Rate of breast biopsy referrals in female BRCA mutation carriers aged 50 years or more: a retrospective comparative study and matched analysis

Adi Pomerantz1 · Daliah Tsoref1 · Ahuva Grubstein2,3 · Sonya Wadhawker4 · Yael Rapson2,3 · Itay Gadiel3 · Hadar Goldvasser1,2 · Ilan Feldhaver5 · Ariel Hammerman5 · Tzipora Shochat6 · Eran Sharon5 · Inbal Kedar7 · Rinat Yerushalmi1,2

Received: 25 August 2021 / Accepted: 20 December 2021 / Published online: 7 April 2022
© The Author(s) 2022

Abstract
Purpose To evaluate the total biopsy and positive biopsy rates in women at high risk of breast cancer compared to the general population.
Methods The study group consisted of 330 women with pathogenic variants (PVs) in BRCA1/2 attending the dedicated multidisciplinary breast cancer clinic of a tertiary medical center in Israel. Clinical, genetic, and biopsy data were retrieved from the central healthcare database and the medical files. Patients aged 50 years or older during follow-up were matched 1:10 to women in the general population referred for routine breast cancer screening at the same age, as recommended by international guidelines. The groups were compared for rate of biopsy studies performed and percentage of positive biopsy results. Matched analysis was performed to correct for confounders.
Results The total biopsy rate per 1000 follow-up years was 61.7 in the study group and 22.7 in the control group (p < 0.001). The corresponding positive biopsy rates per 1000 follow-up years were 26.4 and 2.0 (p < 0.001), and the positive biopsy percentages, 42.9% and 8.7% (p < 0.0001).
Conclusion Women aged 50+ years with PVs in BRCA1/2 attending a dedicated clinic have a 2.7 times higher biopsy rate per 1000 follow-up years, a 13.2 times higher positive biopsy rate per 1000 follow-up years, and a 4.9 times higher positive biopsy percentage than same-aged women in the general population.

Keywords Biopsy · BRCA · Breast cancer · Screening · High risk

Introduction

Background
Breast cancer is the most frequent diagnosed cancer and the leading cause of cancer-related death in women. It accounts for 23% of total cancer cases and 14% of cancer mortality worldwide [1]. In addition to clinical parameters, namely female sex, older age, and exposure to estrogen, genetic factors play an important role in breast cancer risk [2]. In the mid-1990s, genomic sequencing techniques revealed a link between germline PVs in the tumor-suppressor genes BRCA1 and BRCA2 with breast and ovarian cancer [3, 4]. Women with PVs in BRCA1/2 were found to have up to an 80% lifetime chance of developing cancer, primarily of breast and ovarian origin. These PVs were inherited in an autosomal dominant manner with high penetrance.
With the increasing public awareness of breast cancer and the identification of women at high risk, including the establishment of dedicated preventive breast clinics, it is important to ensure that rigorous multidisciplinary follow-up is initiated by international guidelines [5–7]. In our BRCA multidisciplinary follow-up from age 25 years, as recommended by international guidelines [5–7], women are encouraged to start taking part in rigorous follow-up algorithms. She is made aware of the significance of the results, namely, the risk of developing various malignancies, the potential preventive treatment options available, and recommended follow-up algorithms. She is encouraged to start rigorous multidisciplinary follow-up from age 25 years, as recommended by international guidelines [5–7].

When a woman is identified as a carrier, the identification of a family member with PVs in BRCA1/2 is triggered. Women with a family history of multiple malignancies, especially breast and ovarian carcinoma, are offered genetic counseling, and in some cases, testing is recommended. Testing is offered at the Breast Imaging-Reporting and Data System (BI-RADS), with scores ranging from 0 (incomplete) to 6 [10].

The confirmation of a carrier state may be overwhelming to the patient and, indeed, constitutes a life-changing event. Women have many imaging tests during their lifetime and may well be prone to undergo an increased number of biopsies for suspicious lesions, perhaps because knowledge of the greater risk of breast cancer in these patients lowers the threshold for recommending biopsies compared to the general population. This assumption is in line with studies showing that biopsy rates are higher, and the diagnostic yield lower, in women who undergo screening MRI, regardless of a personal history of breast cancer, than in women screened with mammography alone [11]. The increase in needle biopsy rates is associated with rapidly diminishing returns in cancer detection and a marked increase in benign results. The harm caused by screening in terms of false-positive recall rates and non-cancer biopsies is true also for incident screens, but the rates are much lower [12].

