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# Advancing Precision Medicine for Breast and Ovarian Cancer Patients Through Mainstream Genetic Testing: A Pilot Program in Saskatchewan

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## Abstract

Mainstream genetic testing integrates germline analysis directly into oncology care, streamlining access and reducing reliance on genetics referrals. This pilot program evaluated the implementation of a mainstream testing model for patients with breast or ovarian cancer in Saskatchewan from February 2024 to April 2025. Eligible patients were offered testing by oncology and surgical teams at two provincial cancer centres. Clinicians received training on eligibility, consent, and counselling procedures. Mainstreaming reduced the average time from diagnosis to results from 737 to 201 days, representing a 3.7-fold improvement in turnaround time. These findings demonstrate that mainstream genetic testing is feasible, scalable, and effective within a publicly funded Canadian healthcare system, supporting national efforts to expand routine oncology-led genetic testing for improved access, equity, and patient care for hereditary breast and ovarian cancer.

## Introduction

Breast cancer is the most common cancer in Canada after non-melanoma skin cancer.[1] Individuals with germline BRCA variants face a significantly elevated risk of developing breast, ovarian, and other cancers.[2,3] Approximately 13% of Canadians will be diagnosed with breast cancer in their lifetime; however, for those with *BRCA* variants, this risk increases up to 72% by age 80.[2] Timely identification of pathogenic or likely pathogenetic variants is critical, as it informs treatment decisions and enables preventive strategies for patients and their families.[4] Mainstreaming models of care are increasingly adopted across Canadian health systems to meet growing demand for genetic testing amid a stable genetics workforce. Mainstream genetic testing integrates testing into routine oncology care, bypassing traditional referrals to genetics services **(Figure 1)**.[5–8] A recent pan-Canadian framework describes mainstreaming as "*the shifting of all or part of the clinical genetic testing process to clinicians outside of the genetics service to facilitate patient access to genetic testing.*"[8] This approach aims to improve accessibility, reduce delays, and optimize resource use.[9] The primary objective of this pilot program was to implement mainstream genetic testing for people with breast and ovarian cancer in Saskatchewan.

## Methods

### Study Design

A pilot program of mainstreaming genetic testing was implemented at the Saskatoon Cancer Centre in Saskatoon and the Allan Blair Cancer Centre in Regina to assess its impact on reducing cancer genetic testing access wait times. The program was reviewed and approved by the University of Saskatchewan's Research Ethics Board, the Saskatchewan Cancer Agency, and the Saskatchewan Health Authority. Clinicians who were involved in the program (breast surgeons, gynecologic oncologists, and medical oncologists) received education and training on mainstreaming, eligibility criteria, informed consent, and genetic testing protocols. All patients provided their informed consent prior to participating in the study.

### Eligibility Criteria

The target population of this study included individuals with breast cancer in the province of Saskatchewan. Patients were eligible for mainstream genetic testing if they had a personal history of breast cancer, including triple-negative breast cancer (TNBC) diagnosis age ≤60 years, male breast cancer, breast cancer diagnosis age ≤35 years, bilateral breast cancer with at least one diagnosis age ≤50 years; strong family history of breast cancer; or met criteria for companion drug access for olaparib. These criteria were used to identify patients at high risk of harbouring pathogenic or likely pathogenic *BRCA* variants. Eligible patients who met genetic testing criteria were offered enrollment in the program. Patients diagnosed prior to February 2024 and on the waitlist for genetic testing were also eligible for mainstreaming.

