Asian Journal of Current Research in Clinical Cancer
ISSN: 3062-4444
2026, Volume 6, Issue 1, Page No: 18-26

Available online at: www.galaxypub.co/page/journals

Galaxy Publication

Galaxy Publication

Expanding Germline Genetic Testing in Breast Cancer: Universal versus ASCO-Guided Approaches

Maria Silva[1]*, Joao Pereira[1]

[1]Department of Clinical Cancer Research and Oncology, Faculty of Medicine, University of Coimbra, Coimbra, Portugal.

***E-mail** ✉ maria.silva@gmail.com
Received: 19 October 2025; **Revised:** 27 January 2026; **Accepted:** 28 January 2026

ABSTRACT

A notable fraction of breast cancer occurrences stems from hereditary pathogenic mutations. Germline genetic testing (GGT), especially focused on BRCA1 and BRCA2, is an indispensable component of precision oncology, enabling tailored risk classification and the formulation of individualized treatment plans. Within this report, we investigate the practicality of performing blanket testing on all freshly diagnosed breast cancer patients, without regard for age, personal or familial cancer background, in a setting marked by resource constraints. Consecutive patients newly presenting with breast cancer who satisfied the criteria for GGT under the most current American Society of Clinical Oncology (ASCO) recommendations were included. Across the study timeframe, 1,570 individuals were recruited, with a median age of 51 (range 22-96) years, of whom 1,352 (86.1%) were of Jordanian nationality. According to age-related benchmarks, 1,346 (85.7%) patients qualified for testing. A further 134 (8.5%) were deemed eligible owing to other indications, such as a personal or familial background of breast and other malignancies (n = 121, 7.7%), triple-negative pathology (n = 9, 0.57%), and male sex (n = 4, 0.25%). Cumulatively, 1,480 (94.3%) patients met the GGT eligibility requirements set by ASCO recommendations, resulting in merely 90 (5.7%) patients who were not candidates. Pathogenic or likely pathogenic alterations were uncovered in 23 (7.8%) patients. Adopting a universal GGT policy for every newly diagnosed breast cancer case, without consideration of age or risk determinants, would marginally broaden the pool of qualifying patients. This added load is warranted by its potential to boost referral completion rates.

Keywords: Germline genetic testing, GGT, Breast cancer, BRCA1, BRCA2, Resource-limited settings

How to Cite This Article: Silva M, Pereira J. Expanding Germline Genetic Testing in Breast Cancer: Universal versus ASCO-Guided Approaches. Asian J Curr Res Clin Cancer. 2026;6(1):18-26. https://doi.org/10.51847/goUdUiYsfo

Introduction

Breast cancer persists as the predominant malignancy diagnosed in women across the globe [1, 2]. The median age at diagnosis is substantially lower in low-resource nations than in Western populations [3, 4]. Within countries such as Jordan, close to half of all breast cancer cases are identified at or before the age of 50, whereas only a minor segment receives a diagnosis past age 65 [5].

Pathogenic or likely pathogenic (P/LP) germline variants (PGVs) situated within cancer-susceptibility genes, most prominently BRCA1 and BRCA2, have been tied to the causation of breast and various other tumors. Spotting carriers of PGVs can diminish the cancer load on the patients themselves, while relatives at heightened risk may profit from rigorous screening protocols and prophylactic measures [6].

The fraction of breast cancer patients harboring BRCA1 or BRCA2 mutations fluctuates based on the detection tactic and the demographic under study. In non-selected breast cancer series, the reported prevalence of BRCA1 and BRCA2 P/LP variants typically ranges from 1.8% to 2.6% for BRCA1 and 1.3% to 2.1% for BRCA2 [7-9]. Crucially, these alterations are concentrated in specific subsets, such as those possessing a familial background of breast or ovarian cancer, those exhibiting particular breast cancer subtypes like triple-negative disease [10], and in defined ethnicities such as women of Ashkenazi Jewish heritage, where frequency can be elevated [11, 12].

The amplified uptake of multigene panel assays has facilitated the detection of additional variants; some, like PALB2, correlate with a higher breast cancer likelihood and may sway decisions surrounding risk-reduction tactics and surveillance schedules. Other alterations in genes, including CHEK2, BARD1, ATM, RAD51C, and RAD51D, are implicated in breast and other tumor types [13, 14].

