Factors Associated With the People Preferences for the Breast Cancer Genetic Tests: a Systematic Review

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Abstract

Background: Despite the genetic test's benefits in early detection of disease, many people do not have the test performed. This study aimed to systematically review the associated factors with a preference for the gene tests regarding breast cancer.

Methods: It was a systematic review study. Data were collected from Scopus, PubMed, Web of Science (WOS), ProQuest, and Embase databases. All full-text English language studies up to 2020 that addressed the preference for the gene screening tests for early detection of breast cancer were included. Data extracted and assessed for quality by two independent reviewers. Disagreements were resolved by a consensus meeting with a third reviewer. The vote counting was determined for identifying the associated factors with the preference.

Results: From 1269 initially retrieved citations, 25 studies were included. According to vote counting analysis, age was identified as strongly negative factor while being married, income, family history of breast cancer, personal history or presence of breast cancer, BRCA-related knowledge were identified as strongly positive factors with preference of genetic tests for breast cancer. About 96% of articles were in high quality.

Conclusion: There was low evidence in associated factors with a preference on gene tests, especially for psychological factors. So, further research is needed to help policymakers to develop early detection strategies and increase people's participation that leads to the success of the strategies and avoiding the high cost of treatment as well.

Systematic review registration: PROSPERO 2020 (ID: CRD42020190811).

Background

Identifying the health risks of a gene mutation for any disease is possible by progressing in the Human Genome Project. People can obtain information about their risk of disease by genetic analysis. Breast cancer (BC) is a disease that can be early detected by genetic tests (1).

BC has become a common non-communicable disease that health managers and susceptible individuals are searching ways to eradicate or reduce its incidence and prevalence rate (2). The incidence and mortality rate from BC has increased by about 50 percent from 2002 to 2020. The prevalence of BC in North America was 91.6 per 100,000, compared to 43 per 100,000 in the Middle East and North Africa (3). The high cost of treating the progression of BC and reducing quality of life is a major worry for those who succumb (4).The treatment cost, for stages one to four of the disease, was about $283,000, $58,000, and $26,000 in the U.S., Italy, and China, respectively, in 2017 (5–7).

Five to ten percent of BC is a gene mutation, especially BRCA 1 and BRCA 2. Based on U.K. statistics in 2015 the risk of BC in women without gene mutation was 12%, while it was 60% and 50% in women with a genetic mutation of BRCA 1 and BRCA 2, respectively (8). BRCA gene mutation carriers are at risk of 40–60% and 20–40% of breast and ovarian cancer, respectively, in their lifetime (9). Determining the risk of cancer for first-degree family members, identifying the risk of ovarian cancer, and managing prevention strategies are benefits of the BRCA gene test (10).

Traditionally, the results of genetic tests were presented when women had undergone primary surgery where she could use the results for her decision to accept low-risk surgeries, such as bilateral salpingo-oophorectomy. Rapid BRCA gene tests are possible today because of new technologies and equipment. Rapid-response allows people to have more time to manage preventive interventions. The benefits are in avoiding a second surgery or having a risk-reduction surgery parallel to treatment surgery for affected breasts (11).

Hospitals, as well as other medical centers, are presented the genetic tests and provide a direct-to-consumer (DTC) opportunity for obtaining the information of interest about risks of disease, in at least the first 6 to 8 weeks (12). The increasing availability of genetic testing in various settings and the importance of genetic tests for reducing the mortality rate of BC, and early detection of the disease, raises critical questions: Who is getting BRCA tested, and what are the associated factors for performing genetic tests?

Because of the importance of the associated factors with a preference for gene tests as early detection method of breast cancer, the present study was performed. The result can help policymakers with prevention strategies in this area of work.

Method

Search strategy

A systematic review of the literature was performed to identify relevant published factors associated with the preference of gene tests, especially BRCA tests for breast cancer following the standard Cochrane Collaboration methods and adhering to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (PRISMA) reporting recommendations (13).

The search question was regarding the factors that affect people-preference for the genetic test of BC. The search was conducted in Scopus, PubMed, ProQuest, Embase, and WOS databases.

Due to limitations of the published papers for the study goal, a broad search strategy was performed based on keywords in articles and from experts. One concept near the preference category was "willingness-to-pay" and its related concepts such as "stated preference", and was used in the search strategy. "Patient Acceptance of Healthcare" and "stated preference" were added as search terms.

Although the search question was in case of associated factor, the words such as ‘factor*’, ‘predict*’, ‘associat*’, ‘relat*’ and ‘determin* were excluded from the search strategy because of more outputs in the absence of them as well as available to qualitative studies.

The strategy terms involved some keywords or medical subject headings (MeSHs) that identified by a research librarian. Specific search strategies are presented in Appendix 1.

The protocol for this review was registered on PROSPERO in July 2020 (ID: CRD42020190811).

Inclusion and exclusion criteria

Studies were selected for inclusion if the full-text was written in the English language up to 2020 and addressed the preference for the gene screening tests for early detection of breast cancer.

