilotto et al. (2015). Carriers of the BRCA1/2 gene mutations have a decrease in the ovarian pool and a decrease in fertility Smits et al. (2021). The authors recommend several strategies for preserving fertility for carriers of BRCA1/2 gene mutations, including cryopreservation of oocytes, taking into account the development of premature ovarian failure. Gonadotropin stimulation of women carriers of BRCA1/2 gene mutations revealed a sharply reduced number of oocytes; in women with a BRCA1 mutation, the number of oocytes is significantly lower than in healthy women and in carriers of BRCA2 gene mutations Nash and Davies (2024). A series of studies is devoted to the effect of BRCA gene mutations on the density of follicles in ovarian tissue. All researchers confirm a reliable decrease in the number of follicles in women carriers of BRCA1/2 gene mutations, despite various research methods. [Zhang et al. (2020),El et al. (2023)]. The density of primordial follicles in the ovaries of women with BRCA1\2 mutation is lower than in the control group. El et al. (2023). The same article provides data indicating that women carriers of BRCA1\2 mutations who underwent infertility treatment were significantly more likely to have a negative treatment outcome.

A separate line of research into the influence of BRCA gene mutations is related to the search for causes of repeated spontaneous miscarriages. There is a report Dias et al. (2023) that among Ashkenazi Jewish women one of the causes of early spontaneous miscarriages is fetal homozygosity for recurring BRCA1/BRCA2 mutations. However, the authors failed to observe reliable differences in spontaneous abortions in the groups of carriers and non-carriers of BRCA1/BRCA2 mutations. Similar results were obtained by researchers from North Africa Di et al. (2024). The authors explain the absence of reliable differences in the groups of carriers and non-carriers in the probability of early spontaneous abortions by the possibility of other lethal mutations in the so-called control groups.

Another approach to assessing the fertility of carriers of BRCA1 and BRCA2 gene mutations is based on assessing the number of children born. A study by Israeli scientists Dias et al. (2023) provides information on a significantly smaller number of children in carriers of BRCA1/2 gene mutations than in groups of non-carriers. However, the article does not provide adjustments for the influence of such factors as the development of tumors in mutation carriers and differences in reproductive age. On the other hand, some researchers believe that BRCA1/2 gene mutations do not have a significant effect on the fertility of women carriers of these mutations

Buonomo et al. (2021). The authors conducted an epidemiological study of the effect of BRCA gene mutations on fertility. The strength of this study is the large number of observations: 764 non-carriers and 2254 carriers of BRCA1/2 gene mutations. All women were carefully compared by age, use of oral contraceptives, and reproductive history. Nulliparous women were compared separately. According to the questionnaire and stratification by the above-mentioned characteristics, the authors did not reveal any reliable differences and they conclude that BRCA1/2 gene mutations have no effect on female fertility. Unfortunately, the researchers do not link epidemiological indicators with the biological state of the ovaries. In another study Ben et al. (2021), the authors emphasize the need for individual counseling of women carriers of BRCA1/2 gene mutations in order to help women become mothers of desired children, regardless of genetic problems. Several ways of implementing this direction are proposed, including assessment of serum anti-Müllerian hormone or the number of antral follicles, as well as cryopreservation of oocytes after assessment of the ovarian reserve. The authors acknowledge that the fertility of carriers of BRCA1/2 gene mutations in the current state of medicine is more of a social than a biological problem. Earlier studies Dellino et al. (2024) did not find significant differences in the frequency of spontaneous abortions between carriers of BRCA1/2 gene mutations and non-carriers. A total of 1878 BRCA1 mutation carriers, 950 BRCA2 mutation carriers and 657 linked non-carriers from families with BRCA1/2 gene mutations were studied. The authors conclude that BRCA1/2 gene mutations do not serve as a risk factor for spontaneous abortions. In our opinion, the absence of an association between spontaneous abortions and BRCA1/2 gene mutations does not argue for the absence of a decrease in fertility in carriers of BRCA1/2 gene mutations.

