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Patients' experiences with pre-test genetic counseling provided by breast cancer healthcare professionals: Results from a large prospective multicenter study

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ABSTRACT

Background: Pre-test genetic counseling of patients with breast cancer is increasingly being offered by non-genetic healthcare professionals. We aimed to evaluate the experiences of patients with breast cancer receiving pre-test genetic counseling from a non-genetic healthcare professional (i.e., surgeon or nurse).
Methods: Patients who were diagnosed with breast cancer and received pre-test counseling from their surgeon or nurse (mainstream group), and patients who received pre-test counseling from a clinical geneticist (usual care group) were invited to participate in our multicenter study. Between September 2019 and December 2021, patients received a questionnaire after pre-test counseling (T0) and four weeks after receiving their test results (T1) to evaluate psychosocial outcomes, knowledge, discussed topics and satisfaction.
Results: We included 191 patients in our mainstream and 183 patients in our usual care group and received, respectively 159 and 145 follow-up questionnaires. Levels of distress and decisional regret were comparable in both groups. Decisional conflict was higher in our mainstream group ($p = 0.01$), but only 7% had clinically relevant decisional conflict (vs 2% in usual care group). The possible implications of a genetic test on (secondary) breast or ovarian cancer risks were less frequently discussed in our mainstream group ($p = 0.03$ and $p = 0.000$, respectively). In both groups knowledge about genetics was comparable, satisfaction was high and the majority of patients in both groups preferred to give both verbal and written consent for genetic testing.
Conclusion: Mainstreamed genetic care provides sufficient information for the majority of breast cancer patients to decide about genetic testing with minimal distress.

Abbreviations: HCP, healthcare professional.

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1. Introduction

Genetic test results in patients with breast cancer can impact both patients' treatment and preventive options [1,2]. Previously, only surgical treatment was impacted by genetic test results, such as risk-reducing mastectomy of the contralateral breast [3]. Nowadays, there is increasing evidence that systemic treatment options should also be influenced by these test results, especially in patients who are carrier of a germline pathogenic variant (PV) in a *BRCA1/2* gene. In the NCCN guidelines platinum-based agents (cisplatin and carboplatin) are described as preferred treatment for patients with triple-negative recurrent/stage IV breast cancer and a germline *BRCA1/2* PV [4]. Recently, it was shown that one year adjuvant treatment with Poly Adenosine Diphosphate-Ribose Polymerase (PARP) inhibitors leads to significantly improved invasive disease-free survival (IDFS) and distant disease-free survival (DDFS) in patients with high-risk, Her 2-negative, early breast cancer who are also carrying a (likely) PV in a *BRCA1/2* gene [5] and to significantly improved overall survival [6]. With these increasing implications of genetic testing on treatment, one can also expect an increase in the number of eligible patients [7]. However, the workforce of genetics departments is insufficient to meet this growing demand [8,9].

This imbalance between supply and demand has led to innovative ways of offering genetic testing. This includes the mainstreaming of genetic testing, with non-genetic healthcare professionals (HCPs) such as surgeons, oncologists and nurses providing pre-test genetic counseling and ordering genetic tests, instead of usual genetic care provided by genetic HCPs (i.e., clinical geneticists and genetic counselors) [10,11]. Mainstream genetic testing pathways have been successfully introduced for ovarian cancer [12,13]. Given the high acceptability and feasibility for both patients and HCPs, these pathways are increasingly being implemented for breast cancer [14–24].

Pre-test counseling by a non-genetic HCP is different from pre-test counseling by a genetic HCP because of differences in expertise and available time. This raises concerns that with mainstream genetic testing informed consent may not be obtained, it may lead to increased psychosocial problems (e.g., more distress or regret), or patients may receive insufficient information to make an informed decision about genetic testing. So far, studies have shown positive experiences in breast cancer patients [16–18,21,23,24]. However, these studies were either qualitative in nature [18,23], focused only on acceptability [16], did not compare experiences with a group of patients receiving usual genetic care [16,18,23], or involved only a limited number of breast cancer patients [16,17,24]. To our knowledge, no studies have evaluated outcomes such as distress and anxiety at different time points between patients who received pre-test counseling from different HCPs (non-genetic versus genetic).

We have developed and implemented a mainstream genetic testing pathway for patients with breast cancer. We recently reported that surgical oncologists and nurse specialists feel motivated and competent to provide pre-test counseling to patients with breast cancer [25]. In the current paper, we report on the experiences of patients with mainstream genetic testing. We aimed to assess patients' psychosocial outcomes, knowledge about genetics and satisfaction both after pre-test genetic counseling and after receiving the genetic test result and to compare these outcomes with patients who received usual genetic care.

2. Patients and methods

2.1. Study design and participants

First, our mainstream genetic testing pathway for breast cancer was implemented as standard care in nine hospitals [25]. In the current multicenter, prospective, observational study, we evaluated patients' experiences with mainstream genetic testing and compared these with experiences of patients who received usual genetic care. Between September 2019 and December 2021, patients who received pre-test genetic counseling from a non-genetic HCP were invited to participate in our mainstream group and patients who received pre-test genetic counseling from a genetic HCP were invited to participate in our usual care group (Fig. 1). Both newly diagnosed patients and patients with breast cancer in their history could participate. After pre-test counseling, patients could opt for genetic testing (*BRCA1, BRCA2, CHEK2, PALB2*, and *ATM*). Patients were excluded if they did not speak Dutch, if a PV in one of the breast cancer susceptibility genes had been previously identified in a family member, or if the patient had had testing of some of these genes previously.

