Scientific Research Publishing

Advances in Breast Cancer Research, 2025, 14(1), 16-28
https://www.scirp.org/journal/abcr
ISSN Online: 2168-1597
ISSN Print: 2168-1589

Hypothetical Willingness to Share the Genetic Test Results among the Relatives of Individuals with HBOC: A Study on the Japanese Population

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How to cite this paper: Kataoka, I., Itaki, C. and Miura, T. (2025) Hypothetical Willingness to Share the Genetic Test Results among the Relatives of Individuals with HBOC: A Study on the Japanese Population. *Advances in Breast Cancer Research*, **14**, 16-28.
https://doi.org/10.4236/abcr.2025.141002

Received: October 25, 2024
Accepted: January 6, 2025
Published: January 9, 2025

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Abstract

Objective: Hereditary breast and ovarian cancer syndrome (HBOC) increases the risk of developing breast, ovarian, prostate, and pancreatic cancers. With the insurance coverage for BRCA genetic testing, the number of individuals diagnosed with HBOC has increased. To use these test results effectively, cascade genetic testing (CGT) is recommended for at-risk relatives; however, it is not yet widely available. The purpose of this study was to investigate the willingness of the general population to share genetic test results and undergo CGT, as well as to analyze the factors influencing these decisions. Based on these findings, the study aimed to identify the types of support needed to support the sharing of genetic test results and promote the use of CGT. **Methods:** An online survey was conducted with 500 participants (50 men and women from each of the five generations, ranging from 20 to 69 years). **Results:** Among the HBOC blood relatives, 51.2% wanted to share the genetic results and 71.9% expressed a willingness to undergo CGT. "Matters to be shared with relatives" and "Helpful for my cancer prevention" were identified as key factors promoting the willingness to share the BRCA genetic test results and undergo CGT. The motivation for "Helpful for my cancer prevention" had a particularly strong influence on the decision to undergo CGT. **Conclusion:** In the general population, there is an emerging understanding that the genetic information impacts not only the individuals but also their entire families and can be valuable for cancer prevention. To promote the sharing of BRCA genetic test results and CGT uptake, the healthcare providers should offer support tailored to each family's circumstances and establish cancer prevention measures recommended for HBOC.

Keywords

Hereditary Breast and Ovarian Cancer, Cascade Genetic Testing, Japanese

1. Introduction

Hereditary breast and ovarian cancer syndrome (HBOC) are characterized by an increased risk of cancers, such as breast, ovarian, prostate, and pancreatic cancers, due to pathogenic germline mutations in BRCA1 and BRCA2 genes (hereafter referred to as BRCA genes), which are involved in DNA repair [1]. In the Japanese population, pathogenic mutations in BRCA genes are reported to be present in 4% and 5% - 10% of patients with breast and ovarian cancers, respectively, and one in every 200 - 500 individuals in the general population [2] [3]. Since 2020, the BRCA genetic testing and related cancer preventive measures (risk-reducing surgery and surveillance) have been covered for all ovarian cancer patients and for breast cancer patients meeting certain criteria [4], leading to an increase in the use of BRCA genetic testing. Consequently, the number of relatives who may inherit the same pathogenic mutations is also increasing.

The results of the BRCA genetic testing provide valuable information on the potential cancer risks for relatives, offering an opportunity to consider whether cascade genetic testing (CGT) should be performed within the family based on these results. The CGT helps determine the need for detailed cancer preventive measures from an early stage, thereby contributing to early cancer detection. Preventive measures based on genetic test results are reported to be more cost-effective than mass screening [5]. The Japan Organization for Hereditary Breast and Ovarian Cancer recommends CGT for relatives, considering that the benefits outweigh the disadvantages [6]. However, it has been reported that Asians are significantly less likely than Westerners to share the genetic test results with relatives or recommend genetic testing [7]-[9]. Not sharing genetic test results means relatives lose the opportunity for CGT. In Western countries, studies on CGT have reported on the acceptance, implementation rates, barriers, and promoting factors [10]-[13]. Such research provides insights into strategies for encouraging the sharing of genetic test results and increasing the use of CGT. However, in Japan, CGT is not as widespread as in Western countries, and such studies are still lacking.

