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BRAZILIAN AND GLOBAL OVERVIEW OF GENETIC PREDISPOSITION FOR HEREDITARY BREAST AND OVARIAN CANCER SYNDROME: A SYSTEMATIC REVIEW

PANORAMA BRASILEIRO E MUNDIAL DA PREDISPOSIÇÃO GENÉTICA PARA A SÍNDROME DO CÂNCER HEREDITÁRIO DE MAMA E OVÁRIO: UMA REVISÃO SISTEMÁTICA

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ABSTRACT: Objective: This study aimed to perform a systematic literature review on the scenario of genetic predisposition testing for the Hereditary Breast and Ovarian Cancer Syndrome in Brazil and worldwide, specifically regarding the BRCA1 and BRCA2 genes. Method: Through the search of the keywords "Hereditary Breast and Ovarian Cancer Syndrome," "Genetic Testing," "BRCA1 Gene," and "BRCA2 Gene," and the application of exclusion and inclusion criteria. Results: The total of articles identified was 116,159, with 36 meeting the inclusion criteria. The results highlighted the importance of tailoring guidelines to meet the specific needs of different populations, crucial for patient follow-up, considering factors beyond the test itself. Conclusion: It was concluded that there is an advantage in identifying specific mutations in the demographic regions considering the country's great heterogeneity and that the inclusion of genetic predisposition testing for HBOC Syndrome in the Unified Health System is feasible and beneficial for the Brazilian population.

KEYWORDS: Hereditary Breast and Ovarian Cancer Syndrome; Genetic Testing; BRCA1 Gene; BRCA2 Gene.

RESUMO: Objetivo: Este estudo objetivou uma revisão sistemática da literatura sobre o cenário dos testes de predisposição genética para a Síndrome Hereditária do Câncer de Mama e Ovário no Brasil e no mundo, especificamente quanto aos genes BRCA1 e BRCA2. Método: Busca pelas palavras-chave "Síndrome Hereditária do Câncer de Mama e Ovário", "Teste Genético", "Gene BRCA1" e "Gene BRCA2", e da aplicação dos critérios de exclusão e inclusão. Resultados: Foram identificados 116.159 artigos, com 36 atendendo aos critérios de inclusão. Ressaltou-se a importância da adequação das diretrizes às necessidades específicas das populações, cruciais para o acompanhamento, considerando fatores além do teste em si. Conclusão: Concluiu-se que há vantagem em identificar mutações específicas nas regiões demográficas considerando a grande heterogeneidade do país e que a inclusão do teste de predisposição genética para a Síndrome HBOC no Sistema Único de Saúde é viável e benéfica para a população brasileira.

PALAVRAS-CHAVE: Síndrome Hereditária do Câncer de Mama e Ovário; Testes Genéticos; Gene BRCA1; Gene BRCA2.

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INTRODUCTION

Cancer represents a group of more than 100 tumors characterized by uncontrolled cell growth[1], which occurs when cellular proliferation and differentiation lose direct or indirect regulation by tumor suppressor genes or proto-oncogenes. Rapid division makes the cells aggressive and invasive, giving them the ability to spread to other tissues and organs[2,3].

Due to the unpredictability of the disease, cancer is the second leading cause of death worldwide, with one in every six deaths related to the disease. In 2018, cancer was responsible for 9.6 million deaths globally[3].

Among the types of cancer with the greatest relevance and epidemiological impact, breast cancer stands out. It is the second most common cancer in the world and the most diagnosed. However, despite high diagnostic rates, it still has a high mortality rate[3]. It is estimated that by 2030, 2.74 million new cases will be registered worldwide[4,5]. In Brazil, it is estimated that one in every twelve women will develop this condition during their lifetime.

Aligned with the global landscape, Brazil reported 73,610 new cases of the disease in 2020 and 17,825 deaths, with projections suggesting an increase to 110,000 new cases annually by 2030[4,6,7]. Over recent decades, this alarming scenario has prompted significant shifts in cancer approaches, driven by advancements in medicine and technology that have transformed the disease from a nonspecific and incurable condition to one that is preventable and often treatable[8].

Concerning biological factors involved in the disease's genesis, 5% to 10% of all breast cancer cases are linked to hereditary high-penetrance genetic mutations[9]. The Hereditary Breast and Ovarian Cancer (HBOC) Syndrome predisposes carriers to a higher risk of developing breast and ovarian cancers at an early age, as well as other cancers such as melanoma, pancreatic cancer, and prostate cancer[6,10,11].

Mutagenic assessment exams are conducted through blood sample collection, primarily focusing on the BRCA1, BRCA2, and TP53 genes due to their clinical importance, with the option to perform multigenic panels. DNA sequencing techniques demonstrate high sensitivity and specificity for detecting mutations[12–14].

These procedures are integral for an accurate assessment of the risk for hereditary cancer and consistently support the diagnosis of breast carcinoma, though they are less definitive for ovarian cancer[12,15]. This approach is widely adopted in the United States, Canada, most of Western Europe, Poland, and Israel, yet remains limited in many Latin American countries due to the high costs and limited availability[16].

In Brazil, genetic tests are not included in the list of services covered by the Unified Health System (SUS) and are therefore confined to the private sector. They are available only to individuals who meet specific criteria based on personal and family medical history, thus restricting access to necessary assessments, risk stratification, and management for those suspected of having HBOC[17–19].

Given the significant epidemiological impact of breast carcinoma and the pivotal role of genetic mutations in prevention, early diagnosis, treatment, prognosis, and genetic counseling[6,14], this study delineates the landscape of genetic predisposition tests for HBOC Syndrome in Brazil in comparison to the rest of the world, acknowledging the limited focus on genetic testing within the Brazilian population.

METHODOLOGY

This study consists of a systematic literature review aimed at providing a theoretical review of the concept of reproductive justice, its foundations, and its relationship with human rights, gender equity, and health promotion, analyzing historical milestones and practical implications.

To enhance the robustness of the article and align with the aforementioned article type, an eligibility and data analysis protocol was applied based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) model, followed by the creation of a flowchart with the proposed methodological protocol[20].

After defining the research question, the search protocol was developed using search terms, databases, inclusion/exclusion criteria, and the inclusion of selected articles.

The search terms were based on the Health Sciences Descriptors (DeCS) in Portuguese. These were: Hereditary Breast and Ovarian Cancer (HBOC) Syndrome, Genetic Testing, BRCA1 Gene, BRCA2 Gene.

Sources for article selection included PubMed and the Virtual Health Library (VHL). Complementary criteria included statistical data provided by the World Health Organization (WHO), the Pan American Health Organization (PAHO), the National Cancer Institute (NIH), and the Ministry of Health.

Data collection took place between December 2022 and December 2023, followed by screening and eligibility in the subsequent months. Identification, selection, and elaboration norms were employed, such that the analyzed works were selected based on the initial objectives of the analysis and by applying an explicit selection method[21].

After identifying the articles containing the selected keywords, an initial time filter (2013 to 2023) and language filter (Portuguese, English, and Spanish) were applied.

Exclusion criteria during the screening and selection process included: duplication, inter and intra-database overlap, language, publication year, incomplete texts, editorial articles, title, keywords, and abstract.

The selected articles were subjected to exploratory reading, considering the article's objectives, results with interventions or analyses appropriate for this review.