The exclusion criteria were the studies (1) in the form of abstracts and conference papers, (2) addressed the breast cancer screening methods other than genetic testing such as mammography, breast self-assessment, (3) focused on the preference of people for treatment intervention for breast cancer, (4) focused on genome sequencing or Gene-Panel, (5) focused on the preference of genetic tests for other types of cancers, and (6) longitude studies that addressed the effect of an intervention on the preference of genetic tests.

We assumed that all researchers' studies were published as articles, so the gray literature was excluded from the present study.

Study selectionandData extraction

All citations were imported into an electronic database, Endnote version 8, with duplicates subsequently removed. The retrieved articles after deleting duplicated were collected into a separate Excel sheet and disagreements between researchers were examined by Cohen’s kappa coefficient. A 0.6 to 0.8 for the kappa coefficient is substantial for the studies, although more than 0.8 for the coefficient is almost perfect based on accepted standards (14).

The selection of studies was done in two stages. First of all, titles and abstracts of retrieved articles were screened against the inclusion and exclusion criteria. After that, the full text of eligible studies was examined.

Two reviewers (Z.M., A.A.) independently applied inclusion and exclusion criteria to screen titles and abstracts of the remaining articles.

The full text of eligible articles was screened thoroughly by two independent reviewers (Z.M. and N.M. or M.L.). Decisions regarding the inclusion of studies, where it was not clear as to whether or not the material was inclusion criteria, were resolved by a consensus meeting with a third reviewer (A.GH.). Finally, reference lists and citations of eligible articles were checked manually for additional relevant studies.

One author (Z.M.) performed data extraction independently and, then, these were checked by a second author (N.M). A self-assessment form was designed for extracting data. Information retrieved from the researches included the first author, year, title, study design, sample size, methodology, the location, and associated factors with the preference for genetic testing.

Quality assessment

Two reviewers (Z.M. and N.M.) assessed the quality of the studies independently, and the final quality assessment was based on consensus. For quality assessment of the selected studies using the criteria developed by Johannesen and LoGiudice. It contains 8 items that cover inclusion and exclusion criteria, a good response rate (i.e., ≥80%), minimized the selection bias, well-defined outcome, valid and reliable instrument for measuring the outcomes, valid and reliable instrument for measuring risk factors, and adjusting the findings for confounding risk factors. It has been used in previous study (15-17).

All criteria were scored. Items that covered the criteria were given a perfect score (=1), and those that did not cover the criteria, a score of zero was assigned. In case the necessary information was unclear, a negative score was provided, too. Therefore, the sum and percentage of quality assessment of articles was calculated from 8 points. The studies that awarded 50% or more than 50% of points, were of high quality (15, 16).

Data analysis

Meta-analysis were not performed because of a number of reasons: 1) inclusion and exclusion criteria for sample size were not the same (i.e. some studies considered patients and some healthy as well as first degree relatives of breast cancer patients), 2) a number of studies were performed in a quantitative and some qualitative, and 3) the method of the selected studies in terms of measuring related factors were different. So, the results synthesized by the vote counting as used in previous studies. The factors were categorized by their signs as well as significance. Factors categorized to positive, negative, or non-significant effects on preference of genetic tests. Finally, gave a vote to each of factors and the votes were counted. Factors with the same sign as well as significance and factors that obtained at least three votes was considered as an affecting factor on preference of genetic tests for breast cancer (18).

Results

The literature search identified 1269 articles; 193 from PubMed, 428 from Embase, 354 from Scopus, 68 from ProQuest, 214 from WOS, and 12 from other sources. After removing 547 duplicates, 722 titles and abstracts were screened for eligibility, of which, 667 articles were excluded because of irrelevant title and abstracts, and 30 articles because of focusing on attitude of genetic tests, Gene-Panel, and measuring the effect of intervention on preference were excluded. Finally, 25 articles were included.

Inclusion and exclusion criteria to screen titles and abstracts of the identified articles were independently applied by two reviewers (Z.M., A.A.). There was disagreement in the first steps of the study selection but the remaining stages gained authors agreement to the terms of including the articles. The Cohen's kappa coefficient between researchers authors (Z.M. and N.M.), was 0.72 that is substantial based on accepted standards. The study selection is shown in Fig. 1 based on the PRISMA diagram.

Quality assessment

According to the quality assessment, the average percent of items reported in the studies was 80%. All selected studies except one of them (19) were rated high-quality in reviews. Low (20-27) or unclear (10, 19, 28-41) respondent rates and unclear the adjustment for confounding risk factors (10, 19, 20, 22, 23, 28, 29, 31, 35, 36, 39, 42) were the reasons why the studies did not achieve 100% of the criteria.

Study Characteristics

The characteristic of the selected studies was summarized in Table 1. Publication year of the selected articles ranged from 1999 (27) to 2019 (19, 20) and the studies at 2002 were frequent (10, 24, 37, 38).

Twelve studies were conducted in the USA (10, 22-25, 27, 35-37, 39, 40, 42) four in the Asia (India, South Korea, Singapore, and Saudi Arabia) (19, 28-30), five in Canada (21, 26, 31, 38, 41), and four in Israeli (32), Italy (34), Germany (33), and UK (20).

