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The impact of a mainstream genetic testing pathway and socioeconomic factors on the uptake of germline genetic testing in breast cancer patients: results of the nationwide GENE-SMART study

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Summary

Background Genetic testing in breast cancer patients is important for the patient's local and systemic treatment choices and follow-up, as well as for their family members. Not all eligible patients currently undergo genetic testing and disparities persist in genetic testing uptake. It is unknown on the large scale whether pre-test counselling by non-genetic healthcare professionals (HCPs)–mainstream genetic testing (MGT) – improves overall genetic testing uptake and reduces disparities. We examined the impact of MGT on germline genetic testing uptake in general and in subgroups of socioeconomic status (SES) in particular.

Methods In this retrospective nationwide cohort study, we selected all breast cancer patients from the Netherlands Cancer Registry who were eligible for genetic testing according to patient and tumour characteristics under the Dutch guidelines and who were diagnosed between 1-Jan-2017 and 31-Dec-2022. The primary outcome was genetic testing uptake. The influence of MGT and SES on overall uptake and uptake across different SES levels was evaluated using chi-squared tests and multivariable logistic regression analyses.

Results A total of 12,071 breast cancer patients were included. Overall genetic testing uptake was 67%: 78% for MGT versus 63% in referral to a genetics department (RGD) ($p < 0.001$) with significantly higher odds of receiving genetic testing for MGT versus RGD (OR 2.48, 95% CI 2.14–2.87). Patients with low SES showed significantly lower odds of receiving genetic testing compared to those with a high SES (OR 0.71, 95% CI 0.61–0.83). In MGT, no significant difference was found between low and high SES in the likelihood of receiving genetic testing (OR 0.75, 95% CI 0.50–1.13).

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Conclusions MGT significantly increases genetic testing uptake among all eligible patients and across all SES subgroups, strongly encouraging further implementation of MGT. Educating HCPs about current disparities in genetic testing is essential to improve health equity in breast cancer care.

Keywords Breast cancer, Genetic testing, Socioeconomic status, Disparities, Mainstream genetic testing.

Introduction

Approximately 6% of breast cancer cases have a genetic cause underlying their disease, with around 2% linked specifically to *BRCA1* or *BRCA2* [1, 2]. Genetic testing can detect these pathogenic variants (PVs) and is relevant for patients' risk of secondary breast, ovarian or other malignancies, surgical and oncological treatment options and preventative options, as well as for family members [3, 4]. Moreover, germline genetic testing has become increasingly important to guide adjuvant or neoadjuvant therapy [5, 6]. However, not all eligible patients receive a genetic test [7, 8] with genetic testing rates such as 52% reported when referring patients to a genetic healthcare professional (HCP) [9].

The increasing importance of genetic testing for treatment selection combined with the limited capacity of genetics departments has paved the pathway for implementing mainstream genetic testing (MGT). In standard genetic care, a patient is referred to a genetic HCP whereas in MGT, pretest counselling and ordering of the germline genetic test is performed by a non-genetic HCP in the hospital where the diagnosis is made. A few studies have shown that MGT has increased genetic testing uptake among eligible breast cancer patients [9–11]. However, these were single-centre studies with relatively small study populations over relatively short times.

Furthermore, several studies have shown that patients with lower levels of education, lower incomes, migrant backgrounds or lower health literacy levels have limited access to genetic testing and are even less frequently referred to a genetic HCP than patients with higher incomes and literacy levels [7, 12–14]. Up to now, these socioeconomic factors have been studied separately. The influence of socioeconomic status (SES), as a comprehensive concept, on the likelihood of undergoing genetic testing, remains unstudied. In healthcare, low SES (a composite variable involving education, occupation and income) translates to limited access to the resources needed for maintaining a healthy lifestyle [15]. Moreover, religious affiliations are associated with negative attitudes to genetic testing [16–19]. Additionally, travel time to the nearest genetic HCP could affect patients' decisions to undergo genetic testing as travel time was found in general to impact the decision to access healthcare services [20].

In this nationwide study, we therefore aimed to examine the impact of MGT on the uptake of germline genetic

testing in general and in SES subgroups in particular between 2017 and 2022 in the Netherlands.

Method

Data collection

The data for the GENE-SMART study (Genetic Evaluation for breast cancer in the Netherlands: Studying a Mainstreaming Approach for Redefining Testing pathways), a nationwide retrospective cohort study, was obtained from the Netherlands Cancer Registry (NCR), kept by the Netherlands Comprehensive Cancer Organization (IKNL). Specially trained registrars gathered data about patient, diagnostic, tumour, treatment characteristics and whether genetic testing was performed, directly from patient files in almost all Dutch hospitals (73 of 75 hospitals). Two hospitals were excluded from the study as data from these hospitals was not collected by data registrars employed by IKNL. In the remaining hospitals ($n=73$), patients were excluded if they had undergone genetic testing before their breast cancer diagnosis or if data about the hospital of diagnosis, tumour stage or postcode was unknown.

Study sample.

The study included newly diagnosed Dutch breast cancer patients diagnosed between 1 January 2017 and 31 December 2022. Patients aged 18 or older were eligible for genetic testing if they met the patient characteristics as described in the Dutch guidelines [21].

Variables

Organization of genetic care

Three pathways to access to genetic testing apply in the Netherlands: (1) referral to a genetic HCP in one of the eight hospitals with a genetics department (seven UMCS – university medical centres – and the Antoni van Leeuwenhoek cancer hospital), (2) referral to an academic genetic HCP at a satellite outpatient clinic embedded in a general hospital (which is still run by genetic HCP from a genetics department) or (3) the MGT pathway, which is the pre-test counselling by the physician who is treating the patient. Information from the genetics departments indicated that a period of six months was generally considered a reasonable timeframe for the full implementation of MGT. Therefore, the MGT pathway was subdivided in the MGT start-up phase (<6 months after the start of the implementation of the MGT pathway) and fully-implemented MGT (≥ 6 months after the start of the implementation of MGT pathway).

