Evaluating the Effectiveness of a Telehealth Cancer Genetics Program: A BRCA Pilot Study

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Abstract
Introduction: Ashkenazi Jewish (AJ) individuals face a 1 in 40 (2.5%) risk of having a BRCA mutation, which is 10 times the general population risk. JScreen launched the PEACH BRCA Study, a telehealth-based platform for BRCA education and testing, with the goal of creating an effective model for BRCA testing in low-risk AJ individuals who do not meet national testing criteria. Other goals were to determine the rate of BRCA mutations in this group, to assess the adequacy of screening for the 3 common AJ founder mutations only, and to assess satisfaction with the telehealth model to help inform a national launch of a broader cancer genetic testing program. Methods: Criteria for participation included those who were AJ, resided in the metro-Atlanta area, were aged 25 and older, and had no personal or close family history of BRCA-related cancers. Pre-test education was provided through a video and written summary, followed by complimentary \textit{BRCA1}/2 sequencing and post-test genetic counseling. Participants responded to pre- and post-test surveys, which assessed knowledge and satisfaction. Those who were not eligible to participate were sent genetic counseling resources and later surveyed. Results: Five hundred one participants were tested and the results included 4 positives (0.8% positivity rate), 494 negatives, and 3 variants of uncertain significance. Overall satisfaction with the study process was high (96.9/100), knowledge about BRCA was high (97.5% of participants passed a pre-test knowledge quiz), and satisfaction with pre- and post-test education was high (97.9% of participants were satisfied with the pre-test video and written summary, and 99.5% felt that their post-test genetic counseling session was valuable). Many participants expressed interest in receiving broader cancer testing. Conclusions: The BRCA founder mutation rate in a low-risk AJ population was significantly lower than the previously established AJ rate of 1 in 40. It was also determined that a telehealth model for a cancer genetics program is effective and acceptable to the population tested. This study established interest in broader cancer genetic testing through a telehealth platform and suggested that testing may be successful in the Jewish community at a national level and potentially in other populations, provided that patient education and genetic counseling are adequately incorporated.

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**Introduction**

Significant advances in genetic research have allowed us to learn about genetic predispositions to cancer. While most cases of breast and ovarian cancer are believed to be sporadic, about 5–10% are inherited [1]. About 60% of cases of hereditary breast and ovarian cancer are caused by mutations in the BRCA1 and BRCA2 genes [2, 3].

The exact prevalence of clinically significant BRCA1 or BRCA2 mutations in an unselected general population has not been published; however, models estimate it to be about 1 in 300 to 1 in 500 (0.2–0.3%) [4]. Studies have shown that this rate is significantly increased in individuals of Ashkenazi Jewish (AJ; Eastern and Central European) ancestry. About 1 in 40 (2.5%) AJ individuals carry a BRCA mutation, which is tenfold the carrier rate of the general population [5, 6]. Two founder mutations in BRCA1 (185delAG and 5382insC) and 1 in BRCA2 (6174delT) comprise about 95% of mutations in individuals with AJ ancestry [7]. In this group, these 3 mutations account for about 11% of cases of breast cancer [8] and about 40% of ovarian cancer cases [9, 10]. While higher rates of mutations in the AJ population have been established, it remains unclear whether mutation rates in AJ individuals without a history of cancer are as significant as rates in those with personal and family histories of cancer.

Females with a BRCA mutation are at increased risk of developing breast, ovarian, and pancreatic cancer, as well as melanoma, while males with a mutation are at increased risk for breast, prostate, and pancreatic cancer, as well as melanoma [8, 11]. In addition to these cancer risks, an individual with a BRCA mutation has a 50% chance to pass on the mutation to each of his or her children (autosomal dominant inheritance), where the same cancer risks would apply [12].

Both females and males with a BRCA mutation should receive genetic counseling about their options for cancer risk-reduction and management. For example, risk-reducing salpingo-oophorectomy is recommended for all BRCA-positive females between ages 35 and 45 and upon completion of childbearing. Other options for management include vigilant breast cancer screening and risk-reducing mastectomy. Males with a BRCA mutation are advised to have yearly clinical breast exams starting at age 35 and prostate cancer screening starting at age 40. In addition, those who would like to prevent passing on their BRCA mutation to their children are counseled about reproductive options, such as in vitro fertilization with pre-implantation genetic testing, prenatal diagnosis, gamete donation, and adoption. Furthermore, screening of a reproductive partner would be recommended to an individual with a mutation to define their risk to have a child with a recessive Fanconi anemia subtype [12]. Medical management may be personalized for those who are at increased risk.