**Methods**

**Design and setting**

A retrospective study was conducted at the tertiary BRCA Clinic of Davidoff Cancer Center, Rabin Medical Center in Israel, which provides comprehensive follow-up, including psychological counseling, to women with PVs in BRCA1/2, based on international guidelines. Rabin Medical Center belongs to Clalit Health Services, the largest of four health maintenance organizations in Israel, which manages a central computerized healthcare warehouse that integrates data from its hospitals, community clinics, laboratories, and pharmacies nationwide. For purposes of this study, clinical, imaging, biopsy, and operative data were retrieved from the central database and hospital medical records.

The cohort for the first part of the study consisted of 330 consecutive women at high risk of development of breast cancer attending the BRCA Clinic between May 2000 and September 2019. Women in whom breast/ovarian cancer developed before they were identified as having a PV in BRCA1/2 were excluded as they did not undergo follow-up at the clinic. The rate of biopsies performed (number of biopsies/screening episodes in years), including the leading test to biopsy, was calculated and the results assessed.

The second part of the study was restricted to women among this cohort who were older than 50 years during follow-up between January 2002 and June 2019. This cutoff was chosen because the screening program for women at average risk for breast cancer starts at age 50 years [5–7]. Of the 113 women who met this criterion, we excluded 34 who had reached their 50th birthday before or at the beginning of the follow-up period to ensure that all patients analyzed had undergone strict follow-up as recommended. Also excluded were 7 women who were ineligible for regular screening tests through Clalit Health Services and 11 women in whom breast cancer developed before the beginning of follow-up or before age 50 years, for a final group of 61 women.

To form the control group for the second part of the study, we identified 319,187 women who underwent routine breast cancer mammography screening for the first time between 2002 and 2018 at age 50 to 68 years, according to the Clalit Health Services database and were followed for the same period, from January 2002 to June 2019. We excluded 30,202 women in whom breast cancer was diagnosed before the first mammography and 12,067 women who underwent breast MRI on a regular basis and were considered high risk. The inclusion and exclusion criteria for each group are presented in Fig. 1.

The 61 women aged 50+ at follow-up were analyzed for breast biopsy rate and positive biopsy rate, and the
findings were compared to 610 subjects from the control group matched 1:10 for clinical characteristics with the study patients.

The study was approved by the local Institutional Ethics Committee.

The selection process for the study is shown in Fig. 1.

**Statistical analysis**

The rate of biopsies performed per exposure period was compared between groups using the conditional test with mid-P adjustment. The positive biopsy ratio was calculated using chi-square test (with df = 1). Matching analysis
was performed for the following parameters: age group (50, 51–55, 56–60, and 61–65 years), socioeconomic status, Charlson Comorbidity Index score (0, 1, 2–3), sector (Orthodox Jewish, non-Orthodox Jewish), use of hormone replacement therapy, and prior use of oral contraceptive pills. Sector was chosen as a parameter because orthodox Jewish women have a unique lifestyle which is suspected to impact their life time risk to develop breast cancer [13]. Statistical analyses were performed with Microsoft Excel, SPSS version 25, and WinPepi software.

Results

Clinical characteristics

The 330 patients in the study cohort included 198 women with PVs in BRCA1 and 108 women with PVs in BRCA2; 2 women had PVs in both BRCA1 and BRCA2. Of the remainder, one woman had PVs in PTEN, 16 had a family history of breast cancer but no recognized PVs, and 5 had a family history of PVs in BRCA1/2 but had opted not to have a genetic test themselves. The median duration of follow-up was 5.4 years (range, 0.03–18.2 years), and the median age at the beginning of follow-up at the clinic was 37.4 years (range, 18.3–73.7 years). Table 1 shows the specific PVs identified and cancer histories of the study group.

Biopsy analysis

A total of 142 lesions were identified in the study group: 76 (53.5%) by MRI, 31 (21.8%) by physical examination, 17 (12%) by ultrasound, and 11 (7.7%) by mammography; in 7 patients (4.9%), the modality was unknown (Table 2). Of the 31 lesions discovered by physical examination, 13 were found on the first or second visit at the clinic, before MRI was performed, and 10 (32.2%) were identified a short time after a negative MRI. Of the remainder, 2 were found on self-examination, and 6 were breast skin lesions.