The organization of genetic care during the study period was determined for each Dutch hospital, based on information obtained from the eight genetics departments in the Netherlands. At the end of the study period, 26 out of 73 hospitals had implemented the MGT pathway, compared to 3 hospitals at the start. Patients diagnosed at a hospital where patients were referred to a genetics department (i.e. from a general hospital or from the hospital in which the genetics department was situated) were categorized as ‘referral to genetics department (RGD)’. Patients diagnosed at a hospital where patients were referred to a satellite outpatient clinic were categorized as ‘satellite outpatient clinic’. If MGT was the current practice in a hospital at the patient’s date of diagnosis, a comparison was made between the patient’s date of diagnosis and the date when MGT was started. Patients diagnosed less than 6 months after the start of the implementation of the MGT pathway were assigned to the ‘MGT start-up phase’ group and patients with a date of diagnosis more than 6 months after the start of the MGT pathway in their hospital were assigned to the ‘MGT’ group.

Eligibility criteria for genetic testing

Based on the Dutch national breast cancer guideline [21] patients eligible for genetic testing were divided into four groups: breast cancer diagnosis at age < 40, triple negative breast cancer (TNBC) at age < 60, bilateral breast cancer with the first diagnosis at age < 50, or male breast cancer (Table 1). These groups were not mutually exclusive. The four eligibility criteria were included in the logistic regression model as separate binary variables, allowing for overlap between criteria. Other genetic testing criteria (e.g. family history, Ashkenazi Jewish ancestry) exist, but are not included in this study, since this data was not available.

Tumour stage

Tumours were grouped according to the TNM staging system: Ductal Carcinoma In Situ (DCIS) and tumour stages I, II, III and IV. When the pathological stage was unknown, the clinical stage was used.

SES

Median household income was used as a proxy for socioeconomic status. Statistics Netherlands provided data

about household incomes broken down by detailed postcodes for 2016, with each postcode covering an average of 17 households. Median household income was clustered into 9 groups, covering 99% of the Dutch population. SES scores were classed as ‘low’ (1–3), ‘middle’ (4–7) or ‘high’ (8–9), adapted from Van Maaren et al. [22]. Previously, SES was determined using a score derived from mean household income, the proportion of residents with low income, the percentage of individuals with limited educational attainment, and the unemployment rate [22]. However, this method is not used anymore since July 2023 due to the lack of data. The correlation between the prior methodology and the current approach is strong ($r = 0.72$, $p < 0.0001$).

Orthodox religion

The patient’s postcode was also used for determining whether a patient lived in a Reformed church municipality, as a proxy for orthodox religion. Based on a recent study [23] we created a list with the percentage of votes per municipality for the Staatkundig Gereformeerde Partij (SGP), the religious orthodox Christian political party, during the 2017 Dutch parliamentary elections [24]. Municipalities were grouped based on the percentage of votes for the SGP there: ‘low’ (less than 5%), ‘moderate’ (5 to 10%), ‘high’ (10 to 20%), and ‘very high’ (more than 20%). Although the proportion of votes for the SGP in the 2017 parliamentary elections were similar to those in the 2021 parliamentary elections, mergers of various municipalities in 2019 that led to more postcodes per municipality made the 2021 parliamentary election results less accurate. We therefore only used the results of the 2017 parliamentary elections.

Travel time to genetic care

Travel time to the nearest HCP for genetic care at the time of the patient’s diagnosis (i.e. to one of the eight clinical genetics departments, a satellite outpatient genetics clinic or an MGT hospital) was calculated using the Drive Time Matrix (Geodan, version 2.1), containing all travel times between Dutch postcode areas. Travel times were grouped into < 10, 10–20, 20–30 min and > 30 min.

Statistical analysis

Genetic testing uptake was determined based on the percentage of eligible patients who received germline genetic testing. Chi-squared tests were carried out to identify differences in genetic testing uptake based on the organization of genetic care, both for eligible patients overall and for specific clinical genetic testing criteria defined by patient characteristics. Multivariable logistic regression analysis was performed to determine the effect of MGT and SES on the uptake of genetic testing by eligible patients. For estimating the odds ratios (ORs) of MGT

Table 1 Genetic testing criteria for breast cancer patients based on patient characteristics as described in the Dutch guidelines

Genetic testing criteria
Woman with a breast cancer diagnosis at age < 40
Woman with triple negative breast cancer at age < 60
Woman with bilateral breast cancer with the first diagnosis at age < 50
Man with breast cancer regardless of age at diagnosis

and SES for the uptake of genetic testing, the four clinical genetic testing criteria based on patient characteristics (each criterion included individually), tumour stage, year of diagnosis, orthodox religion and travel time to a genetic HCP were included as confounding variables. The same confounding variables were used for estimating the effect of the MGT on the uptake of genetic testing for patients within different SES groups. To determine the effect of MGT on the disparities in uptake of genetic testing between patients in different SES groups, 'MGT' was compared against 'RGD', 'satellite outpatient clinic' and 'MGT start-up phase'.

We assessed multicollinearity among predictor variables by calculating the Variance Inflation Factor (VIF). All VIF values were below 5 (mean VIF = 1.93), indicating no significant multicollinearity. The analyses were carried out using Stata 17.0. A p-value of <0.05 was considered statistically significant.

Results

Between 2017 and 2022, a total of 111,772 patients were diagnosed with breast cancer in the Netherlands. Based on predefined criteria, 4,146 patients were excluded (Supplementary Fig. 1), leaving 107,006 patients. Of these patients, 12,071 (11%) met at least one of the four patient characteristics in the guideline and were eligible for genetic testing. Of these, 8,212 (67%) actually received genetic testing (Table 2). Genetic testing uptake was 80% for patients with a breast cancer diagnosis <40, 77% for patients with TNBC diagnosed <60, 44% for patients with bilateral breast cancer with a first diagnosis at age <50, and 41% for male breast cancer patients.

The overall uptake of genetic testing for patients eligible for genetic testing differed by type of organization: 63% for 'referral to genetics department', 66% for 'satellite outpatient clinic', 72% for 'MGT start-up phase' and 78% for 'MGT'. Moreover, compared to RGD, genetic testing uptake increased for all clinical genetic testing criteria in MGT (Table 3). Since pre-existing differences between the hospitals that implemented MGT and those that did not could exist, we analysed the genetic testing uptake in the hospitals that had implemented MGT at the end of the study period ($n=26$) individually. Most hospitals showed an increase in genetic testing uptake after the implementation of MGT (Supplementary Fig. 2).