The preference on genetic tests were measured in different dependent variables. Out of 25 articles, fifteen (20, 21, 24-27, 29, 30, 32-35, 38, 40), six (10, 22, 28, 37, 39, 42), one (19), one (36), and one (23) articles were addressed interest or intention, decision making, acceptance, participant in genetic cancer risk ,and willingness to pay to genetic tests, respectively. A study were addressed the factors for withdrew from BRCA genetic testing (31). Study designs as reported by all of the selected studies included cross- sectional except two of them that were cohort studies (19, 20).

A number of ten studies were performed in hospital or clinic or medical university setting (10, 19, 20, 24, 26, 28, 29, 34, 37, 42), a study were considered medical university and community as setting (41), and remind were performed in the community.

Sample sizes varied from 28 (36) to 2410 (21) with one study including patients with breast and ovarian cancer (19), six studies including high risk (22, 23, 28, 31, 36, 39) as well as breast cancer patients relative, a number of nine studies including people in general population (10, 21, 24, 25, 30, 32-34, 37), and three studies including Jewish people (20, 35, 42) as sample size, although a number of six studies including a combination of patients, high risks or people from the general population (26, 27, 29, 38, 40, 41). Although all considered women as samples, four papers included men as a sample group, too (20, 28, 31, 39).

Socio-demographic (10, 19-25, 31, 34-42), knowledge (20, 38) as well as awareness (30), health related factors (20-24, 28, 32, 38, 39, 41), Psychological factors (10, 21-23, 27, 30, 33, 34, 37, 39-42), family function (35), cultural factors (36) were the factors in which assessed by the selected articles.

Three studies were used interview (25, 27, 31). Although all of the articles were designed a self-administered questionnaire, for some dimensions of the questionnaire used identified scales, especially for psychological factors. Anxiety/depression was assessed by the Hospital Anxiety and Depression scale (HADS) (20), Health/Illness Orientation Scale (HIOS) (32), and the Health Belief Model (HBM) were measured for measuring a number of physiological factors (26).

Family functioning was measured by the Cohesion subscale of the FACES, the Family Crisis Oriented Personal Evaluation Scale (F-COPES). The stressful encounters of everyday living were measured by The Ways of Coping Questionnaire. Social support was measured by the Medical Outcomes Study (MOS), and mental health was measured by the SF-36 questioner (35). Cultural beliefs and values were assessed in terms of communalism (was measured by Communalism Scale), temporal orientation (was measured by the Temporal Orientation Scale (TOS)), and religious coping style (was measured by Religious Coping Style Scale (RCSS)). Cancer fatalism was measured by the Cancer Fatalism Inventory (CFI) (36). The intrusive thoughts subscale of the IES was used to assess breast cancer-specific distress (10). The Family Environment Scale (FES), the Center for Epidemiologic Studies Depression (CES-D) Scale, the Spiritual Well-Being Scale (SWBS), the Rosenberg Self-Esteem Scale, and the Life Orientation Test (LOT) were measured for dimensions of family relationships, depressive symptomatology, personal spiritual meaning and satisfaction, global self-esteem, and dispositional optimism, respectively (39). Health locus of control (HLOC) was measured by internal, powerful others, and chance (37).

Although a study was used structural equation modeling (33) and a study was used content analysis (31), the remains were used regression as well as statistical analysis to identify the relationship between variables of interest.

Factors associated with the interest in BRCA gene screening test

Presented in Table 2 are the selected factors of the studies organized into five categories; namely, sociodemographic, health related factors, knowledge as well as awareness, psychological variables, and cues to action.

Sociodemographic factors

A number of eleven factors were identified in the selected articles that their association between preferences of genetic tests were addressed. Age were assessed in 19 articles that one (39) study declared a positive relationship and five (21, 24, 28, 30, 31) of the selected articles were displayed a negative relation between age and preferences for genetic tests. Based on vote counting there is strong negative relation between age and preferences for genetic tests.

Marital status (20, 21, 27, 31, 34, 39) and income (19, 21, 29, 30) were the factors that displayed a clear relationship with preferences for genetic tests. Based on vote counting there is strong positive relation between marital status as well as income and preferences for genetic tests.

Between gender as well as religion and preferences did not find any positive and negative relation while a number of five (20, 28, 31, 39) and two (26, 41) articles displayed any relation between them, respectively.

The evidence for relationships involving ethnicity (20, 23-25, 40, 42), employment status (24, 34, 36, 42), education level (10, 19-26, 28-30, 34, 36, 37, 41, 42), geographical region (19, 24), having children (26, 31, 34), and insurance status (20, 42) was more unclear and they are inconclusive based on vote counting.

Health related factors

There were seven factors regarding health related factors identified in the included studies. Family history of breast cancer (21, 27, 28, 30, 38) and personal history of breast disease or presence of BC (30, 31, 41, 42) were identified as positively strong association with preference on genetic tests. Based on vote counting there is inconclusive result for the relation of family history of other cancer (24, 28), the number of previous breast biopsies (21), presence of first-degree relatives affected with cancer (39), presence of family members testing positive (22, 23), and prior hormonal treatment member(s) testing positive (29) with the preference because of any evidence of positive or negative effects of the variables.