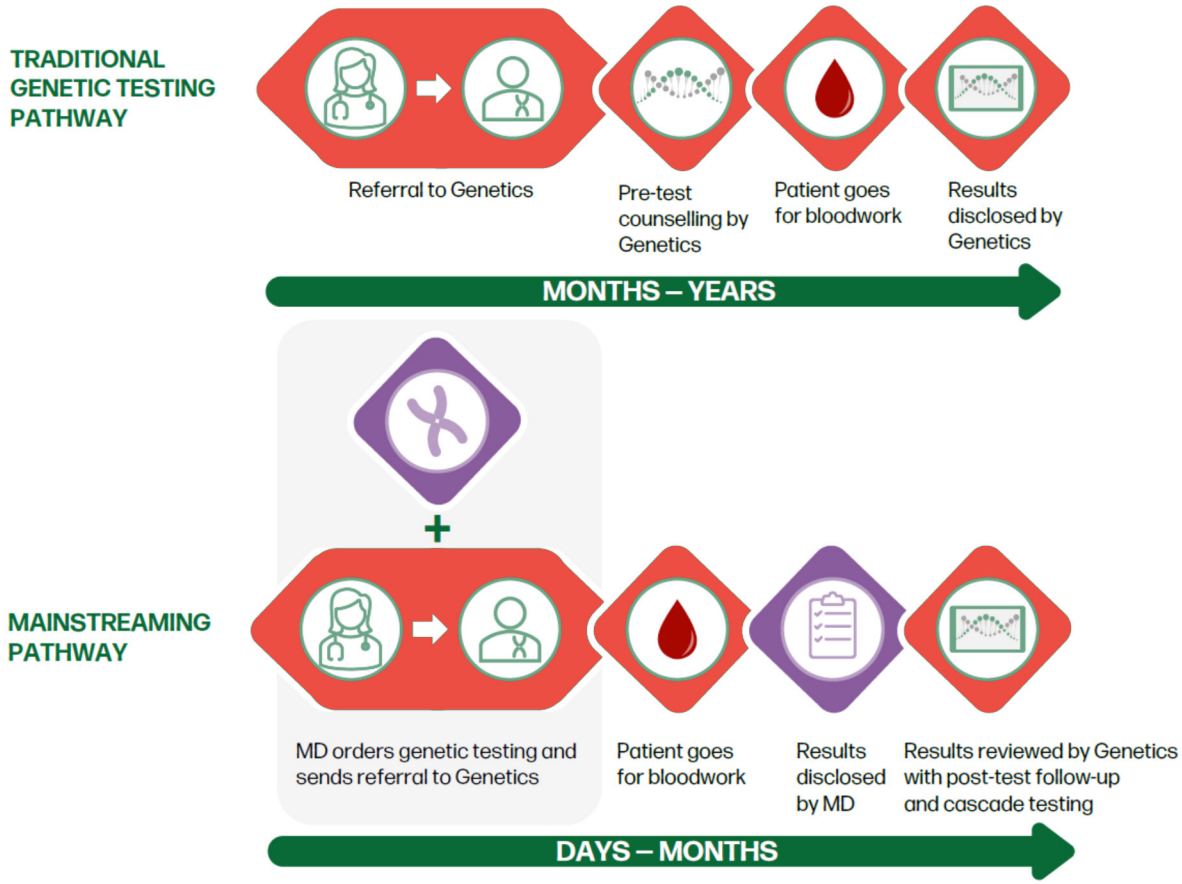


**Figure 1.** Traditional and mainstream genetic testing pathways. In a traditional genetic testing pathway, eligible patients are referred to Medical Genetics, undergo pre-test counselling, obtain bloodwork for testing, and then undergo post-test counselling. In a mainstream genetic testing pathway, pre-test genetic counselling is performed by non-genetic healthcare professionals, thereby making genetic testing more accessible to all eligible patients who might benefit from it; *courtesy of the Canadian Association of Genetic Counsellors (CAGC), adapted with permission.*[10]

Higher-risk patients, according to eligibility criteria, were defined as individuals for whom genetic testing could result in an immediate change in medical management (e.g., surgical planning or limited survivability) or who had characteristics associated with hereditary cancers (e.g., TNBC, male breast cancer, age <35). All other patients met testing criteria primarily based on personal or family history.

## Study Procedures

Informed consent was requested by the ordering physician. Participants who consented to data collection in the pilot program and were eligible for genetic testing automatically received a lab requisition and provided blood samples, which were sent to the Roy Romanow Provincial Laboratory (RRPL) in Regina.

Genetic testing was conducted at the RRPL in accordance with the American College of Medical Genetics and Genomics (ACMG)[11] and ClinGen[12] guidelines, as well as gene-specific recommendations and standards for interpretation of sequence variations. Next-generation sequencing was performed to target the coding regions of genes associated with hereditary cancers. Multiplex ligation-dependent probe amplification was used to detect copy number variants across all 13 genes in the expanded breast/ovarian cancer testing panel (*ATM, BRCA1, BRCA2, BRIP1, CDH1, CHEK2, NBN, PALB2, PTEN, RAD51C, RAD51D, STK11, TP53*).