Patients are offered germline genetic testing guided by international consensus, inclusive of the National Comprehensive Cancer Network (NCCN) [15] and ASCO [8, 16]. These protocols undergo periodic revision, and a considerable portion of practitioners, including both medical and surgical oncologists, may not keep abreast of these ongoing changes—a circumstance that could account for a diminished referral of eligible individuals for testing and counseling. Over the last several years, the NCCN-designated age threshold for commencing testing, independent of personal or familial cancer history, has been incrementally raised from 40 to 45, then to 50, and most recently to 65 by ASCO and the Society of Surgical Oncology (SSO). Conversely, certain professional bodies, exemplified by The American Society of Breast Surgeons, champion blanket testing for all women diagnosed with breast cancer, irrespective of age or risk factors. This emerging standpoint is supported by contemporary studies showing elevated missed-opportunity rates when testing is constrained to guideline-specified candidates [17, 18].

Routine universal germline genetic testing (GGT) using multigene panels (MGP) is not unfamiliar in oncology care; this approach is currently endorsed for patients with ovarian, pancreatic, and metastatic prostate cancers [15].

The convoluted nature of prevailing guidelines, their incessant updates, the deficiency of specialized cancer genetics services, and the paucity of genetic counselors collectively erect obstacles that curtail access to genetic assessment for qualifying oncology patients [19]. Within this report, we investigate the practicality of performing blanket testing on all freshly diagnosed breast cancer patients, without regard for age, personal or familial cancer background, in a setting marked by resource constraints.

Materials and Methods

Study design

This investigation is structured as a retrospective cohort analysis gauging the deployment of universal GGT across all patients receiving a breast cancer diagnosis within a resource-constrained environment. The study was conducted at King Hussein Cancer Center (KHCC) following Institutional Review Board (IRB) approval.

Study population

All successive adult patients, aged 18 and above, newly diagnosed with breast cancer, were recruited between 1 January 2023 and 30 April 2024. Information compilation was concluded by 15 May 2024, which functioned as the data analysis closure date. Individuals with both invasive and non-invasive breast carcinoma, including ductal carcinoma in situ (DCIS), qualified for inclusion. Grounds for exclusion comprised past receipt of genetic testing for hereditary cancer syndromes. Given the study's retrospective design and the omission of identifiable details, informed consent was waived for enrollment; however, every patient had consented to GGT testing at the time it was conducted. The research was conducted in alignment with ethical norms for human investigations. All records were stripped of identifiers, and patient confidentiality was rigorously maintained.

Germline genetic testing

Subjects meeting testing criteria per NCCN or ASCO guidelines received GGT using next-generation sequencing (NGS) platforms that screen for recognized breast cancer-linked genes, including BRCA1, BRCA2, TP53, CHEK2, PALB2, and ATM. Analyses were performed at an overseas reference facility using an authenticated, clinically accepted platform, and the results were delivered within 2 to 4 weeks. Testing was performed on DNA obtained from peripheral blood specimens procured within 4 weeks after the breast cancer diagnosis. A proportion of relatives of patients identified with P/LP variants were offered cascade screening after suitable counseling and were omitted from this cohort.

Clinical data collection

Demographic and clinical parameters were recorded at baseline, encompassing age, sex, nationality, familial cancer status, and tumor histopathology. For those who proceeded with genetic testing, supplementary information on the eligibility framework used (NCCN or ASCO criteria) was collected.

Data analysis

The principal endpoint of the study is to determine the proportion of breast cancer patients who meet GGT eligibility criteria under the latest ASCO recommendations. Secondary endpoints cover the detection rates of P/LP variants within the tested cohort, juxtaposing those qualifying under NCCN parameters against those under ASCO parameters. Additionally, an evaluation of P/LP variant frequency stratified by age was undertaken. Descriptive metrics were applied to outline demographic and clinical profiles, while Chi-square analyses were used to contrast reported P/LP variant outcomes across divergent genetic test eligibility classifications.

Results and Discussion

Throughout the enrollment period, a total of 1,570 subjects were identified with breast cancer; the median age at presentation was 51 years (spanning 22 to 96), and the preponderance (n = 1,346, 85.7%) fell within the 65-or-younger bracket. The stratification by age category is portrayed in **Figure 1.**

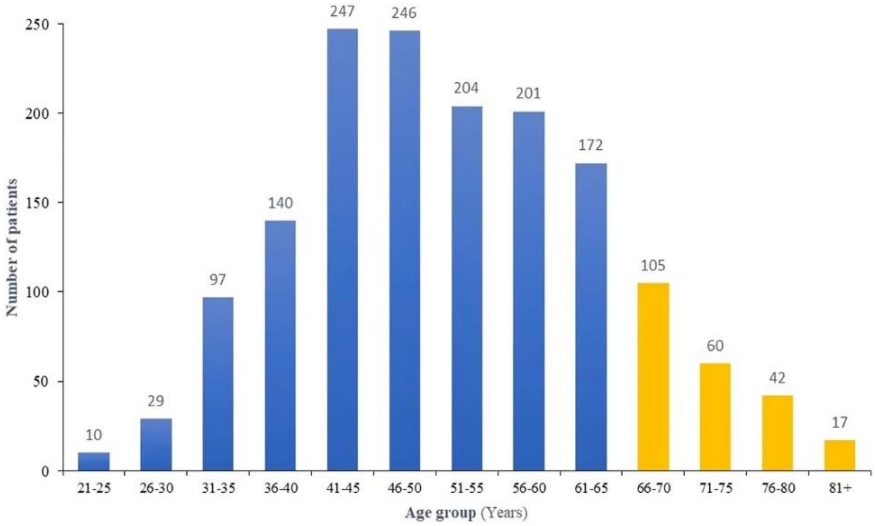

Figure 1. Age distribution of enrolled patients.