Knowledge/Awareness

Knowledge (10, 20, 37) and awareness (29, 30) about BRCA gene tests as well as breast cancer and its risk factors (27, 37) were assessed by a number of selected studies. Although there were not enough evidence for association between knowledge as well as awareness about breast cancer and its risk factors with preference of genetic tests, the evidence were confirmed the strongly positive relation between BRCA-related knowledge and preference for genetic tests for breast cancer.

Women's positive attitude regarding the genetic tests stated as predictor of genetic tests although the significance did not assesse (33).

Psychological variables

The evidence were more frequent regarding psychological variables by 21 associated factors, although just breast cancer risk perception (20-22, 27, 30, 40, 42) and perception of the benefits of BRCA testing (20, 41, 42) were identified as positively strong association with preference on genetic tests based on vote counting and for other variables such as perception of the barriers of BRCA testing (10), health / illness orientation (32), perception of susceptibility (22, 23), perceived costs (26, 41), concern about the risk of relatives developing BC (41), confidentiality (20), emotional impact (20), inability to prevent cancer (20), lack of trust in modern medicine (20), illness prevention motivation (32), emotional reassurance motivation (32), breast cancer-specific distress (34), stigma (40) (10), uncertainty (20), cancer anxiety (20) (32) and worry (22, 23), family-related guilt (10), highly optimistic (21) (39) the results were inconclusive because of low evidence.

Cues to action

Having a locus of control (21) (37), number relatives provide social support (35), being a high monitor (21), family function (35), family Communication (35), greater family cohesion (39), ways of coping (seeking social support) (35), family conflict (39), family expressivity (39), spirituality (39), self-esteem (39), general communication (35), breast cancer communication (35), beliefs and values surrounding familial relationships (36), interdependency (36), collaborative religious coping (36), access to testing (40) were defined in the selected studies as cues to action for preference for genetic tests although based on vote counting and because of low evidence they are inconclusive for decision making as factors associated with preference.

Reasons for refuse the genetic tests

Financial hardship (28) as well as the high cost of genetic tests (19, 28, 29), implications of a positive BRCA tests result on insurance (29), lack of expert consensus in recommending genetic testing (29), not satisfying with the treatment before the symptoms appear (19), lack of knowledge about the heritability of cancer (19), unavailability of decision makers (19), fear of the result as well as finding tumors (19), disrupting the life's projects, concern about the effect on your family, feel labeled or singled out, not remaining confidential of the results, do not trust modern medicine (34) were stated as the reasons for refusing for opting genetic tests.

Discussion

Genetic susceptibility testing is the newest in the medical science that has the potential to transform the practice of preventive care. Although its benefits, many people do not have the test performed. The present systematic review study was assessed to identify the associated factors to preference of peoples for genetic tests.

The selected studies vary in terms of sample sizes, the associated factors with, and tools to measure the factors for preference of genetic tests. In sum, 80%, 40%, and 56% of selected articles were assessed socio demographic, health related factors, and physiological variables, while 12% and 8% of studies addressed knowledge as well as awareness and cues to action variables for preference of genetic tests, respectively.

Although the vote counting was used, the findings about the associated factors with preference especially for knowledge and physiological variables should be interpreted with caution because of low evidence as well as different tools for measuring the factors.

Overall, based on the results age was identified as strongly negative factor while being married, income, family history of breast cancer, personal history or presence of breast cancer, BRCA-related knowledge were identified as strongly positive factors with preference of genetic tests for breast cancer.

The associations between sociodemographic characteristics and preference for genetic tests were complex, although base on vote counting age, marital status, and income were the important associated factors. Based on vote counting there was strong negative relation between age and preferences for genetic tests (21, 24, 28, 30, 31), although a study (39) declared a positive relationship. Based on the results there was strong positive relation between marital status (20, 21, 27, 31, 34, 39) as well as income (19, 21, 29, 30) and preferences for genetic tests. Insurance status is a variable that even low income persons have an opportunity for getting the medical services with lower price that it was confirmed in two studies (20) (42). The reaction of peoples for price changing, leads us to the conclusion that predictive tests such as genetic tests are elastic and by lower price the demand increase. It is confirmed in the Sun et al study, too. They were assessed the effect of costs for high risk Korean females on preference the tests after the implementation of national health insurance coverage for the tests and based on the results refusal rate were decreased (28).

Gender as well as religion and preferences did not have any positive and negative relation while a number of five (20, 28, 31, 39) and two (41) (26) articles displayed any relation between them, respectively.

Although the number of the selected articles confirmed the positive relation between preference for genetic tests and ethnicity, especially Ashkenazi Jewish (42) (25), education level (24, 29, 30, 37), employment status (24), live in urban areas (19) and, having children (31), there were evidence in contrast. So, the result for the stated variables was more unclear and they are inconclusive based on vote counting.

