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Public Health clinics: The frontline for expanding reach of family history screening for Hereditary Breast and Ovarian Cancer

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By

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B.S. in Biology &

Anthropology (Global Health and the Environment)

Washington University in St. Louis

2019

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By: Julia Veitinger

Abstract:

Objectives: To evaluate the impact of increased access to genetic services for underserved and racial/ethnic minority Georgians through a statewide initiative. Additionally, to evaluate any racial uptake differences that exist among the various genetic services.

Methods: Georgia CORE and its collaborators provided training on how to use an online familial history referral tool to all public health clinics in the state. Healthcare providers were responsible for screening their patients during routine care and to refer those identified as high risk for an HBOC mutation to Georgia CORE for further evaluation to determine if genetic testing was warranted. The program was active from 11/1/2012-12/31/2020.

The data collected was analyzed using Chi-Square tests to assess differences between Caucasian and racial minority populations in the uptake of screening, counseling, and testing.

Results: The program reached 79 underserved counties in Georgia. The program screened 29,090 with 26,938 individuals providing their ethnicity and 15,592 (63%) self-identifying as racial minority. The uptake of genetic counseling and testing among minorities was found to be 67.7% (793/1,172) and 52.5% (416/589), respectively. The limited sample size only allowed us to assess differences among Caucasians, African Americans, and Hispanics. African American (63.1% vs. 74.0%, p-value<0.001) and Hispanic (63.1% vs. 72.9%, p-value= 0.028) populations engaged with screening and counseling at statistically significant higher rates than Caucasian populations. However, once the individuals made it to genetic testing, there was no statistically significant difference in uptake between minority and Caucasian populations; only Hispanic populations participated in genetic testing at statistically significantly higher rates than Caucasian populations (69.1% vs. 80.5%, p-value=0.037).

Conclusions: Georgia CORE substantially expanded genetic services in rural settings with large racial minority populations. Racial minorities utilize genetic services when available, sometimes even at higher rates than Caucasian populations. Public health clinics seem like an appropriate setting to provide genetic services to minority populations. The results contradict published literature citing that minority populations do not participate in genetic services. Therefore, access to such services should be expanded in settings such as public health clinics. To expand access genetic services infrastructure needs to be improved.

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Section 1: Introduction:

Breast and ovarian cancers are serious public health problems. In 2020, globally 2.3 million women were diagnosed with breast cancer- and 313,000 were diagnosed with ovarian cancer [1]. Approximately 5-10% of these cancers are associated with known genetic mutations [2]. While this is a very small percentage of the total breast and ovarian cancer burden it nevertheless presents a unique population for enhanced surveillance and early detection. Currently there are more than 65 identified loci found to be associated with increased risk of developing breast cancer and ovarian cancers [3]. About 2/3 of the hereditary genetic breast and ovarian cancer diagnoses can be linked back to a *BRCA1/2* mutation [2]. Women carrying a *BRCA1/2* mutation have an between 4-5 times the increased lifetime risk of developing breast cancer by age 80 [4]. Ovarian cancer impacts a smaller percentage of the population with only approximately 1.2% of women being affected, however *BRCA* mutations confer a significantly higher risk of developing the disease These mutations are known to be passed down through families [3 5].

Decreasing costs of genetic testing and availability of evidence-based screening tools has made it possible to identify individuals who have a mutation more efficiently and in a cost-effective manner [6]. These individuals when appropriate can be referred for genetic counseling regarding preventive options (e.g., enhanced surveillance or prophylactic surgeries) [7].

Currently most genetic services are located in urban academic settings, which are most frequently visited by well-educated Caucasian populations [8]. Such services are rarely offered in medically underserved areas that comprise predominantly of minority communities since the clinics lack the infrastructure knowledge and personnel to provide access to genetic services [8].

For this reason, minority women, are underutilizing genetic services; this leads to later detection of cancers and higher mortality rates [9]. The disparity in mortality is especially pronounced in African American women, despite having lower a lower incidence of breast cancer diagnoses, African American women have a significantly higher mortality rate than Caucasian women [10 11]. African American women also have a greater proportion of breast cancers that are classified as triple negative, meaning that the cancer cells are missing the estrogen receptor (ER), progesterone receptor (PR), and the human epidermal growth factor receptor 2 (HER2), these cancers are the most difficult to treat and have the lowest survival rate [10]. This finding has generated the hypothesis that African American women have an increased risk for having a genetic mutation for triple negative breast cancer promoting increased research into a potential genetic founder-effect [10]. This also means that African American women could stand to benefit significantly from breast cancer screening programs.

In addition to inequitable access to genetic services minority women, are referred for genetic counseling and testing at lower rates than their Caucasian counterparts [12 13]. Genetic services are consistently underutilized, especially by African American, Hispanic, Asian, Native American/Alaskan Native, and Pacific Islander/Hawaiian Native, and other non-Caucasian (minorities) racial groups[14 15]. There are many reasons why non-white individuals have been using genetic screening, counseling, and testing at lower rates than Caucasian populations. Some of the driving factors include, lack access to such services, insufficient trained healthcare providers, fear that the information will not stay private, and more. Additionally, work has been done that highlighted the fact that African American populations may not want to participate in genetic screening, counseling, and testing, citing that their choice to not participate aligns with

their “family values” [12]. Nevertheless, the differing rates of participation in genetic services could be a confounding factor to the differing mortality rates from breast cancer by race.

Despite, HBOC familial history screening tools have been available for over a decade they are still not being widely implemented on a population level, even after studies demonstrated its efficacy and cost-effectiveness [6 16]. The current approach in HBOC genetics is cascade testing, conducting tests and familial screens after diagnosis of a family member [17]. This is a very reactionary approach and does not take advantage of the full early detection/preventative potential of familial screens.

In 2012 with funding from the CDC, the Georgia Department of Public Health (GDPH) in collaboration with the Georgia Center for Oncology Research and Education (CORE) launched a family history-based screening in women’s health clinics. Public health clinics serve rural communities with low socio-economic status and generally individuals without health insurance [18]. Women were approached to complete an online seven question screener indicating any family history of breast or ovarian cancer. Women identified as high risk carrying an HBOC mutation were referred to free genetic counseling and when genetic testing if appropriate. For an eight-year period (2012-2020) HBOC screenings and follow up counseling were provided to all public health clinics in the state. While all clinics were trained and invited to participate in the program, not all clinics were able to partake in it. This thesis will discuss successes and lessons learned from this program about providing genetic services in a public health clinic setting. As well as present some options on how the program could be expanded and improved in a sustainable and equitable manner.

The Genetics services screening program was funded through a grant with the Georgia Department of Public Health (GDPH) and was jointly administered with Georgia CORE and

other collaborators in the Georgia Public Health Clinics. For ease of understanding I will be referring to this program as the GDPH's Genetics Services Program.

Section 3- Literature Review:

Georgia's Hereditary Breast and Ovarian Cancer (HBOC) Family History Screening Program:

The data for this thesis is drawn from a family history-based screening program to evaluate women's risk of HBOC conducted in Georgia Public Health Clinics from 2012-2020. Family history screening for HBOC was integrated into routine care in women's health clinics. The genetics program relied on public health clinic staff administering the screening test and referring the subsequent high-risk individuals to Georgia Center for Oncology Research and Education's (CORE) advanced practice nurse in genetics (APNG). The genetics nurse further evaluated the individual and decided if genetic testing was warranted.

Provision of genetic services has been limited to urban academic settings, where minority and low income individuals are less likely to seek care [19]. This has contributed to low uptake of genetic services by patients of color and the belief that these populations may be reluctant to engage with genetic services [15 20]. Therefore, Georgia CORE and its collaborators set out to expand access to genetic services (screening, counseling, and testing) to rural community settings within Georgia where women with low income and no insurance seek care. In Georgia Public Health Clinics, a sizeable proportion of these women self-identify as African American.

In Georgia 151/159 counties are considered to be medically underserved areas (MUA) or to have medically underserved populations by the Georgia State Office of Rural Health (SORH) [21]. Many of these communities rely on the state public health clinics for their healthcare needs, therefore this made these communities ideal for evaluating the impact of increasing the availability and knowledge of genetic services on the uptake of such services, and if uptake differed by race.

Benefits of HBOC Population-Based Screening:

Current public health recommendations for genetic testing relies largely on cascade testing, meaning that if one person is diagnosed with breast or ovarian cancer then they and their relatives are tested for genetic mutations such as *BRCA1/2* [22]. Cascade testing does not take advantage of the power of population-based screening. Genetic mutations are very rare therefore it is necessary to screen thousands of people to identify the 8-12% who could be at risk [22].