No differences in fertility were found among carriers and non-carriers of BRCA1/2 gene mutations in a study conducted by analyzing the reproductive history of 260 carriers of BRCA1/2 gene mutations and 331 non-carriers. However, the authors showed that the number of pregnancies among the cohort of BRCA1/2 gene mutation carriers was significantly ($p= 0.0049$) lower than in the control group. The authors explain this fact not by a decrease in fertility, but by the fear of having a child in a family with hereditary cancer Peccatori et al. (2018). Another interesting observation, which we did not find confirmation for in the available literature, concerns the imbalance in the birth of male and female children, which in the cohort of BRCA1/2 gene mutation carriers was 0.71 compared to 0.99 in the control. The researchers interpret this observation as a positive selection of BRCA1/2 mutations. We give special attention to studies that classify the presence of BRCA1\2 mutations as factors that increase fertility. Most studies supporting this point of view associate an increase in female fertility with the length of telomeres in reproductive cells. Telomere length is the factor that determines the number of mitoses in a cell. Differences in telomere length in healthy women of the same age reflect differences in the telomeres of the primary germ cells in the prenatal period. Women with long telomeres presumably had their primary germ cells with long telomeres early in life. Thus, these cells should have had more mitotic divisions and a greater number of follicles in the ovaries than short ones. It has been shown that in mutation carriers, the average telomere length is significantly longer than in their relatives who are not carriers ($P = 0.0018$), especially in families with BRCA2 mutations ($P = 0.0016$) Friedman et al. (2006). The authors rely on the judgment that that overexpression of BRCA1/2 inhibits telomerase activity and reduces telomere length. Consequently, mutations of BRCA1/2 genes lead to telomere lengthening and are a protective factor. Higher fertility in families with BRCA1/2 gene mutations is based on greater telomere length and, as a consequence,

increased fertility, compensating for the high mortality of carriers of BRCA1/2 gene mutations in the premenopausal period.

The main idea that unites this group of studies is based on such a well-known phenomenon as antagonistic pleiotropy Moslehi et al. (2010). In this direction, several more works can be cited. There is a report Dorkins et al. (2014) that in women - carriers of BRCA1/2 mutations, the average number of children ever born was higher than in the control group (3.3 and 3.0).

An extensive study French et al. (2006) showed an analysis based on a prospective study of pedigrees of BRCA1/2 gene mutation carriers up to the founders, based on data on family predisposition to breast cancer and ovarian cancer. The authors attach particular importance to the birth rate data in these families for the 30-40s of the last century, when contraception was not widely used. In families of BRCA1/2 gene mutation carriers of this period, there is a significantly larger number of children, a higher frequency of birth of children and later terms of the last pregnancy. At the same time, a significantly higher early mortality was recorded in families of BRCA1/2 gene mutation carriers. The authors believe that the absence of negative selection for BRCA1/2 gene mutations is explained by the reproductive advantages of women carriers of BRCA1/2 gene mutations, which from a biological point of view is more important than the life expectancy of an individual who has completed the task of procreation. This concept is broader and concerns other cancer localizations Magaton et al. (2024). A sufficient number of publications have accumulated demonstrating a positive correlation between telomere length and reproductive health in women. Thus, telomere length was measured in 37 female volunteers of the same age using the FISH fiber method and a positive correlation was found between the duration of the reproductive lifespan and telomere length. Analysis of eggs obtained during in vitro fertilization showed that telomere length was longer in eggs from women who became pregnant compared to those who did not become pregnant Smith et al. (2012). Oocytes, having the initial telomere length at the early stages of development, are subject to endogenous and exogenous oxidative damage, which shortens telomeres. This process largely explains the age-related decline in fertility Tsatsakis et al. (2023). Women with repeated miscarriages and early menopause had significantly shorter telomeres than healthy women from the control group. The authors believe that this observation confirms the relationship between telomere length and reproductive aging in women Mikheev et al. (2023). Since BRCA1/2 gene mutations contribute to telomere lengthening Robinson et al. (2024)