For many years, national BRCA testing guidelines were defined by personal and significant family histories of cancer and/or the presence of familial mutations. These guidelines are often adopted by health insurance companies to set policies for coverage [13, 14]. Recently, the national testing criteria have expanded [12, 15]. In 2014 and again in 2019, the United States Preventative Services Task Force (USPSTF) recommended that asymptomatic women be screened by primary care providers to identify those who might warrant genetic testing, and specified AJ ancestry as a risk factor [16, 17]. Similarly, the National Comprehensive Cancer Network (NCCN) has updated its guidelines and mentions the low-risk AJ population (those without a significant personal or family history of cancer) for testing consideration [12]. These updated criteria have increased the opportunities for testing when a person is of AJ descent.

Even with these guideline updates, it is still not standard-of-care to offer BRCA testing to all AJ individuals. Those without family histories are often not approved for coverage by their insurance companies, despite their ancestry-related risk. Those seeking testing are often required to pay out-of-pocket to test through their healthcare provider or a direct-to-consumer testing company.

Some genetics professionals have suggested that all AJ individuals be offered BRCA testing, regardless of their personal and family histories of cancer [18, 19]. A 2010 community-wide BRCA testing initiative in Toronto [20] and a similar 2015 initiative in New York City [21] were successful at identifying low-risk AJ individuals with BRCA mutations and supported the notion that a greater number of mutation carriers will be detected if testing criteria are expanded to include anyone of AJ ancestry. In 2014, an Israeli group found that rates of cancer are the same among BRCA carriers who do and do not have family histories of cancer, which further supports the value of testing all AJ individuals [6]. In addition, a 2014 study in the UK maintained that population screening in AJ individuals reduces the number of cases of breast and ovarian cancer, which will effectively save money and lives, as the costs of preventative interventions are significantly lower than the costs of cancer treatment [22]. Collectively, these studies support the notion of population-wide BRCA testing for individuals with AJ ancestry as it would iden-
Telehealth-Based BRCA Testing in Ashkenazi Jews

In addition to support from the medical genetics community for population screening, there is also interest among members of the AJ community. Shekdi-Rafid et al. [23] found that in a group of asymptomatic females with BRCA mutations, support for population-based BRCA testing was high due to the perceived benefits of knowledge of results and options for detection and prevention. Of note, many of the women stressed the importance of pre- and post-test genetic counseling as part of the testing experience. Similarly, Lieberman et al. [24] found that in a group of low-risk AJ individuals, the majority would recommend population screening.

Despite professional and community support for population screening for individuals with AJ background, there are concerns about implementation of such a program. Fewer restrictions on testing will likely elicit more requests for tests and, subsequently, a higher demand for genetic counselors (GCs) and other healthcare professionals who are qualified to interpret genetic test results [25]. There is currently a shortage of GCs in direct patient care that is not expected to be ameliorated for years [26]; therefore, increasing numbers of genetics providers are turning to alternate service delivery models to address growing demands for genetic counseling services [27–29]. Another concern is that if health insurance companies do not allow for coverage of genetic testing for the low-risk AJ population, there may be low test uptake [30]. In order to allow for adequate patient education and interpretation of results and testing, especially in populations that are most in need, creative solutions are necessary.

Telehealth provides a number of solutions to the problems posed above. For the purposes of this discussion, we will define telehealth to include both telephone and video-based genetic counseling service delivery. A plethora of studies have demonstrated noninferiority of telehealth compared to in-person genetic counseling for a variety of indicators such as cancer-related stress, genetic testing decision-making, and decisional conflict [31–36]. Telehealth has been shown to improve knowledge and decrease anxiety and depression [35, 37, 38], while maintaining patient satisfaction [33, 37, 39, 40]. It can provide a significant cost reduction for the provision of genetic counseling services [39, 41] and enable access for rural populations [42]. While telehealth has many advantages, it should be noted that there are also disadvantages to this mode of delivery. Technical issues related to voice delay and internet connectivity as well as challenges due to limited use of nonverbal cues have been cited as common disadvantages to telehealth. In addition, providers have voiced concerns about billing for these services and licensure issues related to providing counseling across state lines [29, 36]. Despite these potential disadvantages, telehealth provides many benefits to both providers and patients [38] and is a versatile medium for delivery of cancer genetic services.