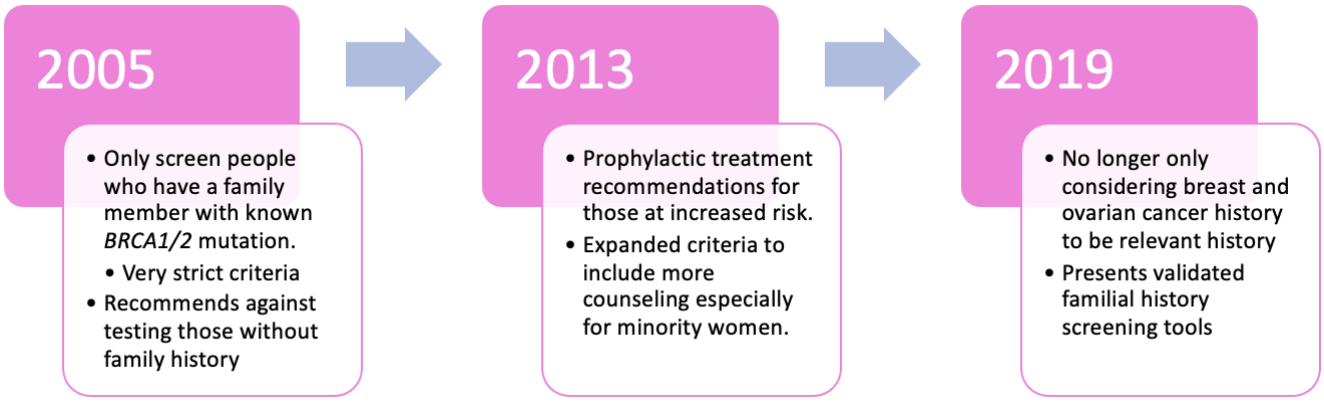
Population-based screening programs by comparison aim to screen the whole population. This approach has the potential to greatly increase the reach of genetic services and identify asymptomatic individuals and at-risk families [22 23]. Broad screening identifies the few who are at the greatest risk of having a genetic mutation related to HBOC. Those individuals can subsequently be counseled and referred for genetic testing. Early detection and diagnosis is crucial in increasing the survival rate of breast and ovarian cancer [23].

Today, many HBOC risk screening tools exist but not all are validated by the USPSTF. As of the 2019 guidelines the following seven tools were validated by the Task Force: "the Ontario Family History Assessment Tool, Manchester Scoring System, Referral Screening Tool, Pedigree Assessment Tool, 7-Question Family History Screening Tool, International Breast Cancer Intervention Study instrument (Tyrer-Cuzick), and brief versions of BRCAPRO [7]." These tools alone are not sufficient to diagnose an individual with having a hereditary genetic mutation; rather they provide additional information and guidance on who should undergo further evaluation and genetic counseling [7].

HBOC screening tests are largely free, and the main constraint is healthcare provider time and knowledge of implementation [24]. The low cost is one of the major benefits of familial history screening tools in primary healthcare settings and that it can reach large and diverse

proportions of the population where they normally seek care, without the need for specialty equipment [22 24 25].While Genetic screening is inexpensive and relatively easy to administer. The subsequent genetic testing is the limited resource that constrains the genetic services sphere. The cost of genetic testing has lessened significantly over the past two decades, decreasing from about $5,000 to around $250 today [22]. Nevertheless, the current price is still a barrier preventing many individuals from undergoing testing. Additionally, the interpretation of testing results requires a genetic counselor, which are in short supply especially in rural, low-income, and minority communities [26]. Without access to a counselor, the individual may not know what the proper next step should be for them.

Figure 1: Key Changes in the USPSTF Genetic Testing Guidelines for HBOC:



[7 27 28]

Barriers to Enacting Population Based Screening: Inadequate Genetic Infrastructure

While the expansion of genetic services is a prudent and necessary next step, the current genetic services infrastructure cannot handle an increase in demand. Rural southern areas in the US already suffer from genetic counselor shortages [19 26]. Counselor shortages are not the only barrier to access and implementation experienced, counselors in these communities highlight obstacles related to: "travel distance and low referral rates due to lack of awareness or

skepticism [19].” Therefore, if genetic services are to expand to address the disparities in access that exist; concurrent steps need to be taken to bolster the current genetic services infrastructure. Examples of this could be to provide programs to increase physician awareness about HBOC to increase referral rates, and encouraging more genetic counselors to practice in rural, medically underserved communities potentially through incentives through the government. Lastly, general education campaigns should also be launched in health centers to increase patient awareness of their risk and options.

Barriers to access

Rurality:

Genetic service began as a highly specialized complicated healthcare provision, being offered in primarily urban and academic centers. [29]. Over time as science and technology improved, the price for genetic services dropped; additionally modalities evolved that could provide genetic testing in non-specialized community settings [29]. With genetic services becoming easier to implement, access has expanded into more communities [19]. Nevertheless, the expansion did not occur in a uniform manner; the communities that were already the most disadvantaged: the MUAs, were still lacking access to such services [30]. Despite many screening tools being free of charge, rural providers do not consistently administer them for various reasons [31]. Insufficient screening and referrals stifles the progress that has occurred in reducing the cost of a genetic test to those who need it most, many tests today only cost about $250 [22]. Nevertheless, rural communities have not benefited nearly as much from these advancements as urban centers, continuing to leave rural communities at a distinct disadvantage.

Yet various interventions have demonstrated that providing genetic services to people living in rural communities is feasible and beneficial [26]. Nevertheless, even when clinics offered screening, education, or testing services additional barriers emerged. Rural communities by definition are more spread out, therefore having the ability to visit a clinic is not always possible [26].

Lack of Physician Awareness

In some circumstances, even when rural communities have access to genetic services individuals are not participating. There is no single reason why rural and minority populations have historically participated in genetic services at lower rates than urban Caucasian populations [19 30]. A frequently cited reason is that healthcare providers in rural and medically underserved areas may not be as aware of genetic services and how to best provide them to their patients [31]. Therefore, some providers do not mention it to their patients during routine visits. A study conducted by the Georgia Breast Cancer Genomics Program sought to evaluate the knowledge that healthcare providers have about HBOC in Georgia and how screening tools can be used to assess a patients genetic risk [31]. In the 13 public health and federally qualified health centers they evaluated, they identified a "profound provider knowledge gaps among physicians and medical residence [existed] and a lack of evidence-based genetic services to survivors [31]." Furthermore, even when services were provided to the at-risk women, providers were unsure of how to advise or counsel these women on next steps. The lack of confidence and knowledge demonstrated by the provider did not help to empower and motivate populations that were already hesitant about utilizing genetic services [26 31].

It is well documented that minority populations, especially African American individuals have a distrust about how their genetic information would be used [13]. Nevertheless, African

American individuals do understand the benefits that cancer screenings provide for themselves, their family and cancer research [13]. If physicians or healthcare providers cannot provide these minority communities with educated informed consent it is unreasonable to expect participation to increase.

Fears of Data Misuse and Violation of Privacy

Populations living in MUAs are already some of the most medically vulnerable communities. In addition to being underserved they also have a significant distrust and hesitancy regarding the protection of their private medical information in the healthcare system [31]. Multiple systematic reviews and articles highlight a "distrust" of how their genetic information would be used if mutations were to be identified [32 33]. Minority populations appear to be more concerned that having a genetic mutation could be used to further discriminate against them, or that the information will not be kept private as promised [33].

While genetic testing results are protected information by the Health Insurance Portability and Accountability Act (HIPAA), the field of genetic testing and information is so rapidly evolving it is understandable that populations fear that the current law may not always be able to fully protect their private data [34]. The federal government has tried to address these concerns through the passing of the Genetic Information Non-discriminatory Act (GINA), but as with other non-discriminatory acts, they are difficult to enforce [34]. While it is important to keep health information private, there are also many researchers that believe that there should be an obligation to share genetic information for "low-risk research" [34]. And sharing this genetic information would be for the benefit of all people. But this desire for access to some confidential genetic information can lead to larger and larger requests for genetic information, validating the lack of privacy concerns expressed by minority populations. Additionally, the very definition of

privacy is being reviewed and revised as a result of the 'Information Age' [34]. People are beginning to argue that privacy does not mean that the information is not shared at all, but rather that you have control about how your data is shared and distributed [34]. For these reasons, the genetic information privacy apprehensions are very valid and should be adequately and thoroughly addressed if we want to build trust that the information will not be misused.

African American Ancestry Risk

Disease risk is not uniformly spread throughout the general population. Some sub-populations are at an increased risk for specific diseases and therefore there is reasoning why resources should be allocated according to the need of a population rather than all populations getting the same [10] . For example, when comparing African American and White women, African American women have a lower risk of developing breast cancer, yet they die at a higher rate than their white counterparts. One explanation for this discrepancy in incidence and mortality could be associated with delayed care/diagnostic seeking behavior; this leads African American to be diagnosed at a later stage in disease [10]. Yet there are other tumor characteristics that are more common in African American women that cannot be attributed to socio-economic factors. For example, African American women are more likely to be diagnosed with breast cancer at younger ages and with more aggressive tumor types such as triple negative breast cancer which is characterized by the following criteria: a missing estrogen receptor (ER) and progesterone receptor (PR), HER/2*neu* a combination, and a chromosomal abnormality, than White women[10].Triple negative breast cancer has also been associated with a *BRCA1/2* mutation; this has led some researchers to associate African ancestry with a predisposition for a *BRCA1/2* mutation [10].

The disparity in incidence holds true for African American males compared to White males as well; it is important to note that men can also be diagnosed with breast cancer [35]. The incidence is very low, accounting for about 1% of breast cancers annually. As with African American women, the men are diagnosed at a younger age and with later stage disease [35]. And regardless of stage, age, of diagnosis, or other confounding factors, African American men had worse overall survival than Caucasian men[35]. And a study conducted by Stark et, al. proposes that African Ancestry should be explored as another potential founder effect [10]. Another community that researchers have identified a potential founder effect is within the Ashkenazi Jewish heritage, meaning *BRCA1/2* mutations are much more common among these individuals than in the general population [10].