2.2. Mainstream genetic care pathway

The development and implementation of our mainstream pathway is described previously [25]. After completing an online training module, non-genetic HCPs could provide pre-test counseling and order genetic tests themselves (Fig. 1). In our study, this was predominantly performed by HCPs working at a surgical department. Two checklists were completed by the non-genetic HCP to determine eligibility for mainstream genetic testing [25]. In addition, these checklists identified patients who required post-test genetic counseling. Patients were eligible for mainstream genetic testing if [1] they met at least one eligibility criterium for genetic testing which was based on patients' characteristics (e.g., breast cancer below the age of 40) and with or without additional eligibility criteria based on family history, and [2] further evaluation at a genetics department prior to testing was unnecessary (e.g., for counseling and testing of the *TP53* gene). After pre-test counseling, HCPs handed out an information sheet about genetic testing to patients and obtained written informed consent before ordering the genetic test. The two checklists and the consent form were sent to the genetics department of the UMC Utrecht.

Test results were sent in a letter by a clinical geneticist to the patient, the HCP who ordered the genetic test and the general practitioner. Patients received an invitation for post-test counseling by a genetic HCP (i.e., clinical geneticist or genetic counselor) if a (likely) PV or variant of uncertain clinical significance was identified. Patients also received this invitation if they had a relevant personal or family history, as identified by the checklist, to receive appropriate screening recommendations for their family members. These consultations with a genetic HCP were considered usual genetic care.

2.3. Usual genetic care pathway

Patients were referred by their treating physician or nurse to the genetics department if [1] this HCP had not (yet) completed the training [2], patients did not meet one of the eligibility criteria for genetic testing based on patients' characteristics but eligibility for genetic testing was solely dependent on family data (i.e., relatives affected with breast, ovarian or prostate cancer), or [3] the HCP or patient preferred referral to the genetics department. Referred patients received pre-test counseling from a genetic HCP, who collected more details about the family to confirm eligibility for testing. Written informed consent was obtained for all patients who consented to genetic testing. Genetic test results were communicated to the patient by telephone, in person or in a videoconference. In addition, a letter was sent to the patient, the HCP who referred the patient and the general practitioner, summarizing the family history, test results, and any advice for patient and family members.

2.4. Procedures

Participants were asked to complete two questionnaires (overview of topics in Online Supplements). The first questionnaire (T0) was handed out after pre-test counseling if counseling was provided face-to-face. For the usual care group, this questionnaire could also be sent with the letter summarizing the pre-test counseling. Information about the study and a form to accept or decline participation were sent with this questionnaire. After two weeks, written reminders were sent to non-responders of our

mainstream group only. The second questionnaire (T1) was sent approximately four weeks after receiving the genetic test result. Written reminders were sent to non-responders of both groups after four weeks and telephone reminders after eight weeks.

Our primary outcomes were the impact of mainstream genetic testing on psychosocial outcomes (i.e., distress, anxiety, depression, decisional conflict and decision regret). Secondary outcomes were patients' knowledge, the topics discussed during pre-test counseling, and patients' satisfaction with the genetic testing process, including the informed consent procedure.

2.5. Clinical data

At the genetics department of the UMC Utrecht, we reviewed the medical records of all participants to obtain their age at diagnosis, number of days between diagnosis and pre-test counseling, test result and eligibility criteria for genetic testing. The date of pre-test counseling for the mainstream group was determined by proxy based on the date the checklist was completed; if that was unavailable, we used the date the consent form was completed. We assessed whether patients were eligible for genetic testing according to national guideline criteria and, if they were eligible, which criteria they fulfilled [26]. Eligibility for genetic testing was assessed based on the family pedigree for all patients in the usual care group and for the patients in the mainstream group who had received post-test counseling at the genetics department. For the other patients in the mainstream group, eligibility for genetic testing was assessed based on the completed checklist.

2.6. Statistical analyses

Between-group analyses were performed using the Chi-square test or Fishers Exact test for categorical outcomes and the independent T-test or Mann-Whitney *U* test for continuous outcomes. Within-group analyses comparing outcomes between T0 and T1 were assessed with the McNemar test for binary outcomes or the Wilcoxon-signed Rank test for continuous outcomes. General Linear Models for repeated measures were used to compare if the difference in anxiety, depression, distress and knowledge were comparable in the mainstream and usual care group over time. IBM SPSS statistics 26.0.0.1 was used to perform the statistical analyses. A (two-sided) p-value <0.05 was considered as significant.

3. Results

3.1. Participants

After exclusion of ineligible patients, 191 patients were included in our mainstream group and 183 patients in our usual care group, of whom respectively 159 (83%) and 146 (80%) patients completed both questionnaires (Fig. 1). The usual care group included significantly more patients with children. The mainstream group included significantly more patients who received pre-test counseling within two weeks after diagnosis, more male patients, and they more often met at least one of the eligibility criteria for genetic testing based on patients' characteristics (Table 1).