## 5. CONCLUSION

It should be recognized that the relationship between BRCA1/2 gene mutations and female fertility rates is not clearly confirmed. Many authors understand female fertility somewhat differently. In the classical definition, female fertility consists of three components: the ability to conceive a child, the ability to bear a child, and the ability to give birth. Undoubtedly, when studying BRCA1/2 gene mutations, researchers mean the first component of this triad. However, while some groups focus their attention on the analysis of biological changes (ovarian reserve, quantity and quality of primordial follicles, etc.), others use statistical and demographic indicators to assess the impact of BRCA1/2 gene mutations on fertility. Hence the opposite conclusions in many studies. Analysis using population genetics methods largely confirms the concept of antagonistic pleiotropy. Women carrying BRCA1/2 gene mutations demonstrate higher fertility in conditions of maintaining natural fertility but also had increased mortality. Another problem leading to discrepancies

in the results is social aspects. In modern society, women have full opportunity to plan offspring, including contraceptive measures. Women who are carriers of BRCA1/2 gene mutations consciously limit their desire to have children due to the risk of transmitting a high probability of cancer to them. Thus, the mechanisms linking BRCA1 and BRCA2 mutations with female fertility remain a subject of debate and are not fully understood. Perhaps, model studies on animals can reveal new mechanisms of the influence of BRCA1/2 gene mutations on female fertility.

## CONFLICT OF INTERESTS

None.

## ACKNOWLEDGMENTS

None.

## REFERENCES

Schlottmann, F., Strauß, S., Ziesing, S., Reineke, C., Ipaktchi, R., Weyand, B., Krezdorn, N., Vogt, P. M., & Bucan, V. (2024). Organization of Hannover Skin Bank: Sterile culture and procurement protocols for viable cryopreserved allogeneic skin grafts of living donors. International Wound Journal, 21 (1), e14374. https://doi.org/10.1111/iwj.14374

Pianigiani, E., Ierardi, F., Cuciti, C., Brignali, S., Oggioni, M., & Fimiani, M. (2010). Processing efficacy in relation to microbial contamination of skin allografts from 723 donors. Burns, 36 (3), 347–351. https://doi.org/10.1016/j.burns.2009.04.020

Sung, H., Ferlay, J., Siegel, R. L., Laversanne, M., Soerjomataram, I., Jemal, A., & Bray, F. (2021). Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: A Cancer Journal for Clinicians, 71 (1), 209–249. https://doi.org/10.3322/caac.21660

Harbeck, N., Penault-Llorca, F., Cortes, J., Gnant, M., Houssami, N., Poortmans, P., Ruddy, K., Tsang, J., & Cardoso, F. (2019). Breast cancer. Nature Reviews Disease Primers, 5, 11–66. https://doi.org/10.1038/s41572-019-0111-2

Dyba, T., Randi, G., Bray, F., Martos, C., Giusti, F., Nicholson, N., Gavin, A., Flego, M., Neamtiu, L., Dimitrova, N., Negrão Carvalho, R., Ferlay, J., & Bettio, M. (2021). The European cancer burden in 2020: Incidence and mortality estimates for 40 countries and 25 major cancers. European Journal of Cancer, 157, 308–347. https://doi.org/10.1016/j.ejca.2021.07.039

Zheng, Y., Li, Y., Zhou, K., Li, T., VanDusen, N. J., & Hua, Y. (2024). Precise genome-editing in human diseases: Mechanisms, strategies, and applications. Signal Transduction and Targeted Therapy, 9 (1), 21–47. https://doi.org/10.1038/s41392-024-01750-2

Polizio, A. H., Park, E., & Walsh, K. (2023). Clonal hematopoiesis: Connecting aging and inflammation in atherosclerosis. Current Atherosclerosis Reports, 3 (1), 105–111. https://doi.org/10.1007/s11883-023-01083-5