Access to Genetic Services:

There is a great need to expand genetic services in rural communities. Currently genetic services (screening, counseling, and testing) are available in mostly specialty or cancer clinics, typically located in affluent, and urban settings [36]. Low income and minority women are historically less likely to seek care from these academic specialty centers [36]. A recent systematic review demonstrated that of the 16 articles published between 2005-2019 about the implementation of genetic services in evaluating women for HBOC risk levels revealed that despite genetic services being available they were not widely implemented in routine care [37]. Of the 16 studies, 11 were conducted in clinical settings with only five being conducted in a public health setting [37]. Additionally, regardless of the setting only 10 of 16 clinics used a brief screening tool, meant to identify women at an increased risk for HBOC [37]. While the implementation and utilization of genetic screening varied significantly across studies, patients who underwent screening in a public health clinic were more likely to proceed to the next step of

genetic counseling to further evaluate their risk; women at public health clinics who screened high risk 65% continued to counseling compared to only 26% in clinic settings [37]. This speaks to the potential impact an expansion of genetic services into public health settings could have on the individuals who depend on such clinics for care.

Rural Southeast America already ranks as having one of the most severe genetic counselor shortages [19]. About 38% of the U.S. population lives in Southern America, with 20% being considered to having poor health [19]. The Southern US consists of 17 states, nine of which belong to the top 20 states with the most MUAs [19]. This entire region only has slightly under 700 registered genetic counselors during the 2017-2018 time period [19]. This data demonstrates the dire need for additional support for genetic services not only in Georgia, but also in other medically underserved states.

Access to these services is not limited by their location and availability, but also by the fact that health care providers were found to be 16 times less likely to discuss genetic testing options with African American women as compared to non-Hispanic, White women [37]. Additionally, with Hispanic women, the provider was two times less likely to discuss genetic testing with them as compared to White women [20]. Lower rates of genetic testing in preventative and treatment settings could influence the disproportionate mortality burden that African American women bear. There are known genetic mutations that result in a significantly higher risk of developing breast or ovarian cancer diagnoses. *BRCA1* mutations confer a risk 34.6 times higher of developing ovarian cancer than the general population [4]. *BRCA2* mutations have a slightly lower risk at 11.6 times the risk of developing ovarian cancer than the general population by age 80 [4]. Less testing leads to later diagnoses and not maximizing the implementation of targeted treatments both of which contribute to increased mortality [20 36].

Family History Screening in Georgia

Georgia CORE and its collaborators set out to make genetic services more readily available where minority populations seek routine. Through this they sought to evaluate if there is a disparity in uptake of genetic services between minority and Caucasian populations truly exists, as well as to evaluate the feasibility of introducing genetic services into public health clinics. They hypothesized that the reason minority populations did not participate in genetic services as frequently as their white counterparts was the result of different degrees of access and knowledge of such services.

A 2019 study conducted by the Georgia CORE and Emory University leveraged data from the Georgia Cancer Registry found that breast cancer screening and outcome disparities not only vary by race but also by geographic region within Atlanta, a large populous metropolitan area with many academic hospitals and clinics [38]. Their results showed that non-Hispanic Black (NHB) women were on average diagnosed at younger ages, with more aggressive and advanced disease, when compared to non-Hispanic White women (NHW) [38]. These findings agreed with other studies supporting that Atlanta's breast and ovarian cancer rates and diagnoses match national trends [10]. Race is not the only confounder for mortality and late-stage diagnosis in Atlanta. Geographically the southeastern portion of Atlanta appeared to have the most pronounced disparity in breast cancer mortality. The southeast part of Atlanta is predominantly comprised of non-White residents, with most neighborhoods having upwards of 90% African American residents [39]. Socio-economic status (SES) is a known factor contributing to disproportion in mortality from breast and ovarian cancer between Caucasian and racial minorities [40 41].

Even when controlling for SES, NHB women were more likely to die than NHW women, even at higher SES [38]. Individuals with low SES often seek care later than people with higher SES; this delayed care seeking behavior contributes to worse health outcomes not just in cancer but also in other diseases such as diabetes, and coronary artery disease [42].

Parts of the Affordable Care Act (ACA) were passed during the study period and aimed to increase the capacity of these clinics and centers, by financial grants to better serve the communities need [43]. The ACA also expanded the eligibility of Medicaid, expanding the patient population the clinics are expected to serve [43]. Georgia opted not to expand Medicaid, therefore the public health and community health centers did not receive the grants and resources to improve care for those they serve [44]. It was calculated that for every one million dollars in federal grants received, centers were able to serve approximately 8,000 additional patients [43]. Therefore, accepting the expansion of Medicaid could be a promising first step to improve the public health infrastructure in public health clinics, allowing them to consider providing genetic services to their patients while providing care to more individuals in the community. Especially here in Georgia increasing the sustainability and feasibility of the GDPH's Genetics Services program.

Additionally, when comparing the stage of the cancer identified between NHB and NHW women, disparities become even more apparent. In NHW the earliest two stages (1 &2) indicating minimal or localized spread made up 86% of tumors identified [40 41]. In NHB women Stage 1 or 2 tumors only were only 76% of tumors. Furthermore, when looking at the most advanced stage of tumor (4) NHB had nearly double the rate of diagnosis as compared to NHW, 4.8% and 9.4% respectively. This demonstrates that the differences in mortality and age of diagnosis cannot be solely attributed to race, but rather that it is complex and multi-layered.

In 2010, the Center for Disease Control and prevention (CDC) recognized the importance of assessing and addressing the observed disparities in access to life saving cancer screening. Therefore, Georgia CORE in conjunction with the Georgia Breast Cancer Coalition (BCC) received a grant to implement a breast and cervical cancer screening tool in all public health clinics within the state. The following manuscript presents and analyzes the data collected by the program over the first eight years of its implementation.

Section 3: Manuscript

Introduction:

Brief family history-based screening, endorsed by national guidelines (e.g., United States Preventative Services Task Force or USPSTF) and public health organizations (e.g., CDC Tier 1), is a frontline public health approach used to identify individuals at high risk for hereditary breast and ovarian cancer syndrome (HBOC). In 1996, the American College of Medical Genetics (ACMG) began recommending genetic counseling and testing for *BRCA1/BRCA2* mutations based on personal or family history of breast or ovarian cancer and Ashkenazi Jewish heritage [28]. In 2005, USPSTF published its first recommendation that "women whose family history is associated with an increased risk for deleterious mutation *BRCA1* or *BRCA2* gene be referred for genetic counseling and evaluation for *BRCA* testing" [28]. The recommendation mentions three screening tools, but none were validated in the general population resulting in limited generalizability and validity [27]. In 2013, USPSTF updated their recommendations highlighting specific screening tools validated as eliciting the information necessary to identify individuals at a higher risk of a *BRCA1/2* mutation [27]. The USPSTF restated its position that individuals at increased risk based on family history be considered for genetic counseling while men continued to be excluded from consideration [27]. In 2019, the USPSTF published additional guidelines reaffirming the benefits of counseling and testing while citing increased evidence of effectiveness in identifying individuals at risk and highlighting recommendations for preventative medications [7].

Current specialty-clinic-centric approaches, despite efforts to expand reach, are not achieving the Healthy People 2030 objective to ensure that all groups benefit from increasing knowledge about hereditary cancer. This is especially critical for subgroups that are more

difficult to reach. Those who live in rural settings, racial/ethnic minorities, and those with low education and income are less likely to have access to genetic services ([45-47] For example, screening is particularly essential for African American/Black (Black) women who are at greater risk of developing aggressive breast cancers at a younger age and dying than Caucasian/White (White) women, often linked to genetic mutations [10 48]. However, Black women are significantly less likely to be referred for and seek cancer genetic services than White women ([15 20 49-51].

Little empirical work has been conducted outside specialty care settings to increase access to genetic services [37]. This is especially critical for those least likely to have access to genetic services including ethnic minorities, those living in rural settings, or individuals with low education and income [45 47]. Recent evidence suggests that family history-based screening programs implemented in public health settings are effective, especially for racial/ethnic minorities living in low-resource settings, when they partner with programs already serving vulnerable populations (e.g., healthcare call centers) [37 51 52].

The state of Georgia has been a trailblazer since 2012, implementing the GDPH's Genetics Services Program for HBOC family history-based screening in public health districts around the state, especially among ethnically diverse and medically underserved areas [25 31 53]. Approximately 33% of Georgia residents are Black and considered 78% less likely than White women to utilize genetic services [15 48]. Such disparities generated a need to launch a genetic screening program targeting racial/ethnic minorities, and underserved communities, and areas lacking public transportation, but with access to public health centers. Georgia CORE, in collaboration with GDPH, Emory University School of Medicine, Morehouse School of Medicine, and Georgia State University, received funding from the CDC to "develop or enhance

activities related to promotion of breast cancer genomics" [15]. The program was funded from 2011-2014 as the Georgia Breast Cancer Genomic Health Consortium to reduce disparities among racial/ethnic minority women in Georgia. Since 2014, the collaboration has continued between Georgia CORE and the GDPH with program funding from GDPH.

The purpose of this paper is to evaluate the capacity of this ongoing collaboration to achieve the goal of expanding genetic risk screening, counseling, and testing uptake among racial/ethnic minority and underserved women throughout the state, and to examine the relationship between race/ethnicity and the use of these cancer genetic services.