Therefore, this study aimed to elucidate the willingness to share the BRCA genetic test results and undergo CGT among individuals aged 20 - 69 years in the general population, and analyze the factors influencing these intentions. These results are expected to contribute to the establishment of support systems for relatives and a broader utilization of the BRCA genetic test results.

2. Methods

2.1. Objects of Study and Methods

The research design is shown in **Figure 1**. The study targeted individuals aged 20

- 69 who were registered in the panel list of an internet research company. No exclusion criteria were established, allowing all eligible individuals to participate. The survey was conducted via electronic means, utilizing a dedicated application and email, with requests for cooperation disseminated through an internet research company. The survey concluded that a total of 500 individuals, with 50 men and 50 women from each age cohort ranging from their 20s to 60s, were collected. The survey was conducted on December 12, 2022.

The research company that conducted this study obtained the "Privacy Mark" from the Japan Information Processing Development Corporation and ISO/IEC27001 (ISMS) certification, which attests to its adherence to the highest standards of data protection and information security. This study was approved by the Ethics Committee of the Graduate School of Health Sciences of Hirosaki University (approval no: 2022-017). The survey was conducted voluntarily, and informed consent was obtained from all participants. Prior to participation, each individual was provided with a detailed explanation of the purpose of the survey and asked to provide consent for their participation and the subsequent publication of the resulting data.

2.2. Survey Questions

The questionnaire comprised three main sections: 1) basic information of participants (age, sex, marital status, presence of children, household income, and presence of cancer in the participant or their close relatives), 2) knowledge of HBOC, and 3) willingness to share the BRCA genetic test results and undergo CGT and motivation for.

The items of knowledge regarding HBOC were derived from the National Center for Human Genome Research, Cancer Genetics Research Consortium's knowledge scale [14], and previous studies [15] [16], with additional unique items included. Correct answers were required across eight items: two items on the concept of HBOC, three items on genetic patterns, and three items on cancer risk.

The participants were asked to read the following explanatory text before responding about their willingness to share the BRCA genetic test results and undergo CGT: "HBOC involves genetic changes that increase the risk of certain cancers and may be inherited by relatives, potentially predisposing them to cancer. There are both benefits, such as cancer prevention, and psychological burdens, such as anxiety over increased cancer risk." The participants were then asked two questions about what they would do if they were relatives of someone diagnosed with HBOC: "Would you want to share the BRCA genetic test results?" and 'Would you want to undergo CGT?' The motivations behind these responses were assessed using six items: four derived from prior studies identifying promoting and barrier factors [13] and two original items. The responses were recorded on a seven-point Likert scale, comprising the following categories: "Strongly disagree", "Disagree", "Slightly disagree", "Neutral", "Slightly agree", "Agree" and "Strongly agree".

2.3. Statistical Analysis

To understand the factors affecting the willingness to share the BRCA genetic test results and undergo CGT, multiple regression analyses were performed. The willingness variables were the dependent variables, whereas the knowledge level (correct answer count) and motivation were the independent variables. Age, sex, marital status, presence of children, household income, personal history of cancer, and family history of cancer were also examined as independent variables. The Likert-scale responses were treated as numerical values.

All statistical analyses were performed using Excel 365 (Microsoft, Redmond, WA, USA) and R (version 4.4.1; R Foundation for Statistical Computing, Vienna, Austria [17]) software programs. The statistical significance was set at $P < 0.05$.

3. Results

3.1. Information of Participants

The basic information of the participants is presented in **Table 1**. A total of 500 participants aged 20 - 69, 50 men and 50 women from each age group, respectively. Regarding household income, 31.4% of the participants were in the low-income group (less than 3 million yen), and 35.6% were in the middle-income group (3 - 6 million yen), accounting for a combined 67.0% of the total participants.