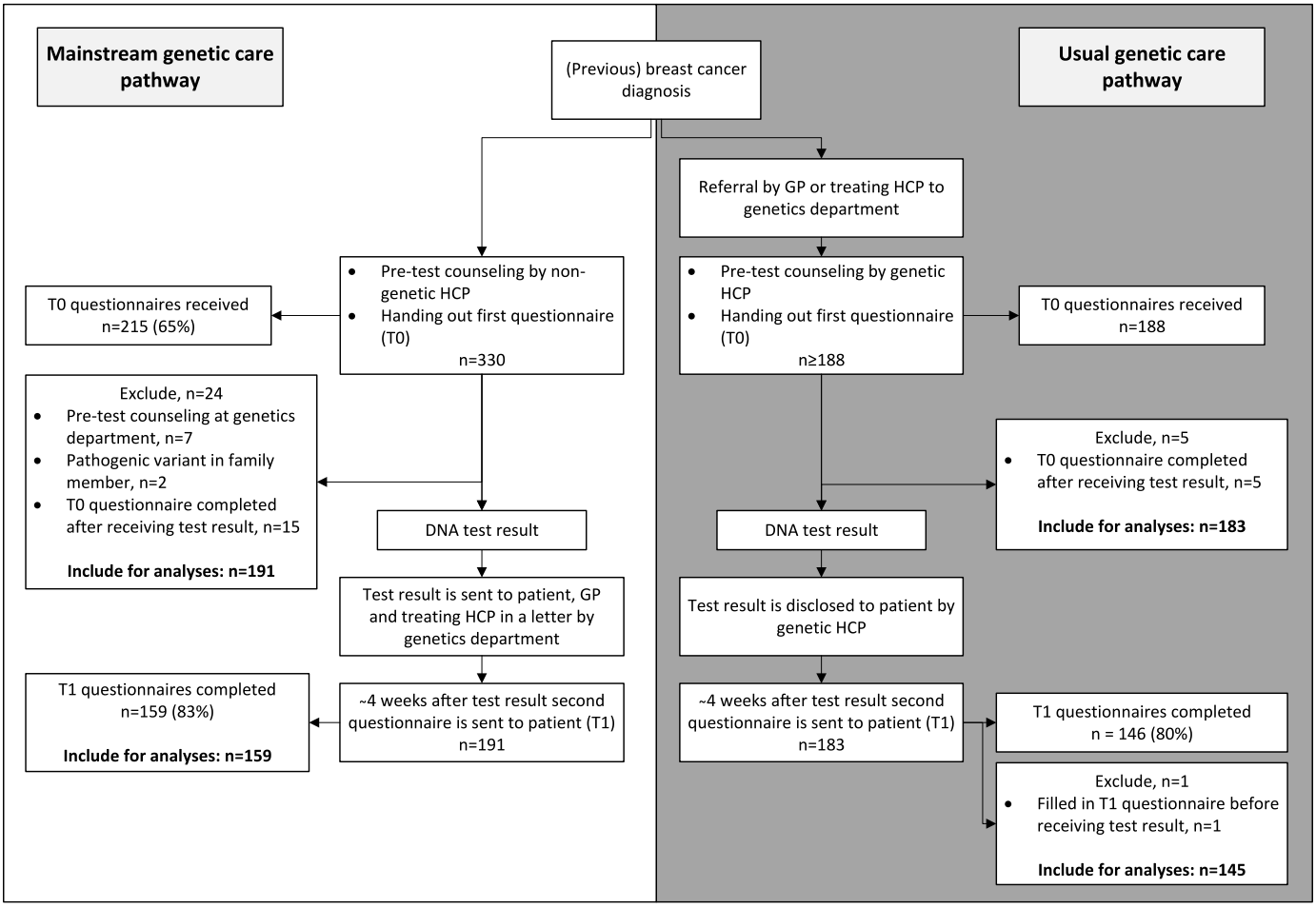

Fig. 1. Mainstream and usual genetic care pathways for breast cancer patients including response rates. GP: general practitioner, HCP: healthcare professional.

Table 1
Characteristics of respondents.