All 142 lesions were biopsied: 117 Tru-cut breast biopsies, 13 fine-needle aspirations, 8 breast skin biopsies, and 4 diagnostic lumpectomies. The median patient age at biopsy was 41.5 years. The biopsy characteristics and pathology results are presented in Table 3. A malignancy was identified in 37 samples (26.1%), including 7 prompted by physical examination. The total biopsy rate per 1000 follow-up years was 69.8. The positive biopsy rate per 1000 follow-up years was 18.2, and the positive biopsy percentage [(number of positive biopsies/number of total biopsies) × 100] was 26.1%.

Comparison with the general population

Findings for the 61 women aged 50 years or more with PVs in BRCA1/2 and 610 women of the same age who underwent routine breast cancer screening are presented in Tables 4 and 5, and the parameters used in the matched analysis are shown in Table 6. The incidence rate ratio (IRR) and significance were calculated using mid-P values. All IRRs for negative, positive, and total number of biopsies were found to be significant. The total biopsy rate per 1000 follow-up years was 61.7 in the study group and 22.7 in the control group (p < 0.001). The positive biopsy rate per 1000 follow-up years was 26.4 in the study group and 2.0 in the control group (p < 0.001), and the corresponding positive biopsy percentages [(number of positive biopsies/number of total biopsies) × 100] were 42.9% and 8.7% (p < 0.0001).

Discussion

BRCA mutation carriers undergo intensive breast follow-up, including radiological studies such as mammography and MRI. Each test has its own false-positive rate (FPR). Mutation carriers are referred for an annual screening protocol which is associated with a higher FPR than standard screening [14, 15]. The present study evaluated the total biopsy
rate, positive biopsy rate, and positive biopsy percentage among women with PVs in BRCA1/2 compared to the general population of women referred for routine screening. We sought to investigate the biopsy load of women with PVs in BRCA1/2 who attend a dedicated clinic.

Our matched analysis revealed that in women with PVs in BRCA1/2, the biopsy rate per 1000 follow-up years was 2.7 times higher than in the general population. Additionally, their positive biopsy rate per 1000 follow-up years was 13.2 times higher, and their positive biopsy percentage, 4.9 times higher. Nevertheless, it is noteworthy that despite the higher percentage of positive biopsies in the BRCA1/2 carriers, most of the biopsies performed in this patient group at the clinic (73.9%) yielded benign results. This finding is in accordance with the 72% rate of benign biopsies reported in a study of healthy women with PVs in BRCA1/2 followed at another high-risk clinic in Israel [16]. Others examined biopsies of women with dense breast tissue who underwent breast MRI as part of their follow-up. Although the results cannot be directly compared with ours because of the different screening structure, as in our study, the cohort was comprised of high-risk women who required MRI analysis as part of their screening program. The rates of malignant results were comparable: 26.1% in our study and 31% in the dense breast study [17]. Together, these findings reflect the need for personalized screening regimens [18]. Our review of the literature failed to reveal a matched analysis similar to that performed here.

An unexpected incidental finding of the present study was the important role of physical examination, second after MRI, in the identification of suspicious lesions during follow-up. Of note, in one-third of cases in which suspicious lesions were first discovered by physical examination, the requested MRI test was not performed on time.

| Table 2 | Screening modalities leading to biopsy for 142 lesions identified. MRI magnetic resonance imaging |
| Modality | Malignant | Benign | Total |
| | N | % of malignant | N | % of benign | N | % of total |
| Physical examination | 7 | 18.9 | 24 | 22.9 | 31 | 21.8 |
| Ultrasound | 4 | 10.8 | 13 | 12.4 | 17 | 12 |
| MRI | 19 | 51.4 | 57 | 54.3 | 76 | 53.5 |
| Mammography | 6 | 16.2 | 5 | 4.8 | 11 | 7.7 |
| Unknown | 1 | 2.7 | 6 | 5.7 | 7 | 4.9 |