JScreen is a national Jewish genetic disease screening program based out of Emory University School of Medicine’s Department of Human Genetics that provides online education, at-home saliva-based genetic screening, and post-test genetic counseling via telephone or secure video conferencing [43]. The program launched in 2013 and, until 2019, focused exclusively on reproductive carrier screening. Over the years, many members of the AJ community were concerned about their ancestry-related cancer risks and requested BRCA testing as well.

According to its mission, JScreen is “dedicated to preventing Jewish genetic diseases” [44]. In an effort to fulfill this mission in relation to BRCA-related cancers, JScreen sought to run a pilot study to assess the feasibility and effectiveness of a cancer genetic testing initiative. “The Program for Evaluation of Ashkenazi Jewish Cancer Heritability Involving the BRCA Genes” (the PEACH BRCA Study) was launched in the summer of 2019 in the metro-Atlanta area and offered complimentary education and testing using its existing at-home model of telehealth. This was the first-known testing program to provide sequencing and reporting of variants of uncertain significance (VUSs) in a low-risk AJ population. The objectives of this study were to assess interest and satisfaction with a telehealth-based BRCA testing program in a low-risk AJ group. Additional objectives were to determine whether the established mutation rate of 1 in 40 applies to this group and to assess the adequacy of screening for the 3 common AJ mutations. Other goals were to evaluate the feasibility and value of introducing a more comprehensive cancer genetic testing program on a national level. The pilot program, results of the study, and lessons learned are described below.

Materials and Methods

The PEACH BRCA Study was approved by the Institutional Review Board (IRB) at Emory University (IRB00104759). Enrollment began in July 2019 and was closed in July 2020. The overall design of the study is shown in Figure 1. Interested individuals who met initial study criteria were directed to complete a personal and family history questionnaire in the secure, Web-based software...
Recruitment

Participants were recruited primarily by social media and word of mouth, coverage in local media outlets, and email blasts to past JScreen (reproductive carrier screening) patients who consented to being notified about research opportunities. Other notable recruitment sources were a live educational event with an Atlanta-based Hadassah group and an article published in the widely distributed Atlanta Jewish Times.

Eligibility

In order to participate in the study, individuals were required to meet the following criteria: be age 25 or older, reside in the metro-Atlanta area, have at least one AJ grandparent, have never had BRCA testing or a known BRCA mutation in the family, and have no significant personal or close family history of breast, ovarian, or pancreatic cancers, and no personal history of metastatic or high-grade prostate cancer. Non-English speakers were not specifically excluded from the study; however, the educational materials and registration were provided in English only.

All registrations were initially reviewed electronically by REDCap, which excluded individuals with a personal history of breast, ovarian, pancreatic, or metastatic or high-grade prostate cancers, as well as those who had previous BRCA testing, a family member with a known BRCA mutation, a bone marrow transplant, or a history of a hematological malignancy. Those who had a bone marrow transplant or history of blood cancer were excluded because their samples may have contained DNA from a donor or malignant cells. Participants in any of these categories were not given the opportunity to complete their registrations.

Completed questionnaires were reviewed by a certified GC, and a 3-generation pedigree was constructed for each registrant. Eligibility was determined based on the NCCN Clinical Practice Guidelines in Oncology (NCCN guidelines) for Genetic/Familial High-Risk Assessment: Breast and Ovarian, version 3.2019 [47]. Those who met guidelines for BRCA testing were deemed ineligible for the study. Registrants with incomplete family history information were emailed for further clarification. Those who noted a family history of prostate cancer were not excluded, as it was determined that many registrants were unaware of the grade and type of prostate cancer, 2 criteria which are required to establish NCCN guideline-based testing eligibility.

Eligible Participants

Clinical Testing

Individuals who met eligibility criteria were emailed pre-test requirements, which included viewing a 4-minute educational video, reading a written summary of the video, and completing a knowledge quiz (shown in online suppl. Fig. S1; for all online suppl. material, see www.karger.com/doi/10.1159/000525658) and laboratory and study consents. Factors such as education level and ability to access online videos were considered when designing the video, and participants were instructed to contact a GC from the study team with any questions. Those who completed these requirements were mailed a saliva kit and were instructed to submit their samples to the laboratory. Accommodations for blood draws were made for those who could not submit a saliva sample or following a saliva sample failure. Sequencing and deletion/duplication analysis of the BRCA1 and BRCA2 genes was performed by Invitae, a Clinical Laboratory Improvement Amendments (CLIA) certified laboratory [48]. This testing was provided at no cost to the participants. Those who withdrew from the study after initial eligibility were sent a survey asking for their reasons for withdrawal.