After this stage, the articles were read and analyzed (qualitative theme) [22], to identify the main approaches to genetic testing for HBOC and subsequently systematized into standardized analysis sheets containing relevant information such as article title, journal, year, target country, field of study, study type, general objective, methodology, concepts, themes, results, and additional observations deemed necessary.

The initial search resulted in the identification of 116,159 articles using the initial filter (described previously in the methodology). The number of articles was reduced by half just with the application of the initial filters for the time frame and the languages previously described; consequently, the number continued to decrease as the exclusion criteria were Applied (Figure 1).

After applying the inclusion and exclusion criteria 36 articles were included in the final work. The selected articles were displayed in Table 1 along with the country of origin of the respective study and the central objective of the work (Figure 2).

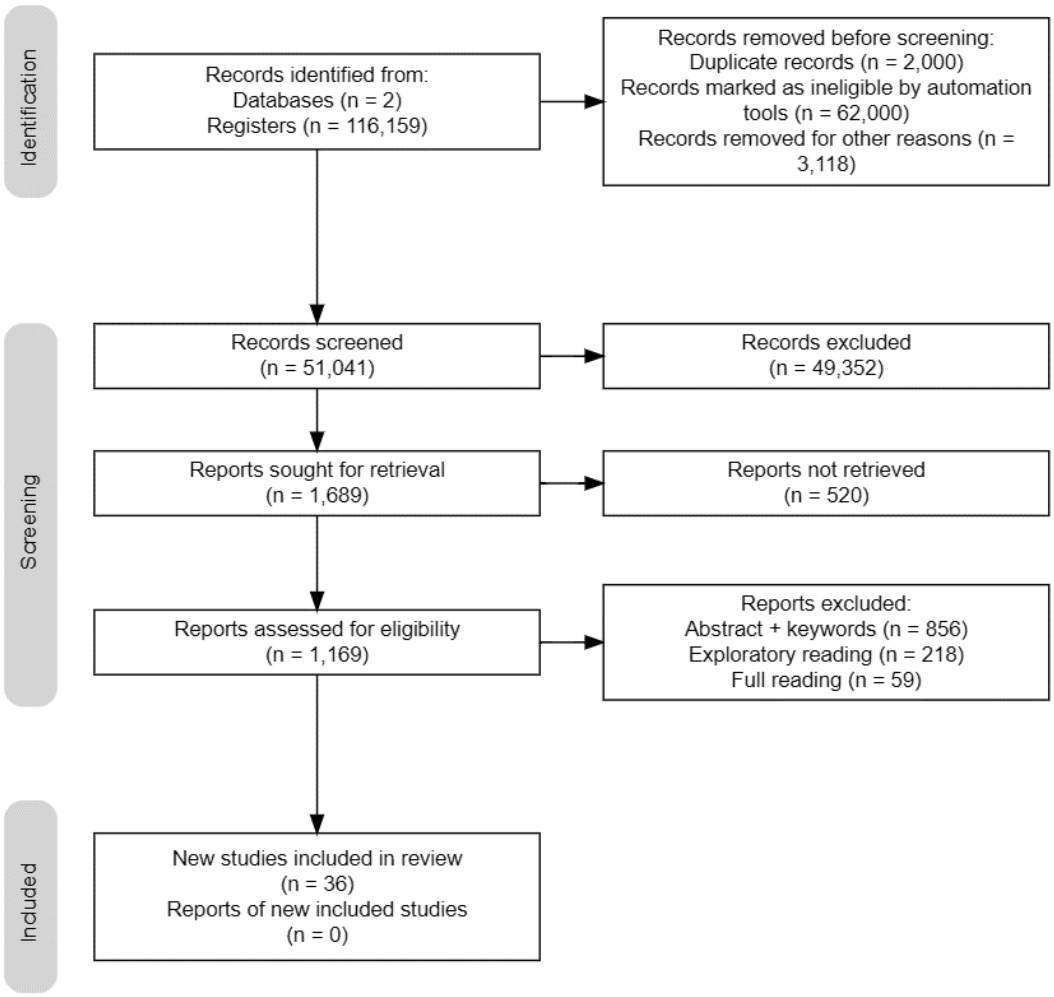

Figure 1. Screening of articles identified in the PubMed and VHL databases based on the pre-established search protocol in the methodology.
Source: The authors.

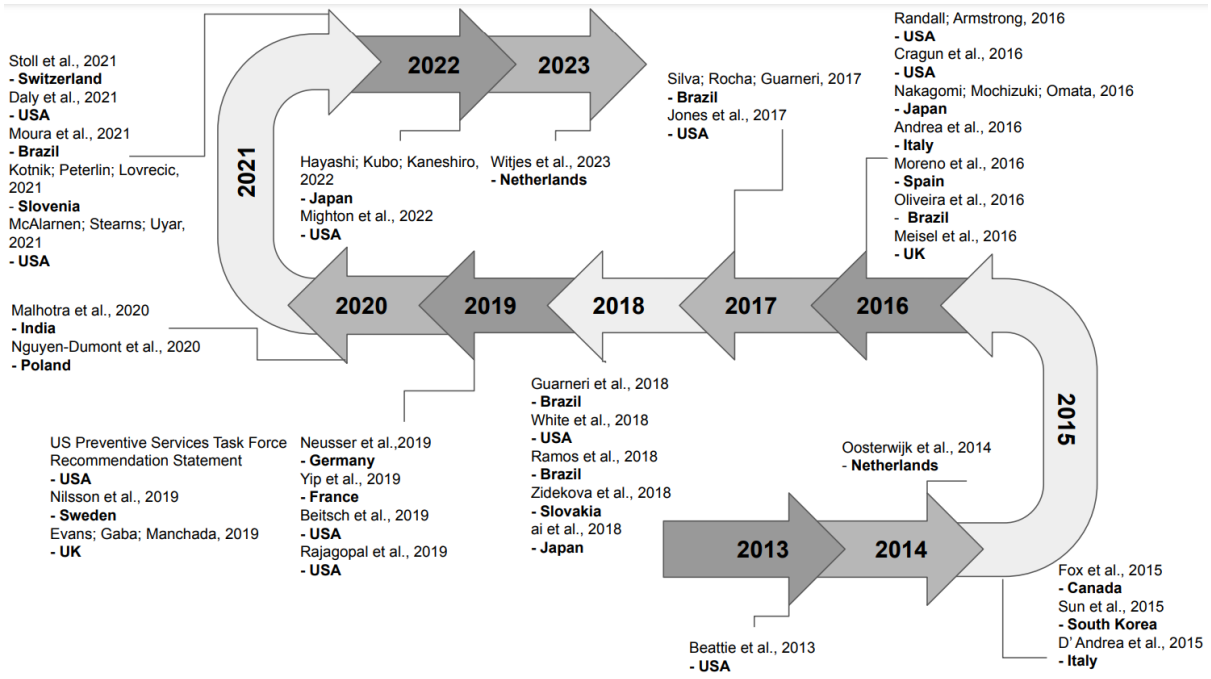

Figure 2. Timeline showing the distribution of global studies included in the final study.
Source: The authors.

While this study has significantly contributed to the understanding of the topic at hand, it is important to acknowledge its limitations. These limitations should be considered when interpreting the results and extrapolating the conclusions to broader contexts. One of the main limitations of this study is the possibility of selection bias. Due to the established inclusion and exclusion criteria, certain specific population groups may have been underrepresented or overrepresented in the sample, affecting the generalization of the results to the entire target population.