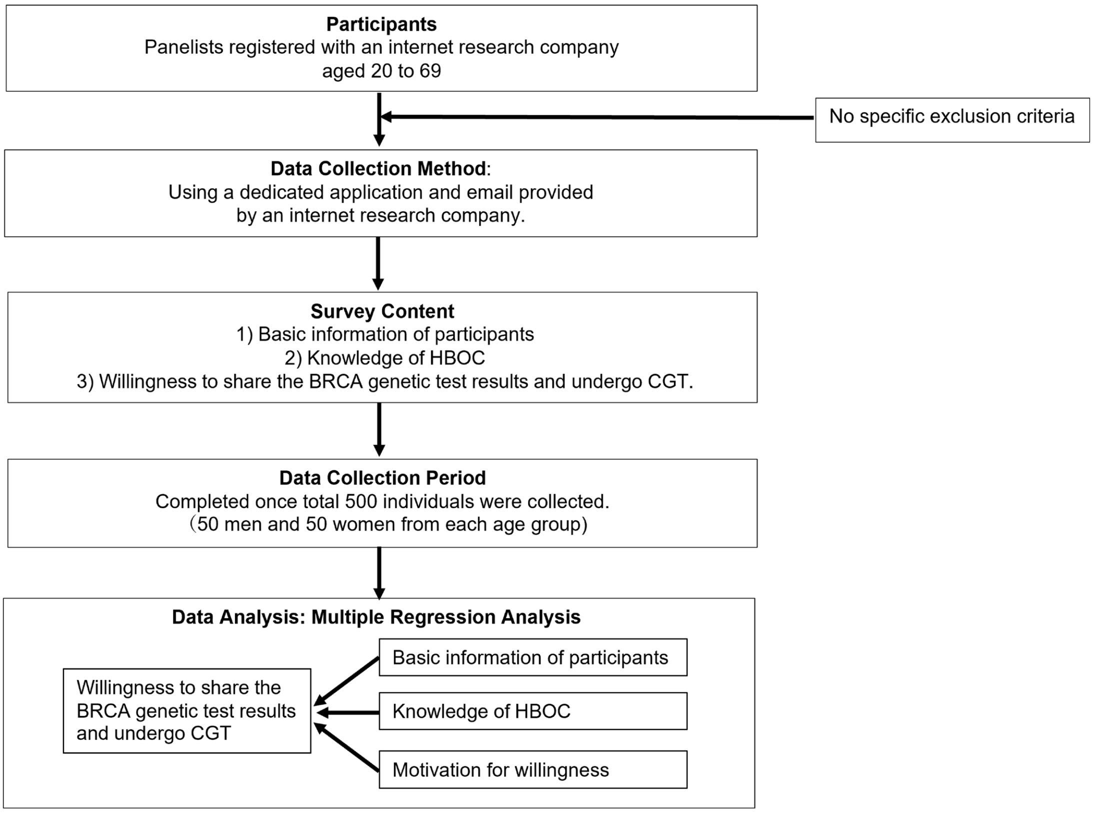

Figure 1. The design of the study.

3.2. Knowledge of HBOC

The correct and incorrect answer rates for the knowledge regarding HBOC are shown in Table 2. The total number of correct answers for knowledge about HBOC ranged from 0 to 8, with a mean of 1.41 ± 1.87, which was significantly low. Notably, women the question "HBOC is a disease of women" had a correct answer rate of 16.4% and an incorrect answer rate of 42.6%, with the incorrect rate exceeding the correct rate.

Table 1. The basic information of the participants ($n = 500$).

Subjects	Categories	*n*	(%)
Age	20 - 69 (mean 45.2 ± 14.1)		
Sex	Men	250	(50.0)
	Women	250	(50.0)
Marital status	Yes	233	(46.6)
	No	267	(53.4)
Presence of child	Yes	186	(37.2)
	No	314	(62.8)
Household income	Low	157	(31.4)
	Intermediate	178	(35.6)
	Higher-intermediate	88	(17.6)
	High	77	(15.4)
Cancer experience	Yes	19	(3.8)
	No	474	(94.8)
	Not known	7	(1.4)
Family history of cancer (first relative)	Yes	146	(29.2)
	No	341	(68.2)
	Not known	13	(2.6)

Table 2. The correct and incorrect answer rates for knowledge regarding HBOC.