In general, MGT showed higher odds of receiving a genetic test compared to RGD (OR 2.48, 95% CI 2.14–2.87) (Table 4). Low SES showed significantly lower odds of receiving a genetic test compared to high SES (OR 0.71, 95% CI 0.61–0.83). No significant difference was found between medium and high SES (OR 0.90, 95% CI 0.79–1.02). The odds of receiving a genetic test increased with advancing tumour stage compared to DCIS, except for tumour stage IV. Patients diagnosed in 2021 had

significantly higher odds of undergoing genetic testing than patients diagnosed in 2017 (OR 1.18, 95% CI 1.02–1.37). Patients living in a municipality in which the SGP received more than 20% of the votes had significantly lower odds of receiving a genetic test than patients living in a municipality where the SGP received less than 5% of the votes (OR 0.69, 95% CI 0.48–0.98). No significant difference was found between different travel times to genetic care.

Socioeconomic status

With the patients stratified into SES groups, MGT is seen to have significantly increased the odds of receiving a genetic test compared to RGD within all SES groups (Fig. 1). The increase in odds was comparable for high SES (OR 2.09, 95% CI 1.39–3.14), medium SES (OR 2.67, 95% CI 2.25–3.18) and low SES (OR 2.23, 95% CI 1.57–3.19).

Conversely, stratifying patients by the type of organization of genetic testing in the hospital of diagnosis revealed that, in the case of being diagnosed in a hospital where RGD was common practice, patients with medium SES (OR 0.73, 95% CI 0.58–0.92) and low SES (OR 0.70, 95% CI 0.53–0.92) had significantly lower odds of receiving a genetic test compared to patients with high SES (Table 5). In patients diagnosed in a hospital in which MGT was implemented at the time of their breast cancer diagnosis, no significant difference in the odds of receiving a genetic test was seen for patients with medium SES (OR 1.13, 95% CI 0.81–1.57) and low SES (OR 0.75, 95% CI 0.50–1.13) when compared to patients with high SES.

Discussion

To our knowledge, this is the first nationwide multicentre study on the impact of MGT on the uptake of genetic testing, showing that the chance of eligible breast cancer patients receiving a genetic test is about 2.5 times higher when MGT is applied than with the RGD usually applied. An increase in genetic testing uptake was observed in MGT compared to RGD, with the largest increases seen among patients with bilateral breast cancer and male breast cancer patients. Furthermore, the results show that lower SES clearly has a negative effect on the uptake of genetic testing, and implementation of an MGT pathway significantly improves the uptake of genetic testing in patients in all SES groups and even seems to reduce disparities in genetic testing uptake. These findings underscore the importance of further implementation of the MGT pathway.

Recent studies have shown a positive relationship between MGT and the uptake of genetic testing in patients with breast cancer [9–11]. However, these studies were limited by their small sample size (230–410 patients), a small number of hospitals (1 to 10) and a

Table 2 Clinical and socioeconomic characteristics of all breast cancer patients and for patients eligible for genetic testing for each test criterion