	Mainstream group n = 191	Usual care group n = 183	p-value
Age at diagnosis, mean (sd)	48.7 (11.8)	50.3 (11.0)	0.184
Gender, n (%)			
Male	10 (5.2)	1 (0.5)	0.01[b]
Female	181 (94.8)	182 (99.5)	
Days between diagnosis and pre-test genetic counseling, n (%)			
0–14	160 (83.8)	49 (26.8)	0.000[b]
> 14	31 (16.2)	134 (73.2)	
Previously diagnosed with BC, n (%)			
Yes	35 (18.3)	26 (14.2)	0.28
No	156 (81.7)	157 (85.8)	
Genetic test results, n (%)			
Normal	170 (89.0)	165 (90.2)	0.71
Pathogenic variant or VUS	21 (11.0)	18 (9.8)	
Children, n (%)			
Yes	146 (76.4)	155 (84.7)	0.04[b]
No	45 (23.6)	28 (15.3)	
Education, n (%)			
Low	4 (2.1)	6 (3.3)	0.31
Intermediate	91 (47.6)	100 (54.6)	
High	93 (48.7)	77 (42.1)	
Missing	3 (1.6)	0	
Migrant status, n (%)			
Dutch background	168 (88)	159 (86.9)	0.94
Migrant, Western	12 (6.3)	12 (6.6)	
Migrant, non-Western	10 (5.2)	11 (6.0)	
Missing	1 (0.5)	1 (0.5)	
Personal history of another type of cancer, n (%)			
Yes	26 (13.6)	29 (15.8)	0.54
No	165 (86.4)	154 (84.2)	
Eligibility criteria for genetic testing, n (%)			
BC < 40 years			
Yes	58 (30.4)	35 (19.1)	0.01[b]
No	133 (69.6)	148 (80.9)	
Triple-negative BC < 60 years			
Yes	61 (31.9)	23 (12.6)	0.000[b]
No	130 (68.1)	160 (87.4)	
Multiple tumors with 1st diagnosis <50 years			
Yes	42 (22.0)	29 (15.8)	0.13
No	149 (78.0)	154 (84.2)	
Personal history of OC			
Yes	1 (0.5)	0	1.00
No	190 (99.5)	183 (100)	
Jewish background			
Yes	6 (3.1)	3 (1.6)	0.50
No	185 (96.9)	180 (98.4)	
Eligible based on family history			
Yes	33 (17.3)	53 (29.0)	0.007[b]
No	158 (82.7)	130 (71.0)	
Eligible according to guidelines			
Yes	172 (90.1)	130 (71.0)	0.000[b]
No	19[a] (9.9)	53 (29.0)	

BC: breast cancer, VUS: variant of uncertain clinical significance, OC: ovarian cancer.
[a] 8/19 (42%) DNA tests were conducted in the mainstream group with consent of a genetic healthcare professional.
[b] $p < 0.05$.

3.2. Psychosocial outcomes

After pre-test counseling, levels of anxiety, distress and decisional conflict were significantly higher for patients in the mainstream group compared with patients in the usual care group (Table 2). After adjusting for the number of days between diagnosis and pre-test counseling with multivariate analysis, this difference between the two groups regarding anxiety and distress disappeared (respectively, $p = 0.53$ and $p = 0.62$). The higher decisional conflict in our mainstream group remained significant after adjustment for time between diagnosis and pre-test counseling, having children and the differences in eligibility criteria between the two groups ($p = 0.02$).

After receiving test results, there were no significant differences for most psychosocial outcomes except for the 'support and effective decision' score of the decisional conflict scale. Within analyses for both groups are presented in the online Supplements.

3.3. Knowledge and discussed topics

There were no significant differences in knowledge between the mainstream and usual care group at both time points (Online Supplements).

In the mainstream group, 'the consequences of genetic testing for chemotherapeutic treatment' were discussed significantly more often than in the usual care group, whereas in the usual care group 'the increased risk of a second breast cancer and ovarian cancer for carriers of a PV in a *BRCA1/2* gene' was discussed more often (Fig. 2a). In both groups, patients considered 'the consequences of genetic testing on family members' most important (Fig. 2b).

3.4. Satisfaction

In both groups, the majority of patients were satisfied with pre-test

Table 2
Comparison of psychosocial outcomes between groups at T0 and T1.