Furthermore, the exclusion of certain subgroups may have influenced the internal validity of the study. As a means of minimizing this bias, not only articles manually found by the authors were considered; all articles containing the selected keywords were downloaded and analyzed in some way. In addition, there are also reporting biases as the studies included in the review may not report all relevant results or outcomes, especially if the results are negative or not statistically significant. To reduce this issue, all articles were analyzed and systematized based on the same topics, allowing for a comprehensive analysis of all pre-selected articles.

Since it is a literature review, it was not necessary to request approval from the Research Ethics Committee. The research conducted ensures transparency and integrity by affirming the absence of conflicts of interest. Through meticulous adherence to ethical guidelines and disclosure practices, the study maintains a rigorous standard of impartiality.

This commitment to objectivity fosters trust and confidence in the findings, reinforcing the credibility of the research outcomes. The work in question is an eloquent example of an initiative devoid of financial motivation or material gains.

The thematic analysis of them allowed the identification of three main categories of results: (1) availability and accessibility of genetic tests, (2) criteria for conducting and the impact of the results on medical conduct, and superficially, (3) cost-benefit for health systems around the world

RESULTS

Among the 36 articles selected from the databases, more than 18 nationalities were identified, demonstrating that the results reflect the reality experienced around the world. However, more than one-third were conducted or targeted towards the U.S. population. This can be explained not only by the familiarity of U.S. researchers with the topic but also by the greater availability of academic resources, research funding, and the country's centrality (Table 1).

Overall, there was a noticeable similarity in the number of publications over the years, indicating that the topic has not lost research relevance over time, despite the large number of works already published.

N.	TITLE	CITATION	COUNTRY	OBJECTIVE
1	Update Swiss guideline for counseling and testing for predisposition to breast, ovarian, pancreatic and prostate cancer	Stoll et al., 2021	**Switzerland**	Literature review aiming to update recommendations for genetic testing in individuals at high risk for developing cancer
2	USPSTF recommendations for BRCA1 and BRCA2 testing in the context of a Transformative National Cancer Control Plan	Rajagopal et al.,2019	**USA**	USPSTF describes new recommendations for risk management, counseling, and genetic testing for the BRCA1 and BRCA2 genes
3	The sooner the better: Genetic testing following ovarian cancer diagnosis	Fox et al., 2015	**Canada**	Understand at what point during treatment for serous ovarian cancer patients opt for genetic testing, and the factors influencing this decision
4	The most efficient and effective BRCA1/2 testing strategy in epitelial ovarian cancer: Tumor-First or Germline-First?	Witjes et al., 2023	**Netherlands**	An analytical model comparing two testing strategies for BRCA1 and BRCA2 in ovarian cancer patients: I) Using tumor DNA as a test preceding genetic testing. II) Genetic testing prior to tumor DNA testing
5	Participation of Korean families at high risk for HBOC in BRCA1/2 genetic testing	Sun et al., 2015	**South Korea**	Determine adherence to BRCA genetic testing for high-risk breast cancer patients; Also highlight reasons why some individuals do not participate in testing despite having indications
6	The budgetary impact of genetic testing for hereditary breast cancer for the statutory health insurance	Neusser et al., 2019	**Germany**	Perform an analytical model to verify the economic impact of BRCA and other gene testing in high-risk individuals within the German health system
7	Genetic and clinical characteristics in JapaneseHBOC: first report after establishment of HBOC registration system in Japan	Arai et al., 2017	**Japan**	Analyze the data registration system for BRCA1 and BRCA2 testing on an electronic platform and “Japanese HBOC Consortium” (JHC) system
8	Genetic and demographicfactors of a brazilian population sample at-risk of HBOC	Guarneri et al., 2018	**Brazil**	Survey the genetic and sociodemographic characteristics of patients considered high risk for developing HBOC
9	Genetic medicine is acceleratingin Japan	Hayashi; Kubo; Kaneshiro, 2022	**Japan**	A multi-site phase III study to compare the safety and effectiveness of Olaparib as adjuvant therapy for patients at high risk for developing BRCA-related breast cancer and for HER2 negative patients who are on neoadjuvant chemotherapy
10	Genetic counseling, cancer screening, breast cancer characteristics, and generalhealth among a diverse population of BRCA genetic testers	Beattie et al., 2013	**USA**	Compare the socio-demographic characteristics of patients undergoing BRCA testing, genetic follow-up, diagnosis, and cancer treatment at two different hospitals, one public and one university-based
11	Genetic counseling, testing, and management of HBOC in India: An expert consensus document from Indian Society of Medical and Pediatric Oncology	Malhotra et al., 2020	**India**	Create recommendations for HBOC genetic testing in India based on existing guidelines from other countries
12	Genetic testing and familial implications in breast–ovarian cancer families	Oosterwijk et al., 2014	**Netherlands**	Indications and implications of the genetic testing process in index patients and their relatives
13	Genetic testing and personalized ovarian cancer screening: a survey of public attitudes	Meisel et al., 2017	**UK**	Identify personal and demographic predictors influencing decisions for genetic testing and risk stratification screening for developing ovarian cancer in women in the United Kingdom

14	Genetic testing for hereditary breast cancer: The decision to decline	White et al., 2018	**USA**	Explore how socio-demographic characteristics influence patients' decisions to adhere to BRCA1 and BRCA2 genetic testing
15	Genetic testing in Poland and Ukraine: should comprehensive germline testing of BRCA1 and BRCA2 be recommended for women with breast and ovarian cancer?	Nguyen-Dumont etal., 2020	**Poland**	Assess the characteristics of pathogenic BRCA1 and BRCA2 mutations in Polish and Ukrainian women diagnosed with breast or ovarian cancer
16	Genetic/Familial high-risk asesssment: breast, ovarian,and pancreatic, Version 2.2021	Daly et al., 2021	**USA**	Evaluate the risk for developing breast cancer and provide a practical guideline for managing patients with variants in the BRCA1 and BRCA2 genes
17	Germline BRCA testing is moving from cancer risk assessment to a predictivebiomarker for targeting cancer therapeutics	Moreno et al., 2015	**Spain**	Review new technologies related to BRCA1 and BRCA2 testing for HBOC and their new clinical implications
18	Global disparities in breast cancer genetics testing, counseling and management	Yip et al., 2019	**France**	Transcript of a workshop held in Switzerland in August 2017 focusing on the genetics of breast cancer around the world
19	Health care disparities inhereditary ovarian cancer: are we reaching the underserved population?	Randall; Armstrong,2016	**USA**	Highlight the disparities found in BRCA1 and BRCA2 gene testing and the clinical implications that result from them
20	HBOC screening syndrome profile in women diagnosed withbreast cancer from paraná state southwest	Moura et al., 2021	**Brazil**	Assess the risk of HBOC in breast cancer patients using the Familial History Screening 7 (FHS-7) tool
21	Hereditary cancer: example of a public health approach to ensure population health benefits of genetic medicine	Cragun et al., 2016	**USA**	Emphasize the identification, prevention, and treatment of hereditary cancer as a significant public health concern
22	Written pretest information and germline BRCA1/2 pathogenic variant testing in unselected breast cancer patients: predictors of testing uptake	Nilsson et al., 2018	**Sweden**	Evaluate the predictors of testing among breast cancer patients who underwent germline BRCA1 and BRCA2 testing
23	Willingness of japanese patients with breast cancer to have genetic testing of BRCA without burden of expenses	Nakagomi; Mochizuki; Omata,2015	**Japan**	Gather data on acceptance and participation in genetic testing in less urban areas outside of Tokyo
24	Which BRCA genetic testing programs are ready for implementation in health care? A systematic review of economic Evaluations	Andrea et al., 2016	**Italy**	Identify the main BRCA1 and BRCA2 testing strategies and their respective cost-benefits
25	Validation of NCCN criteria for genetic testing in HBOC syndrome in Brazil	Silva; Rocha; Guarneri, 2017	**Brazil**	Identify in the Brazilian population the relevant variables that meet the NCCN testing criteria and identify in the studied population the genetic mutations and their frequency
26	Underdiagnosis of hereditary breast cancer: are genetic testing guidelines a tool or an obstacle?	Beitsch et al., 2019	**USA**	Determine if there is a difference in the incidence of actionable variants between patients who met the 2017 NCCN testing guidelines and those who did not