All test results were disclosed by a GC at no cost to the participants through phone or secure video conferencing, depending on the preference of the participant. Participants were then sent their laboratory reports and consultation letter through secure email. Those with positive results were referred to Winship Cancer Institute at Emory University for a consultation with a medical oncologist. In addition, they were recontacted by their GC 1 week after their initial consultation and once again over the next 5 months for emotional and clinical support.

Complimentary reflex testing to Invitae’s expanded cancer panels was offered to all participants. As this testing was not included in the PEACH BRCA Study protocol, interested participants were instructed to ask their personal healthcare providers to order the test on their behalf, and the results were released directly to those providers. De-identified results in aggregate were released to the study team upon completion of the study.

Survey-Based Research

One of the pre-test requirements was a pre-test knowledge quiz that assessed participant understanding of the information they would receive from their genetic test (shown in online suppl. Fig. S1). In addition, all participants were emailed post-test surveys which included the same questions as the pre-test knowledge quiz, as well as questions related to satisfaction with the study process and interest in further testing options. The first 4 questions in the pre- and post-test knowledge quiz were closely matched to items from prior scales that were tested and validated to assess cancer genetics knowledge [49, 50]. An additional question that was added to our survey (question 5) was not closely matched to an item on a prior validated scale. It was chosen as a representation of the content of our educational offering that was not articulated in the same way in prior validated scales.

Ineligible Participants

Individuals who did not meet eligibility criteria due to significant personal or family history of BRCA-related cancers were emailed regarding their ineligibility for this study. Included in the email was information about local genetic counseling services and the National Society of Genetic Counselors’ (NSGC) “Find A Genetic Counselor” resource [51], where participants could find a GC to discuss, and potentially help them pursue, appropriate genetic testing. In addition, those who consented to be recontacted for research were emailed a survey 1 week after the closing of the study. The survey included questions about whether they followed up with genetic counseling or testing after their exclusion from the PEACH BRCA Study.
Results

Characteristics of Study Participants

Over the course of the study, 1,167 individuals completed registration. Of these, 622 (53.3%) met eligibility criteria and 545 (46.7%) did not (shown in Fig. 1). The most common reasons for ineligibility were having a family history of BRCA-related cancers (95.2%), prior BRCA testing (2.2%), and family history of a known BRCA mutation (1.1%). Eight participants were disqualified from the study due to family histories of BRCA-related cancers that were reported after results were disclosed. Of the eligible participants, 97.5% passed the pretest knowledge quiz, which was achieved by correctly answering all of the knowledge-based questions (see online suppl. Fig. S1). When asked how they heard about the study, the most common sources were family/friend, social media, (primarily one Facebook group called “Jewish Moms of Atlanta”), synagogue, and/or a JScreen representative.

Five hundred one (80.5%) of the eligible participants completed testing. Those who did not complete testing (n = 121, 19.5%) did one of the following: failed to send their sample to the laboratory, needed a recollection that was not completed, or formally withdrew from the study. The most common reasons cited for withdrawal were no longer wanting to learn BRCA status and concerns about future insurance coverage should they test positive. Additional characteristics of the 501 eligible participants are presented in Table 1.

Four female participants, ranging from 36 to 53 years of age, tested positive for a BRCA mutation. Three of them had 4 AJ grandparents and carried the common AJ BRCA2 mutation (617delT). The fourth individual also had a mutation in BRCA2, though not the common AJ variant (c.1054dup). This makes the founder mutation...
positivity rate 3 in 501 (0.6%) and the overall positivity rate 4 in 501 (0.8%). The fourth participant’s maternal grandparents were AJ and her paternal grandparents were Scottish/English. After participating in the study, she reported that her mother was tested and was negative for her variant. Three of the participants who tested positive later reported that they consulted with a healthcare provider, and 2 of those participants had or planned to have their ovaries removed. In addition, 2 reported planning for increased breast surveillance. Of note, there were 3 study participants who had a VUS in BRCA1 or BRCA2. Two of them were sisters who were found to have a shared variant in BRCA1 (c.4115G>A). The other had a VUS in BRCA2 (c.5126A>C).