Barring 11 individuals (0.7%), the cohort was entirely female. The dominant share (n = 1,352, 86.1%) held Jordanian citizenship, while the remaining portion (n = 218, 13.9%) consisted of Arabs from bordering states or long-term residents in Jordan. Invasive ductal carcinoma (IDC) stood as the most frequently recorded histology, accounting for 1,253 cases (79.8%), followed by invasive lobular carcinoma (ILC) in 150 (9.6%) and ductal carcinoma in situ (DCIS) in 102 (6.5%), as compiled in **Table 1.**

Table 1. Patients' characteristics (n = 1,570).

Characteristic	n (%)
Age (years)	
Median (range)	51 (22–96)
≤ 65 years	1,346 (85.7%)
> 65 years	224 (14.3%)
Sex	
Female	1,559 (99.3%)
Male	11 (0.7%)
Nationality	
Jordanian	1,352 (86.1%)
Other nationalities	218 (13.9%)
Histopathology	

Invasive ductal carcinoma (IDC)	1,253 (79.8%)
Invasive lobular carcinoma (ILC)	150 (9.6%)
Ductal carcinoma in situ (DCIS)	102 (6.5%)
Others	65 (4.1%)
Genetic testing	
Performed	1,142 (72.7%)
Not performed	428 (27.3%)
Eligibility assessment guidelines	
ASCO 2024	309 (19.7%)
NCCN	1,261 (80.3%)

Abbreviations: IDC = invasive ductal carcinoma; ILC = invasive lobular carcinoma; DCIS = ductal carcinoma in Situ; NCCN = National Comprehensive Cancer Network; ASCO = American Society of Clinical Oncology.

Of the 1,570-person cohort, genetic testing was performed on 1,142 (72.7%). The determination of testing suitability relied on NCCN frameworks for those 1,261 (80.3%) patients whose diagnoses were made through January 2024, after which point the refreshed 2024 ASCO standards were adopted for the subsequent 309 (19.7%) patients. Within the ASCO-evaluated subset, 293 individuals (94.8%) met the threshold for testing, whereas the corresponding figure under NCCN-based appraisal was 849 (67.3%) ($P < 0.001$). Among the 1,142 qualified patients who received testing, P/LP alterations were identified in 23 cases (7.8%) under ASCO-directed assessment and in 77 cases (9.1%) under NCCN-directed assessment ($P = 0.524$), as shown in **Table 2.**

Table 2. ASCO guidelines-based versus NCCN guidelines-based germline genetic testing.

Variable	ASCO (n = 309)	NCCN (n = 1,261)	P-value
Eligibility			
Eligible	293 (94.8%)	849 (67.3%)	< 0.001**
Not eligible	16 (5.2%)	412 (32.7%)	
Test results among eligible#			
Negative	270 (92.2%)	772 (90.9%)	0.524
Pathogenic/likely pathogenic variants	23 (7.8%)	77 (9.1%)	

Testing suitability was judged per NCCN guidelines for 1,261 patients diagnosed through January 2024, with the updated 2024 ASCO guidelines taking effect for the 309 patients diagnosed afterward.
Pearson's Chi-squared test.
#
1142 eligible patients.

All enrolled patients' records were re-examined irrespective of which guideline had initially been applied, and their candidacy was recalculated using ASCO benchmarks. Solely by virtue of age (i.e., being ≤ 65 years old), 1,346 (85.7%) patients would have been deemed eligible. Scrutiny of the clinical files for the remaining 224 (14.3%) revealed additional triggers for GGT beyond the early age of onset. An additional 134 subjects (8.5%) met eligibility criteria based on a personal or familial history of breast cancer and other neoplasms (n = 121, 7.7%), a triple-negative subtype (n = 9, 0.57%), or male sex (n = 4, 0.25%). Summing these figures, 1,480 patients (94.3%) would have satisfied the latest ASCO stipulations, leaving a small minority of 90 (5.7%) who would not have been testing candidates under the updated rules, as captured in **Table 3**. When disaggregated by age bracket, the yield of P/LP variants was markedly richer in the younger age strata. The rate of variant detection reached 13.9% among those aged ≤ 39 years, dropped to 8.0% in the 40–65 years band, and fell further to 4.0% in the over-65 group ($P = 0.005$).