Methods

Study Population Recruitment:

Women 18 years and older who visited a Georgia public health center for any services from 11/1/2012-12/31/2020 were eligible to participate. Most women were living at or below 200% of the Federal Poverty Level (FPL). According to the definitions used by the State Office of Rural Health (SORH), there are 149 counties in Georgia that are considered medically underserved areas (MUA), meaning areas that have a shortage of primary care services within the county; eight counties in the state have medically underserved populations, meaning that specific populations within the counties have unique barriers to accessing primary health services, including homelessness, language barriers, eligibility for Medicaid, and being Native American or a migrant farmworker [21 54]. Since such populations live in 149 of the 159 counties in Georgia, these 149 counties make up 71.3% (826078/1158558) of Georgia's population, meaning that most of the target population is essentially medically underserved [21 36 54]. These findings are consistent with a report published by the Georgia Budget and Policy

Institute with 149 counties falling below the state average for primary care doctors, as well as being defined as federally health professional shortage areas [21 36 54].

Family history screening tool

For the study from 1/1/2012-12/31/2020, B-RST™ 2.0 was used as the screening tool [55]. This online screening tool was cited by the USPSTF (2013) as one of several simple validated screening tools that are clinically useful for estimating the probability of *BRCA1/2* mutations for identifying women who should be referred for cancer genetic counseling [27]. The 2.0 version included the following risk factors: breast and/or ovarian cancer (over or under age 50), two or more cases of breast cancer on the same side of the family after age 50, male breast cancer, and Ashkenazi Jewish ancestry [56]. It should be noted that B-RST™ does not incorporate race, or other breast cancer risk factors (e.g., smoking, alcohol consumption, age at menarche, age at first live birth of child) for breast cancer risk assessment [57]. B-RST™ provides three categories of risk for *BRCA1/2* mutation based on family history: "positive-high risk," "negative-moderate risk," and "negative-low risk." In this study, individuals who screened "positive-high risk" were recommended for additional genetic education. The "negative" category is sub-divided into "negative-low risk" and "negative-moderate risk" for breast cancer, reflective of the expected familial risk for breast cancer aside from a *BRCA1/2* mutation.

Family History Screening, Counseling, Genetic Testing Process:

Of the 187 public health centers that received training on the use of the screening tool during the provision of women's health services, 81 centers actively implemented the tool. Women completed the online tool during a health department visit and immediately received results while at the clinic. Nursing staff used a district-specific login and password allowing the

screening results to be attributed to the district for reporting and follow-up by Georgia CORE for genetic education.

For positive high-risk screens, nursing staff informed the client of the option to receive additional information and, if she accepted, was referred to the Georgia CORE advanced practice nurse in genetics (APNG) for genetic education and potential testing. Women who screened negative-low or moderate risk were referred to the APNG only at their request or nursing staff recommendation. Clients were contacted by phone for initial risk assessment and to determine eligibility for testing by the APNG. If eligible for testing, the APNG set up an appointment at the public health center for additional education, informed consent, and specimen collection during which the client and APNG would meet face to face. Once completed, test results were provided directly to the client and public health center. If the client was found to have a clinically significant mutation in the genes linked to HBOC, the public health center provided referral to a local breast surgeon, primary care physician or specialist for discussion of options regarding surveillance, chemoprevention, or risk reduction surgery. After May 2020, the program shifted to a telehealth format with all education and testing occurring remotely at the client's home during the COVID-19 pandemic.

Measures:

Outcomes*:*

For the purposes of this study, to describe the extent of which the program has been successful in expanding the reach of genetic services, we measured three outcome variables: (1) family history screening uptake (the number of individuals who completed genetic risk screening divided by the total number of women in Georgia living at or below 200% of the FPL), (2) genetic counseling uptake (the number of individuals who completed counseling divided by the

number of individuals identified to be at high genetic risk for HBOC), and (3) genetic testing uptake (the number of individuals who completed genetic testing divided by those who were recommended to undergo testing).

Sociodemographic Characteristics: Age, race, county of residence, and public health district visited were measured by self-report. For the purposes of this study, we categorized racial/ethnic groups into non-Hispanic White, non-Hispanic Black, Hispanic/Latino (Hispanic), and Other (i.e., American Native / Alaskan Natives, Pacific Islanders / Native Hawaiian, Asian, and other).

Statistical analyses*:*

Descriptive statistics for demographic and outcome variables were assessed. To generate the most accurate estimate of the eligible screening population in Georgia, the U.S. Census Small Area Health Insurance Estimates (SAHIE) survey information for women aged 18-64 with incomes at or below 200% of the FPL for the years 2012-2019 were used. Bivariate relationships of race/ethnicity and service uptake were explored through Chi-square tests [58]. Individuals who did not specify their ethnicity or county of residence were excluded from the analysis. Statistical analyses were conducted using Microsoft Excel 16.5, 2021 and SAS Studio 3.81.

Results

Program reach:

Figure 1 demonstrates the programs reach throughout the state of Georgia. Overall, 81 public health centers in 75 of 159 (47.2%) counties participated. 149/159 (93.7%) counties in Georgia are considered MUA and the program was able to successfully reach 69 of 149 MUAs (46.3%) [21 54]. The vast majority of Georgia's female population that lives under the 200% FPL lives in MUAs, 1084624/1157749 (93.7%), according to the SAHIE datasets from 2012-2019.

The state has 18 public health districts, and 14 (77.8%) actively implemented the genetic screening program. North Georgia (1.2), Fulton (3.2), South Central (5.1), and Southeast (9.2) public health districts did not offer the services. For the genetic education and testing portion, 15 of the 18 (83.3%) public health districts participated (with individual referrals); the three districts with no involvement due to other priorities were North Georgia (1.2), South Central (5.1), and Southeast (9.2). Public health districts were unable to participate for various reasons including prioritization of other services, inconsistent and insufficient personnel, and the complexity of data collection login process. The participation of Fulton (3.2) was minimal with only one individual undergoing genetic testing. While all districts were provided with the resources to participate, not all had the capacity to do so.

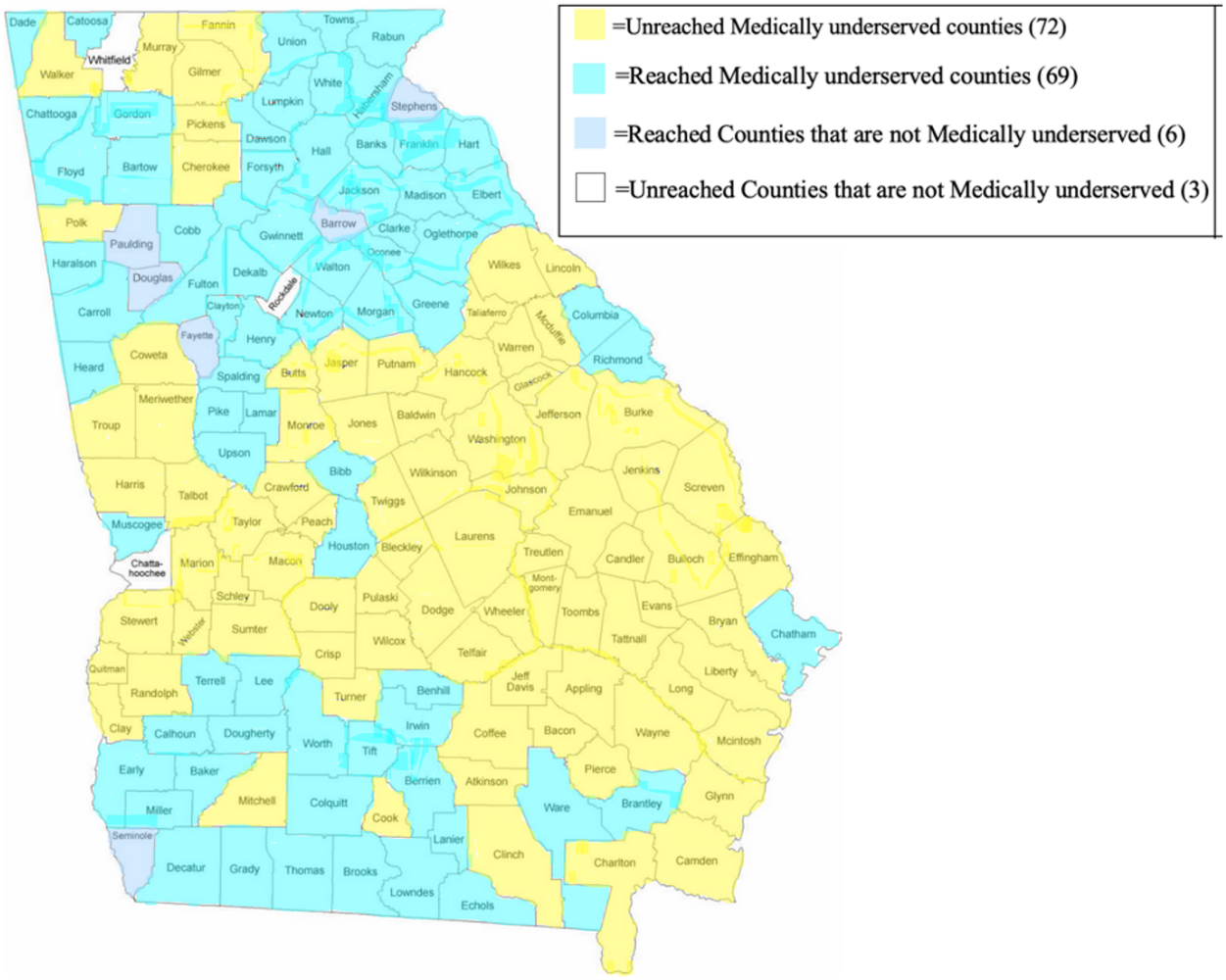
Family history screening:

Of the 29,090 participants who completed family history screening, 26,319 (90.4%) provided their self-identified race/ethnicity (**Table 1**). Over half of clients (63%) self-identified as a racial/ethnic minority (n=15,592); 39.9% were Black; 33.4% were White; and 16.5% were Hispanic.