Genetic test results were provided within 6 to 8 weeks. Patients with a positive genetic result (clinically significant variant or variant of uncertain significance [VUS]) received an automatic referral to the Medical Genetics department at the Royal University Hospital (RUH) in Saskatoon.

## Data Analysis

We collected and analyzed data from the Saskatchewan Cancer Agency electronic records pre- and post-mainstreaming. Pre- and post-implementation metrics assessed included ordering providers (medical oncologists vs. surgeons), region of testing (Saskatoon vs.

| Clinical characteristic | Patients with genetic variants n=50 |
|---|---|
| **Age, average** | 53 years |
| **Gender** | |
| Female | 50 (100%) |
| Male | 0 |
| **Family history of cancer** | |
| Breast | 11 (22%) |
| Ovarian | 0 |
| Both | 2 (4%) |
| **Genetic variants** | |
| *BRCA1/2 or VUS* | 16 (32%) |
| *BRCA1* | 6 (12%) |
| *BRCA2* | 3 (6%) |
| VUS | 7 (14%) |
| *Other* (*ATM, PALB2, PTEN, BRIP1, PMS2*) | 34 (68%) |
| **Surgery*** | |
| Bilateral salpingo-oophorectomy | 2 (4%) |
| Bilateral mastectomy | 5 (10%) |

**Table 1.** Clinical characteristics of all patients identified with a genetic variant through mainstream genetic testing; *courtesy of Mita Manna, MD, FRCPC.*

*Two women underwent bilateral salpingo-oophorectomy and bilateral mastectomy; both carried a germline *BRCA1* variant. Among the three additional women who underwent a bilateral mastectomy, two carried *BRCA1* variants, and one carried a *BRCA2* variant.

**Abbreviations: VUS:** variant of uncertain significance

Regina), time from sample collection to receipt of results, lab turnaround times, and indications for testing.

## Results

Between February 2024 and April 2025, 348 patients met eligibility criteria for mainstreaming genetic testing. Of these, 132 patients consented to data collection, 109 completed testing, and results were available for 97 patients. The testing uptake rate was 82.6%. In total, 90 patients were enrolled at the Saskatoon Cancer Centre in Saskatoon and 42 at the Allan Blair Cancer Centre in Regina. Genetic tests were ordered by medical oncologists (n=71) and surgeons (n=61). Among 97 evaluable patients, 67% (65/97) had hormone receptor-positive human epidermal growth factor receptor 2-negative (HR+/HER2-) cancer, 21% (20/97) had TNBC, and 12% (12/97) had hormone receptor-negative HER2-positive (ER-PR-HER2+) cancer.

We examined the clinical characteristics of patients who underwent mainstream genetic testing and were identified as carriers of a genetic variant **(Table 1)**. Fifty patients (52%) had a genetic variant linked to breast cancer. Of these patients, 16 had germline pathogenic or likely pathogenic variants classified as *BRCA1/2* or a VUS. Of the six women with *BRCA1* variants, two underwent bilateral mastectomy, and two had both a bilateral mastectomy and bilateral salpingo-oophorectomy. One of the three women with a *BRCA2* variant underwent a bilateral mastectomy.

Among the women with an identified genetic variant (n=16), seven had TNBC, including four (25%) with a germline *BRCA1* variant, one (6%) with a *BRCA2* variant, and two (13%) with a VUS. Among those with an identified genetic variant and HR+/HER2- breast cancer, two (13%) had a *BRCA1* variant, two (13%) had a *BRCA2* variant, and four (25%) had a VUS. A single patient with HR-/HER2+ breast cancer was found to have a VUS.

### Mainstream Testing Turnaround Time

Mainstream genetic testing markedly reduced the time from diagnosis to receipt of genetic testing results from 737 days to 201 days **(Figure 2)**, representing a 3.7-fold reduction in turnaround time. Among patients considered at higher risk based on eligibility criteria, the mean turnaround time decreased from 770 to 90 days with mainstream genetic testing. The time from receipt of test results to genetic counselling also decreased from 54 to 51 days, reducing the total time from diagnosis to counselling from 791 to 252 days.