27	Screening of the BRCA1 gene in brazilian patients with breast and/or ovarian cancer via high-resolution melting reactionanalysis	Oliveira et al., 2015	**Brazil**	Evaluate the mutation profile in the BRCA1 gene among Brazilian women affected by cancer with defined risk factors for hereditary breast and ovarian cancer (HBOC) in the Midwest region of Minas Gerais
28	Risk assessment, genetic counseling, and genetic testingfor BRCA-related cancer	US Preventive Services Task Force Recommendation Statement	**USA**	Update the recommendation of the US Preventive Services Task Force (USPSTF) from 2013 on risk assessment, genetic counseling, and genetic testing for BRCA-related cancer
29	Rapid screening test of most frequent BRCA1/BRCA2 pathogenic variants in the ngs era	Zidekova et al., 2017	**Slovakia**	Describe a rapid and comprehensive approach to the detection of the most common pathogenic mutations in BRCA1 and BRCA2 in the population affected by HBOC
30	Population-based genetic testing for women's cancer prevention	Evans; Gaba; Manchada, 2020	**UK**	Review population-based genetic testing (differences between PBGT and FHM tests)
31	Predictors of BRCA1/2 genetic testing among black women with breast cancer: a population- based study	Jones et al., 2017	**USA**	Identify the predictors of BRCA testing among Black women treated for breast cancer and examine the differences between those who were previously tested for BRCA and not tested
32	Identification of women at risk for HBOC in a sample of 1000 slovenian women: a comparison of guidelines	Kotnik; Peterlin; Lovrecic, 2021	**Slovenia**	Compare guidelines from three organizations: NCCN, ACMG/NSGC, and SGO
33	Genetic testing and economic Evaluations: a systematic reviewof the literature	Andrea et al., 2015	**Italy**	Evaluate the cost-effectiveness of genetic testing
34	Cost effectiveness of the cancer prevention program for carriers of the BRCA1/2 mutation	Ramos et al., 2018	**Brazil**	Analyze the cost-effectiveness relationship of the diagnosis program for the germline mutation in the BRCA1/2 genes and preventive strategies for relatives of patients diagnosed with ovarian cancer associated with this mutation
35	Challenges of genomic testing for HBOC	McAlarnen; Stearns; Uyar, 2021	**USA**	Examine the issues arising from the use of germline genetic testing for HBOC
36	From the patient to the population: use of genomics for population screening	Mighton et al., 2022	**USA**	Identify inclusion criteria for screening tests and their characteristics

Table 1. Tabulation of Selected Articles Included in the final paper.
Source: The authors.
USPSTF: United States Preventive Services Task Force; NCCN: National Comprehensive Cancer Network; ACMG/NSGC: American College of Medical Genetics in cooperation with the National Society of Genetic Counselors; SGO: Society of Gynecologic Oncology; HBOC: Hereditary Breast and Ovarian Cancer.

AVAILABILITY AND ACCESSIBILITY OF GENETIC TESTS

Genetic testing, like other screenings, has various factors that influence its proper execution. A study was conducted in the United Kingdom to identify personal predictors of women in the country regarding HBOC testing and concluded that over 65% of the interviewees agreed with genetic testing, with the vast majority having completed higher education, thus correlating adherence to testing with education level[23].

Corroborate these, about the country and add that psychological aspects are also predictors of testing, thus suggesting that delaying the procedure to seek more information about it may increase the cost-effectiveness of testing[24]. Moreover, in a study in South Korea agree with this finding, identifying that personalized care reduces anxiety about the test and increases patient adherence[25].

Beyond the academic aspect, various studies have identified ethnic disparities in decision-making and timing of the test: ethnically diverse women are less likely to undergo testing compared to white women, even with similar risks[26–28].

This premise is supported by a North American study highlighting a significant disparity in the diagnosis and follow-up care for HBOC syndrome between African-descendant and white women. Although the prevalence of BRCA1/2 mutations is similar or potentially higher in African-descendant women, studies reveal that only one in seven women in this group with BRCA1/2 mutations meeting testing criteria undergo testing. Furthermore, African-descendant women are less likely to access BRCA1/2 testing, receive genetic counseling, and adhere to recommended treatments[29].

A comparative study between two North American hospitals—one public and one university-based—reaffirmed differences in the profile of tested patients, which led to variations in post-test counseling. In contrast, a Canadian study did not identify a relationship with age, ethnicity, or education[30,31].

The predominance of studies indicates social disparities in testing. In a Swedish study, support this premise that adherence to testing varies among different subgroups according to factors related to the patient, which helps health professionals identify those less likely to undergo genetic testing[32].

However, this also raises concerns about whether health professionals are adequately trained, as were noted in Japan that even though the service is free, the counseling system could not meet demand and might be insufficient to persuade the high-risk population to undergo genetic testing[33].

The number of trained professionals is very limited; in the United States there are only 700 specialized health professionals. In Switzerland, psychological counseling is mandatory before and after testing, so health insurance plans only cover the cost of testing after counseling[27,34,35].

SOCIODEMOGRAPHIC DESCRIPTIONS AND THE REPERCUSSIONS ON MEDICAL PRACTICE (TESTING AND CONDUCT)

The lack of awareness, misinformation, understanding of risk, equitable access to specialized care, resources, and costs are factors that contribute to inequality in access to testing, its benefits, access to information, treatment, and genetic counseling[27–29].

In France, a well-developed European country, genetic services are advanced in richer countries while scarce in developing/emerging countries. The authors also discussed the GenTEE project, which aims to identify the current knowledge gap in emerging countries (Argentina, Brazil, China, Egypt, India, Oman, Philippines, and South Africa) and promote international collaboration to increase preparedness and knowledge among professionals in the field of cancer genetics[36].

In a north-american study, was proposed involving and educating non-geneticist physicians and/or oncologists to ensure that patients have access to competent genomic services. The interpretation of results is complex and typically requires post-test genetic counseling for the family carrying the mutation, allowing for risk quantification and management options[37,38].

Care must be taken to avoid biases in research, data analysis, and interpretation of these results, minimizing mutations of undetermined clinical relevance because if there are deficiencies in the process, they can cause unnecessary concerns and uncertainties for families[39–41].

The United States Preventive Services Task Force (USPSTF) recommends that primary care physicians assess women with a personal or family history of breast, ovarian, tubal, or peritoneal cancer or who have ancestry associated with mutations in BRCA1 and BRCA2 with a brief appropriate tool for family risk assessment. Routine risk assessment, genetic counseling, or genetic testing is not recommended for women whose history or ancestry does not suggest potentially harmful diseases[42].