| Table 3 | Biopsy characteristics in patients with PVs in BRCA1/2. IDC invasive ductal carcinoma, DCIS ductal carcinoma in situ, ILC invasive lobular carcinoma |
| Characteristics | No. (%) |
| Type of biopsy (n = 142) | |
| Tru-cut breast biopsy | 117 (82.4) |
| Fine needle aspiration | 13 (9.2) |
| Breast skin biopsy | 8 (5.6) |
| Excisional biopsy | 4 (2.8) |
| Type of malignancy (n = 37) | |
| Invasive | 33 (89.2) |
| DCIS | 3 (8.1) |
| Other | 1 (2.7) |
| Type of benign lesions (n = 105) | |
| High-risk lesions (ADH, ALH, and LCIS) | 2 (1.9) |
| Fibroadenoma | 11 (10.5) |
| Others | 92 (87.6) |

| Table 4 | Results of biopsy studies in the BRCA and the general population groups |
| Biopsy studies | Study group (N = 61) | Control group (N = 610) |
| | Years of follow-up = 340.6 | Years of follow-up = 6088.2 |
| No | % of biopsies performed in the study group | No | % of biopsies performed in the control group |
| Total biopsies | 21.0 | 138.0 |
| Positive biopsies | 9.0 | 42.9 | 12.0 | 8.7 |
| Negative biopsies | 12.0 | 57.1 | 126.0 | 91.3 |

| Table 5 | Biopsy rate per 1000 years of follow-up |
| Biopsy studies | Study group | Control group | Ratio | p value |
| Total biopsies | 61.7 | 22.7 | 2.7 | < 0.001 |
| Positive biopsies | 26.4 | 2.0 | 13.4 | < 0.001 |
| Negative biopsies | 35.2 | 20.7 | 1.7 | 0.048 |
This occurred mainly in patients who were new to the clinic.

This study has several limitations. Besides the retrospective design, which has inherent biases due to unknown or unrecorded confounders, the main limitation of the study was our inability to perform a matched analysis for the under-50 age group because routine screening mammography in Israel is recommended only for women above this age, whereas screening in women with PVs in \textit{BRCA1/2} starts much earlier. Furthermore, a different screening protocol was used in the two groups. The high-risk protocol includes more frequent imaging, including MRI, which is known to be associated with a relatively high prevalence of false-positive results [19]. In addition, as noted above, most of the women with PVs in \textit{BRCA1/2} started screening at an earlier age, and the false-positive in the first year of screening is known to be higher than in later years. This may suggest that the difference between the groups is even larger than observed in this study [20]. Finally, we did not stratify the patients by duration of use of oral contraceptives and hormone replacement therapy.

The high biopsy rates found here highlight the limitations of current imaging studies, including MRI. The literature suggests that the innovations in artificial intelligence and radiomics will improve image analysis in the future, making it easier to distinguish benign from malignant small breast masses and lead to changes in the guidelines [21]. The results also imply that studies of personalized screening programs should include women with PVs in \textit{BRCA1/2} [22].

It should be emphasized that this study was intended to mirror a given situation in the context of adherence to the national and international guidelines. From that perspective, it clearly describes the differences in biopsy load and outcomes between patients with PVs in \textit{BRCA1/2} and the general population of women aged 50 years or more.

### Clinical implications

To our knowledge, this is the first study to evaluate total biopsy and positive biopsy rates among women aged 50 years or more with PVs in \textit{BRCA1/2} and without a personal history of breast cancer compared to the general population. Our data are relevant both to patients and caregivers, improving their understanding of the “carrier journey” in a dedicated clinic. Repeated imaging and biopsies are very stressful, and for some women, may have a considerable negative impact on quality of life. Providing these patients with detailed information on the process and outcomes of follow-up can contribute to their feeling of health safety and can be a major psychological predictor when considering a prophylactic surgery [23, 24]. This information is also helpful for health authorities in terms of regulating resources and costs.

The findings of the present study are particularly timely given the increasing awareness of the importance of \textit{BRCA} testing in the high-risk population and the concerns raised regarding the use of biopsies as a screening test for women of Ashkenazi Jewish ancestry [25]. About 2.5% of Ashkenazi Jewish women have PVs in \textit{BRCA1/2} [4], so we may expect many more such patients in the future.

The high positive biopsy percentage in our study group is in line with current international recommendations for follow-up of women with PVs in \textit{BRCA1/2} and should be part of the quality assurance considerations of teams assessing the requirements for biopsy tests.