## Discussion

### Improved Access Through Mainstreaming

This pilot study assessed the implementation of mainstream genetic testing for patients with breast and ovarian cancer across Saskatchewan, beginning in February 2024. Over the 15-month study period, this initiative demonstrated that a mainstreaming approach substantially reduced turnaround times compared with the traditional genetic referral pathway.

The most notable outcome of mainstreaming was a marked reduction in time from diagnosis to receipt of genetic results. With mainstreaming, turnaround time decreased 3.7-fold, from over two years (737 days) to approximately 201 days, and to 90 days for those classified as higher risk based on eligibility criteria. These reductions are clinically meaningful, as timely access to genetic test results can directly influence surgical planning, systemic therapy selection (e.g., eligibility for poly (ADP-ribose) polymerase [PARP] inhibitors), and cascade testing for at-risk relatives.[13]

The results achieved in our program align with Canadian and international evidence supporting a mainstreaming approach.[5,7,14–18] A systematic review of 15 studies across various cancers (ovarian, breast, endometrial, and prostate cancer) found that the quality of genetic care was maintained with mainstreaming, test results were typically disclosed within 3 to 6 weeks of the testing referral, and turnaround times were consistently shorter with the mainstream approach.[17]

In the Canadian setting, an observational study from British Columbia found that among 149 patients with a personal history of breast and ovarian cancer, oncology clinic-based testing significantly reduced the time from date of referral to the return of test results, from 403 to 191 days.[18] In Alberta, a provincial mainstreaming initiative reported an average of 2.7 months from provider appointment to result disclosure, with a laboratory turnaround of 2.1 months.[5] Our results in Saskatchewan are therefore consistent with these provincial experiences, indicating that mainstream genetic testing can be effectively implemented across diverse Canadian healthcare systems.

Internationally, evidence similarly demonstrated significantly shorter turnaround times and higher testing uptake with mainstream genetic testing.[14–16] The GENE-SMART study, a large, national study in the Netherlands spanning a 6-year period, found that the uptake of genetic testing among patients with breast cancer was 2.5x higher with mainstreaming than with direct referral to genetics.[15] In Australia, mainstream genetic testing improved patient access to testing and reduced pressure on genetic counselling services.[14] In that setting, test results impacted treatment decisions for most (88.6%) patients with a detected pathogenic variant.

Collectively, these data demonstrate that mainstreaming minimizes the need for pre-test genetics consultations without compromising quality, enabling genetic specialists to focus on patients with positive or complex results. The present study confirms that similar outcomes are achievable in the Canadian healthcare context, particularly when supported by provincial funding and institutional commitment.

## Canadian Consensus Recommendations and Mainstreaming Framework

A recent pan-Canadian expert working group (comprising medical oncologists, a geneticist, a surgical oncologist, and a genetic counsellor) recommended reflexive and broad germline testing at the time of initial cancer assessment for patients with breast cancer.[9] This recommendation aligns with our findings and underscores the clinical importance of mainstreaming to improve timely access to hereditary risk information and personalized treatment planning. Another pan-Canadian expert group comprising medical geneticists, medical genetics resident physicians, a laboratory geneticist, and a genetic counsellor developed a national conceptual mainstreaming framework comprising four models for different testing scenarios across the diagnostic care