The screening recommendations of the National Comprehensive Cancer Network (NCCN) are based on performing self-exams of the breasts beginning at age 18 and having a clinical breast exam every 6 to 12 months beginning at age 25. Between 25 and 29 years, an annual MRI is recommended, and post-testing follow-up is also recommended for those with a confirmed pathogenic or possibly pathogenic variant, to begin the validation of preventative consultation[43].

Conversely, in a study in the USA, 49.95% of women met the NCCN criteria, and 50.05% did not—a statistically insignificant difference, indicating that even though the criteria have high validity, they do not apply to all populations in the same way[44]. So, the NCCN criteria were a poor predictor of deleterious mutation in the BRCA1 and BRCA2 genes[45].

Thus, countries globally should analyze the specific variables of their resident populations to standardize genetic assessment by adapting guidelines for each health system. According to a swiss study, established that individuals under 18 years of age and tumors with low malignancy should not undergo genetic testing. However, relatives of a cancer patient who has not been tested, high-risk individuals, or those who already have a risk factor for the syndrome should be tested. Specifically for Ashkenazi Jews, it was defined that specific mutations in BRCA1 (BRCA1: c.68_69delAG, c.5266dupC) and BRCA2 (BRCA2: c.5946delT) should be tested first before conducting a comprehensive test[35].

Similarly, a study developed in Brazil emphasizes the importance of identifying specific mutations of the region or country to optimize the testing process[46]. In contrast, analyzing Ukrainian and Polish women, identified greater benefits with massive sequencing of BRCA1 and BRCA2 compared to only analyzing the most prevalent mutations (founder mutations) as is done in other countries[47].

In India, was recommended testing every individual diagnosed with breast cancer before the age of 45, triple-negative breast cancer diagnosed before 60, ovarian cancer diagnosis, and men with breast cancer, in addition to adhering to the NCCN guidelines[48]. Meanwhile, in Italy, concluded it is not cost-effective to test all women with ovarian cancers[49].

In Slovenia, a similar method was applied, comparing the NCCN and NSGC (National Society of Genetic Counselors) guidelines to identify which best applies to the Slovenian population. As a conclusion, the NCCN criteria identified a larger at-risk population, thus being deemed the most appropriate guideline[50].

A similar application occurred in Japan using an electronic registration system (Japanese HBOC Consortium). One of the merits of this system is that individuals who tested for a mutation in BRCA1 and BRCA2 are eligible for annual follow-ups and updates, allowing the analysis of patient data and new data on HBOC that may be relevant in clinical practice[51].

In 2014, in the Netherlands, it was found that triple-negative breast cancer is more closely related to BRCA1, and this alone is enough to indicate testing. Furthermore, the detection of an undetermined mutation requires additional molecular testing to interpret and categorize it according to its possible pathogenicity. Until pathogenicity is confirmed, the diagnosis of hereditary breast/ovarian

cancer is not confirmed. Furthermore, there are no recommendations for testing family members in this case[52].

A study in Italy observed that programs based on family history are considered promising. Until then, only risk-cascading screenings were applied in the country due to a lack of knowledge about the costs of other testing models[53]. Because of genetic heterogeneity, in the last 30 years, various pathogenic variations related to HBOC beyond the well-known ones in BRCA1 and BRCA2, such as variants in BARD1, RAD51C, RAD51D, ATM, PALB, CDH1, CHEK2, PTEN, and TP53, have been found[54–57].

A study conducted in Italy compared two types of multigene panels, one with 12 genes and another with 48 genes and portions of DNA that are not exons, both identified pathogenic variations in various genes such as TP53, ATM, CHEK2, and BARD1[39].

In addition to these, a research developed in France identified cancer-susceptible genes: BRIP1, CDH1, MLH1, MSH2, MSH6, PALB2, PSM2, RAD51C, and STK11[40]. These studies suggest that with the application of multigene panels, there is greater identification of individuals who have mutations that would go unnoticed in traditional testing, thus favoring genetic counseling and follow-up.

COST-BENEFIT FOR HEALTH SYSTEMS AROUND THE WORLD

Besides the testing parameters, even though in the last decade the tests have been democratized, research in the United States and the United Kingdom shows that high costs remain a barrier to the execution of HBOC genetic tests[24,27].

To address the high costs, a Brazilian study suggested using high-resolution melting (HRM) to increase the screening of unknown mutations, thus reducing the gene sequencing of BRCA1 and BRCA2 aimed at lowering the test cost[58]. Furthermore, in other study, was applied the Historical Screening Questionnaire 7 (FHS-7), a simple, low-cost, sensitive, and easily applicable instrument in Primary Health Care (PHC) to identify high-risk individuals for HBOC[59].

In the Netherlands, a study evaluated the “Tumor first strategy,” which is a pre-screening test of tumor DNA (lower cost) followed by germline testing only of those who meet the criteria[60]. In Slovakia, it was proposed to apply simple, fast, low-cost screening tests sensitive enough to identify individuals in the population with an increased lifetime risk of developing cancer, with only those with negative results undergoing complex exams to analyze BRCA1 and BRCA2 to identify less common mutations in the population[61].

As an alternative to reducing or waiving costs, some countries already have certain tests available, and others are conducting studies to assess the feasibility of implementing the test in health consortia. An example of this is Japan, which already includes BRCA testing in the national health plan for eligible individuals[62].

A german study, demonstrated the application of the “German consortium for HBOC” in Germany, which aims to manage, counsel, and treat women at high risk for developing breast/ovarian cancer. However, they observed that the increase in testing leads to the identification of mutations and a larger volume of people needing follow-up, and even though there is a decrease in the costs of cancer treatment, the increase in cost related to testing and follow-up outweighed this cheapening[63].

Raising such a question is valid to cite a study previously developed in Spain which suggests that age should be better directed to perform testing based on previous diagnoses to facilitate the reallocation of health system resources and improve the follow-up of individuals[64].

Meanwhile, in Brazil, a study identified the opposite. The cost per case of cancer prevented with post-test positive preventive strategies was lower than the values normally spent on cancer treatment, suggesting cost-effectiveness in testing all those who meet the risk criteria[65].

Besides testing for specific populations, population-wide genetic testing has been speculated as a way to significantly improve health outcomes. Studies focusing on the United Kingdom and the USA, identified that despite logistical challenges, this method would enhance the detection of individuals with pathogenic variants compared to traditional approaches and would be more cost-effective[66,67]. It is worth noting that in developing countries, the effectiveness of such measures depends on the type of test applied.

After an initial diagnosis, patients with BRCA1/2 mutation who are candidates for breast conservation receive conservative breast with a guarantee of adjuvant therapy. Consideration may also be given to contralateral prophylactic mastectomy for breast cancer with BRCA1/2 mutations; if performed, immediate breast reconstruction is recommended[68].

Advances in identifying genetic predispositions to cancer, such as Hereditary Breast and Ovarian Cancer Syndrome (HBOC), have significant implications for public health. This study, by exploring demographic, socioeconomic, and cultural variables related to the application of genetic tests, provides valuable insights for the development of public policies and health strategies that promote equity and efficiency in the early diagnosis of hereditary conditions.

SYSTEMATIZATION

The presented work is essential for understanding and systematizing the variables that impact adherence to, implementation of, and benefits derived from genetic testing for Hereditary Breast and Ovarian Cancer Syndrome (HBOC).