	Eligible BC patients*	BC diagnosis <40*	TNBC diagnosis <60*	Bilateral BC + 1st BC at age <50*	Male BC*	Ineligible BC patients**	All BC patients
Total	12,071 (11.3)	4,737 (4.4)	5,028 (4.7)	2,994 (2.8)	782 (0.7)	94,935 (88.7)	107,006
Gender							
Male	782 (6.5)	17 (0.4)	3 (0.1)	1 (0.03)	782 (100)	-	782 (0.7)
Female	11,289 (93.5)	4,720 (99.6)	5,025 (99.9)	2,993 (99.97)	-	94,935 (100)	106,224 (99.3)
Age at diagnosis							
18–29	550 (4.6)	550 (11.6)	140 (2.8)	28 (0.9)	3 (0.4)	-	550 (0.5)
30–39	4,187 (34.7)	4,187 (88.4)	936 (18.6)	194 (6.5)	14 (1.8)	-	4,187 (3.9)
40–49	2,827 (23.4)	-	1,726 (34.3)	1,154 (38.5)	35 (4.5)	11,186 (11.8)	14,013 (13.1)
50–59	2,906 (24.1)	-	2,226 (44.3)	637 (21.3)	110 (14.1)	22,352 (23.5)	25,258 (23.6)
60–74	1,184 (9.8)	-	-	806 (26.9)	378 (48.3)	41,459 (43.7)	42,643 (39.9)
75+	417 (3.5)	-	-	175 (5.9)	242 (31.0)	19,938 (21.0)	20,355 (19.0)
Year of diagnosis							
2017	1,996 (16.5)	773 (16.3)	796 (15.8)	550 (18.4)	128 (16.4)	16,303 (17.2)	18,299 (17.1)
2018	1,996 (16.5)	765 (16.2)	847 (16.9)	505 (16.9)	122 (15.6)	15,865 (16.7)	17,861 (16.7)
2019	2,005 (16.6)	797 (16.8)	818 (16.3)	497 (16.6)	127 (16.2)	16,043 (16.9)	18,048 (16.9)
2020	1,996 (16.5)	808 (17.1)	804 (16.0)	479 (16.0)	131 (16.8)	13,559 (14.3)	15,555 (14.5)
2021	2,030 (16.8)	786 (16.6)	922 (18.3)	483 (16.1)	118 (15.1)	16,822 (17.7)	18,852 (17.6)
2022	2,048 (17.0)	808 (17.1)	841 (16.7)	480 (16.0)	156 (20.0)	16,343 (17.2)	18,391 (17.2)
Tumour stage							
DCIS	863 (7.2)	337 (7.1)	-	509 (17.0)	77 (9.9)	11,717 (12.3)	12,580 (11.8)
I	3,746 (31.0)	1,269 (26.8)	1,363 (27.1)	1,233 (41.2)	242 (31.0)	39,550 (41.7)	43,296 (40.5)
II	5,109 (42.3)	2,108 (44.5)	2,632 (52.4)	803 (26.8)	305 (39.0)	30,821 (32.5)	35,930 (33.5)
III	1,602 (13.3)	715 (15.1)	763 (15.2)	258 (8.6)	96 (12.3)	7,859 (8.3)	9,461 (8.8)
IV	751 (6.2)	308 (6.5)	270 (5.4)	191 (6.4)	62 (7.9)	4,988 (5.2)	5,739 (5.4)
SES							
Low	2,193 (17.72)	888 (18.8)	869 (17.3)	503 (16.8)	158 (20.2)	19,039 (20.1)	21,178 (19.8)
Medium	8,337 (69.1)	3,333 (70.4)	3,438 (68.4)	2,094 (69.9)	516 (6.0)	63,160 (66.5)	71,497 (66.8)
High	1,595 (13.2)	516 (10.9)	721 (14.3)	397 (13.3)	108 (13.8)	12,736 (13.4)	14,331 (13.4)
Orthodox religion***							
Low	10,996 (91.1)	4,353 (91.9)	4,549 (90.5)	2,719 (90.8)	719 (91.9)	85,510 (90.1)	96,506 (90.2)
Moderate	503 (4.2)	172 (3.6)	223 (4.4)	142 (4.7)	30 (3.8)	4,167 (4.4)	4,670 (4.4)
High	410 (3.4)	152 (3.2)	191 (3.8)	90 (3.0)	23 (2.9)	3,753 (4.0)	4,163 (3.9)
Very high	162 (1.3)	60 (1.3)	65 (1.3)	43 (1.4)	10 (1.3)	1,505 (1.6)	1,667 (1.6)
Travel time to genetic care							
< 10 min	3,270 (27.1)	1,411 (29.8)	1,308 (26.0)	760 (25.4)	219 (28.0)	23,216 (24.5)	26,486 (24.7)
10–20 min	5,935 (49.2)	2,304 (48.6)	2,468 (49.1)	1,507 (50.3)	374 (47.8)	46,160 (48.6)	52,095 (48.7)
20–30 min	2,365 (19.6)	858 (18.1)	1,033 (20.5)	599 (20.0)	154 (19.7)	20,977 (22.0)	23,242 (21.7)
> 30 min	501 (4.2)	164 (3.5)	219 (4.4)	128 (4.3)	35 (4.5)	4,682 (4.9)	5,183 (4.8)
Genetic care organization							
RGD	3,654 (30.3)	1,443 (30.5)	1,579 (31.4)	857 (28.6)	219 (28.0)	28,620 (30.2)	32,274 (30.2)
Satellite outpatient clinic	5,922 (49.1)	2,326 (49.1)	2,446 (48.7)	1,502 (50.2)	377 (48.2)	46,849 (49.4)	52,771 (49.3)
MGT start-up phase****	417 (3.5)	178 (3.8)	154 (3.1)	107 (3.6)	28 (3.6)	3,237 (3.4)	3,654 (3.4)
MGT****	2,078 (17.2)	790 (16.7)	849 (16.9)	528 (17.6)	158 (20.2)	16,229 (17.1)	18,307 (17.1)
Genetic test performed							
Yes	8,116 (67.2)	3,797 (80.2)	3,867 (76.9)	1,323 (44.2)	319 (40.8)	7,376 (7.8)	15,492 (14.5)
No	3,955 (32.8)	940 (19.8)	1,161 (23.1)	1,671 (55.8)	463 (59.2)	87,559 (92.2)	91,514 (85.5)

Data items are n and percentage (%). BC=breast cancer, TNBC=triple negative breast cancer, DCIS=ductal carcinoma in situ, SES=socioeconomic status, RGD=referral to genetics department, MGT=mainstream genetic testing. * The total number of eligible patients is not equal to the sum of the number of patients fulfilling one of the four clinical genetic testing criteria because the criteria are not mutually exclusive. ** 'Ineligible patients' includes all patients who are not eligible for genetic testing based on the four clinical genetic testing criteria based on patient characteristics [21]. *** Orthodox religion represents the percentage of votes for the Staatkundig Gereformeerde Partij (the religious orthodox Christian political party), during the 2017 Dutch parliamentary elections in the patient's municipality. Low=0–5%, moderate=5–10%, high=10–20%, and very high=>20%. **** MGT start-up phase: mainstream genetic testing implemented within the last 6 months at the date of diagnosis. MGT refers to a mainstream genetic testing pathway implemented more than 6 months before date of diagnosis

Table 3 Uptake of genetic testing for all eligible patients and per clinical genetic testing criterion based on patient characteristics

Uptake of genetic testing	Referral to genetics department	Satellite outpatient clinic	MGT start-up phase < 6 months	MGT ≥ 6 months	p-value
Total eligible patients	2,297/3,654 (62.9)	3,904/5,922 (65.9)	300/417 (71.9)	1,615/2,078 (77.7)	< 0.001
BC < 40	1,096/1,443 (76.0)	1,865/2,326 (80.1)	147/178 (82.6)	689/790 (87.2)	< 0.001
TNBC < 60	1,153/1,579 (73.0)	1,869/2,446 (76.4)	122/154 (79.2)	723/849 (85.2)	< 0.001
Bilateral BC (1st BC < 50)	320/857 (37.3)	641/1,502 (42.7)	66/107 (61.7)	296/528 (56.0)	< 0.001
Male BC	64/219 (29.2)	139/377 (36.9)	9/28 (32.1)	107/158 (67.7)	< 0.001