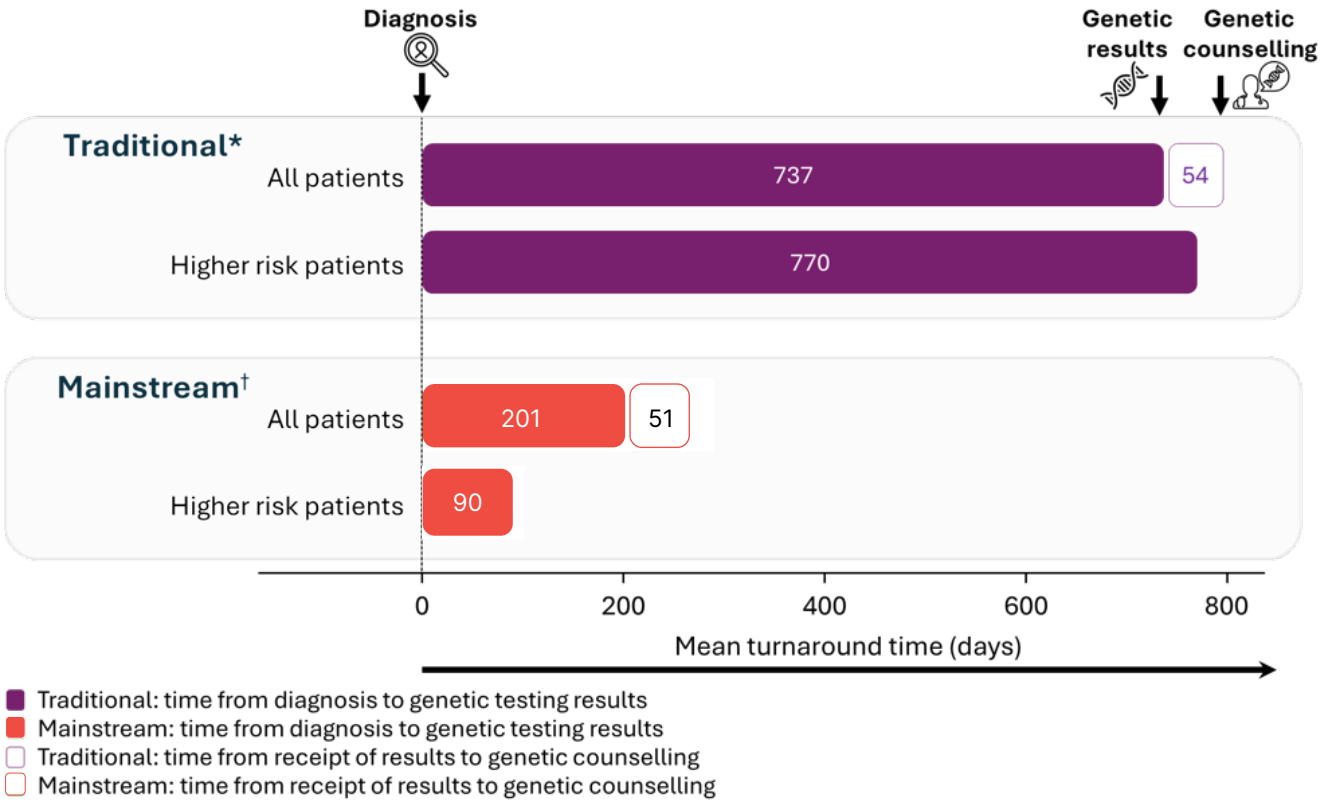


**Figure 2.** Mean time from diagnosis to genetic testing results and genetic counselling with traditional and mainstream genetic testing pathways. Compared with the traditional approach, mainstream genetic testing resulted in a time from diagnosis to genetic results and counselling that was more than 3x shorter. Solid bars indicate mean time to genetic results; white bars indicate mean time to genetic counselling; *courtesy of Mita Manna, MD, FRCPC*.
* Representative of the process where patients are referred to a genetic testing specialist prior to testing.
† All patients were diagnosed after 2023.

pathway.[8] Our implementation aligns with the "to-result" model outlined in the framework, in which oncology clinicians identify eligible patients, obtain consent, provide pre-test counselling, and order testing, while the genetics service provides result disclosure and follow-up support.

### Challenges and Opportunities

Barriers to mainstream genetic testing include inadequate knowledge among referring healthcare professionals, a lack of system infrastructure, and limited human and financial resources.[17] In addition, patients of lower socioeconomic status remain less likely to receive genetic testing, even under a mainstream approach, highlighting a persistent gap in equity.[15] Sustained educational initiatives to improve genomic literacy and competency among non-genetic clinicians, and collaboration across disciplines, are essential to effectively implement mainstream genetic testing. Broader adoption of mainstreaming requires a national structured care program with defined workflows, roles, and responsibilities across oncology, genetics, and laboratory teams.[8,9] Further, there is room for improvement to bring Canada closer to the international average of 3 to 6 weeks from diagnosis to disclosure of test results.[17]