The study may support earlier reports suggesting that dedicated \textit{BRCA} clinics effectively meet the specific short- and long-term needs of this high-risk population [8].

### Funding

None.

### Data availability

The datasets generated during and/or analyzed during the current study are not publicly available but are available from the corresponding author on reasonable request.

### Code availability

NA.

### Declarations

**Conflict of interest** Conflict of interest are reported, all outside the submitted work.
**Ethical approval** The study was approved by the local Institutional Ethics Committee.

**Consent to participate** Need for informed consent was waived by the Ethics Committee.

**Consent for publication** All authors consent to publication of the manuscript.

**Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article’s Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article’s Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by/4.0/.

**References**

1. Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D (2011) Global cancer statistics. CA Cancer J Clin 61:69–90. https://doi.org/10.3322/caac.20107
2. Stuckey A (2011) Breast cancer: epidemiology and risk factors. Clin Obstet Gynecol 54(1):96–102. https://doi.org/10.1097/GRF.0b013e3182080056
3. Whittemore AS, Gong G, John EM, McGuire V, Li FP, Ostrow KL, Dicioccio R, Felberg A, West DW (2004) Prevalence of BRCA1 mutation carriers among U.S. non-Hispanic Whites. Cancer Epidemiol Biomarkers Prev 13:2078–2083
4. Roa BB, Boyd AA, Volcik K, Richards CS (1996) Ashkenazi Jewish population frequencies for common mutations in BRCA1 and BRCA2. Nat Genet 14:185–187. https://doi.org/10.1038/ng1096-185
5. USPSTF (2016) Breast cancer: screening. U.S preventive services task force. Available at https://www.uspreventiveservices.org/Page/Document/UpdateSummaryFinal/breast-cancer-screening. Accessed on 9 Mar 2021
6. ASBrS (2019) Position statement on screening mammography. The American Society of Breast Surgeons. Available at https://www.breastsurgeons.org/docs/statements/Position-Statement-on-Screening-Mammography.pdf Accessed on 9 Mar 2021
7. Daly MB, Pal T, Berry MP, Buys SS, Dickson P, Domchek SM, Elkhanany A, Friedman S, Goggins M, Hutton ML, Karlan BY, Khan S, Klein C, Kohlmann W, Kurian AW, Laronga C, Litton JK, Mak JS, Menendez CS, Merajver SD, Norquist BS, Olfit K, Pederson HJ, Reiser G, Senter-Jamieson L, Shannon KM, Shatsky R, Visvanathan K, Weitzel JN, Wick MJ, Wisinski KB, Yurgelun MB, Darlow SD, Dwyer MA (2021) Genetic/familial high-risk assessment: breast, ovarian, and pancreatic, version 2.2021, NCCN clinical practice guidelines in oncology. J Natl Compr Canc Netw 19(1):77–102. https://doi.org/10.6004/jnccn.2021.0001
8. Yerushalmi R, Rizel S, Zoref D, Sharon E, Eitan R, Sabah G, Grubstein A, Rafson Y, Cohen M, Magen A, Birenboim I, Margel D, Ozlavo R, Sulkes A, Brenner B, Perry S (2016) A dedicated follow-up clinic for BRCA mutation carriers. Isr Med Assoc J 18(9):549–552
9. The Israel Ministry of Health (2019) Summary of the Recommendations of the Committee for Examining the National Program for Detection of Breast Cancer in Israel. Available at https://www.health.gov.il/NewsAndEvents/SpokesmanMessages/Documents/10022021_1_1.pdf. Accessed on 26 Oct 2021
10. D’Orsi CJ, Sickles EA, Mendelson EB, Morris EA et al (2013) ACR BI-RADS® Atlas, breast imaging reporting and data system. American College of Radiology, Reston
11. Buist DSM, Abraham L, Lee CI, Lee JM, Lehman C, O’Meara ES, Stout NK, Henderson LM, Hill D, Wernli KJ, Haas JS, Tosteson ANA, Kerlikowske K, Onega T, Breast Cancer Surveillance Consortium (2018) Breast biopsy intensity and findings following breast cancer screening in women with and without a personal history of breast cancer. JAMA Intern Med 178(4):458–468. https://doi.org/10.1001/jamainternmed.2017.8549