Family history screening uptake was offered to all women over the age of 18 visiting a public health center for women's health services, yet the uptake was low across the state (2.5%, 29,090/1,157,749) among all medically underserved women in Georgia. Hispanic women had the highest uptake at 3.2% (4,473/141,976), followed by Black women (2.4%, n=11,770) and White women (2.1%, n=9,640). The "Other" ethnicities uptake was the lowest at 0.7% (n=463/65,491). It is also important to note that not all medically underserved individuals visit public health centers for care.

As compared to White women, the higher screening uptake rate is statistically significant in Hispanic and Black women, but lower in "Other" races (all p-value < 0.001 after Bonferroni multiple comparison correction).

Figure 1: Reach of the Genetic Service Program within Georgia



*A reached county is a county where an individual received genetic screening, counseling or testing through the public health center

Genetic education:

In total, 1,579 clients were referred to Georgia CORE for genetic counseling based on their positive B-RST™ screen results (n=1,460) or clinical judgment by providers. Of the 1,579, 1,172 clients provided their racial/ethnic identity, and contact was established with 793/1,172 individuals (67.7%).

Black women (74.0%, 259/350, p-value<0.001) and Hispanic women (72.9%, 113/155, p-value=0.03) had a statistically significant higher participation in genetic education when compared to White women (63.1%, 414/656).

Genetic Testing:

Overall, uptake of genetic testing among high-risk individuals was high. Of the 793 clients who received genetic counseling, 589 were recommended for genetic testing based on National Comprehensive Cancer Network (NCCN) guidelines, and 416 completed genetic testing (70.6%). In total, 32 (7.7%) women who completed testing were identified as carrying a deleterious mutation associated with HBOC.

Uptake of genetic testing was higher among Hispanic women (80.5%, 70/87) and Black women (70.1%, 122/174), compared to White women (69.1%, 221/320). Other races/ethnicities had the lowest uptake (42.9%, 3/8) of eligible women undergoing genetic testing.

When comparing the uptake of genetic testing between races/ethnicities there only appears to be a statistically significant difference between White and Hispanic (p-value=0.036). Hispanics appear to participate in genetic testing at a higher rate.

Impact of COVID on genetic services uptake:

During May 2020, the program transitioned to a telehealth model in response to pandemic restrictions. Since the transition, contact and uptake of genetic counseling rates

successfully increased from 66.5% to 100%. The education rate for Black women increased from 73.6% (254/345) to 100% (4/4). A similar increase was seen among Hispanic women, increasing from 71.8% (107/149) to 100% (6/6). Women who identified as Other saw the largest increase in genetic education, increasing from 60.0% (6/10) to 100% (1/1). White women also increased their uptake of genetic counseling, from 61.4% (385/627) to 100% (29/29).

The rate of participation in genetic testing also increased after May 2020 compared to previous years. From November 2012 to May 2020, the genetic testing completion rate was 69.0% (380/551). Beginning in May 2020 to December 2020, the rate improved to 92.1% (35/38). All racial/ethnic groups had improvements in genetic testing rates except Hispanic women which decreased from 79.5% (66/83) to 75.0% (3/4) after May 2020. For Black women, the rate increased from 66.5% (113/170) to 75.0% (3/4) and for White women, the rate increased from 68.4% (199/291) to 96.6% (28/29). For Other races/ethnicities, the rate increased from 28.6% (2/7) to 100% (1/1). See **Table 2** for the complete results comparing counseling uptake before and after the implementation of COVID19 related restrictions. **Table 3** provides insight into the genetic testing completion rates pre and post COVID19 restrictions.

Table 1: Uptake of family history screening, genetic education, and genetic testing*

Race/ethnicity	Uptake of Genetic Risk Screening				Uptake of Genetic Counseling				Uptake of Genetic Testing			
	# Screened[¥]	Total #	Screening Uptake (%)	P-value[†]	# Completed Genetic Counseling	# Eligible for Genetic Counseling	Counseling Uptake (%)	P-value[†]	# Completed Genetic Testing	# Eligible for Genetic Testing	Testing Uptake (%)	P-value[†]
Total that provided a race	26,319	1,157,749	2.3	N/A	793	1,172	67.7	N/A	416	589	70.6	N/A
White	9,640	452,016	2.1	reference	414	656	63.1	reference	221	320	69.1	reference
Black	11,770	498,266	2.4	<.001	259	350	74.0	<.001	122	174	70.1	0.913
Hispanic	4,473	141,976	3.2	<0.001	113	155	72.9	0.028	70	87	80.5	0.037
Grouped Other*	436	65,491	0.7	<.001	7	11	63.6	0.8	3	8	42.9	0.115

[¥] Overall, 29,090 individuals participated in the program, but only 26,319 provided their race, therefore since we are analyzing based on race, we can only include the 26,319 individuals in the analysis.

*Grouped Other=American Indian / Native American, Asian, Native Hawaiian / Pacific Islander, and others.

[†] P-values for pairwise comparisons between races, White clients acted as the reference group for the analysis

Discussion:

Through the implementation of B-RST™, GDPH's Genetics Services Program increased the utilization of genetic services in racial/ethnic minority and medically underserved communities by facilitating access to genetic screening, counseling, and testing. The screening program was available to all 18 public health districts in Georgia and implemented in 15. To

date, 29,090 women have been screened with 40.5% self-identifying as Black and 17% as Hispanic. Our study indicates that introducing genetic services into public health centers that serve racial/ethnic minority populations leads to substantial uptake of these services in populations that historically have not had access to genetic services [31].

Despite its potential, the reach of this screening initiative remains low; only 2.5% of age-eligible women in Georgia were screened through this program at participating public health centers. Of the women screened, 39.2% (n=1,172) were found to be eligible for genetic counseling. Of the 589 women identified as appropriate for genetic testing for a cancer-predisposing mutation, 416 (70.1%) opted to participate in genetic testing. Fifteen of 18 public health districts participated in some aspect of the program, but it is likely that residents from other MUAs participated. Georgia residents can receive services at any public health center in the state, so the reach of the program may be greater than the data shows. Not all public health centers implemented the screening program to the same degree. This could be attributed to various local factors including insufficient funding or staff, local priorities, or differences in the services provided to women at each location. Furthermore, the program had one genetics professional (APNG) for all referrals independent of participant location. It was nearly impossible for one APNG to reach all referred women throughout the state. Contact rates were negatively influenced by inactive phone numbers, time of call, working hours, inadequate bandwidth of phone service, unknown phone numbers, etc. Thoughtful consideration of sustainable and scalable outreach strategies to promote equitable identification and access to genetic services is needed.

We found that Black and Hispanic women had significantly higher uptake of cancer genetic services compared to White women. This finding suggests that the historical

underrepresentation of racial/ethnic minority communities and their lack of participation in genetic services may not be a result of hesitancy or lack of trust, but rather a lack of access to such services [51]. In our study, once racial/ethnic minority women were provided the opportunity to consider genetic services, they were more likely to proceed with genetic education and testing. Deeper consideration of factors that contribute to the observed racial/ethnic differences in service uptake is warranted. Prior studies have shown that family history screening for HBOC provided in settings that serve a large proportion of racial/ethnic minorities had high reach potential for genetic risk screening and genetic counseling [36]. Though the research base is limited, these findings support continued efforts to implement family history screening to reduce disparities in access to cancer genetic services.

It is important to note that the transition to telehealth services because of the COVID-19 pandemic increased the rate of participation in the program. Throughout the whole study period (1/1/2012-12/31/2020) the successful contact rate was 67.7% of the referrals from GDPH. From 5/1/2020-12/31/2020, clients were contacted using a telehealth model and not required to travel to receive education, adhering to the COVID-19 pandemic restrictions. By allowing clients to receive education over the phone and have the testing kits sent to their residences, the contact rates improved to 100% for all races/ethnicities. This improvement may be the result of telehealth reducing barriers to access, including transportation, work schedules, and finding childcare. This improvement may not be solely attributed to the transition to a telehealth model, but rather the circumstances the pandemic produced, including social isolation or being at home in general, which may have made participants more available and willing to answer the phone and speak with someone about their health. The shift to telehealth made the program more accessible to those living in medically underserved areas where barriers such as transportation

made it more difficult for participants to complete sample collection which required a visit to a public health center. Using the telehealth model, the specimen could be collected in the home. Long-term implementation of this telehealth or a hybrid model may increase program scalability and sustainability.

This study has several weaknesses that must be considered in interpreting the results. Our estimation of the target population was based on the population-level census and SAHIE datasets, most likely overestimating the true number of women visiting the public health centers for healthcare. The lack of individual-level data in client demographic characteristics (e.g., age, education) limited our ability to test some associations. Also, the small sample size of genetic testing uptake limited power to explore associations among racial/ethnic subgroups. Screening activities occurred during the provision of women's health services in public health centers, so men were not recruited in this study. We acknowledge that men can benefit from learning their risk of carrying a *BRCA* mutation.

Conclusion

Improving genetic counseling referral rates in racial/ethnic minority groups and medically underserved communities is an increasingly important area as evidenced by numerous regional and state initiatives. Our study presents an effective and sustainable outreach approach to promote population-level reach of cancer genetic services and to increase the likelihood of fair distribution of advances in genomic technology. The implementation of telehealth options including counseling over the phone and mailing clients the testing kits was found to be effective in increasing participation. The study findings will inform a systematic evaluation with public health districts across Georgia and the development of organizational implementation strategies to enable a sustainable expansion of genetic services across the state.