### Limitations

This pilot study has several limitations. First, the sample size was modest, and data were collected from two tertiary cancer centres in Saskatchewan, which may limit generalizability to other jurisdictions or community-based settings. Second, as a program evaluation, outcomes such as patient satisfaction, recall of genetic information, and long-term behavioural or psychosocial impact were not assessed. Finally, as highlighted in the national conceptual framework for mainstreaming genetic testing, variability in clinician expertise, infrastructure, and inter-professional coordination across health systems may influence the scalability and sustainability of this model.[8]

## Future Directions

Future directions for this work include expanding provincial eligibility criteria for genetic testing to improve access for patients who may benefit the most from testing. Specifically, broadening the criteria to include all patients diagnosed with TNBC and HR+ breast cancer at age 50 or younger would align with evolving evidence supporting the clinical utility of early genetic testing in these populations.[19] Integrating the support of cancer specialist nurses, particularly in underserved regions, may contribute to the sustainability and expansion of mainstreaming programs.[20] For example, one study showed that with the support of breast cancer coordinators, expanding testing to patients with early breast cancer treated in a community setting was feasible without increasing the burden on genetic specialists.[21] Additionally, reducing wait times for genetic consultations and prioritizing referrals for patients with identified pathogenic or likely pathogenic variants could facilitate more timely and informed treatment decision-making, particularly for patients whose management may be impacted by genetic findings. Together, these efforts will continue to advance the integration of genetic testing into routine breast and ovarian cancer care.

## Summary

Our results demonstrate the feasibility and effectiveness of mainstreaming genetic testing for breast cancer within a provincial healthcare system. In Saskatchewan, this approach has markedly reduced wait times from more than 2 years to 90 days for those considered higher risk based on eligibility criteria, enabling more timely access to genetic information and facilitating treatment decisions. Mainstreaming is now the provincially funded standard of care, reflecting its established value in advancing precision oncology. Aligned with national recommendations,[9] this model supports broader implementation to improve access and outcomes in hereditary breast cancer care. Continued success of the program at the provincial and national levels will require coordinated strategies that address workforce capacity, provider training, patient education, and system-level communication. Structured care pathways will be essential to ensure long-term program sustainability and equitable access to mainstream genetic testing.

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## Financial Disclosures

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Conceptualization, M.M., L.H., P.M., T.S., G.G.: Funding acquisition, M.M., T.S.; Methodology/ Genetic Testing/Analysis, M.M., N.A., A.H., T.S.; Project administration, M.M., N.A., L.D., A.H.; Supervision, M.M., L.D.; Writing—original draft, M.M.; Writing—review and editing, M.M, N.A. All authors have read and agreed to the published version of the manuscript.