Question	Correct (%)	Incorrect (%)	Unclear (%)
1) Hereditary breast cancer is diagnosed when there are multiple family members with breast cancer	40 (8.0)	161 (32.2)	299 (59.8)
2) HBOC is a disease of women	82 (16.4)	213 (42.6)	205 (41.0)
3) HBOC has a 50% chance of being passed on to children	68 (13.6)	35 (7.0)	397 (79.4)
4) HBOC is not passed on to men	105 (21.0)	36 (7.2)	359 (71.8)
5) HBOC will definitely get breast cancer in their lifetime	127 (25.4)	29 (5.8)	344 (68.8)
6) HBOC is more likely to develop breast cancer at a young age	70 (14.0)	22 (4.4)	408 (81.6)
7) HBOC is more likely to develop breast, ovarian and prostate cancer	68 (13.6)	21 (4.2)	411 (82.2)
8) HBOC recommends more in-depth breast cancer screening than usual	145 (29.0)	12 (2.4)	343 (68.6)

3.3. Willingness and Motivations for Sharing BRCA Test Results and Undergoing CGT

Figure 2 shows the hypothetical willingness of individuals to share the BRCA genetic test results and undergo CGT if they were relatives of someone with HBOC.

Positive motivations: "Helpful for my cancer prevention" (53.0%), "Matters to be shared with relatives" (45.4%). Negative motivations: "Increased worry and anxiety" (45.8%), "Suffering from discrimination or prejudice" (12.2%).

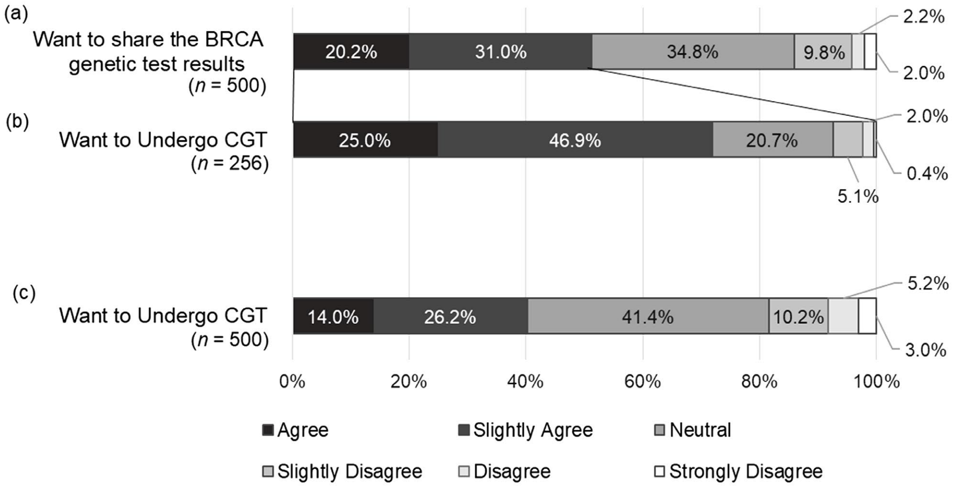

Figure 2. The hypothetical willingness of individuals to share the BRCA genetic test results and undergo CGT if they were relatives of someone with HBOC. (a) Overall agreement on sharing results. (b) Agreement on undergoing CGT among those who agreed or slightly agreed to share the results. (c) Overall agreement on undergoing CGT.