Through a comprehensive analysis of studies conducted globally, it emphasizes the importance of considering demographic, economic, and cultural aspects in the application and accessibility of these tests, while also proposing guidelines adapted to diverse realities.

The standardization of regional protocols can serve as a powerful tool to guide governments in the efficient allocation of resources and to expand access to genetic testing, especially in developing countries, with the potential to reduce inequalities and enhance early detection.

Additionally, the inclusion of historically underrepresented populations in genetic studies, such as women from minority ethnic groups, is crucial to ensuring that the benefits of testing are distributed equitably.

The analyses and interpretation, duly supported by the data, concepts, and information presented in the development, should be inserted here. This is the section in which the results achieved in the research must be made explicit. Verification and comparison with the state of the art of the theoretical framework may also be carried out.

CONCLUSION

Genetic predisposition tests for HBOC Syndrome have predictors that influence both adherence and the outcome of these tests. Among the socioeconomic, the present study identified education, psychological aspects, access to information, ethnic disparities, and the level of country development.

Among healthcare professionals, issues such as inadequate training, numerical incompatibility, and limited availability were noted. The availability and accessibility of genetic tests for detecting HBOC-related mutations varied considerably between the analyzed countries. Despite international guidelines for widespread dissemination, different countries adapted or formulated protocols that better suit their populations.

In developed countries like the United States and Canada, genetic tests are widely available and accessible in both the public and private sectors, facilitating early detection and improved patient management. Conversely, in Brazil, these tests are primarily confined to the private sector and are not widely accessible to the general population because of the high costs.

The feasibility of genetic testing for HBOC is influenced by factors such as cost, accessibility, and healthcare infrastructure. Strategies like low-cost screening tools, government subsidies, and inclusion in national health plans can improve access, but proper training for healthcare professionals is essential for effective implementation.

Sociodemographic factors, including education, income, ethnicity, and cultural perceptions, significantly impact testing uptake. Higher education and income levels often correlate with greater acceptance, while underserved populations face barriers like limited access and cultural stigma. Addressing these disparities requires culturally sensitive outreach and public health initiatives to ensure equitable access.

The impact of the results of genetic tests on medical practice is significant in all the countries analyzed. In countries where genetic tests are widely available, the results are used to guide the clinical management of patients, including conducting additional screening tests and recommending preventive measures.

In Brazil, however, the lack of access to genetic tests means many patients do not receive appropriate genetic counseling and are not referred to cancer prevention and early detection programs. Therefore, the results of this study support the premise that including genetic predisposition testing for HBOC syndrome in SUS is both feasible and beneficial for the Brazilian population, thereby suggesting further research for a more in-depth evaluation.

Finally, genetic testing for HBOC transcends the individual dimension, directly impacting public health by providing tools for disease prevention, reducing inequalities, and promoting equity. Studies like this highlight the importance of multidimensional strategies that combine science, policy, and cultural practices to expand the benefits of this technology, contributing to more inclusive and sustainable healthcare systems.

REFERENCES

1. Macleod K. Tumor suppressor genes. Curr Opin Genet Dev. 1º de fevereiro de 2000;10(1):81–93. https://doi.org/10.1016/S0959-437X(99)00041-6
2. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. novembro de 2018;68(6):394–424. https://doi.org/10.3322/caac.21492
3. Câncer - OPAS/OMS | Organização Pan-Americana da Saúde [Internet]. 2024 [citado 18 de novembro de 2024]. Disponível em: https://www.paho.org/pt/topicos/cancer
4. Cancer Tomorrow [Internet]. [citado 25 de novembro de 2024]. Disponível em: https://gco.iarc.who.int/today/
5. Siegel RL, Giaquinto AN, Jemal A. Cancer statistics, 2024. CA Cancer J Clin. 2024;74(1):12–49. https://doi.org/10.3322/caac.21820

6. Instituto Nacional de Câncer - INCA [Internet]. [citado 18 de novembro de 2024]. Estatísticas de câncer. Disponível em: https://www.gov.br/inca/pt-br/assuntos/cancer/numeros/estatisticas-de-cancer
7. Câncer de mama agora forma mais comum de câncer: OMS tomando medidas [Internet]. [citado 25 de novembro de 2024]. Disponível em: https://www.who.int/pt/news/item/03-02-2021-breast-cancer-now-most-common-form-of-cancer-who-taking-action
8. Teixeira LA, Araújo Neto LA. Câncer de mama no Brasil: medicina e saúde pública no século XX. Saúde E Soc. 2020;29(3):e180753. https://doi.org/10.1590/S0104-12902020180753
9. Rosenthal TC, Puck SM. Screening for Genetic Risk of Breast Cancer. Am Fam Physician. 1º de janeiro de 1999;59(1):99.
10. Amendola LCB, Vieira R. A contribuição dos genes BRCA na predisposição hereditária ao câncer de mama. Rev Bras Cancerol. 30 de dezembro de 2005;51(4):325–30. https://doi.org/10.32635/2176-9745.RBC.2005v51n4.1927
11. Pereira TL, Lima EV, Cardoso PB, Destro LRS, Mattos Z. MUTAÇÃO NOS GENES BRCA 1 E 2 E OS RISCOS PARA CÂNCER DE MAMA. 2019;2(2).
12. Marmolejo DH, Wong MYZ, Bajalica-Lagercrantz S, Tischkowitz M, Balmaña J, Patócs AB, et al. Overview of hereditary breast and ovarian cancer (HBOC) guidelines across Europe. Eur J Med Genet. dezembro de 2021;64(12):104350. https://doi.org/10.1016/j.ejmg.2021.104350
13. Pantoja REDL, Monteiro MCC, Nascimento BDS, Mota DAD, Balla IL, Rocha IMD, et al. A aplicação do mapeamento genético na identificação dos polimorfismos do câncer de mama e o direcionamento da terapia alvo. Res Soc Dev. 7 de agosto de 2022;11(10):e450111032762.
14. Sousa MC, Santos E Silva LD, Sousa CC. Diagnóstico de câncer de mama por exames genéticos: uma revisão de literatura. Braz J Health Rev. 2020;3(2):1786–97.
15. El Ansari FZ, Jouali F, Marchoudi N, Bennani MM, Ghailani NN, Barakat A, et al. Screening of BRCA1/2 genes mutations and copy number variations in patients with high risk for hereditary breast and ovarian cancer syndrome (HBOC). BMC Cancer. dezembro de 2020;20(1):747.
16. Narod SA. Screening for BRCA1 and BRCA2 mutations in breast cancer patients from mexico: the public health perspective. Salud Pública México. 2009;51:s191–6.
17. Buys SS, Sandbach JF, Gammon A, Patel G, Kidd J, Brown KL, et al. A study of over 35,000 women with breast cancer tested with a 25-gene panel of hereditary cancer genes. Cancer. 15 de maio de 2017;123(10):1721–30. https://doi.org/10.1002/cncr.30498
18. Graffeo R, Livraghi L, Pagani O, Goldhirsch A, Partridge AH, Garber JE. Time to incorporate germline multigene panel testing into breast and ovarian cancer patient care. Breast Cancer Res Treat. dezembro de 2016;160(3):393–410.
19. Achatz MI, Caleffi M, Guindalini R, Marques RM, Nogueira-Rodrigues A, Ashton-Prolla P. Recommendations for Advancing the Diagnosis and Management of Hereditary Breast and Ovarian Cancer in Brazil. JCO Glob Oncol. novembro de 2020;(6):439–52. https://doi.org/10.1200/JGO.19.00170
20. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. The BMJ. 29 de março de 2021;372:n71.
21. Cassundé FR de SA, Barbosa MAC, Mendonça JRC. Entre revisões sistemáticas e bibliometrias: como tem sido mapeada a produção acadêmica em Administração no Brasil? Informação Informação. 17 de dezembro de 2018;23(1):311–34. https://doi.org/10.5433/1981-8920.2018v23n1p311
22. Braun V, Clarke V. Using thematic analysis in psychology. Qual Res Psychol. janeiro de 2006;3(2):77–101.
23. Meisel SF, Rahman B, Side L, Fraser L, Gessler S, et al. Genetic testing and personalized ovarian cancer screening: a survey of public attitudes. BMC Womens Health. dezembro de 2016;16(1):46.