Extended Discussion Section Overview:

This next section is comprised of three main themes. The first part will cover the successes of the program, highlighting the significant uptake of genetic services by minority populations, the potential for this program to be highly sustainable in public health clinics, the possibility of integrating tele-health options into the program, and the efficiency of using a familial history screening tool into routine care as a way to screen for HBOC. Next the discussion will move into the problems identified throughout the project including: the low completion rates at each step of the program and the loss to follow up throughout the intervention. The last portion of the discussion will explore some of the limitations in the analysis of this data and program. Limitations include the inaccessibility to the data that would inform the total number of eligible women (and thus a more accurate assessment of screening uptake in the clinics), the small sample sizes for minorities other than African American and Hispanic individuals, and lastly that no supplementary data was gathered to provide context to the participation data collected.

Part 1: Program Successes:

High Genetic Service Uptake by Minority Populations:

Throughout the eight years of the program Georgia CORE and its collaborators were able to screen nearly 27,000 individuals who otherwise would not have had access to these services as a part of their routine care. The experience of the GDPH's Genetics Services Program suggests that African American and Hispanic women participated in genetic screening, counseling, and testing at rates comparable and often higher than White women. This conclusion is contrary to previous studies consistently showing that minority populations are more discerning in their use of genetic services [59]. A potential reason for this could be that these services were not previously offered in these non-academic, rural settings [19]. Previously MUAs like those that this program targeted may not have had access to genetic services and therefore were not able to participate [60]. Now when presented with the opportunity to participate, a proportion of minority women elected to partake. Additionally, minority populations are historically underrepresented in genetics studies that

Documented low rates of participation in genetics programs hinder the progress of precision medicine in minority populations [32]. If minority populations are not adequately represented in large genomic databases, precision medicine for the benefit racial groups with unique founder effect mutations cannot be realized. As Saulsberry et, al. notes the 'genotype-phenotype correlations across many populations furthers general understanding of health and disease and helps identify at-risk populations for certain diseases [32].' This highlights the value of having a diverse genome database to understand the implications of all variants that exist. Low minority participation puts minority populations at a double disadvantage: not only is disease diagnosis occurring at a later stage, but also limits the ability for developing genotype or

mutation specific interventions for conditions [32]. Throughout the eight years of the program Georgia CORE and its collaborators were able to screen nearly 27,000 individuals who otherwise probably would not have had access to such services as a part of their routine care. Expanding genetic services into local care settings has the possibility to not only improve the care and health of the population directly but to also begin to combat the lack of diversity in genomic databases [61]. While diversity is increasing, it is happening at a very slow rate. In 2009, only 13% of genome-wide association studies (GWAS) included individuals of non-European descent [61]. By 2016, this percentage only increased to 20%, but this increase is almost exclusively an increase of studies conducted in Asian population participation [61]. The representation of non-European populations has increased, the "persistent bias" in these databases remain [61]. Persistent bias is the continued dominance of European descendants being tested and recorded. Programs like Georgia CORE's screening program could help combat this bias by increasing the representation and participation of the "most vulnerable and traditionally underserved populations" in the Southern United States [61].

Potential for Sustainability of the Program in Public Health Clinics

This HBOC genetics program relied heavily on the existing health service delivery within the public health clinics. A 2019 literature review demonstrated that integrating health services into a public clinic and primary care setting is a promising way to increase access to care and works to address disparities in access [62]. But for this program to be truly sustainable it needs to be low burden on the public health clinics, quick to administer and it cannot take away from other implemented programs.

Although, there is no single definition for sustainability. For this section I am defining sustainability as it pertains to the feasibly of the implementation of the program while not detracting significant resources from the clinic's other services [63]. Public health clinics in around the United States, especially in the southern regions of the country are already struggling to serve all the individuals they are meant to serve [19 30]. To minimize the burden on the clinics, the program only relied on them for the initial step consisting of consenting and administering the screening questionnaire. A brief training module was provided to all public health clinics in Georgia on how to use the B-RST^{TM} HBOC screening tool. It was simple for the healthcare provider to use and involved verbally asking the patients the seven questions and then recording the answers and the resulting risk stratification. The short nature of the questionnaire allowed it to be administered quickly, in about 5-7 minutes during a routine clinic visit, a key factor making it feasible and realistic to implement. Overall, 74/159 (46.5%) counties participated in the program, through 81 different healthcare centers. It is likely that the reach of the program was greater than the number of counties reported since Georgians can visit any clinic they chose. Despite the sub-optimal county uptake of the program, it was able to demonstrate its feasibility to be integrated into routine public health clinic care settings with adequate personnel.

A major barrier that could negatively influence sustainability is the issue of competing priorities. For example, if a large proportion of clinic patients had HIV, the majority of funding and time went into HIV care and prevention, so HBOC screening was not a health outcome priority. After speaking with the APGN who conducted the counseling and had close ties to the clinics, she mentioned that some clinics did not want to shift resources away from what they felt were the biggest health needs of their population, like HIV and diabetes [64]. Another concern

that arose was the difficulty providers experienced with using their unique log in to administer the screening questionnaire. This led to two major outcomes: first, screens were done but not correctly logged causing data and follow-up issues, or second, the provider opted not to screen. Both shortcomings continued to disadvantage the women the program sought to help. These concerns and others will need to be addressed if the program seeks to expand and increase its impact. For the program to truly be sustainable it would need to be administrable by any healthcare provider during any routine primary care visits. If it is simple and they know it can improve their patients' health, it is likely to suppose that they will utilize it more.

Successful Virtual Counseling:

In 2012, at the inception of the program, genetic counseling was meant to occur using an in-person format that provided informational and educational sessions to validate and respect the sensitivity and emotional gravity of the topic. For nearly the entire program counseling was conducted in-person until April 2020. With the onset of the COVID-19 pandemic, the program had to shift to a virtual counseling format to respect local social distancing guidelines. Virtual counseling consisted of either a video or phone call with Georgia CORES APGN. Shifting the counseling to a virtual format increased contacting rates and participation rates in the counseling portion of the program, independent of race. Every individual that was referred for during this period completed the counseling step of the program **(Table 2).** Subsequent completion of genetic testing rates was also higher that before COVID19 since sample collection kits were mailed to the place of residence **(Table 3).**

Table 2: Pre-Post COVID Successful Counseling rates:

Race	Pre COVID (%)	Post-COVID (%)
White	385/627 (61.4)	29/29 (100)
Black	254/345 (73.6)	4/4 (100)
Latina	107/149 (71.8)	6/6 (100)
Other	7/11 (63.6)	1/1 (100)
Successfully Counseled	753	40
Total Eligible	1132	40
Percent Counseled	66.5%	100%

Table 3: Pre-Post COVID Successful Genetic Testing Rates:

Race	pre-COVID19 Testing Completition (%)	post-COVID19 Testing Completion(%)
White	199/291 (63.4)	28/29 (96.6)
Black	113/170 (66.5)	3/4 (75.0)
Latina	66/83 (79.5)	3/4 (75.0)
Other	2/7 (28.6)	1/1 (100)
Total	380/551 (70.0)	35/38 (86.7)

Because the tele-genetic counseling only occurred for a short period of time (eight months), a definitive conclusion cannot be made if this is a better modality. However, a systematic review demonstrated that telehealth, conducted by phone found to be inferior to in-person interactions, this same shortcoming was not observed as dramatically among telehealth conducted in a video format, however this study did not report on potential differences in health or survival outcomes. [65].

While in-person discussions may seem like a better modality to discuss potentially life-changing information, the tele-genetic delivery modality maybe a promising second choice helping to address barriers to access. To this point, the limited tele-genetic data in this study

appears to suggest that virtual counseling has a better contact rate than the in-person format, 66.5% and 100%, respectively. It is possible that providing virtual counseling helps to remove barriers to access that may exist with the traditional in person counseling. For example, if a person can receive the education while at home, he or she may not have to find childcare to go to the visit, or must organize transportation, it would also require less time since travel would be eliminated. Virtual counseling may also reduce the burden on the APGN, who no longer has to travel to the health centers around the state. Additionally, this allows the APGN to conduct more counseling sessions each day, since travel time is eliminated and the APGN can now reach more areas of the state which previously had been too far away to travel to.

However, virtual counseling has its' limitations. For example, it requires that the participant have reliable private access to a phone or the internet. It also relies on the contact information gathered at the health visit, which was not always accurate.

A combination of in-person and virtual counseling would be ideal to meet the needs of the largest proportion of the population in Georgia. Additionally, this expansion of counseling modalities would likely increase participation and increase the demand for genetic counselors, something which Southern Georgia is not ready to handle [19]. Other factors to consider are preferences and follow through with the recommended testing between in-person and tele-genetic counseling. In larger sample sizes it has been discovered that individuals who under tele-phone-based counseling had lower rates of completing the referred genetic testing [15]. This is an important distinction because this means there could be another barrier or concern that could not be addressed over the phone. Therefore, the program would be sacrificing quality of counseling and genetic testing rates in exchange for expanding the reach of genetic counseling.

One of the motivations of this program was to reduce the disparities in access and participation in genetic services between white and minority races. The aforementioned tele-genetic study found that minority women receiving tele-genetic counseling were less likely to complete the recommended testing [15]. Therefore, while there may be benefits to the tele-genetic modality such as being able to reach more people by reducing the travel burden on both the participant and counselor, there are still shortcomings and obstacles that would need to be addressed with this modality.