Table 3. Indications for germline genetic testing (n = 1,570).

Indication	Number (n)	Percentage (%)	Cumulative n (%)
Age ≤ 65 years	1,346	85.7	1,346 (85.7)
Family history of cancer	121	7.7	1,467 (93.4)
Triple-negative breast cancer	9	0.57	1,476 (94.0)
Male breast cancer	4	0.25	1,480 (94.3)
Not eligible for testing	90	5.7	1,570 (100)

Carrying a BRCA1 or BRCA2 mutation weighs heavily on the therapeutic trajectory of breast cancer, largely because these tumors possess discrete biological behaviors and react distinctively to certain classes of drugs. BRCA1/2-deficient cancers display pronounced susceptibility to agents that inflict DNA injury, especially poly (ADP-ribose) polymerase (PARP) inhibitors like olaparib and talazoparib, both of which have garnered evidence of extending progression-free survival (PFS) in BRCA-mutated, HER2-negative breast cancer across early-stage [20-23] and late-stage scenarios [24-26]. Clinical practice guidelines codify the integration of PARP inhibitors into routine care and have become a standard component of therapeutic protocols for BRCA-altered breast cancer [27]. Recent data have additionally documented an overall survival (OS) advantage [28]. Platinum-salt chemotherapeutics also retain notable activity in BRCA-mutated malignancies, attributable to their mode of action—creating interstrand DNA crosslinks that prove catastrophic to cells already handicapped in homologous recombination repair [29]. These drugs are commonly deployed in the preoperative window to boost pathologic complete response (pCR) figures, most conspicuously in triple-negative breast cancer (TNBC) harboring BRCA defects [29, 30]. Beyond pharmacotherapy, the confirmation of a BRCA alteration shapes surgical consultations and prophylactic interventions. Affected individuals frequently contemplate bilateral mastectomy or salpingo-oophorectomy as a means to curtail the likelihood of metachronous primary tumors [31].

Several global professional organizations, among them the NCCN, have put forward guidance endorsing GGT for breast cancer patients classified as high-risk. The algorithms currently in force are arguably convoluted for a sizeable segment of the clinical workforce to consistently apply, a circumstance that arguably fuels the suboptimal frequency with which qualifying patients are actually referred for GGT. Such under-referral is by no means unique to low-resource environments. Investigators working with California-derived pooled cross-sectional data from the National Health Interview Survey identified eligible respondents as women with a personal history of either breast or ovarian cancer who fulfilled specified 2017 NCCN eligibility thresholds predicated on age at diagnosis and family pedigree. Within this weighted sample of 47,218 women, 2.7% reported a prior breast cancer diagnosis. More than one-third (35.6%) were adjudged eligible for GGT according to NCCN standards; among those eligible, only 29.0% recalled discussing GGT with a healthcare professional, 20.2% were actively advised to get tested, and only 15.3% ultimately underwent the procedure [32].

A variety of models have been piloted to widen the reach of and shorten waiting times for genetic evaluation. A policy of universal germline testing—whereby every woman newly diagnosed with breast cancer is offered a panel irrespective of her age or family background—constitutes a transformative shift. Yet obstacles to uptake persist, spanning expense, logistical deployment, the nuanced task of variant interpretation, and ethical quandaries surrounding unsolicited findings [33]. Whereas the NCCN currently endorses routine universal testing for epithelial ovarian, metastatic prostate, and exocrine pancreatic carcinomas, it has not extended this recommendation to breast cancer [34, 35].

The recently published ASCO–Society of Surgical Oncology Guideline now advises BRCA1/2 testing for all newly presenting breast cancer patients up to the age of 65, with selective testing beyond 65 dictated by personal oncologic history or familial clustering. This roadmap is straightforward and can be operationalized via either dedicated genetics clinics or mainstream oncology pathways [8].

In Western contexts, such as the United States (US) and much of Europe, the median age at breast cancer discovery approximates 63 years. By contrast, resource-limited settings routinely report a median onset that lags by at least a decade [36-38]. Such geographic variation in the age at diagnosis stems from disparities in population age structure, hereditary background, and environmental/lifestyle exposures [39, 40]. Jordan exhibits a markedly youthful demographic profile, with over 95% of its population under 65 years old. Our dataset confirms that 85% of incident breast cancer cases in countries with this demographic profile meet the testing bar based solely on chronological age (per ASCO guidelines), as illustrated in **Figure 1** [5]. A supplemental proportion of elderly individuals (> 65 years) enters the eligible pool when factoring in personal or familial cancer burden, triple-negative receptor status, or male sex, bringing the cumulative total close to 95%.