Data items are number n and percentage (%). The table presents the uptake of genetic testing across different types of organizations for genetic care for each genetic testing criterion based on patient characteristics. The p-values are derived from a chi-squared test, indicating whether the differences in uptake between types of genetic care organization are statistically significant ($p < 0.05$). BC = breast cancer, TNBC = triple negative breast cancer, MGT = mainstream genetic testing

relatively short study period (2 to 3.5 years). Our study has significantly substantiated these findings, using a larger patient population, at a national level, examined over a longer period (6 years). Moreover, we found that genetic testing was performed in only 44% of patients with bilateral breast cancer with a first diagnosis under the age of 50 and in only 41% of male breast cancer patients. The logistic regression supported these findings, with patients with bilateral breast cancer and male breast cancer patients showing around 50% lower odds at receiving genetic testing compared to patients who did not meet these criteria (but who did meet one of the other criteria). Although the uptake of genetic testing was higher among patients with breast cancer aged under 40 and patients with TNBC aged under 60, around 20% of these patients were still not tested. Comparable results regarding genetic testing uptake were found in earlier studies in Norway and the US [9, 11]. Although a 100% uptake is unrealistic – and not necessarily desirable, given that some patients may refrain from genetic testing – the uptake as shown in the results (especially for patients with bilateral breast cancer and male breast cancer) is unexpectedly low. This indicates that HCPs often fail to identify or refer patients eligible for genetic testing. MGT significantly improved genetic testing uptake overall and for all four eligibility criteria taken separately. However, there are still discrepancies in genetic testing uptake between the four eligibility criteria. These discrepancies regarding eligibility criteria can be remedied by enhancing HCPs’ knowledge of testing criteria (and thereby increasing non-genetic HCPs’ awareness of genetic testing) through targeted training. In addition, fully informing patients and empowering them to choose their degree of involvement in decisions about their care can have a positive influence on equitable access to genetic testing [25].

In our study, we found that patients with tumour stage IV received genetic testing less frequently than patients with tumour stages I, II and III. These discrepancies were also shown in an earlier study [26]. This may be explained by the fact that newly diagnosed patients with metastatic breast cancer often primarily visit a medical oncologist, whereas the surgical oncologist is usually the first

physician for patients with non-metastatic breast cancer. Moreover, in the Netherlands surgical oncologists are used to referring for or requesting genetic testing, whereas in other countries medical oncologists are (also) involved in discussing and requesting genetic testing [10, 11, 27, 28]. Due to the patients’ disease status, medical oncologists could decide not to discuss genetic testing (or to do so later) in patients with tumour stage IV. As a result, genetic testing may be postponed and ultimately forgotten. Obviously, this is undesirable because patients with metastatic breast cancer can also benefit from genetic testing in their therapy choices (e.g. PARP-inhibitors) and by enabling their relatives to take preventive measures [10]. The involvement of a medical oncologist in MGT is therefore strongly recommended, especially regarding the increasing importance of therapeutic criteria for germline genetic testing. Future studies are needed to explore the causes for the observed discrepancies in uptake of genetic testing by patients with different tumour stages.

Although the evidence suggests that MGT has a beneficial impact, it is critical to recognize that patients with low SES still had less access to genetic testing than patients with high SES. An earlier study found that HCPs perceive difficulties in recognizing patients with low health literacy and in adapting communication to the needs of such patients [29]. These inequalities highlight the need for ongoing efforts to ensure that all patients, regardless of their SES, can benefit from genetic testing. We showed that MGT seemed to reduce the gap between access to genetic testing for patients with low and high SES. A recent study on improving the access of genetic testing for patients with ductal pancreatic carcinoma found a comparable result, that MGT reached a more ethnically diverse patient population, thereby reducing disparities [30]. Our study underlines that MGT has the potential to reduce existing disparities in access to genetic testing. However, increasing HCPs’ awareness of the current inequitable access to genetic testing and further education on recognizing patients with low SES is needed in order to reduce these disparities.

Although travel time to genetic care was not a significant factor, patients diagnosed in hospitals with a

Table 4 Independent variables associated with the uptake of genetic testing in breast cancer patients eligible for genetic testing ($n = 12,071$)

	OR (95% CI)	<i>p</i> -value
Genetic care organisation		
RGD	ref	ref
Satellite outpatient clinic	1.19 (1.07–1.31)	0.001
MGT start-up phase (< 6 months)	1.67 (1.30–2.15)	< 0.001
MGT (≥ 6 months)	2.48 (2.14–2.87)	< 0.001
SES		
High	ref	ref
Medium	0.90 (0.79–1.02)	0.10
Low	0.71 (0.61–0.83)	< 0.001
BC diagnosis < 40*		
No	ref	ref
Yes	2.57 (2.21–2.99)	< 0.001
TNBC diagnosis < 60*		
No	ref	ref
Yes	1.69 (1.45–1.98)	< 0.001
Bilateral BC (1st BC at < 50)*		
No	ref	ref
Yes	0.53 (0.45–0.62)	< 0.001
Male BC*		
No	ref	ref
Yes	0.42 (0.34–0.52)	< 0.001
Tumour stage		
DCIS	ref	ref
I	2.45 (2.07–2.91)	< 0.001
II	4.00 (3.37–4.75)	< 0.001
III	4.74 (3.88–5.80)	< 0.001
IV	1.34 (1.08–2.67)	0.008
Year of diagnosis		
2017	ref	ref
2018	1.06 (0.92–1.22)	0.43
2019	1.09 (0.94–1.25)	0.25
2020	1.13 (0.97–1.31)	0.11
2021	1.18 (1.02–1.37)	0.03
2022	1.02 (0.88–1.19)	0.77
Orthodox religion**		
Low	ref	ref
Moderate	0.96 (0.78–1.18)	0.68
High	1.02 (0.80–1.29)	0.89
Very high	0.69 (0.48–0.98)	0.04
Travel time to genetic care		
< 10 min	ref	ref
10–20 min	0.98 (0.88–1.09)	0.71

Table 4 (continued)

	OR (95% CI)	<i>p</i> -value
Genetic care organisation		
20–30 min	0.96 (0.84–1.10)	0.55
≥ 30 min	0.82 (0.65–1.02)	0.07

Multivariable logistic regression analysis on the influence of independent variables on genetic testing. RGD=referral to genetics department, MGT=mainstream genetic testing, SES=socioeconomic status, BC=breast cancer, TNBC=triple negative breast cancer, DCIS=ductal carcinoma in situ. * These four clinical genetic testing criteria are not mutually exclusive. Each genetic testing criterion was included individually. For each criterion, the reference group includes all patients that do not meet that specific criterion. However, these patients do meet one (or more) of the other criteria, since all included patients are eligible for genetic testing. ** Orthodox religion represents the percentage of votes for the Staatkundig Gereformeerde Partij (the religious orthodox Christian political party) during the 2017 Dutch parliamentary elections in the patient's municipality. Low=0–5%, moderate=5–10%, high=10–20%, and very high=>20%

genetics satellite outpatient clinic were more likely to receive genetic testing than those referred to a genetic HCP elsewhere. This suggests that on-site access to a genetic HCP influences testing rates, implying that travel time does influence the chance of receiving genetic testing.