Making HBOC Screening more Efficient: HBOC Family History Screening Tool

Currently public health relies on cascade genetic screening, counseling and testing, this necessitates a first or second degree relative receiving a breast or ovarian cancer diagnosis and sharing this with their family members who may also be at risk [66]. Cascade testing relies on the initiative of a proband, meaning that a family member receives a breast or ovarian cancer diagnosis and undergoes genetic testing, and a mutation is identified, which they share with family members. Upon receiving this information, proband testing is initiated, referring all first- and second-degree relatives to genetic counseling or testing for a suspected hereditary risk [66 67]. Familial history screening still requires a family member to receive a breast or ovarian cancer diagnosis, but it is more proactive on identifying and screening all relatives that could be at risk.

This program finds evidence to support the possibility of adding population- based screening strategies testing for HBOC risk, which could help increase screening efficiency. The advantages of population-based screening is that it expands the reach of services with the potential to identify more at-risk families [37]. Early detection and risk stratification allows more

individuals to participate in prophylactic risk mitigation measures, including medication, surgery, or enhanced surveillance [31]. Early interventions are known to decrease the mortality of breast cancer among those at with a *BRCA* mutation by 95% and by 80% for ovarian cancer [31]. Such benefits can only be realized if the number of individuals screened increases and genetic services are made more available to those who currently do not have access [31].

Part 2: Identified Problems:

Low Reach and Participation in the Program:

Although the Georgia CORE's APGN did their best to follow-up with all referred individuals in the program, individuals were lost at every stage. The sub-optimal uptake of the program could be the result of hesitancy among the women to participate. Hesitancy is a documented barrier to participation in genetic services [32]. This hesitancy is exacerbated in minority populations [32]. African American women have the highest rate of variants of unknown significance (VUS), and with continued low participation in genetic testing it will be harder to determine the true nature of these variants [32]. Once individuals agreed to participate in the program and were screened, those who screened as high-risk were referred for genetic counseling. Upon referral, the APGN from Georgia CORE would contact the individual to see if she was interested in undergoing genetic counseling. If she was interested, a face-to-face meeting was scheduled. The genetic counseling served to ascertain those who truly needed to undergo genetic testing for an HBOC related mutation. Women who were identified were referred for testing, however not all that were referred underwent testing. Despite these individuals knowing that they had an increased risk of having a deleterious mutation, a significant proportion elected

not to follow through with the genetic testing. While it is not possible to ascertain the reason why individuals elected not to undergo testing, literature combined with the APGN's experiences point to residual concerns and apprehension about how the information will be used and stored, forgetting to go get tested, and a fear of the results [13 64]. While the APGN did everything they could to educate and empower the individual it was ultimately their choice if they felt comfortable undergoing testing or not. Those who elected not undergo testing, were provided with information about what early detection practices they could engage with or how they could get tested in the future if they changed their mind.

Since no additional data was collected other than the race, and age of the participants, there is no way to identify or classify the barriers to participation in genetic testing, and therefore must rely on the literature for common barriers to participation. General distrust of the genetic process was cited as a barrier to participating in genetic testing [22]. The literature also cited financial strain as a reason why women did not undergo testing. The cost of genetic testing has decreased significantly over the last 20 years it can still present a significant financial strain to a low-income family [22]. However, the GDPH Genetics Screening Program in collaboration with Myriad Genetics provided all the genetic testing free of charge. Myriad saw this as an opportunity to help diversify and build their genetics database, motivating them to provide this service [64]. This partnership increases the sustainability of the program since they are hoping to transition the counseling to Myriad Genetics as well, continuing to reduce the cost and burden of the program [64]. External stakeholders like Myriad Genetics are integral in the continuation and sustainability of this program. A significant proportion of the individuals seeking care at public health clinics are uninsured and so providing this service free of charge is likely an integral factor in participation with genetic testing [58].

Loss to Follow-up at Subsequent Steps of the Program

After the screening portion of the program 1,172 individuals were referred for genetic counseling. However only 739, or 63.5%, of those people followed through with the recommended counseling. This leaves a significant proportion of the individuals who could benefit from genetic counseling underserved. While we cannot understand all the factors why people did not participate in genetic counseling, some of the recorded reasons were: inability to contact (incorrect contact information, or simply never responded) and not wanting to participate/not interested [64].

Initially contacting individuals proved to be very challenging [64]. Therefore, the APGN integrated some new steps to increase the contacting rate and by proxy improve program retention. Efforts included establishing contact with the genetic counselor while the individual was still at the clinic immediately after the screen or verifying on-file phone numbers during their visit and sending letters to the individuals who may not have access to phones. Towards the end of the program the genetic counselor also began texting individuals which seemed to be a preferred mode of communication [64]. Loss-to-follow-up and low initial participation was a significant short coming of the program, and innovative steps need to be taken to increase engagement and retention at all stages of the intervention.

Then in the last step of genetic testing, a similar trend of loss was observed with only 416/589 (70.6%) of those referred for genetic testing following through with the test. Not much supplementary data was gathered on why individuals did not undergo testing, but the limited documentation demonstrates that some individuals missed their appointments, and never rescheduled [64]. In the literature commonly reported factors included financial strains, which the program addressed by making the test free of charge [50 60]. Additional documented factors

were fear of privacy violation, lack of transportation to the test, fear of the results, and others [50 68]. Unfortunately, there is no way to assess which of these is relevant to this population in Georgia. Therefore, in the future it would be beneficial to gather additional data about motivators and obstacles to participation.

Part 3: Limitation of the Study and Analysis:

Lack of Precision in Screening Uptake Estimates

Unfortunately, the accuracy of the denominator used to calculate the uptake of genetic screening by race is not precise. Access to the appointment records of the public health clinics to assess how many women visited the clinics during the study period was denied. Therefore, it was difficult to determine the appropriate denominator for how many women could have been screened.

Since the data for how many individuals visited the participating health clinics during the study period was not available, a proxy had to be identified. The best option was the Small Area Health Insurance Estimates (SAHIE) to approximate the number of individuals that would have been eligible to visit a clinic and potentially get screened. The SAHIE data is collected annually by the U.S. Census Bureau. SAHIE assesses the insurance status at the state and county level, for individuals under the age of 65 [58]. This dataset likely overestimates the number of people that were eligible to participate in the program, because not everyone visited a clinic each year. Additionally, since not all clinics participated in the program there was no way to discount the people who went to clinics outside of the program. Also, the SAHIE datasets do not provide breakdown by race, so the Census racial breakdown of Georgia in 2020 was used to estimate the racial composition of those who visited the clinics.

Accuracy of the uptake of genetic screening could be improved if we had access to the raw number of people who visited a participating clinic each year. This would likely increase the participation percent. Without an accurate understanding of how many people were truly eligible and able to participate, we cannot truly understand how the different racial groups interacted with and participated in the screening program.

Small Sample size for Racial Minorities

Some of the racial groupings used by the B-RST^{TM} Tool yielded very small sample sizes, sample sizes that were too small to run a chi square test for independence (less than 5 observations for an expected observation number) [69]. Therefore, we can only really analyze the data by Caucasian, African American, and Hispanic populations. The other races classifications from the B-RST^{TM} Tool like, American Native / Alaskan Natives, Pacific Islanders / Native Hawaiian, Asian, and other populations yielded sample sizes that were too small for reliable and representative statistical analysis[69]. Therefore, these four groups were grouped together for a general "grouped other" category. It is likely that these races have differences in the uptake of genetic services. Previously published literature demonstrated that these racial groups have differences in knowledge and attitude towards genetic services [13], which provides evidence that race maybe a confounding factor for participation at any stage of the utilization of genetic services [13]. However, there was not sufficient sampling power to analyze this potential difference. If Georgia CORE seeks to identify differences within these racial groups, recruitment practices may have to change to reach more people from these communities. Georgia CORE could launch targeted messaging to increase the re

Extended Discussion Conclusion:

The genetics services program successfully integrated into the public health clinics around the state and managed to screen 29,090 individuals, with demonstrating that it is possible to improve access to genetic services for minority and underserved populations. There were some challenges with the program, raising questions of sustainability and ways to increase the reach to screen more people. With the lack of supplemental data, it is very difficult to accurately assess how the program performed and how it can be improved to increase utilization. In the last section, I will be discussing potential next steps for the program and how it could grow and be more effective and efficient in serving its target population.

Section 6: Future Directions

Reducing the number of participants lost throughout the program:

Despite Georgia CORE's best effort to enroll and keep as many individuals in the program as possible, a significant amount of people was lost at each step, between those eligible for counseling and those who underwent counseling, and those eligible for genetic testing and those who underwent testing.

By the end of the study period the program began to implement new strategies to increase follow-up. For example, extra steps were taken to verify that the phone number on file was accurate and the best number to reach the individual at. Georgia CORE's APGN mentioned that outdated or incorrect phone numbers was a common occurrence.

Nevertheless, even when the phone number was correct people did not want to talk on the phone about the genetic screening result or were not? willing to set up a time to meet to undergo counseling. With the COVID-19 pandemic, counseling shifted to a virtual format (via phone or videocall) and this format increased counseling participation rates. The sample size was very limited, but the change in participation appear to be dramatically higher. Anecdotally Georgia CORE's APGN also began texting with individuals to set up a time to talk instead of cold calling, which also seemed to be favored.