Post-Test Surveys

Of the 497 participants who received their results in a genetic counseling consultation (99.2% of tested participants), 373 (75.5%) completed the post-test surveys. Three hundred twenty-eight (87.9%) respondents were female and 45 (12.1%) were male. Three of the 4 participants with a positive result completed the post-test survey, as did 2 of the 3 participants with a VUS.

The mean overall satisfaction with the study process was 96.9 out of 100. The mean overall satisfaction for those with a negative result was 97.1 (SD = 6.48), for those with a positive result was 71.0 (SD = 21.5), and for those with a VUS was 96.0 (SD = 5.7). The mean satisfaction with different aspects of the study process was measured as well. Ease of registration was 92.5, and communication with study staff was 96.3. In addition, 92.8% of the respondents passed the knowledge quiz portion of the post-test survey.

When asked whether they would have made any changes to the pre-test education process, a majority of participants responded “no” (n = 334, 89.5%). The remaining responses are shown in Figure 2. Three hundred seventy-one (99.5%) participants felt that their discussion with the GC about their results was valuable. When asked if alternative modes of results disclosure (including in-person genetic counseling, pre-recorded videos, written materials explaining the results, or receiving a laboratory report only) would have been better, 351 (94.1%) responded “no.”

As seen in Table 2, when asked if they would have been willing to pay for testing if it had not been fully subsidized, 293 (78.6%) participants responded affirmatively. When asked which testing option they would have chosen if given the choices of a multigene cancer panel and BRCA-only panel, 325 (87.1%) participants responded that they would have preferred a multigene panel. After the study period was over, 84 (16.9%) participants followed through with upgrading to a larger cancer panel through their healthcare providers (data provided by Invitae laboratory). In this group, there were 10 positive results in 4 different genes (CHEK2, APC, NF1, and RECQL4) and 17 VUS results in 14 different genes. Of the positive results, 7 of them were the common AJ APC low-risk allele (p.Ile1307Lys) and 1 was the common CHEK2 AJ founder mutation (p.Ser428Phe).

| Table 1. Characteristics of PEACH BRCA Study participants |
|---------------------------------|-------------|
| Total participants with results | 501 |
| Age range                       | n (%)     |
| 25–34                           | 86 (17.2) |
| 35–44                           | 155 (30.9) |
| 45–54                           | 127 (25.3) |
| 55–64                           | 70 (14.0)  |
| 65–74                           | 57 (11.4)  |
| 75+                             | 6 (1.2)    |
| Sex                             | n (%)     |
| Female                          | 439 (87.6) |
| Male                            | 62 (12.4)  |
| Ancestry                        | n (%)     |
| 4 AJ grandparents               | 369 (73.7) |
| 3 AJ grandparents               | 36 (7.2)   |
| 2 AJ grandparents               | 83 (16.6)  |
| 1 AJ grandparent                | 13 (2.6)   |

| Table 2. Interest in testing outside of the study |
|---------------------------------|-------------|
| Total participants who completed post-test survey | 373 |
| Willingness to pay for testing   | n (%)     |
| Not willing to pay               | 80 (21.4)  |
| Willing to pay                   | 293 (78.6) |
| USD 100                          | 184 (49.3) |
| USD 200                          | 65 (17.14) |
| USD 300                          | 29 (7.8)   |
| USD 400                          | 2 (0.5)    |
| USD 500                          | 13 (3.5)   |
| Interest in BRCA-only versus multiple gene panel | n (%)     |
| BRCA-only                        | 48 (12.9)  |
| Multigene panel                  | 325 (87.1) |

Ineligible Participants

Of the 524 registrants who were deemed ineligible by GC review and received an email recommending that
they see a GC, 500 (95.4%) agreed to be recontacted and received the ineligible survey. Two hundred ninety-five (59.0%) of those individuals completed the ineligible surveys. Of these respondents, only 21 (7.1%) had met with a GC in person or virtually and only 39 (13.2%) reported that they were planning to consult with a GC. When the remaining participants were asked why they had not followed up with a GC, there was a wide range of reasons related to the accessibility, impact, and necessity of genetic counseling. The most common reasons cited were concern about insurance coverage and costs for the consultation, lack of time, lack of concern about risk, desire to have testing without genetic counseling, and not knowing how to find a GC (shown in Fig. 3). There were also a few free-text responses related to healthcare providers suggesting that the counseling was not necessary, difficulty meeting with a GC during the COVID-19 pandemic, believing testing is unnecessary when periodic cancer screening is already being done, and believing that a family member’s negative result applied to them as well. When asked in what way(s) they found value in their brief involvement in the study, the most common responses were no value gained, glad to be part of research, learned about family health history, shared information about the study with others, and discussed cancer risks with relatives.