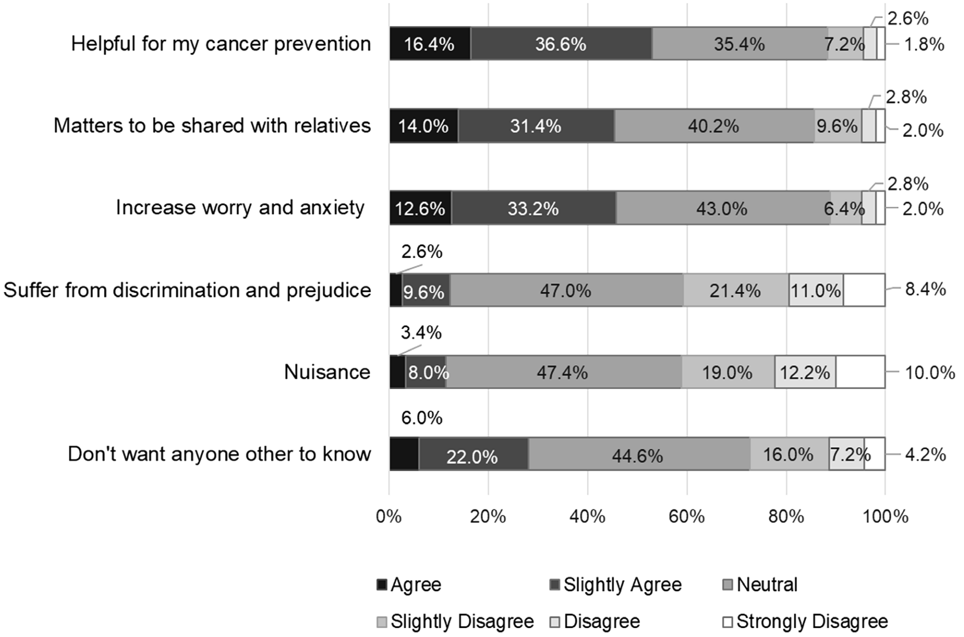

Figure 3. Proportions of responses regarding motivations influencing the willingness to share the BRCA genetic test results and undergo.

For sharing the BRCA genetic test expressed results, 51.2% of the participants answered "Agree" or "Slightly agree," and among them, 71.9% "Agree" or "Slightly agree" to undergoing CGT. In addition, 20.7% answered "Neutral." Not all those who wanted to share the genetic test results wished to undergo CGT. Additionally, among the 14.0% who answered, "Strongly disagree," "Disagree," or "Slightly disagree" to sharing the BRCA genetic test results, 71.4% indicated that they would not undergo CGT. This suggests that the individuals who do not intend to undergo CGT may not perceive a need to share their BRCA genetic test results.

Figure 3 shows the proportion of responses regarding the motivations influencing the willingness to share the BRCA genetic test results and undergo CGT. The positive motivations included "Helpful for my cancer prevention" and "Matters to be shared with relatives" chosen by 53.0% and 45.4% of the respondents, respectively. The negative motivations included "Increased worry and anxiety" and "Suffering from discrimination or prejudice", which were selected by 45.8% and 12.2% of the respondents, respectively. However, "Suffering from discrimination or prejudice" was notably lower compared to "Increased worry and anxiety".

3.4. Factors Influencing the BRCA Genetic Test Results Sharing and Undergoing CGT

The results of the multiple regression analysis on the willingness to share the BRCA genetic test results and undergo CGT in relation to motivation and knowledge are shown in **Table 3**. Both the willingness to share the BRCA genetic test results and undergo CGT were promoted by the factors "Helpful for my cancer prevention" and "Matters to be shared with relatives," with a stronger motivation for "Helpful for my cancer prevention" particularly influencing the decision to undergo CGT. Additionally, sharing the BRCA genetic test results was weakly associated with "Increased worry and anxiety," and the willingness to undergo CGT was weakly related to knowledge about HBOC.

Table 3. Regression analysis of willingness to share and Undergo CGT on motivations and knowledge.

Motivation and knowledge	Want to share the genetic test results			Want to undergo CGT		
	Estimate	*p*-value		Estimate	*p*-value	
Helpful for my cancer prevention	0.38	<0.001	***	0.46	<0.001	***
Matters to be shared with relatives	0.37	<0.001	***	0.27	<0.001	***
Increased worry and anxiety	0.09	0.012	*	0.00	0.953	
Suffer from social discrimination and prejudice	−0.07	0.074		0.06	0.143	
Annoying	−0.07	0.104		0.03	0.555	
Don't want anyone other to know	−0.04	0.302		−0.06	0.098	
Amount of knowledge	−0.02	0.520		0.10	0.002	**
Adjusted R-squared	0.51			0.46		

*<0.05, **<0.01, ***<0.001.