Increasing follow through with genetic testing is more complex. Despite minority populations having a documented distrust of how their genetic information will be used, they underwent testing at statistically significant higher rates than Caucasian individuals [13]. However, rates could be improved for all racial groups. Ideally the vast majority of who is referred to undergo genetic testing should do so. Increasing testing rates is not as easy as double checking a phone number or texting someone. Hesitancy about testing often rooted in a distrust

of the medical system and the providers who are supervising their care [31 32 59]. The Southern portions of the United States suffer from severe shortages of genetic counselors, and often providers who are meant to administer these services are not comfortable with the topic themselves, and therefore are hesitant to discuss or encourage patients to participate [19 31]. Lack of physician knowledge is a documented reason why providers do not provide a service.

A potential way to improve genetic testing follow through is to increase confidence in the physician's knowledge. This avenue was explored in a 2009 intervention seeking to evaluate the effect of introducing a genetics workshop into primary care physicians' continuing education program. The program was an interactive workshop with supplementary modules for the providers to increase knowledge and confidence about implementing genetics into routine care for their patients [70]. Unfortunately, the study did not detect a significant change in the reported awareness, or use of genetic services, however they did report a significant increase in the providers ability to assess risk of developing a hereditary disorder. Most importantly there was an increase in confidence in referring the appropriate individuals for genetic counseling [70]. Additionally, a statistically significant number of physicians acknowledged that they understand how genetic testing can be beneficial in the care of their patients. The study produced mixed results the providing physicians had more knowledge about how to integrate genetic services to better care for their patients; however, this knowledge did not lead to a significant increase in the utilization of such services. Nevertheless, over time I think it is reasonable to assume that if providers are confident and understand the impact of knowing if their patient has a deleterious mutation and how it would impact how they care for them, then providers would become more confident and begin to incorporate HBOC screening into routine care.

Increasing provider knowledge could be coupled with an awareness campaign to help make the community more aware of the benefits of HBOC screening. A screening awareness campaign was implemented in Australia that proved to be very successful. The Australian National Bowel Cancer Screening Program (NBCSP) had low screening participation rates despite it being a free and potentially lifesaving intervention [71]. Therefore, the NBCSP launched a seven-week mass media campaign to educate the public about the benefits of undergoing bowl cancer screening, how to access the service, and that it is free of charge [71]. The short awareness and education campaign increased the participation in the screening program by 1.31-fold [71]. The successes of this bowl cancer screening campaign could be applied to help increase participation in an HBOC screening setting. Increasing provider knowledge and public awareness of the service could be a powerful combination to increase participation in this HBOC screening program.

Privacy Fears Driving Participation Hesitancy

But individuals also need to be confident that if they chose to undergo genetic testing that their health data will remain private and not be used for other purposes. Our knowledge and understanding of genetic information is evolving so rapidly that it is hard for privacy laws and related regulations to keep up and provide adequate protection to protected health information [34 72]. One's genome is protected health information, but scientists are pushing for genomes to be made publicly available for "low-risk" research [34].

There is also a fear that having a genetic mutation will turn into another way to discriminate against individuals for example when purchasing insurance [73].Without addressing the privacy and trust concerns of the people, it is unlikely that we will see an increase in

participation. According to various published studies and systematic reviews privacy fears are not limited to minority populations in the United States, it is a concern evident around the world [73-75].

While Georgia CORE may be unable to address global privacy concerns about maintaining the privacy of one's genetic information. They could introduce additional safeguards into the clinics to help reassure participants that the information will be maintained under doctor patient confidentiality, such as an additional form signed by both parties outlining that information will not be shared and will only be discussed in an agreed upon modality (in-person, over the phone, or if information may be mailed to the house). Additionally, depending on funds, Georgia CORE could help introduce a deidentified way to store the information, therefore it would be harder to trace the genomic information back to an individual. This could help make participants feel more secure and protected. Nevertheless, Georgia CORE can still participate in applying pressure on national legislature to pass and update current privacy laws to protect private genetic information, as well as creating clear guidelines on what information can be shared for research and how the individual should be informed and consented.

Meeting The Community Where They Are:

The program was administered through public health clinics which is a great way to reach people who are likely interested in staying healthy and may be more inclined to participate in genetic services. However, this can also be seen as a limitation of the program. By only being implemented in one setting (the public health clinic), the program is limited in its ability to reach a greater proportion of the community. Social determinants of health play a significant role in how individuals can get access to healthcare and health services. For example, by only providing

the program in public health clinics we are limiting our reach to people who have access to transportation and time off allowing them to go to the clinic for care [76].

While public health clinics were a very promising and logical place to start since these individuals may be more inclined to participate in additional preventative measures, it is still disadvantaging the most vulnerable who are unable to seek healthcare [76]. But if Georgia CORE and its collaborators would like to increase the screening uptake within the general population changes need to be made to expand access. For example, Georgia CORE could provide community outreach screening days, where they staff an individual with the screening tool at an easily accessible location in the community, like a church, a park, or outside of a grocery store. This way, people would not have to go as far out of their way to undergo HBOC screening. Extremely large number of people need to be screened to identify those who have an HBOC mutation putting them at an increased risk for developing breast or ovarian cancer. For example, best estimates for shifting the screening portion out of the public health clinics would be about $12-15 per hour per screener at each event [53]. And with Myriad Genetics covering the cost of counseling and testing, this could prove to be a sustainable way for the program to operate in the future while relieving the burden placed on public health clinics. Genetics screening programs are a validated and effective evidence based intervention, as demonstrated by a Taiwanese study demonstrated that screening for breast cancer through mammogram in 1.4 million women resulted in a 41% reduction in breast cancer mortality [77].

Another benefit of shifting the initial screen into a community setting instead of a public health clinic is that it would further reduce the burden that the already stressed and underfunded public health clinics experience [78]. Community based medicine and care is an area of rapid

growth in healthcare right now, and it is possible that GDPH's Genetics Screening program could substantially increase its reach and impact through this modality [79].

Building Trust with the Communities:

Another presumed barrier to uptake and participation within the program based on the literature is the lack of trust between minority communities and the healthcare system [32]. Building confidence with minority populations is not an easy undertaking. It is going to require both the public health clinics and Georgia CORE's program to educate their target population about how genetic testing can benefit not only their health and healthcare but also that of their family but identifying hereditary mutations that may put their family members at a greater risk. Research has shown that family members are not always keen to share their mutation status despite knowing that it would be beneficial for their family [66]. A recent systematic review highlighted that only an estimated 30% of family members who should be screened or tested are undergoing the process [66]. This is believed to be the result of "lack of communication" between family members. With proper education and reassurance that their genetic information will remain private it is possible to increase the percentage of individuals sharing their concern with family members. This is especially important for HBOCs, since most of the known mutations are passed down through an autosomal dominant manner, meaning that first and second degree relatives have between a 12.5-50% chance of inheriting the deleterious mutation [66].

There is no simple way to repair trust between the medically community and minority populations but as previously discussed, it will be vital for the practitioners administering the screen or counseling to be highly knowledgeable and able to answer all questions the individuals

may have. While knowledge and transparency alone is not enough to repair the distrust it can be a step in the right direction. Another manner to build trust would be to hire professionals from the minority community because individuals may be more likely to trust and believe someone who they can relate to. The current genetics professional shortage within Georgia should be filled by professionals who are from the minority community to help establish a relatable team [30].

While building trust is not an easy task and there is not much literature on the topic, two of the main themes that have been presented are creating community partnerships, as well as enhancing communications between the community and the healthcare system [80]. Choosing the appropriate partnership is critical to promote trust, commonly identified partnerships include faith-based organizations or leadership members, schools, and organizations already serving the vulnerable communities [80]. In order to maintain and grow trust through partnerships, open honest and continuous communication is needed. Communication has been identified as one of the critical components determining the success or failure of a partnership. For example it is important to conduct communications in a way that is acceptable in the community, this pertains to the language, the level of health literacy, and modes of communication (written, audio, verbal, social media, and others) [80]. By creating trustworthy partnerships community members maybe more likely to participate in the screening program.

Next Step: Investigating further the drivers of uptake and participation:

It is unlikely that all motivating factors for participation in genetic services have been considered. Therefore, it is advisable to collect additional supplementary data at each stage of the program (screening, counseling, and testing) with both individuals who opted to participate as

well as with those who decided against it. While it is difficult to know how many interviews, or surveys would be required, a reasonable approximation might be about 10 per strata for interviews (participation/or not, and each level of the program) [81] .This number may need to be adjusted once data collection begins. Analysis of these interviews can provide invaluable insight into minority communities motivations and perspectives about the program. It would provide a rich context for the already collected data, allowing us to have a deeper more informed understanding. I think this data would be especially informative surrounding the best way to make the program assessable to the community, and how trust could better be built. Depending on the results of this research the program would need to be adjusted as necessary.

Conclusions:

While Georgia CORE's HBOC screening program only reached about 2.5% of the eligible population in Georgia, it still proved itself to be a valuable tool that is acceptable among minority populations with minority races participating at a higher rate than their Caucasian counterparts. This finding helps to disprove the fear that minority communities do not want to participate [32]. While the true uptake of genetic screening cannot be assessed because of the lacking proper denominator. The uptake of genetic counseling and subsequent testing can be used as a proxy, since we have a valid denominator of who was able to participate. When looking at this data minority races have significantly higher rates of participation than Caucasian populations.

Overall, the program demonstrated that minority races participate in genetic services where they seek routine care. Nevertheless, with these findings proposing that minority communities do participate it raises the question of how we can reach a larger proportion of

medically vulnerable and underserved communities. Subsequent research needs to be done to determine the best way to expand and continue the program in the most efficient way possible.

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