Study Enrollment during COVID-19

Of note, the COVID-19 pandemic began about halfway through the study period. The rate of registrations and testing dropped significantly in April 2020, about a month after the pandemic began. There was a small up-tick in registrations in June 2020, but the numbers remained low until the close of the study.

Discussion

Mutations among Low-Risk AJ Individuals

BRCA Testing for All AJ Individuals

Based on a one-sample test of proportions, the JScreen positivity rate for an AJ founder mutation of 3 in 501 (0.6%) is statistically different than the established AJ founder mutation frequency of 1 in 40 (2.5%), \( p = 0.0064 \). This established mutation rate was calculated by studying individuals with and without personal or family histories of BRCA-related cancer [5]. Given a general population prevalence of all mutations near the midpoint of the modeled range of 0.2–0.3%, our overall positivity rate of 4 in 501 implies a higher mutation risk in the low-risk AJ cohort at the 5% significance level [52]. As such, even without a family history, AJ individuals may be considered a “high-risk” group and, therefore, could be considered for national testing criteria guidelines. Indeed, recent NCCN clinical practice guidelines have been updated and state that “testing may be considered for an Ashkenazi Jewish individual” in the absence of family history or other related risks [12]. With our data and these recent NCCN updates, there is mounting justification for insurance companies to broaden their criteria and allow for coverage for BRCA testing for all AJ individuals.

Fig. 2. Pre-test education preferences.
Fig. 3. Reasons for no GC follow-up.
BRCA Sequencing in the AJ Population

Testing only for the 3 common AJ founder mutations has been demonstrated to be effective for the low-risk AJ population in a prior study [7]. However, JScreen’s data have shown that ethnic-specific testing may not be a sufficient means to meeting the goal of identifying mutation carriers. One reason carriers will be missed if founder mutation testing is performed is that many individuals who identify as AJ are actually of mixed Jewish ancestry. In the PEACH BRCA Study, 26.5% of participants had 3 or fewer Ashkenazi grandparents (see Table 1). In fact, 1 of the participants who tested positive for a non-founder BRCA2 mutation was of mixed AJ/non-Jewish ancestry. Had she been screened for the AJ founder mutations only, her mutation would have gone undetected.

Another limitation to founder mutation testing is that it relies on the participants accurately reporting their AJ ancestry. JScreen has seen that family health history information can be overlooked or unknown. A cursory review of family history information submitted by participants who reported to be relatives demonstrated that there are discrepancies and gaps in knowledge about family history among family members. Furthermore, with the availability of direct-to-consumer ancestry testing, it has been observed that a great number of individuals are surprised by their ancestry results [53] because their genetic ancestry does not match what they were told about their background. If family information, such as ancestry and health history, may not be accurate, caution should be taken when using such information to inform testing choices.

AJ individuals should consider BRCA testing due to their ancestry, but this testing should not be limited to founder mutations. Additional considerations for more extensive testing should also be made for AJs with personal and/or family histories of cancer or for individuals who are interested in learning their hereditary cancer risks.

Low Rates of Genetic Counseling in a High-Risk Group

It was observed that the majority of individuals who registered for the study but did not meet eligibility criteria due to family history did not follow-up with genetic counseling and testing. These high-risk individuals were sent information about the importance of genetic counseling and were given options for accessing a GC for appropriate care; however, the rate of follow-up or plans to follow-up with genetic counseling was low (approximately 20%).
Finding a Solution: Considering a New Service Delivery Model

One way to improve education about risks and access to genetic testing would be to train general healthcare providers who already have a relationship with their patients to assess risk and to order and interpret appropriate genetic tests. Another solution would be for healthcare providers to guide their patients to GCs, breast surgeons, or gynecologic oncologists for this care [58].

While referring patients for a genetics consultation may be easier for the healthcare provider, meeting with a GC in person may be a barrier for many patients. As seen in Figure 3, there are often concerns about the time commitment, cost, and insurance coverage involved in seeing a GC. Additional concerns relate to a shortage of GCs, especially in nonurban areas [58].