A paramount barrier to the rollout of universal testing in low- and middle-income countries (LMICs) is the prohibitive cost of commercial sequencing assays, which often place them beyond the reach of individual payers and overburdened public health budgets. Compounding this is the downstream financial toxicity associated with follow-on care, including post-test counseling, cascade genotyping of first-degree kin, and ensuing therapeutic interventions—all of which impose a layered economic burden on patients in such regions.

Several investigations have sought to evaluate the economic viability of a universal testing strategy, predominantly within Western health systems. One analysis, conducted in the United Kingdom (UK) and the

United States (US), aimed to assess the cost-effectiveness of panel-based universal testing for all breast cancer patients compared with the existing model of genetic testing driven by family history or clinical thresholds (guideline-based). In the universal arm, every breast cancer patient received testing for BRCA1, BRCA2, and PALB2. In the guideline-driven arm, testing was restricted to those meeting predefined criteria. The economic model accounted for contralateral prophylactic mastectomy among carriers of BRCA/PALB2 P/LP variants, as well as risk-reducing salpingo-oophorectomy (RRSO) for those with BRCA1/2 mutations. The evaluation also incorporated the cost of cascade screening for at-risk relatives, along with corresponding prophylactic measures, including surveillance via magnetic resonance imaging or mammography, chemoprevention, and risk-reducing mastectomy or RRSO. The investigators determined that panel-based universal testing for all breast cancer patients stands as highly cost-effective when set against guideline-directed testing within both the UK and US healthcare frameworks [41]. Researchers reached a similar conclusion when examining universal testing in a Canadian population. However, the same conclusion might not translate to settings with constrained resources [42].

The dearth of clinical geneticists and genetic counselors represents an additional obstacle —a gap that has spurred the uptake of mainstream cancer genetic testing—a model in which non-genetics clinicians, such as oncologists and surgeons, are empowered to request genetic assays without a mandatory genetics counselor referral [43-46]. Still, uneven execution and reduced testing volumes persist, fueled by intricate, rapidly evolving guidelines and the demand for specialized instruction in hereditary cancer risk evaluation for those without formal genetics training.

Emerging data from low- and middle-income countries (LMICs) reveal that unselected germline testing yields substantial numbers of actionable BRCA and other pathogenic alterations, with over half of carriers eluding detection by conventional selection criteria [47]. Extensive cohorts from Brazil and Mexico likewise show that many mutation carriers lack so-called “high-risk” clinical features, resulting in considerable under-detection when selective guidelines are enforced [48]. Economic appraisals from upper-middle-income contexts underscore additional affordability hurdles, demonstrating that, while expanded testing can be cost-effective in Upper MICs, its rollout in LMICs requires meticulous resource evaluation and planning [49].

An increased rate of variants of uncertain significance (VUS) poses yet another difficulty [50]. The frequency of VUS varies across populations, rising notably as testing indications broaden and the number of genes interrogated in a multigene panel increases [51]. The management of patients harboring a VUS fundamentally rests on a watchful, well-informed stance, as such variants lack clinical actionability and must not, on their own, redirect medical management. Affected individuals ought to be counseled that a VUS may undergo reclassification with time, and scheduled reassessments are warranted to revisit the variant’s status [52].

This work carries several constraints. To begin with, its retrospective, single-institution nature may introduce selection bias and curtail the broader applicability of the results. Second, downstream outcomes and cascade testing were not tracked, and over time, certain VUS may be reclassified, a shift that could influence the interpretation of findings. Third, a formal cost-effectiveness analysis was not undertaken, as the financial data fell outside the IRB’s remit for approval. These elements warrant consideration when concluding the data.

Conclusion

Implementing universal germline genetic testing for all newly diagnosed breast cancer patients, without regard to age, tumor features, or personal and familial oncologic history (universal testing), is a practicable strategy that enlarges the eligible candidate pool by only a few percentage points. This added load is justified by its capacity to boost referral rates and reduce reliance on genetic counselors.

Acknowledgments: The author would like to thank Mrs. Alice Haddadin and Ms. Doaa Al-Saadi for their help in preparing this manuscript.