Li, Y., Dong, W., Zhang, P., Zhang, T., Ma, L., Qu, M., Ma, X., Zhou, X., & He, Q. (2021). Comprehensive analysis of regulatory factors and immune-associated patterns to decipher common and BRCA1/2 mutation-type-specific critical regulation in breast cancer. Frontiers in Cell and Developmental Biology, 9, 750897. https://doi.org/10.3389/fcell.2021.750897

Sengodan, S. K., Hu, X., Peddibhotla, V., Balamurugan, K., Mitrophanov, A. Y., McKennett, L., Kharat, S. S., Sanawar, R., Singh, V. K., Albaugh, M. E., Burkett, S. S., Zhao, Y., Tran, B., Malys, T., Sterneck, E., De, S., & Sharan, S. K. (2024). Mismatch repair protein MLH1 suppresses replicative stress in BRCA2-deficient breast tumors. The Journal of Clinical Investigation, 134 (7), e173718. https://doi.org/10.1172/JCI173718

Liu, X., Yue, J., Pervaiz, R., Zhang, H., & Wang, L. (2022). Association between fertility treatments and breast cancer risk in women with a family history or BRCA mutations: A systematic review and meta-analysis. Frontiers in Endocrinology, 13, 986477. https://doi.org/10.3389/fendo.2022.986477

Oktay, K., Kim, J. Y., Barad, D., & Babayev, S. N. (2024). Association of BRCA1 mutations with occult primary ovarian insufficiency: A possible explanation for the link between infertility and breast/ovarian cancer risks. Journal of Clinical Oncology, 28 (2), 240–244. https://doi.org/10.1200/JCO.2009.24.2057

Melnick, A. (2023). Menopause. In P. H. Chung & Z. Rosenwaks (Eds.), Problem-Focused Reproductive Endocrinology and Infertility (pp. 245–251). Springer International Publishing. https://doi.org/10.1007/978-3-031-19443-6

Zhu, Z., Xu, W., & Liu, L. (2022). Ovarian aging: Mechanisms and intervention strategies. Medical Reviews, 2 (6), 590–610. https://doi.org/10.1515/mr-2022-0031

Wang, X., Wang, L., & Xiang, W. (2023). Mechanisms of ovarian aging in women: A review. Journal of Ovarian Research, 16 (1), 67–81. https://doi.org/10.1186/s13048-023-01151-z

Yuan, L., Yin, P., Yan, H., Zhong, X., Ren, C., Li, K., Chin Heng, B., Zhang, W., & Tong, G. (2021). Single-cell transcriptome analysis of human oocyte ageing. Journal of Cellular and Molecular Medicine, 25, 6289–6303. https://doi.org/10.1111/jcmm.16594

Turan, V., & Oktay, K. (2020). BRCA-related ATM-mediated DNA double-strand break repair and ovarian aging. Human Reproduction Update, 26 (1), 43–57. https://doi.org/10.1093/humupd/dmz043

Horta, F., Ravichandran, A., Catt, S., Vollenhoven, B., & Temple-Smith, P. (2021). Ageing and ovarian stimulation modulate the relative levels of transcript abundance of oocyte DNA repair genes during the germinal vesicle-metaphase II transition in mice. Journal of Assisted Reproduction and Genetics, 38 (1), 55–69. https://doi.org/10.1007/s10815-020-01981-6

Bilotto, S., Boni, R., Russo, G. L., & Lioi, M. B. (2015). Meiosis progression and donor age affect the expression profile of DNA repair genes in bovine oocytes. Zygote, 23 (1), 11–18. https://doi.org/10.1017/S0967199413000154

Smits, M. A. J., Janssens, G. E., Goddijn, M., Hamer, G., Houtkooper, R. H., & Mastenbroek, S. (2021). Longevity pathways are associated with human ovarian ageing. Human Reproduction Open, 2021 (2), hoab020. https://doi.org/10.1093/hropen/hoab020