It was expected that risk factors for getting breast cancer such as family history (people with a greater probability of being a carrier of the BRCA1/2 gene) had got a positive association with preference for genetic tests that studies confirmed it for family history (21, 27, 28, 30, 38), although a study was in contrast (24). Gene mutation is frequent in some ethnicity such as Ashkenazi descent and it was expected that they have more interest for genetic tests but the studies did not find the same results. Women with a family history of breast cancer may have learned more about gene tests and be more anxious about undergoing testing (24).

Personal history of breast disease or presence of BC (30, 31, 41, 42) were identified as positively strong association with preference on genetic tests in the number of studies. Based on vote counting there was inconclusive result for the relation of family history of other cancer (24) (28), the number of previous breast biopsies (21), presence of first-degree relatives affected with cancer (39), presence of family members testing positive (22) (23), and prior hormonal treatment member(s) testing positive (29) with the preference because of any evidence of positive or negative effects of the variables.

Although lack of evidence, there were the strongly positive relation between BRCA-related knowledge (10, 20, 37) and preference for genetic tests for breast cancer. Aging had negative relation with preference among knowledgeable women about genetic testing. Knowledgeable 59 and 60 years old women expressing the greatest and lowest interest in genetic testing, respectively (38). Awareness (29) (30) about BRCA gene tests as well as breast cancer and its risk factors (37) (27) did not associated with preference for genetic tests. Women's positive attitude regarding the genetic tests as well as its results stated as a predictor of genetic tests although the significance did not assesse (33).

BRCA testing is a sensitive issue and can lead to a range of opinions and emotions. So, Psychological variables have an important role for preference for the genetic tests and more than half of selected articles were addressed them. Breast cancer risk perception (20–22, 27, 30, 40, 42) and perception of the benefits of BRCA testing (20, 41, 42) were identified as positively strong association with preference on genetic tests based on the results.

The results are in caution for other variables and they are inconclusive because of low evidence and vote counting as well, although based on the selected articles there were positive relation between perception of the barriers of BRCA testing (10), perception of susceptibility (22) (23), concern about the risk of relatives developing BC (41), illness prevention motivation (32), emotional reassurance motivation (32), breast cancer-specific distress (34), uncertainty (20), and family-related guilt (10) and there were negative relation between perceived costs (26) (41), confidentiality (20), emotional impact (20), inability to prevent cancer (20), highly optimistic (21) (39), lack of trust in modern medicine (20), stigma (40) (10) with the preference of genetic tests. There were not any relation between health/illness orientation (32), cancer anxiety (20) (32) worry (22) (23) and preference.

There were negative relation between having a locus of control of others (21) for genetic tests while it was in contrast for having a locus of health providers control for genetic tests (37). being a high monitor (21), greater family cohesion (39), and access to testing (40) were the variables that lead to preference for genetic tests while ways of coping (seeking social support) (35) was reported to negative relation and number relatives provide social support (35), family function (35), family Communication (35), family conflict (39), family expressivity (39), spirituality (39), self-esteem (39), general communication (35), breast cancer communication (35), beliefs and values surrounding familial relationships (36), interdependency(36), collaborative religious coping (36), did not have any relation with preference for genetic tests based on the studies and because of low evidence they are inconclusive for decision making as factors associated with preference.

It is interesting that although women displayed the high rate of interest for genetic tests to identify children's risk, to plan for cancer screening tests or preventive interventions, to help for advance research, to be reassured (34) (38), to make decisions about having (more) children (34), curiosity, to warn the family, to achieve peace of mind, reduced worry and to warn the family (38), it did not lead to opt the gene tests (29).

Limitations And Strengths

Although in our knowledge the present study was the first one that assessed the preference for a new medical technology, genetic tests, for early detection of disease and did not have time-limited and included the qualitative and quantitative studies as well, considering English language studies was our limitation. Low evidence to decision making about cues to action factors that associated with the preference, using different definition for measuring the variables were the other limitation of the present study that need to further studies.

Conclusion

The burden of breast cancer can reduce by early detection interventions such as genetic tests as a new technology in medical science. But before the implication of early detection strategies, the participant's rate of people should be estimated. Identifying the associated factors with a preference for gene tests can help policymakers to remove barriers and had high coverage of people in such plans. Based on the result of the present study a number of factors were associated with preference but there was low evidence, especially for psychological factors. So, further research is needed to help policymakers to develop early detection strategies and increase people's participation that leads to the success of the strategies and avoiding the high cost of treatment as well.

Abbreviations

DTC: direct-to-consumer

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

MeSH: medical subject headings

PROSPERO: The International Prospective Register of Systematic Reviews

WTP: Willingness-To-Pay

Declarations

Ethics approval and consent to participate

The study protocol was approved by the Ethics Committee of the Iran University of Medical Sciences (Ethical Code.IR.IUMS.REC.1398.1051). Consent to participate not applicable for the study.