Conflict of Interest: None

Financial Support: None

Ethics Statement: The King Hussein Cancer Center IRB approved the studies involving humans under IRB Number 20 KHCC 202. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

References

1. International Agency for Research on Cancer. Global Cancer Observatory: Cancer Today. Lyon (France): International Agency for Research on Cancer; 2022. Available from: https://gco.iarc.who.int/today
2. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021;71:209-49. doi:10.3322/caac.21660
3. Abdel-Razeq H, Mansour A, Jaddan D. Breast cancer care in Jordan. JCO Glob Oncol. 2020;6:260-8. doi:10.1200/JGO.19.00279
4. Abdel-Razeq H, Al-Ibraheem A, Al-Rabi K, Shamiah O, Al-Husaini M, Mansour A. Cancer care in resource-limited countries: Jordan as an example. JCO Glob Oncol. 2024;10:e2400237. doi:10.1200/GO.24.00237
5. Abdel-Razeq H, Mansour A. Challenges and opportunities in breast cancer care in low-resourced countries, Jordan as an example. Cancers (Basel). 2024;16:1751. doi:10.3390/cancers16091751
6. Edaily S, Abdel-Razeq H. Management strategies of breast cancer patients with BRCA1 and BRCA2 pathogenic germline variants. Onco Targets Ther. 2022;15:815-26. doi:10.2147/OTT.S369844
7. Li J, Wen WX, Eklund M, Kvist A, Eriksson M, Christensen HN, et al. Prevalence of BRCA1 and BRCA2 pathogenic variants in a large, unselected breast cancer cohort. Int J Cancer. 2019;144:1195-204. doi:10.1002/ijc.31841
8. Bedrosian I, Somerfield MR, Achatz MI, Boughey JC, Curigliano G, Friedman S, et al. Germline testing in patients with breast cancer: ASCO-Society of Surgical Oncology guideline. J Clin Oncol. 2024;42:584-604. doi:10.1200/JCO.23.02225
9. Monticciolo DL, Newell MS, Moy L, Niell B, Monsees B, Sickles EA. Breast cancer screening in women at higher-than-average risk: recommendations from the ACR. J Am Coll Radiol. 2018;15:408-14. doi:10.1016/j.jacr.2017.11.034
10. Abdel-Razeq H, Tamimi F, Abujamous L, Edaily S, Abunasser M, Bater R, et al. Patterns and prevalence of BRCA1 and BRCA2 germline mutations among patients with triple-negative breast cancer: regional perspectives. Cancer Manag Res. 2021;13:4597-604. doi:10.2147/CMAR.S316470
11. Walsh T, Mandell JB, Norquist BM, Casadei S, Gulsuner S, Lee MK, et al. Genetic predisposition to breast cancer due to mutations other than BRCA1 and BRCA2 founder alleles among Ashkenazi Jewish women. JAMA Oncol. 2017;3(12):1647-53. doi:10.1001/jamaoncol.2017.1996
12. Tennen RI, Laskey SB, Koelsch BL, McIntyre MH, Tung JY. Identifying Ashkenazi Jewish BRCA1/2 founder variants in individuals who do not self-report Jewish ancestry. Sci Rep. 2020;10:7669. doi:10.1038/s41598-020-63466-x
13. Schwartz CJ, Khorsandi N, Blanco A, Mukhtar RA, Chen YY, Krings G. Clinicopathologic and genetic analysis of invasive breast carcinomas in women with germline CHEK2 variants. Breast Cancer Res Treat. 2024;204:171-9. doi:10.1007/s10549-023-07176-8
14. Graffeo R, Rana HQ, Conforti F, Bonanni B, Cardoso MJ, Paluch-Shimon S, et al. Moderate penetrance genes complicate genetic testing for breast cancer diagnosis: ATM, CHEK2, BARD1 and RAD51D. Breast. 2022;65:32-40. doi:10.1016/j.breast.2022.06.003
15. National Comprehensive Cancer Network. Breast, ovarian and pancreatic cancer: genetic/familial high-risk assessment. 2025. Available from: https://www.nccn.org/guidelines/guidelines-detail?category=1&id=1419
16. Kurian AW, Bedrosian I, Kohlmann WK, Somerfield MR, Robson ME. Germline testing in patients with breast cancer: ASCO-Society of Surgical Oncology guideline Q and A. JCO Oncol Pract. 2024;20:466-71. doi:10.1200/OP.23.00771
17. Culver JO, Freiberg Y, Ricker C, Comeaux JG, Chang EY, Banerjee V, et al. Integration of universal germline genetic testing for all new breast cancer patients. Ann Surg Oncol. 2023;30:1017-25. doi:10.1245/s10434-022-12595-w