A strength of this nationwide retrospective cohort study is the use of data from the NCR that includes all patients diagnosed with breast cancer over a relatively long period, which enhances the validity and generalizability of the results. Additionally, including factors such as the travel distance to genetic care and orthodox religion, which are known to influence healthcare accessibility, have been included in the analyses. The study has some limitations. We only included patients eligible for genetic testing based on the four patient characteristics as described in the Dutch guideline. No data was available on other eligibility criteria such as a positive cancer family history, Ashkenazi Jewish ancestry, clinical trial participation and/or therapeutic implications for genetic testing. We therefore do not know which factors influence genetic testing in patients who are eligible based on one of the other genetic testing criteria. Furthermore, the postcode was used for determining a patients' SES and whether a patient lived in a Reformed Church municipality. Although there will indeed be differences in income and religious beliefs among residents of a certain postcode, this approach approximates SES and religion effectively. Another limitation of the study is that SES was not included as a composite SES index, because SES was based on median income in a postal code area. However, a statistically significant association exists between the use of median income and a composite SES index ($r = 0.72$, $p < 0.0001$)²². Another limitation is that since the first Dutch COVID-19 lockdown, hospital visits have increasingly been replaced by video consultations. It is unclear if the implementation of video consultations has had a positive impact on genetic testing uptake,

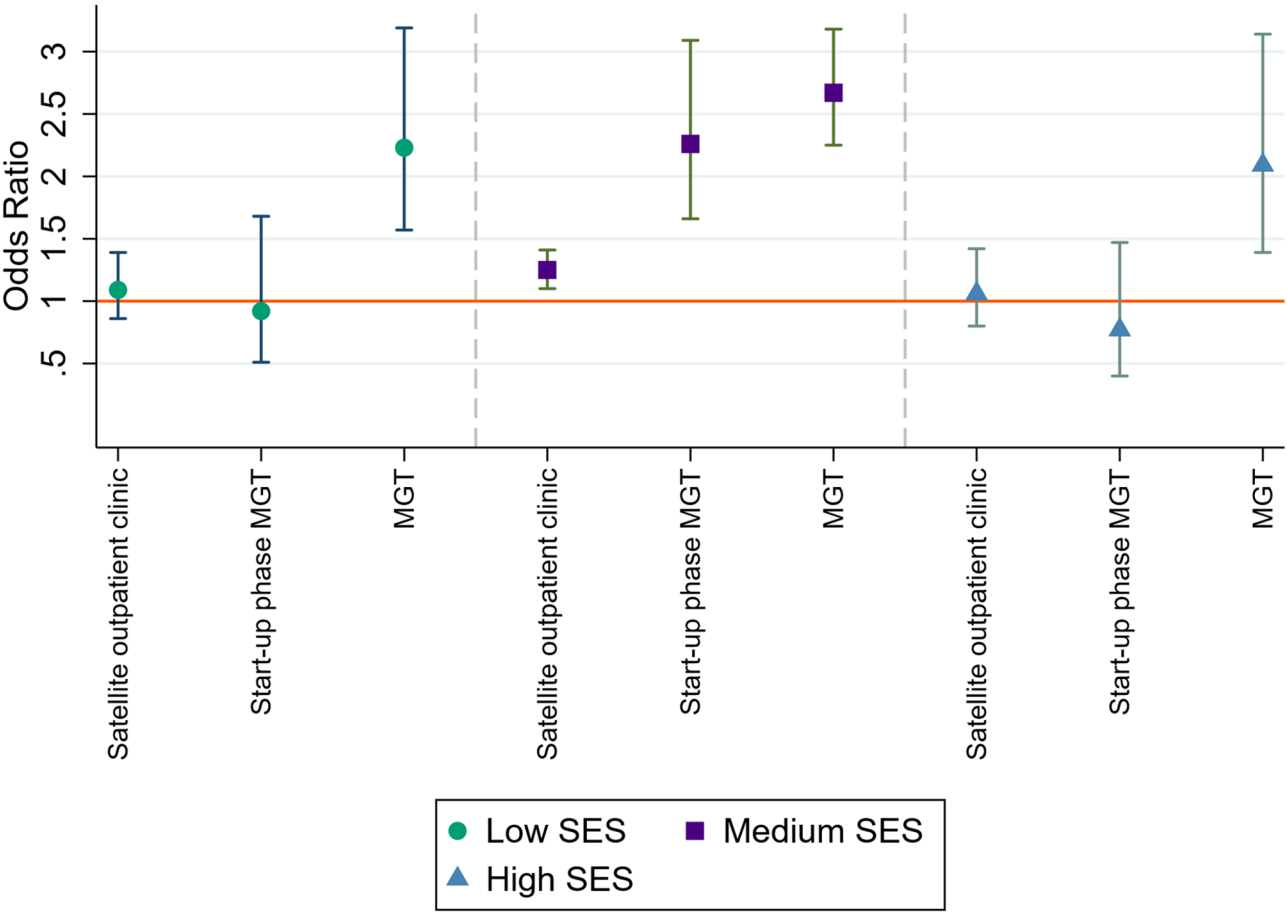


Fig. 1 Effect of the organization of genetic care on the uptake of genetic testing for patients within groups with different socioeconomic status. Odds of receiving a genetic test for referral to a satellite outpatient clinic, MGT start-up phase and MGT compared to RGD (OR 1.0; orange baseline), corrected for the four clinical genetic testing criteria, tumour stage, year of diagnosis, orthodox religion and travel time to genetic care. MGT=mainstream genetic testing, RGD=referral to genetics department, SES=socioeconomic status

Table 5 Effect of the organization of genetic care in the hospital of diagnosis on the disparities in uptake of genetic testing between eligible patients in different SES groups (n = 12,071)