Variable	T0			T1		
	Mainstream group n = 191	Usual care group n = 183	p-value	Mainstream group n = 159	Usual care group n = 145	p-value
HADS-Anxiety						
Total score, median (IQR)	7.0 (7.0)	5.0 (7.0)	0.002[a]	5.0 (6)	4.0 [5]	0.17
Subgroups, n (%)						
0–7	101 (52.9)	122 (66.7)	0.022[a]	115 (72.3)	113 (77.9)	0.48
8–10	38 (19.9)	21 (11.5)		28 (17.6)	23 (15.9)	
11–21	50 (26.2)	39 (21.3)		15 (9.4)	9 (6.2)	
Missing	2 (1.0)	1 (0.5)		1 (0.6)	0	
HADS-Depression						
Total score, median (IQR)	3.0 (5.0)	3.0 (5.0)	0.58	4.0 (4.0)	4.0 (4.0)	0.47
Subgroups, n (%)						
0–7	155 (81.2)	148 (80.9)	0.96	135 (84.9	118 (81.4)	0.62
8–10	19 (9.9)	20 (10.9)		14 (8.8)	16 (11.0)	
11–21	15 (7.9)	14 (7.7)		9 (5.7)	11 (7.6)	
Missing	2 (1.0)	1 (0.5)		1 (0.6)	0	
Distress Thermometer						
Total score, median (IQR)	6.0 (4.0)	4.0 (5.0)	0.01[a]	4.0 (4.0)	4.0 (4.0)	0.46
Subgroups, n (%)						
≤ 3	55 (28.8)	73 (39.9)	0.01[a]	66 (41.5)	69 (47.6)	0.26
≥ 4	135 (70.7)	104 (56.8)		93 (58.5)	75 (51.7)	
Missing	1 (0.5)	6 (3.3)		0	1 (0.7)	
Influence of genetic testing on tension or distress, n (%)						
Yes, less tension or distress	2 (1.0)	4 (2.2)	0.63	9 (5.7)	10 (6.9)	0.82
No	134 (70.2)	122 (66.7)		89 (56.0)	77 (53.1)	
Yes, more tension or distress	54 (28.3)	54 (29.5)		60 (37.7)	57 (39.3)	
Missing	1 (0.5)	3 (1.6)		1 (0.6)	1 (0.7)	
Decisional conflict						
Total score, median (IQR)	20.3 (18.8)	15.6 (18.8)	0.01[a]	15.0 (20.0)	13.3 (20.0)	0.14
Subgroups, n (%)						
0–37.5	169 (88.5)	176 (96.2)	0.04[a]	152 (95.6)	141 (97.2)	0.45
> 37.5	13 (6.8)	4 (2.2)		5 (3.1)	2 (1.4)	
Missing, n (%)	9 (4.7)	3 (1.6)		2 (1.3)	2 (1.4)	
Uncertainty score	4.2 (25.0)	0 (25.0)	0.65	0.0 (16.7)	0 (25.0)	0.08
Missing, n (%)	1 (0.5)	1 (0.5)		1 (0.6)	2 (1.4)	
Informed score	25.0 (25.0)	16.7 (33.3)	0.02[a]	16.7 (25.0)	16.7 (25.0)	0.61
Missing, n (%)	2 (1.0)	0		1 (0.6)	2 (1.4)	
Support score	25.0 (25.0)	16.7 (25.0)	0.004[a]	16.7 (16.7)	8.3 (25.0)	0.003[a]
Missing, n (%)	5 (2.6)	0		1 (0.6)	2 (1.4)	
Values clarity score	25.0 (25.0)	25.0 (25.0)	0.02[a]	25.0 (33.3)	16.7 (33.3)	0.07
Missing, n (%)	7 (3.7)	2 (1.1)		1 (0.6)	2 (1.4)	
Effective decision score	18.8 (25.0)	12.5 (25.0)	0.002[a]	16.7 (25.0)	0 (25.0)	0.02[a]
Missing, n (%)	2 (1.0)	0		2 (1.3)	2 (1.4)	
Decision regret	N/A	N/A	N/A			
Total score, median (IQR)				0 (10.0)	0 (10.0)	0.93
Subgroups, n (%)						
0–25				153 (96.2)	138 (95.2)	0.49
> 25				3 (1.9)	5 (3.4)	
Missing, n (%)				3 (1.9)	2 (1.4)	

HADS: Hospital Anxiety and Depression Scale, IQR: Interquartile range. N/A: Not applicable. Outcomes are not corrected for 'time since diagnosis'.
[a] $p < 0.05$.

counseling regarding the information received, the amount of time to consider the genetic test and the preferred moment to be offered a genetic test (Table 3). In the mainstream group, significantly more patients were unsure whether they had received sufficient information and amount of time to consider the genetic test and whether they thought the information discussed was clear. In both groups, the majority of patients felt that 'immediately after diagnosis' was the best moment to offer genetic testing.

The majority of patients in both groups were satisfied with how and what information they received about the test result (Table 4). In the mainstream group, for more patients it was unclear how they would receive the test result. In addition, the majority of patients in this group preferred a letter to receive the test result, whereas in the usual care group the majority preferred a telephone consultation.

In both the mainstream and usual care group, the majority of patients gave both verbal and written informed consent and also preferred this (Online Supplements).

4. Discussion

To our knowledge, this is the largest study to evaluate the experiences of breast cancer patients with mainstreamed genetic testing compared with the experiences of patients who received usual genetic care including pre-test counseling by a genetic HCP. This study shows that mainstreamed genetic care allows the majority of patients to make an informed decision about genetic testing, and it results in acceptable levels of distress, decisional conflict and regret.

4.1. Psychosocial outcomes

Adjusting for the time between diagnosis and pre-test counseling, we did not observe statistically significant differences, either after pre-test counseling or after receiving the test result, in distress, anxiety or depression between the patients who received pre-test counseling from a non-genetic HCP and those who received it from a genetic HCP. Only two previous studies compared psychosocial outcomes between breast cancer