Table 4. Relationship between willingness to share, undergo CGT, and participants information.

Subjects	Categories	Want to share the genetic test results			Want to undergo CGT		
		Estimate	*p*-value		Estimate	*p*-value	
Age	20s	1.00 (reference)					
	30s	0.05	0.398		0.01	0.845	
	40s	−0.02	0.681		−0.07	0.250	
	50s	0.14	0.018	*	-0.01	0.852	
	60s	0.03	0.682		-0.06	0.327	
Sex	Women	1.00 (reference)					
	men	−0.10	0.020	*	−0.15	0.001	**
Presence of child	Yes	0.06	0.267		0.00	0.969	
Household income	Low	1.00 (reference)					
	Intermediate	0.14	0.006	**	0.17	0.001	**
	Higher-intermediate	0.06	0.004	**	0.15	0.004	**
	High	0.06	0.21		0.14	0.007	*
Cancer experience	Yes	−0.06	0.15		−0.04	0.308	
Family history of cancer	Yes	0.10	0.03	*	0.15	0.001	**
Adjusted R-squared		0.06			0.06		

*<0.05, **<0.01.

Table 4 shows the relationship between the willingness to share the test results and undergo CGT and the basic information of the participants. Both the willingness to share the BRCA genetic test results and undergo CGT were influenced by the respondents' gender, household income, and family history of cancer. Women with family histories of cancer were more willing to undergo CGT.

4. Discussion

This study targeted the general population of Japan, aged 20 - 69 years, to elucidate their hypothetical willingness to share the BRCA genetic test results and undergo CGT if they were relatives of someone with HBOC, and analyze the factors influencing these decisions. The results showed that 51.2% of the participants expressed a willingness to share the genetic test results ("Agree" or "Slightly agree"), and of these, 71.9% were willing to undergo CGT. The analysis revealed that the key promoting factors for the willingness to share the test results and undergo CGT were "Helpful for my cancer prevention" and "Matters to be shared with relatives," with "Helpful for my cancer prevention" having a particularly strong influence on the willingness to undergo CGT. In the general population, there is an emerging understanding that the genetic information affects not only the individuals but also their entire families and that it is useful for cancer prevention.

Those who were more willing to share the results of the BRCA genetic test considered it valuable to know the results. Negative emotions such as "increased worry and anxiety" have been reported to be both facilitating and barrier factors in previous reports [13]. In this study, "increased worry and anxiety" was a facilitating factor, and although awareness of the results increased concern about cancer risk, we believe it worked in the direction of promoting the desire to know because of worry. Additionally, "Matters to be shared with relatives" was an equally significant promoting factor. Previous reports have indicated that in Asia, people still hesitate to discuss cancer issues within the family due to concerns about "bad luck" and "discrimination", and concerns about discrimination against relatives are barriers to sharing the genetic test results [18] [19]. However, in this study, only 12.2% of the participants believed that being a relative of someone with HBOC would lead to discrimination. This low percentage may be due to cultural changes and shifts in the family structure in Japan. Historically, the Japanese civil law has emphasized large families and the respect for family lineage [20]. However, households with parents, children, and grandparents living together decreased from 62% in 1980 to 32.7% in 2020 [21]. They think that the change to a nuclear family has made them less concerned about the eyes of others. Studies conducted in Japan have reported a declining trend in genetic discrimination [22]. Negative feelings such as discrimination, which had been a barrier to knowing genetic information, have been suppressed, and people are becoming aware that they can make use of the information for cancer prevention because they are concerned about it. However, it is difficult to definitively state whether discrimination has decreased. In this survey, 47.0% of the respondents answered "neither" about the possibility of being discriminated against for being related to an HBOC. It is suggested that some of these people cannot imagine what kind of discrimination they might face, more than a lack of knowledge about HBOC. Additionally, 14.0% of the respondents did not want to share the BRCA genetic test results. This may indicate a potential lack of risk awareness due to insufficient knowledge about HBOC.