24. White VB, Amacker-North L. Genetic Testing for Hereditary Breast Cancer: The Decision to Decline. *The American Surgeon™*. 2018;84(1):154-160. https://doi.org/10.1177/000313481808400139
25. Sun Y, Kang E, Baek H, Jung J, Hwang E, Koo J, et al. Participation of Korean families at high risk for hereditary breast and ovarian cancer in BRCA1/2 genetic testing. Jpn J Clin Oncol. 2 de abril de 2015. https://doi.org/10.1093/jjco/hyv044
26. Jones T, McCarthy AM, Kim Y, Armstrong K. Predictors of *BRCA 1/2* genetic testing among Black women with breast cancer: a population-based study. Cancer Med. julho de 2017;6(7):1787–98. https://doi.org/10.1002/cam4.1120
27. Rajagopal PS, Nielsen S, Olopade OI. USPSTF Recommendations for *BRCA1* and *BRCA2* Testing in the Context of a Transformative National Cancer Control Plan. JAMA Netw Open. 20 de agosto de 2019;2(8):e1910142. 10.1001/jamannetworkopen.2019.10142
28. McAlarnen L, Stearns K, Uyar D. Challenges of Genomic Testing for Hereditary Breast and Ovarian Cancers. Appl Clin Genet. janeiro de 2021;14:1–9. https://doi.org/10.2147/TACG.S245021
29. Randall TC, Armstrong K. Health Care Disparities in Hereditary Ovarian Cancer: Are We Reaching the Underserved Population? Curr Treat Options Oncol. agosto de 2016;17(8):39. https://doi.org/10.1007/s11864-016-0417-1
30. Beattie MS, Copeland K, Fehniger J, Cheung E, Joseph G, Lee R, et al. Genetic Counseling, Cancer Screening, Breast Cancer Characteristics, and General Health among a Diverse Population of BRCA Genetic Testers. J Health Care Poor Underserved. agosto de 2013;24(3):1150–66. https://doi.org/10.1353/hpu.2013.0151
31. Fox E, McCuaig J, Demsky R, Shuman C, Chitayat D, Maganti M, et al. The sooner the better: Genetic testing following ovarian cancer diagnosis. Gynecol Oncol. junho de 2015;137(3):423–9. https://doi.org/10.1016/j.ygyno.2015.03.057
32. Nilsson MP, Nilsson ED, Silfverberg B, Borg Å, Loman N. Written pretest information and germline BRCA1/2 pathogenic variant testing in unselected breast cancer patients: predictors of testing uptake. Genet Med. janeiro de 2019;21(1):89–96. https://doi.org/10.1038/s41436-018-0021-9
33. Nakagomi H, Sakamoto I, Hirotsu Y, Amemiya K, Mochizuki H, Inoue M, et al. Willingness of Japanese patients with breast cancer to have genetic testing of BRCA without burden of expenses. Breast Cancer. julho de 2016;23(4):649–53. https://doi.org/10.1007/s12282-015-0618-7
34. Nelson HD, Pappas M, Cantor A, Haney E, Holmes R. Risk Assessment, Genetic Counseling, and Genetic Testing for *BRCA*- Related Cancer in Women: Updated Evidence Report and Systematic Review for the US Preventive Services Task Force. JAMA. 20 de agosto de 2019;322(7):666.
35. Stoll S, Unger S, Azzarello-Burri S, Chappuis P, Graffeo R, Pichert G, et al. Update Swiss guideline for counselling and testing for predisposition to breast, ovarian, pancreatic and prostate cancer. Swiss Med Wkly. 13 de setembro de 2021;151(3738):w30038. https://doi.org/10.4414/SMW.2021.w30038
36. Yip CH, Evans DG, Agarwal G, Buccimazza I, Kwong A, Morant R, et al. Global Disparities in Breast Cancer Genetics Testing, Counselling and Management. World J Surg. 15 de maio de 2019;43(5):1264–70. https://doi.org/10.1007/s00268-018-04897-6
37. Cragun D, Lewis C, Camperlengo L, Pal T. Hereditary Cancer: Example of a Public Health Approach to Ensure Population Health Benefits of Genetic Medicine. Healthcare. 8 de janeiro de 2016;4(1):6. https://doi.org/10.3390/healthcare4010006
38. Sullcahuaman Allende YC, Loarte Villarreal M, Torres Loarte M. Cáncer ginecológico hereditario en la era de la medicina genómica. Rev Peru Ginecol Obstet. 28 de setembro de 2018;64(3):461–8. http://dx.doi.org/https://doi.org/10.31403/rpgo.v64i2112
39. Eliade M, Skrzypski J, Baurand A, Jacquot C, Bertolone G, Loustalot C, et al. The transfer of multigene panel testing for hereditary breast and ovarian cancer to healthcare: What are the

implications for the management of patients and families? Oncotarget. outubro de 2016;8:1957-1971. https://doi.org/10.18632/oncotarget.12699