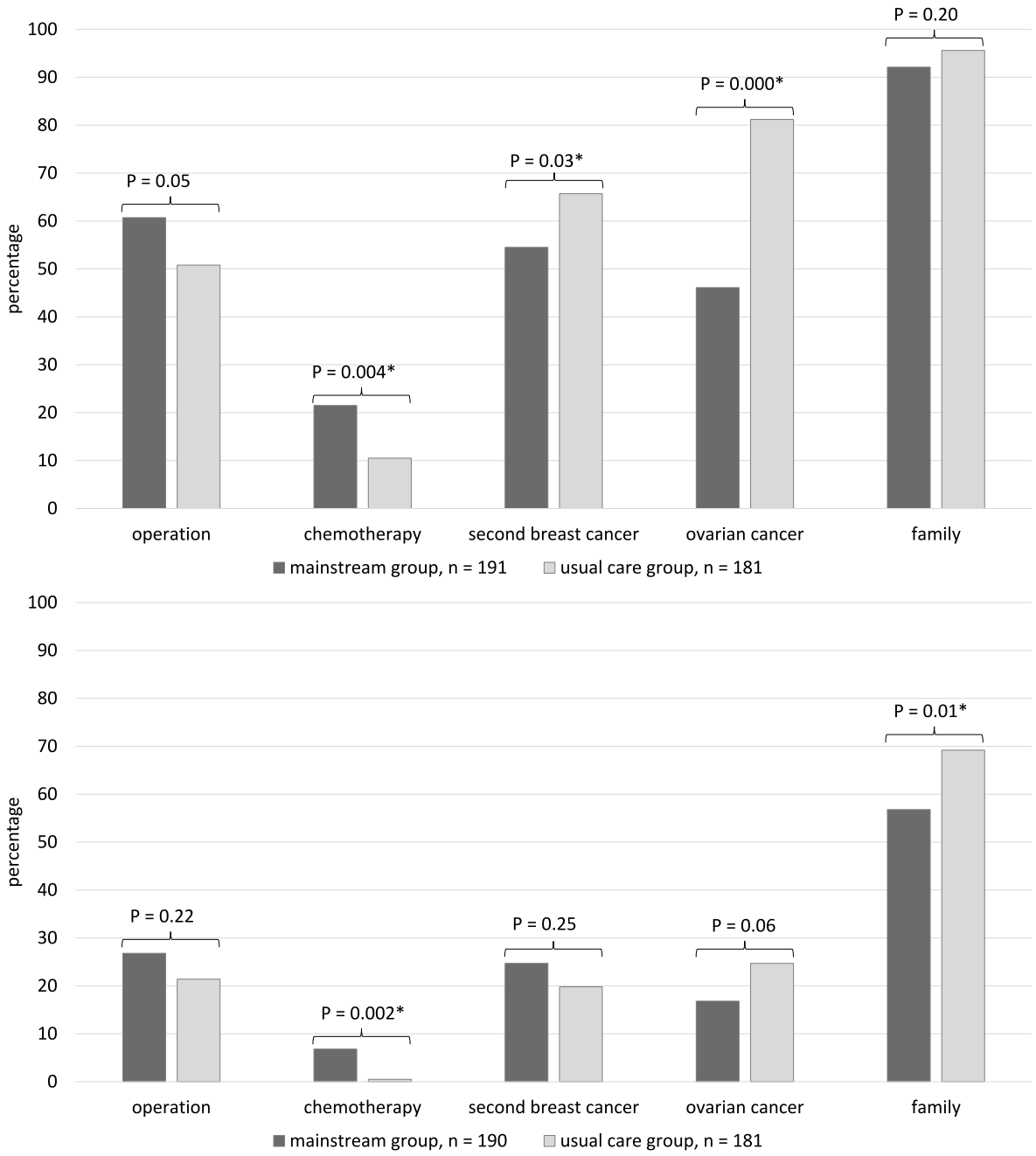

Fig. 2A. Discussed topics during pre-test counseling for the mainstream and usual care group. Patients were asked whether one or more of these topics were discussed. For every topic, the percentage of patients who said that it was discussed is displayed in this bar chart. *p < 0.05. Fig. 2b. Topics that patients in the mainstream and usual care group considered most important. Patients were asked to select the topic they considered most important. For every topic, the percentage of patients who said it was most important is displayed. If patients selected more than one topic, both were included in the bar chart. *p < 0.05.

patients receiving mainstreamed versus usual genetic care. However, these studies included both patients with breast and ovarian cancer, their mainstream groups were limited in size (<50 patients), and these groups only included 11 patients with breast cancer [17,21]. As in our study, no difference in distress levels between the two groups was found in either of the other studies. Only one study compared anxiety and depression levels between two groups [21]. In this study, patients who received mainstreamed genetic care were more likely to screen positive on the 'general emotions' domain of the 'psychosocial aspects of hereditary cancer (PAHC)' questionnaire relating to anxiety and depression amongst others. However, it is unclear whether the number of days between diagnosis and pre-test counseling affected these outcomes.

In our study, decisional conflict after pre-test counseling was higher in patients who had received mainstreamed genetic care. However, only a small proportion of these patients (7%) had clinically relevant decisional conflict, versus 2% of patients in our usual care group. The only study that evaluated this outcome did not find a significant difference in decisional conflict between patients who had received mainstreamed and usual genetic care [17].

As far as we know, decisional regret after performing a genetic test has not been evaluated previously for patients with breast cancer. We showed that regret was comparable and low in both groups, which is in line with previous research for patients with ovarian cancer [27,28]. This suggests that even if some patients experience more decisional conflict after pre-test counseling by a surgeon or nurse (instead of a genetic HCP), the majority will not regret their choice to undergo genetic testing.

Table 3
Questions indicating satisfaction with pre-test genetic counseling.