Telehealth provides a number of solutions to the challenges posed above. Numerous studies have concluded that genetic counseling via telehealth is noninferior to in-person genetic counseling [36]. Indeed, data from the post-test surveys indicated that the telehealth model used for the PEACH BRCA Study was a success.

To further highlight the efficacy of telehealth, it should be noted that the COVID-19 pandemic began about halfway through the study period. In a time when healthy individuals were discouraged from visiting their providers for routine medical matters due to concerns about COVID infection and overloading healthcare systems [59, 60], a shift from in-person consultations to telehealth had become a solution in many areas of healthcare [59, 60]. Bergstrom et al. [61] highlighted the advantages and challenges of utilizing telehealth for genetic counseling in the wake of the COVID-19 shutdown of New York State, and concluded that telehealth may be a sustainable option for genetic counseling services, even after the resolution of a health crisis. The COVID-19 pandemic has underscored that using telehealth for genetic testing and counseling, especially in the context of an already successful service, is a viable and proven solution in the event of a crisis and beyond.

Value of Pre-Test Education

Standardized Educational Resources in the Pre-Test Period

JScreen saw excellent scores on the pre-test quiz (97.5% pass rate). These scores suggest that the standardized video and written summary utilized in this study are effective tools for pre-test education.

Indeed, research has shown that educational videos are effective in achieving goals of genetic counseling. Benefits of using standardized educational videos include practicality (convenience for patients and providers), low production costs, enhancement of patients’ sense of control in the decision-making process, and the ability for patients to rewatch when needed [62, 63]. In addition, the use of multiple formats to present the same information (such as videos and written materials) in the realm of health education has been suggested to improve patient memory and learning [62, 64].

Oliver et al. [65] studied the effectiveness of showing 2 pre-test educational videos about prenatal genetic testing and carrier screening to women at OB/GYN and perinatology offices. They found that the videos elicited a high level of patient satisfaction and understanding of the concepts presented and suggested that pre-test education videos increase efficiency of genetic counseling services and enhance the patient experience. In addition, Hardy et al. [66] assessed the efficacy of a pre-test educational video in the realm of preconception carrier screening. In this study, over 1,000 undergraduate students were given a quiz assessing their knowledge and understanding of carrier screening. Then they watched a pre-test educational video and were quizzed again. Results of this study showed that knowledge about the testing improved significantly post-education [66]. Data from the PEACH BRCA Study’s post-test survey (seen in Fig. 2) support the findings of that study, as the use of a pre-test video and educational summary was associated with high levels of satisfaction. Considering the high passing rate of the knowledge quiz and general satisfaction with the pre-test education provided, an educational video and written summary as a prelude to cancer screening can be considered a suitable model for pre-test education.

Of note, the pass rate for the post-test quiz (92.8%) was significantly lower than that of the pre-test quiz (97.5%), $z = 3.34, p < 0.01$. It is possible that the pass rate declined due to the extended amount of time that had lapsed between receiving pre-test education and taking this quiz, which ranged from 3 weeks to a few months. While every participant consulted with a GC before taking the post-test quiz, most of the topics in the quiz (seen in online suppl. Fig. S1) were likely not addressed by the GC because the majority of patients had a negative test result.

Education about Risk in the Community

The need for family health history education in the AJ community is highlighted in the surveys of ineligible participants. Data from these surveys show that bringing the PEACH BRCA Study to the community helped some ineligible participants develop a newfound awareness that there...
are factors that increase the risk for mutations. Bringing educational events and testing opportunities to other cities with high-risk communities should be considered as an effective way to engage with the community and encourage its members to consider their options for healthcare.

Cancer Panels for the Broader Community

Data from the post-test surveys show that overall satisfaction with the study process among study participants was high. JScreen has designed a patient-approved approach to cancer genetic testing that has been used to inform the national launch of an at-home cancer genetics program.

While JScreen tested for mutations in the BRCA genes only, the majority of study participants who completed the post-test survey would have preferred a multigene panel (Table 2). There is clinical utility to offering panel testing, as demonstrated by the 10 out of 84 participants who received positive results after upgrading to a larger cancer panel. In addition, studies have showed that standard guidelines for genetic testing may be limited, and mutations are going undetected. Neben et al. [67] analyzed the results of over 7,000 individuals who did not meet NCCN criteria for genetic testing and were tested with a 30-gene cancer panel. The frequency of a pathogenic mutation was 8.2%. A significant percentage (21.3%) of these mutations were in genes with well-established genetic testing recommendations, including hereditary breast and ovarian cancer and Lynch syndrome, even though those who tested positive did not meet NCCN criteria for testing of these genes [67]. In addition, panels would reduce reliance on the accuracy of patient-provided information about ancestry and family history.