The willingness to undergo CGT was strongly influenced by "Helpful for my cancer prevention" rather than "Increased worry and anxiety." This suggests that the belief in the health benefits of cancer prevention outweighs the fear of increased anxiety, making people more likely to engage in preventive health behaviors. Not everyone who wanted to share the BRCA genetic test results wanted to undergo CGT. We believe that wanting to know the results is not the same as wanting to undergo CGT and that the perceived significant benefit is necessary to move a person to take action. Previous studies have also reported that health beliefs promote CGT uptake in Western countries, and this study found similar results [13]. In Japan, awareness is increasing that breast cancer is treatable when detected early and that early prevention is essential. [23]. This awareness is reflected in concrete actions, as the breast cancer screening rate in 2022 was approximately 47.4% [24]. While this rate is still lower compared to 70.0% - 76.5% in Western countries [25], it has significantly improved by approximately 20% in 20 years. For patients diagnosed with HBOC, detailed breast cancer surveillance, such as contrast-enhanced breast magnetic resonance imaging (MRI) is recommended [6]. However, in Japan, breast MRI is primarily used for diagnostic purposes and not as widely used for screening high-risk individuals as in Western countries. Many facilities still use mammography and breast ultrasound for HBOC surveillance, similar to the standard screening [26]. To promote the use of genetic test results and CGT uptake, healthcare providers must establish systems that enable them to provide surveillance of relatives. Recognizing genetic information as a valuable tool helps relatives appreciate its importance.

In this study, women and higher-income individuals were more willing to share the BRCA genetic test results and undergo CGT than men and lower-income individuals.

Previous reports have shown that the BRCA genetic test results are more often shared with women, and CGT is rarely performed in families with men [27]. This study found many incorrect responses, identifying "HBOC is a disease of women", which may hinder men from sharing their results and undergoing CGT. The healthcare providers should advise the sharing of BRCA genetic test results with men. CGT and surveillance of relatives without cancer are expensive and not covered by insurance. Low-income households may not be able to afford CGT. Promoting CGT requires raising awareness about HBOC and creating financial systems that make testing affordable.

As the number of individuals diagnosed with HBOC has increased, the number of relatives with HBOC has also increased. The healthcare providers need to offer personalized support tailored to each family's circumstances and establish surveillance systems that utilize genetic information when sharing the BRCA genetic test results. This approach is expected to promote relatives' utilization of genetic information.

Limitations of this study include the use of a hypothetical scenario in which participants were asked to imagine themselves as a relative of someone with HBOC. This could mean that their responses may differ from real-life responses. In addition, the randomly selected population in this study cannot be compared to individuals with a high-risk family history. However, the responses may more accurately reflect the potential reactions of people who consider themselves to be less involved with HBOC.

5. Conclusions

It is necessary to understand the perspectives of relatives regarding the BRCA genetic test results; however, there have been no such research reports in Japan. Understanding the hypothetical intentions of relatives regarding their willingness to share their BRCA genetic test results and undergo CGT is essential for healthcare professionals to recognize the support needed in the future. Therefore, this study elucidated the willingness of the general population to share the genetic test results and undergo CGT and analyze the factors that influence these decisions.

The results of the BRCA genetic testing provide valuable information about the potential cancer risks for relatives, and offer an opportunity to consider whether CGT should be performed within the family based on these results. In the general population, there is an emerging understanding that genetic information affects not only the individual, but also the entire family, and that it is useful for cancer prevention. The CGT helps determine the need for detailed cancer prevention measures at an early stage, thereby contributing to early cancer detection. To promote the sharing of BRCA genetic test results and the uptake of CGT, the healthcare providers should offer support tailored to each family's circumstances and establish cancer prevention measures recommended for HBOC.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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