Consent for publication

Not applicable

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Competing interests

The authors declare that there is no conflict of interest regarding the publication of this article

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Authors 'contributions

Dr. Moradi, N and Dr. Meshkani, Z designed the study. Dr. Moradi, N, Dr. Meshkani, Z and Dr. Aboutorabi searched the articles and Dr. Meshkani, Z and Dr. Aboutorabi, Dr. Ghanbari Motlagh, and Dr. Langari zadeh analyzed the data. Dr. Meshkani, Z wrote the manuscript. Dr. Moradi revised the manuscript. All authors read and approved the final manuscript.

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Tables

Table 1
characteristics of selected studies

Author/ year	Country/ study location	Study design	Study setting	Sample/ sample size	Respondent rate	sampling method	Dependent variable	Method	Instrument
Singh, N, 2019 (19)	India	Cohort study	King George's Medical University	A number of 100 cases of patients with breast and/or ovarian cancer	NA	Convenience sampling	Acceptance	quantitative-descriptive	A self-administere questionna
Manchanda,R, 2019 (20)	UK/ North London	Cohort study	recruitment clinics	A total of 935 Ashkenazi Jews men and women > 18 years (mean age = 53.8)	NA	Cluster sampling	Interest/ Intention	logistic-regression models	A baseline questionna with Likert-scales
Blouin-Bougie, J 2018 (21)	Canada/ Québec	Cross-sectional	Web	A number of 2410 adult women of general population aged 35 to 69 years old	43%	Randomly	Interest	A regression analysis	A self-administere Web-based questionna
Sun,Y 2015 (28)	South Korea/ Seoul	Cross-sectional	A hospital	A number of 804 persons who underwent genetic counseling for cancer (26 to 69 years old)	NA	Randomly	Decision to get genetic test	A logistic regression analysis	A self-administere questionna
Miron-hatz,T 2015 (22)	US	Cross-sectional	Web	A number of 449 high-risk women	48%	Randomly	Decision/ Willingness to test	A Stepwise regression analysis	A self-administere questionna
Miron-hatz,T 2014 (23)	US	Cross-sectional	Web	A number of 299 high-risk women	48%	Randomly	Willingness to pay	A regression analysis	A self-administere questionna
Ngoi,N, 2013 (29)	Singapore	Cross-sectional	A tertiary cancer center	A number of 752 individuals that 200 of them were patients with breast cancer (> = 21 years old)	NA	Convenience sampling	Interest	Univariate and multivariate logistic regression	A self-administere questionna

Author/ year	Country/ study location	Study design	Study setting	Sample/ sample size	Respondent rate	sampling method	Dependent variable	Method	Instrument
Amin,T.T, 2012 (30)	Saudi Arabia/ Al Hassa	Cross-sectional	Community	A number of 599 women aged ≥ 18 years	NA	Randomly	Interest	Multivariate regression model	A self-administere questionna
Godar,B 2007 (31)	Canada/ Quebec	Cross-sectional	Community	A number of 334 high risk French-Canadian population > = 18 years old who declined genetic testing	NA	Randomly	Withdrew from BRCA genetic testing	Content analysis (standard inductive method) as well as statistical analysis	Notes and comments
Shiloh,SH 2005 (32)	Israel	Cross-sectional	Community	A number of 102 adult women with no history of BC (20 to 79 years old)	NA	A snowball method	Interest	A regression analysis	A revised version of t questionna
Bruno,M 2004 (34)	Italy/ Apulia	Cross-sectional	Clinics	A number of 677 healthy women (with or without a FH of BC)	NA	Randomly	Interest	A multivariate logistic regression	A structure questionna
Bowen, D.J 2004 (35)	Seattle/ Washington	Cross-sectional	Community	A number of 221 Ashkenazi Jewish women between 18–74 years old.	NA	Randomly	Interest	Regression analysis	Well-established questionna
Reitz,F 2004 (33)	Germany/ Freiburg	Cross-sectional	Community	A number of 377 low risk women (between 21 to 65 years old)	NA	Randomly	Interest	Structural equation modeling	A self-administere questionna

Author/ year	Country/ study location	Study design	Study setting	Sample/ sample size	Respondent rate	sampling method	Dependent variable	Method	Instrument
Hughes,C 2003 (36)	USA	Cross-sectional	Community	A number of 28 high risk African American women aged 18 and over	NA	Randomly	Participant in genetic cancer risk assessment	Descriptive	Well-established questionna
Armstrong, K 2002 (24)	Philadelphia	Cross-sectional	University-based health system	A number of 400 adult women aged 18 and over	70.6%	A simple random sample	Interest	A multiple logistic regression	A self-administere questionna
Helmes, W 2002 (37)	Washington	Cross-sectional	Clinics	A number of 340 women between 18 and 64 years old	NA	Randomly	Decision making	regression analyses	A questionna packet in th mail
Thompson,H 2002 (10)	New York	Cross-sectional	A community clinic	A number of 76 African-American women (> = 18 years old)	NA	Randomly	Decision making	A statistical analysis (ANOVA)	A structure questionna
Bottorff,J.L 2002 (38)	Canada	Cross-sectional	Community	A number of 761 women without and 260 with BC (totally 1021 women)	NA	Randomly	Interest	A multiple logistic regression	Well-established questionna