40. Nunziato M, Scaglione GL, Di Maggio F, Nardelli C, Capoluongo E, Salvatore F. The performance of multi-gene panels for breast/ovarian cancer predisposition. Clin Chim Acta. janeiro de 2023;539:151–61. https://doi.org/10.1016/j.cca.2022.12.007
41. Thompson ER, Rowley SM, Li N, McInerny S, Devereux L, Wong-Brown MW, et al. Panel Testing for Familial Breast Cancer: Calibrating the Tension Between Research and Clinical Care. J Clin Oncol. 1º de maio de 2016;34(13):1455–9. https://doi.org/10.1200/JCO.2015.63.7454
42. US Preventive Services Task Force, Owens DK, Davidson KW, Krist AH, Barry MJ, Cabana M, et al. Risk Assessment, Genetic Counseling, and Genetic Testing for *BRCA* -Related Cancer: US Preventive Services Task Force Recommendation Statement. JAMA. 20 de agosto de 2019;322(7):652.
43. Daly MB, Pal T, Berry MP, Buys SS, Dickson P, Domchek SM, et al. Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic, Version 2.2021, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw. 6 de janeiro de 2021;19(1):77–102. https://doi.org/10.6004/jnccn.2021.0001
44. Beitsch PD, Whitworth PW, Hughes K, Patel R, Rosen B, Compagnoni G, et al. Underdiagnosis of Hereditary Breast Cancer: Are Genetic Testing Guidelines a Tool or an Obstacle? J Clin Oncol. 20 de fevereiro de 2019;37(6):453–60. https://doi.org/10.1200/JCO.18.01631
45. Silva AVD, Rocha JCCD, Hospital Erasto Gaertner, Pontifícia Universidade Católica do Paraná, Guarneri GO, et al. Validation of NCCN criteria for genetic testing in HBOC syndrome in Brazil. Mastology. dezembro de 2017;27(4):271–5.
46. Hospital Erasto Gaertner, Guarneri GO, Ponte BJ, Hospital Erasto Gaertner, Ferreira JHF, Hospital Erasto Gaertner, et al. Genetic and demographic factors of a brazilian population sample at-risk of hereditary breast and ovarian cancer. Mastology. setembro de 2018;23(3):134–55.
47. Nguyen-Dumont T, Karpinski P, Sasiadek MM, Akopyan H, Steen JA, Theys D, et al. Genetic testing in Poland and Ukraine: should comprehensive germline testing of *BRCA1* and *BRCA2* be recommended for women with breast and ovarian cancer? Genet Res. 2020;102:e6.
48. Malhotra H, Kowtal P, Mehra N, Pramank R, Sarin R, Rajkumar T, et al. Genetic Counseling, Testing, and Management of HBOC in India: An Expert Consensus Document from Indian Society of Medical and Pediatric Oncology. JCO Glob Oncol. novembro de 2020;(6):991–1008. https://doi.org/10.1200/JGO.19.00381
49. D'Andrea E, Marzuillo C, De Vito C, Di Marco M, Pitini E, Vacchio MR, et al. Which BRCA genetic testing programs are ready for implementation in health care? A systematic review of economic evaluations. Genet Med. dezembro de 2016;18(12):1171–80.
50. Kotnik U, Peterlin B, Lovrecic L. Identification of women at risk for hereditary breast and ovarian cancer in a sample of 1000 Slovenian women: a comparison of guidelines. BMC Cancer. dezembro de 2021;21(1):665. https://doi.org/10.1186/s12885-021-08400-8
51. Arai M, Yokoyama S, Watanabe C, Yoshida R, Kita M, Okawa M, et al. Genetic and clinical characteristics in Japanese hereditary breast and ovarian cancer: first report after establishment of HBOC registration system in Japan. J Hum Genet. abril de 2018;63(4):447–57. https://doi.org/10.1038/s10038-017-0355-1
52. Oosterwijk JC, De Vries J, Mourits MJ, De Bock GH. Genetic testing and familial implications in breast-ovarian cancer families. Maturitas. agosto de 2014;78(4):252–7.
53. D'Andrea E, Marzuillo C, Pelone F, Vito CD, Villari P. Genetic testing and economic evaluations: a systematic review of the literature. Epidemiol Prev. 2015;
54. Aganezov S, Goodwin S, Sherman RM, Sedlazeck FJ, Arun G, Bhatia S, et al. Comprehensive analysis of structural variants in breast cancer genomes using single-molecule sequencing. Genome Res. setembro de 2020;30(9):1258–73. http://www.genome.org/cgi/doi/10.1101/gr.260497.119

55. Hu C, Hart SN, Gnanaolivu R, Huang H, Lee KY, Na J, et al. A Population-Based Study of Genes Previously Implicated in Breast Cancer. N Engl J Med. 4 de fevereiro de 2021;384(5):440–51.
56. Miki Y, Swensen J, Shattuck-Eidens D, Futreal PA, Harshman K, Tavtigian S, et al. A Strong Candidate for the Breast and Ovarian Cancer Susceptibility Gene *BRCA1*. Science. 7 de outubro de 1994;266(5182):66–71.
57. Sporikova Z, Koudelakova V, Trojanec R, Hajduch M. Genetic Markers in Triple-Negative Breast Cancer. Clin Breast Cancer. outubro de 2018;18(5):e841–50. 10.1016/j.clbc.2018.07.023
58. De Oliveira ES, Soares BL, Lemos S, Rosa RCA, Rodrigues AN, Barbosa LA, et al. Screening of the BRCA1 gene in Brazilian patients with breast and/or ovarian cancer via high-resolution melting reaction analysis. Fam Cancer. abril de 2016;15(2):173–81. 10.1007/s10689-015-9858-0
59. Moura JBD, Ghedin CC, Takakura ÉT, Scandolara TB, Rech D, Panis C. Hereditary Breast and Ovarian Cancer Screening Syndrome Profile in Women Diagnosed with Breast Cancer from Paraná State Southwest. Rev Bras Ginecol E Obstetrícia RBGO Gynecol Obstet. agosto de 2021;43(08):616–21. https://doi.org/10.1055/s-0041-1733998
60. Witjes VM, Ligtenberg MJL, Vos JR, Braspenning JCC, Ausems MGEM, Mourits MJE, et al. The most efficient and effective BRCA1/2 testing strategy in epithelial ovarian cancer: Tumor-First or Germline-First? Gynecol Oncol. julho de 2023;174:121–8. 10.1016/j.ygyno.2023.04.029
61. Zidekova D, Waczulikova I, Dolesova L, Vavrova L, Hamidova O, Lohajova Behulova R, et al. Rapid screening test of most frequent BRCA1/BRCA2 pathogenic variants in the NGS era. Neoplasma. 2018;65(02):309–15. 10.4149/neo_2018_170507N328
62. Hayashi S, Kubo M, Kaneshiro K, Kai M, Yamada M, Morisaki T, et al. Genetic medicine is accelerating in Japan. Breast Cancer. julho de 2022;29(4):659–65. 10.1007/s12282-022-01342-4
63. Neusser S, Lux B, Barth C, Pahmeier K, Rhiem K, Schmutzler R, et al. The budgetary impact of genetic testing for hereditary breast cancer for the statutory health insurance. Curr Med Res Opin. 2 de dezembro de 2019;35(12):2103–10. 10.1080/03007995.2019.1654689
64. Moreno L, Linossi C, Esteban I, Gadea N, Carrasco E, Bonache S, et al. Germline BRCA testing is moving from cancer risk assessment to a predictive biomarker for targeting cancer therapeutics. Clin Transl Oncol. outubro de 2016;18(10):981–7. 10.1007/s12094-015-1470-0
65. Ramos MCDA, Folgueira MAAK, Maistro S, Campolina AG, Soárez PCD, Bock GHD, et al. Cost effectiveness of the cancer prevention program for carriers of the BRCA1/2 mutation. Rev Saúde Pública. 22 de novembro de 2018;52:94. https://doi.org/10.11606/S1518-8787.2018052000643
66. Mighton C, Shickh S, Aguda V, Krishnapillai S, Adi-Wauran E, Bombard Y. From the patient to the population: Use of genomics for population screening. Front Genet. 24 de outubro de 2022;13:893832. https://doi.org/10.3389/fgene.2022.893832
67. Evans O, Gaba F, Manchanda R. Population-based genetic testing for Women's cancer prevention. Best Pract Res Clin Obstet Gynaecol. maio de 2020;65:139–53. https://doi.org/10.1016/j.bpobgyn.2020.02.007
68. Kwong A, Shin VY, Au CH, Law FBF, Ho DN, Ip BK, et al. Detection of Germline Mutation in Hereditary Breast and/or Ovarian Cancers by Next-Generation Sequencing on a Four-Gene Panel. J Mol Diagn. julho de 2016;18(4):580–94. 10.1016/j.jmoldx.2016.03.005