12. Blanks RG, Given-Wilson R, Alison R, Jenkins K, Wallis MG (2019) An analysis of 11.3 million screening tests examining the association between nipple biopsy rates and cancer detection rates in the English NHS Breast Cancer Screening Programme. Clin Radiol 74(5):384–389. https://doi.org/10.1016/j.crad.2019.01.015
13. Tkatch R, Schwartz K, Shore RD, Penner LA, Simon MS, Albrecht TL (2014) Breast cancer incidence rates among orthodox Jewish women. J Immigr Minor Health 16(5):1007–1010. https://doi.org/10.1007/s10903-013-9822-8
14. Myers ER, Moorman P, Gierisch JM, Havrilesky LJ, Grimm LJ, Ghate S, Davidson B, Montgomery RC, Crowley MJ, McCrory DC, Kendrick A, Sanders GD (2015) Benefits and harms of breast cancer screening: a systematic review. JAMA 314(15):1615–1634. https://doi.org/10.1001/jama.2015.13183
15. Nelson HD, Cantor A, Humphrey L, Fu R, Pappas M, Daeges M, Griffin J (2016) Screening for breast cancer: a systematic review to update the 2009 US preventive services task force recommendation. Preventive services task force evidence syntheses, formerly systematic evidence reviews. Agency for Healthcare Research and Quality (US), Rockville
16. Laitman Y, Madorsky Feldman D, Sklar-Levy M, Yosepovich A, Barshack-Nakar I, Brodsky M, Halshtok O, Shalmon A, Gotlieb M, Friedman E (2018) Abnormal findings detected by multi-modality breast imaging and biopsy results in a high-risk clinic. Clin Breast Cancer 18(4):695–698. https://doi.org/10.1016/j.clbc.2017.12.005
17. Weinstein SP, Korhonen K, Cirelli C, Schnall MD, McDonald ES, Pantel AR, Zuckerman S, Borthakur A, Conant EF (2020) Abbreviated breast magnetic resonance imaging for supplemental screening of women with dense breasts and average risk. J Clin Oncol 38(33):3874–3882. https://doi.org/10.1200/JCO.19.02198
18. Allweis TM, Hermann N, Berenstein-Molho R, Guindy M (2021) Personalized screening for breast cancer: rationale, present practices, and future directions. Ann Surg Oncol 28(8):4306–4317. https://doi.org/10.1245/s10434-020-09426-1
19. Houssami N, Hayes DF (2009) Review of preoperative magnetic resonance imaging for breast cancer: a scoping review to assess AI’s potential in breast screening practice. Expert Rev Med Devices 16(5):351–362. https://doi.org/10.1080/17434440.2019.1610387
20. D’Orsi CJ (2020) The clinically relevant breast imaging audit. J Breast Imaging 2(1):2–6. https://doi.org/10.1093/jbimbim/boz080
21. Houssami N, Kirkpatrick-Jones G, Naguchi N, Lee CI (2019) Artificial intelligence (AI) for the early detection of breast cancer: a scoping review to assess AI’s potential in breast screening practice. Expert Rev Med Devices 16(5):351–362. https://doi.org/10.1080/17434440.2019.1610387

© Springer
22. Saccarelli CR, Bitencourt AGV, Morris EA (2021) Is it the era for personalized screening? Radiol Clin North Am 59(1):129–138. https://doi.org/10.1016/j.rcl.2020.09.003

23. Butler E, Collier S, Hevey D (2020) The factors associated with distress a minimum of six months after BRCA1/2 confirmation: a systematic review. J Psychosoc Oncol 22:1–27. https://doi.org/10.1080/07347332.2020.1836109

24. Segerer R, Peschel C, Kämmerer U, Häussler S, Wöckel A, Segerer S (2020) Factors impacting on decision-making towards prophylactic surgeries in BRCA mutation carriers and women with familial predisposition. Breast Care (Basel) 15(3):253–259. https://doi.org/10.1159/000503370

25. Lieberman S, Tomer A, Ben-Chetrit A, Olsha O, Strano S, Beeri R, Koka S, Fridman H, Djemal K, Glick I, Zalut T, Segev S, Sklar M, Kaufman B, Lahad A, Raz A, Levy-Lahad E (2017) Population screening for BRCA1/BRCA2 founder mutations in Ashkenazi Jews: proactive recruitment compared with self-referral. Genet Med 19(7):754–762. https://doi.org/10.1038/gim.2016.182

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.