Conversely, broad panels may come with higher risks of detecting VUSs or include genes with low-penetrance, unspecified cancer risks, or lack of medical management guidelines. Counseling individuals who test positive for genes in these categories can be challenging, increasing the GC’s workload, and there is often a need for carriers to continue to keep up with evolving guidelines, which poses a burden to the patient [68, 69]. However, by utilizing standardized pre-test education that is appropriate for individuals with varying degrees of risk, and carefully curating a robust panel of genes with well-understood cancer risks and recommendations for clinical follow-up, more mutations would be detected, as seen in high-risk groups [70–72]. This would also allow GCs to operate at the top of their professional scope of practice by concentrating their expertise on counseling and results interpretation, especially for more complex cases [25, 73]. As seen in the post-test survey, overall mean satisfaction with this model of education and testing was quite high, even among participants with VUSs (96.0/100).

Study Limitations

Some study limitations are related to the participants. For example, participants were relied upon to report their personal and family histories to define eligibility, but since family history information may be limited, the BRCA carrier rate of 0.8% in a "low-risk" AJ population may be inaccurate. Also, it is possible that the study participants entered the study with a fair amount of background knowledge about BRCA, especially if they were recruited through an education event. This might have influenced the success on the knowledge quizzes. In addition, there may be participant bias in that the study subjects may have been early adopters who are more proactive than the general population about health, individuals with past JScreen experience, and/or those with interest in contributing to research. Finally, this study assessed the Atlanta-based AJ population only, and study conclusions may not be applicable to other AJ and non-AJ populations.

There are also other limitations to the study design. For example, while the telehealth model was effective for this population, it may not be feasible for individuals with lower health literacy, those who are not proficient in English, and/or those with limited access to computers and smartphones. In addition, the interest in and uptake of the test may have been due to the fact that the testing was fully subsidized and that insurance information was not collected. And finally, since follow-up data were not collected on the participants who reflexed to an expanded panel, satisfaction with broader testing cannot be assessed.

Conclusion

The PEACH BRCA Study was an effective pilot program, demonstrating that a telehealth model for cancer education and testing is effective and acceptable to the AJ community in Atlanta. The data indicate a higher-than-average BRCA mutation rate among low-risk AJ individuals and suggest that all AJ individuals, even those without histories, should consider comprehensive testing for BRCA. The data also point to the interest and clinical utility of broader panel testing in this community.

The study established that the pre-test video and written summary is an effective and satisfactory mode of pre-test education and that the telehealth model for post-test genetic counseling is acceptable. Genetic testing and
counseling via telehealth is a good model for those who will not access traditional in-person genetic counseling and also helps fill the gap for providers who are not ordering testing themselves.

The information gleaned from the PEACH BRCA Study was used to establish a national cancer genetic screening program at JScreen that was launched in January of 2021. It is our hope that there will continue to be improvements in accessibility and that anyone who wants to learn about their genetic cancer risks will have easy access to testing and genetic counseling.

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Statement of Ethics

All participants in the PEACH BRCA Study have given their written informed consent. In addition, the study protocol was approved by the Institutional Review Board at Emory University (IRB00104759).

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Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

The authors confirm contribution to the paper as follows: study conception and design: Esther Rose, Melanie Walker Hardy, Christine Stanislaw, Jane Meisel, and Karen Arnovitz Grinzaid; data collection and analysis and interpretation of results: Esther Rose, Melanie Walker Hardy, and Rachael Gates; and draft manuscript preparation: Esther Rose and Melanie Walker Hardy. All authors reviewed the results and approved the final version.

Data Availability Statement

The data that support the findings of this study are not publicly available due to their containing information that could compromise the privacy of research participants but are available from E.R. upon reasonable request.

Statement of Ethics

All participants in the PEACH BRCA Study have given their written informed consent. In addition, the study protocol was approved by the Institutional Review Board at Emory University (IRB00104759).
Telehealth-Based BRCA Testing in Ashkenazi Jews

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