	RGD (n = 3,654)		Satellite outpatient clinic (n = 5,922)		MGT Start-up phase, < 6 months (n = 417)		MGT, ≥ 6 months (n = 2,078)	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
SES								
High	ref	ref	ref	ref	ref	ref	ref	ref
Medium	0.73 (0.58–0.92)	0.008	0.90 (0.75–1.08)	0.27	1.88 (0.90–3.92)	0.09	1.13 (0.81–1.57)	0.47
Low	0.70 (0.53–0.92)	0.01	0.69 (0.56–0.86)	0.001	0.63 (0.26–1.52)	0.30	0.75 (0.50–1.13)	0.17

The effect of the organization of genetic care on the disparities in uptake between different levels of SES, corrected for the four clinical genetic testing criteria, tumour stage, year of diagnosis, orthodox religion, and travel time to genetic care. RGD=referral to genetics department, MGT=mainstream genetic testing, SES=socioeconomic status

as the odds of receiving genetic testing increased in the year after the first COVID-19 infections in the Netherlands (2021). However, no significant difference was seen between 2017 and 2022. On top of that, we cannot exclude the possibility that the introduction of MGT may have positively influenced the uptake due to increased awareness of genetic testing. The increased awareness could have led to a better identification of eligible patients. Additionally, differences exist between MGT pathways in different hospitals. In some hospitals where MGT was implemented, patients with a positive family history received genetic testing via the MGT pathway, whereas in other hospitals where the MGT pathway was implemented these patients were referred to a genetic HCP. These differences, however, are not expected to interfere with the results, because in this study we only

included patients who meet the testing criteria based on patient characteristics. Finally, when genetic testing was not performed, it was not registered in the data whether genetic testing was not recommended or whether the patient refrained from genetic testing. However, previous research has shown that the proportion of patients not interested in genetic testing is relatively small and that a lack of physician's recommendation is a frequent reason for not being tested [31, 32].

In conclusion, MGT is important for increasing the overall uptake of genetic testing and has the potential to reduce disparities in access to genetic testing. An essential next step would be to motivate and educate HCPs who are as yet unfamiliar with pre-test counselling to embrace the MGT pathway. For hospitals where MGT is already implemented, encouraging medical oncologists to participate in this pathway is crucial, as they can serve as a checkpoint to ensure that eligible patients have undergone genetic testing, including those who might not have been offered genetic testing by other HCPs. Moreover, as newly diagnosed patients with metastatic breast cancer often first see a medical oncologist, these specialists are well-positioned for providing genetic counselling when needed for guiding therapy choices. Also, further education for HCPs about recognizing patients with low SES is needed to reduce disparities in access to genetic testing.

Supplementary Information

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Supplementary Material 1

Supplementary Material 2

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Author contributions

CLdJ and MGEMA performed the literature search, designed the study, interpreted results of the statistical analyses, and discussed and wrote the manuscript. CLdJ analyzed the data. GCWMP was responsible for data-management, supported the statistical methods and reviewed the manuscript. SS and AJ designed the study, interpreted data, reviewed the statistical methods, and discussed and wrote the manuscript.

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Data availability

The data that support the findings of this study are available from the Netherlands Comprehensive Cancer Organisation but restrictions apply to the

availability of these data, which were used under license for the current study, and so are not publicly available.

Declarations

Ethics approval

This study does not fall under the scope of the Dutch Medical Research Involving Human Subjects Act (WMO); this was confirmed by the MEC-U of the UMC Utrecht, which ensures compliance with legislation and regulations (in terms of informed consent, data management, privacy aspects and legal aspects). The request for the use of data has been granted according to the conditions of the privacy committee of the NCR and the NABON-BOOG committee (K23.325).

Competing interests

CLdJ, GCWMP and AJ declare no conflict of interest. SS received a fee for reviewing grant applications for the Pfizer Boost program. MGEMA received consulting fees from AstraZeneca for participation in an international Steering Committee to give advice on a Train-The-Trainer programme and honoraria for a lecture on genetic testing in breast cancer. These payments were made to the institution (University Medical Center Utrecht).

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References

1. Hu C, Hart SN, Gnanaolivu R, et al. A Population-Based study of genes previously implicated in breast Cancer. *N Engl J Med*. 2021;384(5):440–51. <https://doi.org/10.1056/NEJMoa2005936>.
2. Breast Cancer Association Consortium, Dorling L, Carvalho S, et al. Breast Cancer risk Genes - Association analysis in more than 113,000 women. *N Engl J Med*. 2021;384(5):428–39. <https://doi.org/10.1056/NEJMoa1913948>.
3. Cardoso F, Kyriakides S, Ohno S, et al. Early breast cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Ann Oncol*. 2019;30(8):1194–220. <https://doi.org/10.1093/annonc/mdz173>.
4. Daly MB, Pal T, Berry MP, Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic et al. Version 2.2021, NCCN Clinical Practice Guidelines in Oncology. *J Natl Compr Canc Netw*. 2021;19(1):77–102. <https://doi.org/10.6004/jnccn.2021.0001>.
5. Niravath P, Cakar B, Ellis M. The role of genetic testing in the selection of therapy for breast cancer: A review. *JAMA Oncol* [Internet]. 2017 [cited 2023 Dec 11];3(2):262. Available from: <https://pubmed.ncbi.nlm.nih.gov/27560719/>.
6. Tutt ANJ, Garber JE, Kaufman B, et al. Adjuvant Olaparib for patients with BRCA1- or BRCA2-Mutated breast Cancer. *N Engl J Med*. 2021;384(25):2394–405. <https://doi.org/10.1056/NEJMoa2105215>.
7. Kurian AW, Ward KC, Howlader N, et al. Genetic testing and results in a Population-Based cohort of breast Cancer patients and ovarian Cancer patients. *J Clin Oncol*. 2019;37(15):1305–15. <https://doi.org/10.1200/JCO.18.01854>.
8. Kurian AW, Abrahamse P, Furgal A, et al. Germline genetic testing after Cancer diagnosis. *JAMA*. 2023;330(1):43–51. <https://doi.org/10.1001/jama.2023.9526>.
9. Chai TS, Yin K, Wooters M, Shannon KM, Hughes KS. Mainstreamed genetic testing of breast cancer patients: experience from a single surgeon's practice in a large US academic center. *Fam Cancer*. 2023;22(4):467–74. <https://doi.org/10.1007/s10689-023-00342-3>.
10. Beard C, Monohan K, Cicciarella L, James PA. Mainstream genetic testing for breast cancer patients: early experiences from the Parkville Familial Cancer