Author/ year	Country/ study location	Study design	Study setting	Sample/ sample size	Respondent rate	sampling method	Dependent variable	Method	Instrument
Cappelli,M 2001 (26)	Canada / Ontario	Cross-sectional	A hospital	A number of 58 high risk and 50 women from the general population (totally 108 women)	56%	Randomly	Intent to be tested	A logistic regression and A statistical analysis (ANOVA) as well.	A survey designed
Press,N.A 2001 (25)	Washington	Cross-sectional	Community	A number of 246 women over 40 years old	NA	Randomly	Interest	A statistical and qualitative analysis	Semi structured interviews
Armstrong,K 2000 (42)	Pennsylvania	Cross-sectional	A university based clinic	A number of 251 Ashkenazi women without cancer	80%	Randomly	Decision making	A multivariate regression	A self-administere questionna
Bowles Biesecker,B 2000 (39)	Maryland	Cross-sectional	Community	A number of 172 high risk individuals (> = 18)	NA	Randomly	Decision making	A logistic regression	A self-assessed using validated psychomet instrument
Durfy, S.J 1999 (40)	Western Washington	Cross-sectional	Community	Four groups were defined: (1) white women with a FH of BC, as “Main study”; (2) African-American women, (3) lesbian/bisexual women, and (4) Ashkenazi Jewish women. (totally 543 women)	NA	Randomly	Interest	A logistic regression	A baseline questionna

Author/ year	Country/ study location	Study design	Study setting	Sample/ sample size	Respondent rate	sampling method	Dependent variable	Method	Instrument
Cappelli,M 1999 (41)	Canada/ Ottawa	Cross-sectional	Ottawa Regional Cancer Centre and community	A number of 60 women diagnosed with BC and 50 general population women (18 to 50 years old)	NA	Randomly	Interest	Two-by-two analyses of variance (ANOVA) and a logistic regression	A single comprehen questionna
Lipkus, I.M 1999 (27)	US	Cross-sectional	community	A number of 130 female with and 136 without a family history of BC (totally 266 women)	86% response rate for women With FH and 70% for Women without a FH	Randomly	Interest	A multivariate regression	A telephone interview

Table 2
Factors associated with the preference for genetic screening BRCA tests

Category	Factors	N	Number of studies displaying a positive association ($p < 0.05$)	Number of studies displaying a negative association ($p < 0.05$)	Number of studies displaying no association ($p \geq 0.05$)	Vote counting
Sociodemographic factors	Age	19	One (39)	Five (21) (24) (28) (30) (31)	Thirteen (20, 35) (19) (40) (34) (43) (29) (22) (23) (36) (37) (10) (26)	Strongly negative
	Gender	5	0	0	Five (20) (28) (31) (39)	Inconclusive
	Ethnicity	6	Two (42) (25)	One (20)	Three (24) (40) (23)	Inconclusive
	Employment status	4	One (24)	0	Three (34) (42) (36)	Inconclusive
	Religion	2	0	0	Two (41) (26)	Inconclusive
	Education level	17	Four (24) (29) (30) (37)	Two (20) (25)	Eleven (19) (34) (21) (42) (28) (22) (23) (36) (41) (10) (26)	Inconclusive
	Geographical region	2	One (19)	0	One (24)	Inconclusive
	Marital status	11	Six (20) (34) (31) (39) (27) (21)	0	Five (24) (28) (36) (41) (26)	Strongly positive
	Having children	3	One (31)	0	Two (34) (26)	Inconclusive
	Income	9	Four (21) (19) (29) (30)	0	Five (20) (36) (41) (10) (26)	Strongly positive
	Insurance status	2	Two (20) (42)	0	0	Inconclusive
Health-related factors	FH of BC	10	Five (21) (28) (30) (27) (38)	One (24)	Four (20, 34) (29) (25)	Strong positive
	FH of other cancer	2	0	0	Two (24) (28)	Inconclusive
	The number of previous breast biopsies	1	0	0	One (21)	Inconclusive
	Personal history of breast disease or presence of BC	7	Four (42) (31) (41) (30)	One (38)	Two (28) (23)	Strongly positive
	Presence of first-degree relatives affected with cancer	1	0	0	One (39)	Inconclusive
	Presence of family member(s) testing positive	2	0	0	Two (22) (23)	Inconclusive
	Prior hormonal treatment	1	0	0	One (29)	Inconclusive
Knowledge/ awareness	BRCA-related knowledge	3	Three (20) (37) (10)	0	0	Strongly positive
	Knowledge about BC and risk factors	3	Two (37) (27)	0	One (41)	Inconclusive
	Awareness of genetic testing	3	Two (29) (30)	0	One (38)	Inconclusive
Psychological factors	Having a perception of health status	1	One (21)	0	0	Inconclusive
	Breast cancer risk perception	12	Seven (20) (40) (21) (27) (42) (22) (30)	0	Five (41) (23) (32) (26) (27)	Strongly positive
	Perception of the benefits of BRCA testing	5	Three (20) (41) (42)	0	Two (10) (26)	Strongly positive
	Perception of the barriers of BRCA testing	1	One (10)	0	0	Inconclusive