18. De Silva DL, Stafford L, Skandarajah AR, Sinclair M, Devereux L, Hogg K, et al. Universal genetic testing for women with newly diagnosed breast cancer in the context of multidisciplinary team care. Med J Aust. 2023;218:368-73. doi:10.5694/mja2.51906
19. Raspa M, Moultrie R, Toth D, Haque SN. Barriers and facilitators to genetic service delivery models: scoping review. Interact J Med Res. 2021;10(1):e23523. doi:10.2196/23523
20. Robson M, Im SA, Senkus E, Xu B, Domchek SM, Masuda N, et al. Olaparib for metastatic breast cancer in patients with a germline BRCA mutation. N Engl J Med. 2017;377:523-33. doi:10.1056/NEJMoa1706450
21. Robson ME, Tung N, Conte P, Im SA, Senkus E, Xu B, et al. OlympiAD final overall survival and tolerability results: olaparib versus chemotherapy treatment of physician's choice in patients with a germline BRCA mutation and HER2-negative metastatic breast cancer. Ann Oncol. 2019;30:558-66. doi:10.1093/annonc/mdz012
22. Robson ME, Im SA, Senkus E, Xu B, Domchek SM, Masuda N, et al. OlympiAD extended follow-up for overall survival and safety: olaparib versus chemotherapy treatment of physician's choice in patients with a germline BRCA mutation and HER2-negative metastatic breast cancer. Eur J Cancer. 2023;184:39-47. doi:10.1016/j.ejca.2023.01.031
23. Litton JK, Rugo HS, Ettl J, Hurvitz SA, Gonçalves A, Lee KH, et al. Talazoparib in patients with advanced breast cancer and a germline BRCA mutation. N Engl J Med. 2018;379:753-63. doi:10.1056/NEJMoa1802905
24. Henry NL, Somerfield MR, Dayao Z, Elias A, Kalinsky K, McShane LM, et al. Biomarkers for systemic therapy in metastatic breast cancer: ASCO guideline update. J Clin Oncol. 2022;40:3205-21. doi:10.1200/JCO.22.01063
25. Tung NM, Garber JE. BRCA1/2 testing: therapeutic implications for breast cancer management. Br J Cancer. 2018;119:141-52. doi:10.1038/s41416-018-0127-5
26. Tan JZC, Zhang Z, Goh HX, Ngeow J. BRCA and beyond: impact on therapeutic choices across cancer. Cancers (Basel). 2024;17:8. doi:10.3390/cancers17010008
27. Tutt ANJ, Garber JE, Kaufman B, Viale G, Fumagalli D, Rastogi P, et al. Adjuvant olaparib for patients with BRCA1- or BRCA2-mutated breast cancer. N Engl J Med. 2021;384:2394-405. doi:10.1056/NEJMoa2105215
28. Geyer CE, Garber JE, Gelber RD, Yothers G, Taboada M, Ross L, et al. Overall survival in the OlympiA phase III trial of adjuvant olaparib in patients with germline pathogenic variants in BRCA1/2 and high-risk, early breast cancer. Ann Oncol. 2022;33:1250-68. doi:10.1016/j.annonc.2022.09.159
29. t'Kint de Roodenbeke MD, Pondé N, Buisseret L, Piccart M. Management of early breast cancer in patients bearing germline BRCA mutations. Semin Oncol. 2020;47:243-8. doi:10.1053/j.seminoncol.2020.07.006
30. Zattarin E, Taglialatela I, Lobefaro R, Leporati R, Fucà G, Ligorio F, et al. Breast cancers arising in subjects with germline BRCA1 or BRCA2 mutations: different biological and clinical entities with potentially diverse therapeutic opportunities. Crit Rev Oncol Hematol. 2023;190:104109. doi:10.1016/j.critrevonc.2023.104109
31. Manahan ER, Kuerer HM, Sebastian M, Hughes KS, Boughey JC, Euhus DM, et al. Consensus guidelines on genetic testing for hereditary breast cancer from the American Society of Breast Surgeons. Ann Surg Oncol. 2019;26:3025-31. doi:10.1245/s10434-019-07549-8
32. Childers CP, Childers KK, Maggard-Gibbons M, Macinko J. National estimates of genetic testing in women with a history of breast or ovarian cancer. J Clin Oncol. 2017;35:3800-6. doi:10.1200/JCO.2017.73.6314
33. Abdel-Razeq H, Sharaf B, Tamimi F, Hani HB, Alsmadi O, Khalil H, et al. Establishment of a clinical cancer genetics program for breast cancer in a resource-limited country: challenges and opportunities. Front Oncol. 2024;14:1431985. doi:10.3389/fonc.2024.1431985
34. Shore N, Nielsen SM, Esplin ED, Antonarakis ES, Barata PC, Beer TM, et al. Implementation of universal germline genetic testing into standard of care for patients with prostate cancer: the time is now. JCO Oncol Pract. 2025;21:747-53. doi:10.1200/OP-24-00626
35. Whitworth PW, Beitsch PD, Patel R, Rosen B, Compagnoni G, Baron PL, et al. Clinical utility of universal germline genetic testing for patients with breast cancer. JAMA Netw Open. 2022;5:e2232787. doi:10.1001/jamanetworkopen.2022.32787
36. Song QK, Li J, Huang R, Fan JH, Zheng RS, Zhang BN, et al. Age of diagnosis of breast cancer in China: almost 10 years earlier than in the United States and the European Union. Asian Pac J Cancer Prev. 2014;15:10021-5. doi:10.7314/APJCP.2014.15.22.10021