	Response categories	Mainstream group n = 191	Usual care group n = 183	p-value
Clarity of discussed information regarding the genetic test, n (%)	- (Very) clear	168 (88.0)	179 (97.8)	0.001*
	- Unsure	18 (9.4)	4 (2.2)	
	- Not clear (at all)	3 (1.6)	0	
	- Missing	2 (1.0)	0	
Received written information after discussing genetic test, n (%)	- Yes	140 (73.3)	144 (78.8)	0.22
	- No	50 (26.2)	38 (20.8)	
	- Missing	1 (0.5)	1 (0.5)	
Clarity of received written information after discussing the genetic test, n (%)	- (Very) clear	128 (91.4)	136 (94.4)	0.10
	- Unsure	9 (6.4)	4 (2.8)	
	- Not clear (at all)	2 (1.4)	4 (2.8)	
	- Missing	1 (0.7)	0	
There was enough information to decide whether or not to perform the genetic test, n (%)	- Yes	171 (89.5)	177 (96.7)	0.04*
	- No	1 (0.5)	0	
	- Don't know	16 (8.4)	6 (3.3)	
	- Missing	3 (1.6)	0	
There was enough time to decide whether or not to perform the genetic test, n (%)	- Yes	167 (87.4)	177 (96.7)	0.002*
	- No	7 (3.7)	0	
	- Don't know	15 (7.9)	6 (3.3)	
	- Missing	2 (1.0)	0	
I felt I had a choice whether or not to perform a genetic test, n (%)	- Yes	168 (88.0)	165 (90.2)	0.54
	- No	13 (6.8)	13 (7.1)	
	- Don't know	8 (4.2)	4 (2.2)	
	- Missing	2 (1.0)	1 (0.5)	
Satisfaction with being offered a genetic test, n (%)	- (Very) satisfied	183 (95.8)	175 (95.6)	0.77
	- Unsure	7 (3.7)	5 (2.7)	
	- Not satisfied (at all)	0	0	
	- Missing	1 (0.5)	3 (1.6)	
Preferred moment to be offered a genetic test, n (%)	- Directly after (first) diagnosis	160 (83.3)	126 (68.9)	0.000*
	- After the (first) operation	8 (4.2)	6 (3.3)	
	- After completion of treatment	5 (2.6)	26 (14.2)	
	- In case of recurrence	7 (3.7)	4 (2.2)	
	- No preference	2 (1.0)	3 (1.6)	
	- Other[a]	4 (2.1)	8 (4.4)	
	- Missing/unclear	5 (2.6)	10 (5.5)	
It was clear that after talking to the doctor or nurse specialist about the genetic test, I could choose to have an additional conversation with a genetics healthcare professional about it	- Yes	107 (56.0)	N/A	N/A
	- No	79 (41.4)		
	- Missing	5 (2.6)		

N/A: Not applicable. [a]In the mainstream group, two patients preferred genetic counseling in the second consultation after diagnosis, and two preferred counseling after breast cancer was diagnosed in a family member. In the usual care group, four patients preferred genetic counseling in a second or later consultation after diagnosis, two patients preferred to have genetic counseling before diagnosis, one patient considered the best moment to be determined by the doctor or nurse, and one patient preferred genetic counseling after breast cancer was diagnosed in a family member.

4.2. Knowledge and discussed topics

Knowledge about genetic testing was comparable in the two groups in our study. This is in line with the study of Richardson et al. [17], but in contrast to the study of McCuaig et al. where knowledge was higher in their usual care group [21]. However, their study included more extensive knowledge questions than our study. We believe that it is important for patients to have a basic understanding of genetic testing to make a well-informed decision about genetic testing. Detailed information about risks and implications for family members is needed especially when a PV in a breast cancer gene is identified.

A notable finding is that the possible higher risk of a second breast cancer or ovarian cancer after identifying a PV in a *BRCA1/2* gene was discussed less often in our mainstream group.

4.3. Satisfaction

Satisfaction of patients with mainstreamed genetic care was high, as also reported in previous studies [16,17,21,24]. However, only two studies included a limited number of patients in their usual care group as comparison [17,21]. Interestingly, in our mainstream group significantly more patients considered the provided information or time insufficient to consider genetic testing or were unsure about this. Although the majority of patients receiving mainstreamed genetic care were satisfied with the information and amount of time they received, this highlights the importance of recognizing those patients who require more extensive pre-test counseling. In addition, more patients in our mainstream group considered the information discussed during pre-test counseling unclear. This is in line with the study by McCuaig et al., who showed that in the mainstream group fewer patients considered the information helpful or given in a way that they understood [21].

The preferred moment for pre-test counseling in both groups was directly after diagnosing breast cancer, which is in line with previous research [23,29]. The preferred way to receive the test result differed between patients in both group. However, this is probably biased by the way most patients actually received their test result (i.e., in a letter in the mainstream group and by telephone in the usual care group). It also indicates that most patients do not object to receiving their test result in a letter.

One of the concerns about mainstream genetic testing, as identified by previous research, is the inability to obtain proper informed consent for genetic testing, possibly due to HCPs not providing pre-test counseling [30]. With written consent, there is a higher chance that pre-test counseling is provided. Our study is unique in that we evaluated patients' experiences with our informed consent procedure. Although many mainstream genetic testing pathways do include written informed consent for genetic testing [12], this is not standard practice. This study shows that patients do prefer to give both written and verbal informed consent for genetic testing.

Table 4
Questions indicating satisfaction with receiving test result.