Nash, Z., & Davies, M. (2024). Premature ovarian insufficiency. BMJ, 20 (384), e077469. https://doi.org/10.1136/bmj-2023-077469

Zhang, X., Niu, J., Che, T., Zhu, Y., Zhang, H., & Qu, J. (2020). Fertility preservation in BRCA mutation carriers—efficacy and safety issues: A review. Reproductive Biology and Endocrinology, 18 (1), 11–27. https://doi.org/10.1186/s12958-019-0561-0

El Moujahed, L., Philis, R., Grynberg, M., Laot, L., Mur, P., Amsellem, N., Mayeur, A., Benoit, A., Rakrouki, S., Sifer, C., Peigné, M., & Sonigo, C. (2023). Response to

ovarian stimulation for urgent fertility preservation before gonadotoxic treatment in BRCA-pathogenic-variant-positive breast cancer patients. Cancers (Basel), 15 (3), 895. https://doi.org/10.3390/cancers15030895

Dias Nunes, J., Demeestere, I., & Devos, M. (2023). BRCA mutations and fertility preservation. International Journal of Molecular Sciences, 25 (1), 204–226. https://doi.org/10.3390/ijms25010204

Di Nisio, V., Daponte, N., Messini, C., Anifandis, G., & Antonouli, S. (2024). Oncofertility and fertility preservation for women with gynecological malignancies: Where do we stand today? Biomolecules, 14 (8), 943–968. https://doi.org/10.3390/biom14080943

Buonomo, B., Massarotti, C., Dellino, M., Anserini, P., Ferrari, A., Campanella, M., Magnotti, M., De Stefano, C., Peccatori, F. A., & Lambertini, M. (2021). Reproductive issues in carriers of germline pathogenic variants in the BRCA1/2 genes: An expert meeting. BMC Medicine, 19 (1), 205. https://doi.org/10.1186/s12916-021-02081-7

Ben Ayed-Guerfali, D., Ben Kridis-Rejab, W., Ammous-Boukhris, N., Ayadi, W., Charfi, S., Khanfir, A., Sellami-Boudawara, T., Frikha, M., Daoud, J., & Mokdad-Gargouri, R. (2021). Novel and recurrent BRCA1/BRCA2 germline mutations in patients with breast/ovarian cancer: A series from the south of Tunisia. Journal of Translational Medicine, 19 (1), 108. https://doi.org/10.1186/s12967-021-02772-y

Dellino, M., D'Amato, A., Battista, G., Cormio, G., Vimercati, A., Loizzi, V., Laganà, A. S., Damiani, G. R., Favilli, A., Gerli, S., La Forgia, D., Daniele, A., Agrifoglio, V., Cicinelli, E., Vitagliano, A., & Etrusco, A. (2024). Reproductive outcomes in women with BRCA 1/2 germline mutations: A retrospective observational study and literature review. Open Medicine (Wars), 19(1), 20249999. https://doi.org/10.1515/med-2024-9999

Peccatori, F. A., Mangili, G., Bergamini, A., Filippi, F., Martinelli, F., Ferrari, F., Noli, S., Rabaiotti, E., Candiani, M., & Somigliana, E. (2018). Fertility preservation in women harboring deleterious BRCA mutations: Ready for prime time? Human Reproduction, 33(2), 181–187. https://doi.org/10.1093/humrep/dex356

Friedman, E., Kotsopoulos, J., Lubinski, J., Lynch, H. T., Ghadirian, P., Neuhausen, S. L., Isaacs, C., Weber, B., Foulkes, W. D., Moller, P., Rosen, B., Kim-Sing, C., Gershoni-Baruch, R., Ainsworth, P., Daly, M., Tung, N., Eisen, A., Olopade, O. I., Karlan, B., Saal, H. M., Garber, J. E., Rennert, G., Gilchrist, D., Eng, C., Offit, K., Osborne, M., Sun, P., & Narod, S. A. (2006). Spontaneous and therapeutic abortions and the risk of breast cancer among BRCA mutation carriers. Breast Cancer Research, 8(2), R15. https://doi.org/10.1186/bcr1387