- centre. *Eur J Hum Genet.* 2021;29(5):872–80. <https://doi.org/10.1038/s41431-021-00848-3>.
11. Grindedal EM, Jørgensen K, Olsson P, et al. Mainstreamed genetic testing of breast cancer patients in two hospitals in South Eastern Norway. *Fam Cancer.* 2020;19(2):133–42. <https://doi.org/10.1007/s10689-020-00160-x>.
 12. van der Giessen JAM, van Dulmen S, Velthuis ME, et al. Effect of a health literacy training program for surgical oncologists and specialized nurses on disparities in referral to breast cancer genetic testing. *Breast.* 2021;58:80–7. <https://doi.org/10.1016/j.breast.2021.04.008>.
 13. Parikh DA, Dickerson JC, Kurian AW. Health disparities in germline genetic testing for Cancer susceptibility. *Curr Breast Cancer Rep.* 2020;12:11–20. <https://doi.org/10.1007/s12609-020-00354-3>.
 14. Ademuyiwa J, Barrett FO. Disparities in genetic testing for heritable Solid-Tumor malignancies. *Surg Oncol Clin N Am.* 2022;31(1):109–26. <https://doi.org/10.1016/j.soc.2021.08.004>.
 15. Shavers VL. Measurement of socioeconomic status in health disparities research. *J Natl Med Assoc.* 2007;99(9):1013–23.
 16. Botosaneanu A, Alexander JC, Banaszak-Holl J. To test or not to test? The role of attitudes, knowledge, and religious involvement among U.S. adults on Intent-to-Obtain adult genetic testing. *Health Educ Behav.* 2011;38(6):617–28. <https://doi.org/10.1177/1090198110389711>.
 17. Lemons J, Ragsdale J, Vaughn L, Grosseohme D. I didn't know it existed before you called: Protestant clergy experience, education and perceptions regarding genetics. *J Genet Couns.* 2013;22(2):226–37. <https://doi.org/10.1007/s10897-012-9538-2>.
 18. Bartlett VL, Johnson RL. God and genes in the caring professions: clinician and clergy perceptions of religion and genetics. *Am J Med Genet C Semin Med Genet.* 2009;151 C(1):41–51. <https://doi.org/10.1002/ajmg.c.30201>.
 19. Schwartz MD, Hughes C, Roth J, et al. Spiritual faith and genetic testing decisions among high-risk breast cancer probands. *Cancer Epidemiol Biomarkers Prev.* 2000;9(4):381–5.
 20. Mseke EP, Jessup B, Barnett T. Impact of distance and/or travel time on healthcare service access in rural and remote areas: A scoping review. *J Transp Health.* 2024;37:101819. <https://doi.org/10.1016/j.jth.2024.101819>.
 21. Breast Cancer - Criteria for Referral to Clinical Genetics. Guideline Database [Internet]. Accessed February 26, 2024. Available from: http://richtlijndatabase.nl/richtlijn/borstkanker/screening/screening_buiten_het_bvo/criteria_vo_or_verwijzing_kg.html
 22. van Maaren MC, Rachet B, Sonke GS, et al. Socioeconomic status and its relation with breast cancer recurrence and survival in young women in the Netherlands. *Cancer Epidemiol.* 2022;77:102118. <https://doi.org/10.1016/j.canep.2022.102118>.
 23. Hoekman LM, Smits MMV, Koolman X. The Dutch COVID-19 approach: regional differences in a small country. *Health Policy Technol.* 2020;9(4):613–22. <https://doi.org/10.1016/j.hlpt.2020.08.008>.
 24. Electoral Council. Electoral Council - Election Results. www.verkiezingsuitslagen.nl [Internet]. Published 2017. Available from: <https://www.verkiezingsuitslagen.nl/verkiezingen/detail/TK20170315>
 25. Coles CE, Earl H, Anderson BO, et al. The lancet breast Cancer commission. *Lancet.* 2024;403(10439):1895–950. [https://doi.org/10.1016/S0140-6736\(24\)00747-5](https://doi.org/10.1016/S0140-6736(24)00747-5).
 26. Wehbe A, Manning M, Assad H, Purrington KS, Simon MS. Uptake of genetic counseling and testing in a clinic-based population of women with breast cancer. *Cancer Med.* 2022;11(17):3304–11. <https://doi.org/10.1002/cam4.4684>.
 27. Bokkers K, Bleiker EMA, Aalfs CM, et al. Surgical oncologists and nurses in breast Cancer care are ready to provide Pre-Test genetic counseling. *Ann Surg Oncol.* 2023;30(6):3248–58. <https://doi.org/10.1245/s10434-023-1322-9-5>.
 28. Ain Q, Richardson C, Mutebi M, George A, Kemp Z, Rusby JE. Does mainstream BRCA testing affect surgical decision-making in newly-diagnosed breast cancer patients? *Breast.* 2023;67:30–5. <https://doi.org/10.1016/j.breast.2022.12.001>.
 29. Murugesu L, Heijmans M, Rademakers J, Fransen MP. Challenges and solutions in communication with patients with low health literacy: perspectives of healthcare providers. *PLoS ONE.* 2022;17(5):e0267782. <https://doi.org/10.1371/journal.pone.0267782>.
 30. Cremin C, Bedard AC, Hong Q, et al. Improving access to hereditary testing in pancreatic ductal carcinoma. *JCO Precis Oncol.* 2024;810.1200/po.24.00167.
 31. White VB, Walsh KK, Foss KS, et al. Genetic testing for hereditary breast cancer: the decision to decline. *Am Surg.* 2018;84(1):154–60. <https://doi.org/10.1177/000313481808400139>.
 32. Kurian AW, Griffith KA, Hamilton AS, et al. Genetic testing and counseling among patients with newly diagnosed breast Cancer. *JAMA.* 2017;317(5):531–4. <https://doi.org/10.1001/jama.2016.16918>.
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