	Response categories	Mainstream group n = 159	Usual care group n = 145	p-value
It was clear how the test result would be communicated, n (%)	- Yes	120 (75.5)	135 (93.1)	0.000*
	- No	38 (23.9)	7 (4.8)	
	- Missing	1 (0.6)	3 (2.1)	
Clarity of written information about the test result, n (%)	- (Very) clear	148 (93.1)	136 (93.8)	0.18
	- Unsure	10 (6.3)	4 (2.8)	
	- Not clear (at all)	0	0	
	- Missing	1 (0.6)	5 (3.4)	
Clarity of discussed information about the test result	- (Very) clear	N/A	138 (95.2)	N/A
	- Unsure		1 (0.7)	
	- Not clear (at all)		1 (0.7)	
	- Missing		5 (3.4)	
The doctor or nurse specialist discussed the result of the DNA test	- Yes	101 (63.5)	N/A	N/A
	- No, I have not had a new appointment after receiving the result	40 (25.2)		
	- No, I did have an appointment after receiving the result, but the result was not discussed	16 (10.1)		
	- Missing	2 (1.3)		
Looking back, there was insufficient information to decide on the DNA test, n (%)	- Yes	8 (5.0)	5 (3.4)	0.58
	- No	149 (93.7)	137 (94.5)	
	- Missing	2 (1.3)	3 (2.1)	
Ways of receiving test result, n (%)	- Letter	N/A	6 (4.1)	N/A
	- Telephone		122 (84.1)	
	- Video consultation		14 (9.7)	
	- Missing		3 (2.1)	
Satisfied with how test result was received, n (%)	- Yes	117 (73.6)	120 (82.8)	0.09
	- No	12 (7.5)	5 (3.4)	
	- No preference	29 (18.2)	18 (12.4)	
	- Missing	1 (0.6)	2 (1.4)	
Preferred way of receiving the test result	- Letter	127 (79.9)	11 (7.6)	0.000*
	- Telephone	16 (10.1)	96 (66.2)	
	- Consultation at genetics department	6 (3.8)	18 (12.4)	
	- Video consultation	1 (0.6)	9 (6.2)	
	- Both telephone or personal consultation and letter	4 (2.5)	1 (0.7)	
	- No preference	0	3 (2.1)	
	- Other	4 (2.5)	5 (3.4)	
	- Missing	1 (0.6)	2 (1.4)	
In case of a preferred personal conversation: preferred specialist to receive the result of the DNA test from	- Treating doctor	13 (41.9)	16 (12.1)	0.000*
	- Nurse specialist	7 (22.6)	3 (2.3)	
	- Clinical geneticist/genetic counselor	10 (32.3)	107 (81.1)	
	- No preference	1 (3.2)	3 (2.3)	
	- Other	0	3 (2.3)	
It was clear that the result of the genetic test could also have consequences for family members	- Yes	158 (99.4)	142 (97.9)	0.48
	- No	0	1 (0.7)	
	- Missing	1 (0.6)	2 (1.4)	
It was clear when the result of the genetic test would be discussed by a clinical geneticist/genetic counselor	- Yes	87 (54.7)	N/A	N/A
	- No	70 (44.0)		
	- Missing	2 (1.3)		

N/A: Not applicable.

4.4. Limitations

This study has several limitations. First, this study was not randomized and in the mainstream group, there was a high proportion of patients who did not participate in our study. In addition, for both groups we do not know how many eligible patients received pre-test counseling and how many of these patients received the study material. This may have skewed our results because of an ascertainment bias. Although it cannot be excluded that this information was provided to a selection of patients, most sociodemographic characteristics, e.g., migrant status and educational level, were comparable in both groups. In the future, a randomized non-inferiority design may provide stronger evidence to support the conclusions. Second, because of the differences in eligibility criteria for pre-test counseling by a non-genetic HCP (i.e., surgeon or nurse) or by a genetic HCP, the two groups were not comparable. We adjusted for the known differences with multivariate analyses, but there may have been other differences that we did not account for (e.g., current age or stage of treatment). In addition, we did not have detailed family data for all patients and therefore were unable to account for possible differences in family history for breast or ovarian cancer between the two groups. Third, we did not correct for multiple testing. Although we believe that this correction was not needed in our study because of the relatively small number of hypotheses [31], future studies are needed to confirm our findings.

5. Conclusion

This study shows that mainstream genetic testing for the majority of breast cancer patients provides sufficient support and information for decision making without unacceptable distress, decisional conflict or regret.

However, this study also shows that for some patients more personalized attention is necessary. It is important to further investigate for which patients mainstream genetic testing is insufficient and who therefore should be referred for pre-test counseling by a genetic HCP.

Authors' contributions

Conceptualization: KB, MGEMA; Methodology: KB, EMAB, BFH, CMA, EJPS, MGEMA; Formal analysis: KB, RMB; Investigation: KB, RK, JPJB, JHK, APSV, NV, BFH, AJW, TF, WK, EJPS; Resources: KB, MEV; Data curation, KB; Writing – original draft: KB; Writing – review & editing: KB,

EMAB, MEV, RK, JPJB, JHK, APSV, NV, BFH, AJW, TF, RMB, CMA, WK, EJPS, MGEMA; Visualization: KB; Supervision: MGEMA; Project Administration: KB, MEV; Funding acquisition: MGEMA.

Ethics approval and consent to participate

This study is registered at the International Clinical Trials Registry Platform (NL9712) and was reviewed by the Medical Reviews Ethics Committee (MREC) of the UMC Utrecht in August 2019. The Medical Research Involving Human Subjects Act (WMO) did not apply to this study. We obtained written informed consent for all participants. This study was performed in accordance with the Declaration of Helsinki.

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Declarations of competing interest

The authors have no conflicts of interest to declare.

Data availability

The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.breast.2023.03.017.

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