Moslehi, R., Singh, R., Lessner, L., & Friedman, J. M. (2010). Impact of BRCA mutations on female fertility and offspring sex ratio. American Journal of Human Biology, 22 (2), 201–215. https://doi.org/10.1002/ajhb.20978

Dorkins, H., Douglas, F., Eason, J., Houghton, C., Kennedy, M. J., McCann, E., Miedzybrodzka, Z., Murray, A., Porteous, M. E., Rogers, M. T., Side, L. E., Tischkowitz, M., Walker, L., Hodgson, S., Eccles, D. M., Morrison, P. J., Evans, D. G., Eeles, R. A., Antoniou, A. C., Easton, D. F., & Dunning, A. M. (2014). Lymphocyte telomere length is long in BRCA1 and BRCA2 mutation carriers regardless of cancer-affected status. Cancer Epidemiology Biomarkers & Prevention, 23(6), 1018–1024. https://doi.org/10.1158/1055-9965.EPI-13-0635-T

French, J. D., Dunn, J., & Smart, C. E. (2006). Disruption of BRCA1 function results in telomere lengthening and increased anaphase bridge formation in

immortalized cell lines. Genes Chromosomes & Cancer, 45, 277–289. https://doi.org/10.1002/gcc.20290

Magaton, I. M., Arecco, L., Mariamidze, E., Jankovic, K., Stana, M., Buzzatti, G., Trevisan, L., Scavone, G., Ottonello, S., Fregatti, P., Massarotti, C., von Wolff, M., & Lambertini, M. (2024). Fertility and pregnancy-related issues in young BRCA carriers with breast cancer. Breast Cancer (Auckland), 14(18), 11782234241261429. https://doi.org/10.1177/11782234241261429

Smith, K. R., Hanson, H. A., Mineau, G. P., & Buys, S. S. (2012). Effects of BRCA1 and BRCA2 mutations on female fertility. Proceedings of the Royal Society B: Biological Sciences, 279 (1732), 1389–1395. https://doi.org/10.1098/rspb.2011.1697

Tsatsakis, A., Oikonomopoulou, T., Nikolouzakis, T. K., Vakonaki, E., Tzatzarakis, M., Flamourakis, M., Renieri, E., Fragkiadaki, P., Iliaki, E., Bachlitzanaki, M., Karzi, V., Katsikantami, I., Kakridonis, F., Hatzidaki, E., Tolia, M., Svistunov, A. A., Spandidos, D. A., Nikitovic, D., Tsiaoussis, J., & Berdiaki, A. (2023). Role of telomere length in human carcinogenesis (Review). International Journal of Oncology, 63, 178. https://doi.org/10.3892/ijo.2023.5526

Mikheev, R. K., Andreeva, E. N., Grigoryan, O. R., Sheremetyeva, E. V., Absatarova, Y. S., & Loginova, E. V. (2023). Replicative and biochemical ageing features among females with primary ovarian insufficiency. Problemy Endokrinologii, 69 (2), 92–98. https://doi.org/10.14341/probl13253

Robinson, L. G. Jr., Kalmbach, K., Sumerfield, O., Nomani, W., Wang, F., Liu, L., & Keefe, D. L. (2024). Telomere dynamics and reproduction. Fertility and Sterility, 121 (1), 4–11. https://doi.org/10.1016/j.fertnstert.2023.11.012

Pirtea, P., Keefe, D. L., Ayoubi, J. M., & de Ziegler, D. (2024). Telomere length: A marker for reproductive aging? Fertility and Sterility, 121 (1), 1–3. https://doi.org/10.1016/j.fertnstert.2023.10.027

Korneenko, T. V., & Pestov, N. B. (2023). Oncogenic BRCA1/2 mutations in the human lineage—A by-product of sexual selection? Biomedicines, 12 (1), 22–38. https://doi.org/10.3390/biomedicines12010022