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## References

1. Canadian Cancer Statistics Advisory Committee in collaboration with the Canadian Cancer Society, Statistics Canada, and the Public Health Agency of Canada. *Canadian Cancer Statistics 2023*. Canadian Cancer Society; 2023.
2. Kuchenbaecker KB, Hopper JL, Barnes DR, Phillips KA, Mooij TM, Roos-Blom MJ, et al. Risks of breast, ovarian, and contralateral breast cancer for BRCA1 and BRCA2 mutation carriers. *JAMA*. 2017;317(23):2402-2416. doi:10.1001/jama.2017.7112
3. Cheng HH, Shevach JW, Castro E, Couch FJ, Domchek SM, Eeles RA, et al. BRCA1, BRCA2, and associated cancer risks and management for male patients: A review. *JAMA* Oncol. 2024;10(9):1272-1281. doi:10.1001/jamaoncol.2024.2185
4. Eerola H, Aittomäki K, Asko-Seljavaara S, Nevanlinna H, von Smitten K. Hereditary breast cancer and handling of patients at risk. Scand J Surg. 2002;91(3):280-287. doi:10.1177/145749690209100312
5. Alberta Health Services. Mainstreaming cancer genetics 2019/2020 year end report. Accessed December 4, 2025. https://www.albertahealthservices.ca/assets/about/scn/ahs-scn-cancer-mainstreaming-cancer-genetics-2020.pdf
6. Rahman N. Mainstreaming genetic testing of cancer predisposition genes. *Clin Med*. 2014;14(4):436-439. doi:10.7861/clinmedicine.14-4-436
7. George A, Riddell D, Seal S, Talukdar S, Mahamdallie S, Ruark E, et al. Implementing rapid, robust, cost-effective, patient-centred, routine genetic testing in ovarian cancer patients. *Sci Rep*. 2016;6(1):29506. doi:10.1038/srep29506
8. Mackley MP, Richer J, Guerin A, Caluseriu O, Armstrong L, Blood KA, et al. Mainstreaming of clinical genetic testing: A conceptual framework. *Genet Med*. 2025;27(8). doi:10.1016/j.gim.2025.101465
9. Weber E, Carmona-Gonzalez CA, Boucher M, Eisen A, Laing K, Melvin J, et al. Canadian recommendations for germline genetic testing of patients with breast cancer: A call to action. *Curr Oncol*. 2025;32(6):290. doi:10.3390/curroncol32060290
10. Canadian Association of Genetic Counsellors (CAGC). What Is Mainstreaming? PowerPoint presentation. 2023. Accessed December 4, 2025. https://www.cagc-accg.ca/?page=470
11. Richards S, Aziz N, Bale S, Bick D, Das S, Gastier-Foster J, et al. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. *Genet Med*. 2015;17(5):405-424. doi:10.1038/gim.2015.30
12. ClinGen | Clinical Genome Resource. Variant Classification Guidance. Accessed December 4, 2025. https://clinicalgenome.org/tools/clingen-variant-classification-guidance/
13. 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(9):e2232787. doi:10.1001/jamanetworkopen.2022.32787
14. Beard C, Monohan K, Cicciarelli L, James PA. Mainstream genetic testing for breast cancer patients: Early experiences from the Parkville Familial Cancer Centre. *Eur J Hum Genet*. 2021;29(5):872-880. doi:10.1038/s41431-021-00848-3
15. de Jong CL, Siesling S, Puts GCWM, Jager A, Ausems MGEM. The impact of a mainstream genetic testing pathway and socioeconomic factors on the uptake of germline genetic testing in breast cancer patients:

Results of the nationwide GENE-SMART study. *Breast Cancer Res*. 2025;27:129. doi:10.1186/s13058-025-02081-y

16. Kemp Z, Turnbull A, Yost S, Seal S, Mahamdallie S, Poyastro-Pearson E, et al. Evaluation of cancer-based criteria for use in mainstream BRCA1 and BRCA2 genetic testing in patients with breast cancer. *JAMA* Netw Open. 2019;2(5):e194428. doi:10.1001/jamanetworkopen.2019.4428
17. Bokkers K, Vlaming M, Engelhardt EG, Zweemer RP, van Oort IM, Kiemeney L, et al. The feasibility of implementing mainstream germline genetic testing in routine cancer care—A systematic review. *Cancers*. 2022;14(4):1059. doi:10.3390/cancers14041059
18. Richardson M, Min HJ, Hong Q, Compton K, Mung SW, Lohn Z, et al. Oncology clinic-based hereditary cancer genetic testing in a population-based health care system. *Cancers*. 2020;12(2):338. doi:10.3390/cancers12020338
19. Metcalfe KA, Narod SA, Eisen A, Poll A, Zamani N, McCready D, et al. Genetic testing women with newly diagnosed breast cancer: What criteria are the most predictive of a positive test? *Cancer Med*. 2023;12(6):7580-7587. doi:10.1002/cam4.5515
20. Scott N, O'Sullivan J, Asgeirsson K, Macmillan D, Wilson E. Changing practice: Moving to a specialist nurse-led service for BRCA gene testing. *Br J Nurs*. 2020;29(10):S6-S13. doi:10.12968/bjon.2020.29.10.S6
21. Shim V, Karlea A, Brenman LM, Gul J, Hoodfar E, Chan TD, et al. Mainstream germline genetic testing with expanded eligibility for early breast cancer patients in a large integrated health system. *Ann Surg Oncol*. 2025;32(1):75-83. doi:10.1245/s10434-024-16223-7