37. Rodríguez-Cuevas S, Macías CG, Franceschi D, Labastida S. Breast carcinoma presents a decade earlier in Mexican women than in women in the United States or European countries. Cancer. 2001;91:863-8. doi:10.1002/1097-0142(20010215)91:4<863::AID-CNCR1074>3.0.CO;2-Y
38. Johnson HM, Irish W, Muzaffar M, Vohra NA, Wong JH. Quantifying the relationship between age at diagnosis and breast cancer-specific mortality. Breast Cancer Res Treat. 2019;177:713-22. doi:10.1007/s10549-019-05353-2
39. Zahed H, Feng X, Sheikh M, Bray F, Ferlay J, Ginsburg O, et al. Age at diagnosis for lung, colon, breast and prostate cancers: an international comparative study. Int J Cancer. 2024;154:28-40. doi:10.1002/ijc.34671
40. Bidoli E, Virdone S, Hamdi-Cherif M, Toffolutti F, Taborelli M, Panato C, et al. Worldwide age at onset of female breast cancer: a 25-year population-based cancer registry study. Sci Rep. 2019;9:14111. doi:10.1038/s41598-019-50680-5
41. Sun L, Brentnall A, Patel S, Buist DSM, Bowles EJA, Evans DGR, et al. A cost-effectiveness analysis of multigene testing for all patients with breast cancer. JAMA Oncol. 2019;5:1718-30. doi:10.1001/jamaoncol.2019.3323
42. Guo F, Adekanmbi V, Hsu CD, Berenson AB, Kuo YF, Shih YCT. Cost-effectiveness of population-based multigene testing for breast and ovarian cancer prevention. JAMA Netw Open. 2024;7:e2356078. doi:10.1001/jamanetworkopen.2023.56078
43. Monaghan A, Copson E, Cutress R. Hereditary genetic testing and mainstreaming: a guide for surgeons. Ann R Coll Surg Engl. 2024;106:300-4. doi:10.1308/rcsann.2024.0029
44. Young AL, Ip E, Scheinberg T, Harrison M, Beale P, Goodwin A. An Australian mainstream genetic testing program: clinicians' views about current and future practices. Asia Pac J Clin Oncol. 2024;20:119-27. doi:10.1111/ajco.14033
45. Berkman J, DeBortoli E, Steinberg J, Milch V, Yanes T, McInerney-Leo A. Mainstreaming cancer genomic testing: a scoping review of the acceptability, efficacy, and impact. Clin Genet. 2025;107:123-35. doi:10.1111/cge.14660
46. Bokkers K, Vlaming M, Engelhardt EG, Zweemer RP, van Oort IM, Kiemeney LALM, et al. The feasibility of implementing mainstream germline genetic testing in routine cancer care: a systematic review. Cancers (Basel). 2022;14:1059. doi:10.3390/cancers14041059
47. Van der Merwe NC, Combrink HM, Ntaita KS, Oosthuizen J, Kotze MJ. Prevalence of clinically relevant germline BRCA variants in a large unselected South African breast and ovarian cancer cohort: a public sector experience. Front Genet. 2022;13:834265. doi:10.3389/fgene.2022.834265
48. Seewald RA, Silva IAS, Pereira L, Martins LN, Costa E. Characterization of patients with breast cancer and national genetic testing strategy in Brazil. Rev Bras Cancerol. 2023;e-044214.
49. Villarreal-Garza C, Alvarez-Gómez RM, Pérez-Plasencia C, Herrera LA, Herzog J, Castillo D, et al. Significant clinical impact of recurrent BRCA1 and BRCA2 mutations in Mexico. Cancer. 2015;121(3):372-8. doi:10.1002/cncr.29058
50. Goh SP, Lee C, Tan W, Jalaludin MY, Ng CH, Low LL, et al. Economic evaluation of germline genetic testing for breast cancer in upper-middle-income countries. BMC Cancer. 2024;24(1):316. doi:10.1186/s12885-024-12038-7
51. Burke W, Parens E, Chung WK, Berger SM, Appelbaum PS. The challenge of genetic variants of uncertain clinical significance: a narrative review. Ann Intern Med. 2022;175:994-1000. doi:10.7326/M21-4109
52. Abdel-Razeq H, Tamimi F, Abujamous L, Abdel-Razeq R, Abunasser M, Edaily S, et al. Rates of variants of uncertain significance among patients with breast cancer undergoing genetic testing: regional perspectives. Front Oncol. 2022;12:673094. doi:10.3389/fonc.2022.673094