*N: the number of studies that assessed the factors

Category	Factors	N	Number of studies displaying a positive association ($p < 0.05$)	Number of studies displaying a negative association ($p < 0.05$)	Number of studies displaying no association ($p \geq 0.05$)	Vote counting
	Health / illness orientation	1	0	0	One (32)	Inconclusive
	Perception of susceptibility	2	Two (22) (23)	0	0	Inconclusive
	Perceived costs	2	0	Two (26) (41)	0	Inconclusive
	Concern about the risk of relatives developing BC	1	One (41)	0	0	Inconclusive
	Confidentiality	1	0	One (20)	0	Inconclusive
	Emotional impact	1	0	One (20)	0	Inconclusive
	Inability to prevent cancer	1	0	One (20)	0	Inconclusive
	lack of trust in modern medicine	1	0	One (20)	0	Inconclusive
	Illness prevention motivation	1	One (32)	0	0	Inconclusive
	Emotional reassurance motivation	1	One (32)	0	0	Inconclusive
	Breast cancer-specific distress	1	One (34)	0	0	Inconclusive
	Stigma	2	0	Two (40) (10)	0	Inconclusive
	Uncertainty	1	One (20)	0	0	Inconclusive
	Cancer anxiety	2	0	0	Two (20) (32)	Inconclusive
	Cancer worry	2	0	0	Two (22) (23)	Inconclusive
	Family-related guilt	1	One (10)	0	0	Inconclusive
	Highly optimistic	2	0	Two (21) (39)	0	Inconclusive
Cues to action	Having a locus of control highly attributed to powerful others	1	0	One (21)	0	Inconclusive
	Health locus of control (trust in provider)	1	One (37)	0	0	Inconclusive
	Number relatives provide social support	1	0	0	One (35)	Inconclusive
	Being a high monitor	1	One (21)	0	0	Inconclusive
	Family function	1	0	0	One (35)	Inconclusive
	Family Communication	1	0	0	One (35)	Inconclusive
	Greater family cohesion	1	One (39)	0	0	Inconclusive
	Ways of coping (seeking social support)	1	0	One (35)	0	Inconclusive
	Family conflict	1	0	0	One (39)	Inconclusive
	Family expressivity	1	0	0	One (39)	Inconclusive
	Spirituality	1	0	0	One (39)	Inconclusive
	Self-esteem	1	0	0	One (39)	Inconclusive
	General communication	1	0	0	One (35)	Inconclusive
	Breast cancer communication	1	0	0	One (35)	Inconclusive
	Beliefs and values surrounding familial relationships	1	0	0	One (36)	Inconclusive
	Interdependency	1	0	0	One (36)	Inconclusive
	Collaborative religious coping	1	0	0	One (36)	Inconclusive
	Access to testing	1	One (40)	0	0	Inconclusive

*N: the number of studies that assessed the factors

Figures

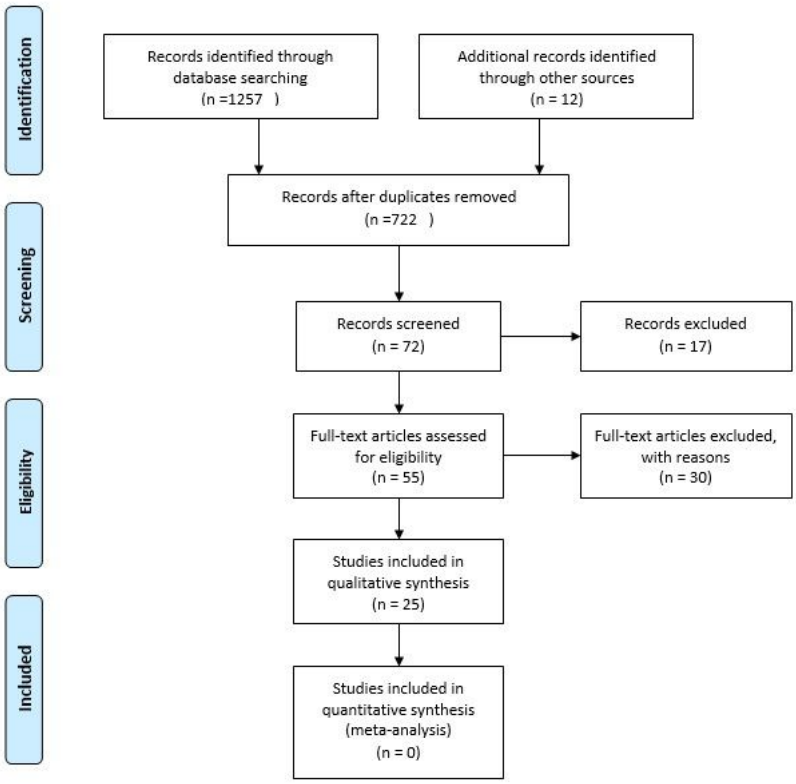

Figure 1

the PRISMA flow diagram for the study selection

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