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Implementing a Population Screening Program for Lynch syndrome and Hereditary Breast and Ovarian Cancer syndrome: An Institutional Experience

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Table of Contents

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Genetics is an ever-evolving field, and progressively continues to make its way to the forefront of personalized medicine. The link between family history, heredity, and cancer, specifically colon cancer, was first described in the 1960s by Dr. Henry Lynch. Hereditary Non-Polyposis Colorectal Cancer Syndrome (HNPCC) and Lynch syndrome (LS) were terms that were used interchangeably to describe a handful of families in which the prevalence of colon cancer was much greater than what one would expect in the general population. In the subsequent decades, thanks to advances in molecular genetics, the underlying histopathology of this syndrome, along with other seemingly heritable cancer syndromes, such as familial early onset breast cancer were clarified. In the 1990s, mutations in the *MSH2, MLH1, PMS2,* and *MSH6* genes were found to be associated with familial colorectal cancer, termed Lynch syndrome (LS), and mutations in the *BRCA1* and *BRCA2* were found to be associated with Hereditary Breast and Ovarian Cancer syndrome (HBOC). LS and HBOC are the two most common hereditary cancer syndromes, and cancer risks due to LS and HBOC have been well-defined. Given the significantly increased risks for cancer associated with these conditions, evidence-based consensus guidelines for managing HBOC and LS patients are well established and widely accepted and have been shown to reduce cancer incidence and mortality.[1,2]

LS and HBOC-Associated Cancer Risks and the Impact of Risk-Management Recommendations and Health Behavior Modifications

Lynch syndrome is associated with elevated lifetime risks for colorectal, endometrial, gastric, ovarian, renal pelvis/ureter, bladder, gastric, small bowel, pancreatic, biliary tract, prostate, female breast, and CNS cancers. It is also linked to increased risks for sebaceous neoplasms. Risk-management recommendations for *LS*-associated cancers have been outlined by the National Comprehensive Cancer Network (NCCN), and include detailed discussions of conferred risk-reduction, procedure-related risks and impacts, side effects, as well as reproductive options for mutation carriers.[1] LS mutation carriers should receive clinical care with medical specialists to ensure appropriate risk-management protocols are followed. The prescribed colon cancer screening protocol outlined has been shown to reduce colorectal cancer mortality by 60 – 70%.[3,4] LS patients following these established screening guidelines could increase their life expectancy by 24 years.[5] Additionally, aspirin use in some studies has been shown to reduce the risk for LS-associated cancers and may be considered, although the optimal dose and duration of therapy is unknown.[6-10]

HBOC is associated with significantly increased risks for female and male breast, ovarian, prostate, and pancreatic cancers as well as melanoma. As with LS, risk-management recommendations for *BRCA*-associated cancers have been outlined by the National Comprehensive Cancer Network (NCCN), and are accompanied by detailed discussions of the impacts of the recommendations.[2] Those with *BRCA* mutations should receive care under the guidance of medical specialists to ensure appropriate risk-management protocols are followed. The breast imaging protocol for women described has a sensitivity of 86 – 94% for detection of breast cancer in *BRCA*1/2 gene mutation carriers.[11, 12] This screening regimen increases the detection of early, more treatable breast cancers and has been associated with improved outcomes.[13] Bilateral risk-reducing mastectomy has been shown to decrease the risk of developing breast cancer by at least 90% in known *BRCA1/2* mutation carriers as well as other moderate-and-high-risk women.[14-17] Use of Tamoxifen in *BRCA1/2* mutation carriers has been shown to reduce the risk for breast cancer by up to 62%.[18-20]

Due to the lack of reliable surveillance methods for early detection of ovarian cancer and poor prognosis of advanced ovarian cancer, bilateral risk-reducing salpingo-oophorectomy (RRSO) typically between ages 35-40 years and upon completion of childbearing remains the gold standard and has been shown to reduce the risk for ovarian, fallopian, or peritoneal cancer by 80-85%.[21-23] Additionally, bilateral RRSO has also been shown to reduce breast cancer incidence by up to 50%.[22, 24, 25, 26, 27] Studies show that oral contraceptive use by BRCA mutation carriers can further reduce the risk for ovarian cancer by up to 60%.[28-31]

Though more longer-term studies are needed, recent data suggests that pancreatic cancer surveillance for select high-risk individuals can lead to improved survival and downstaging, where 75-90% of pancreatic cancers detected via screening have been surgically resectable at diagnosis compared to historical data where detection of cancer was based on identification of symptoms.[32, 33, 34]

Aside from screening and surgical interventions, health behaviors can further impact cancer risk in individuals with LS and HBOC. Tobacco use and increased body mass index (BMI) have been shown to increase colorectal cancer risk within the LS population, and breast cancer risk in *BRCA* mutation carriers. Smoking cessation and increased physical activity and/or weight reduction have the potential to counteract these elevated risks. Most patients undergoing genetic testing have at least one modifiable risk factor and could benefit from health behavior intervention. Genetic testing has the potential to motivate individuals to increase physical activity, change dietary habits, and quit smoking, all of which are primary cancer prevention activities.[35-37]

LS and HBOC are Under-Diagnosed Despite the Potential for Cancer Prevention

LS and HBOC have a prevalence of approximately 1/300 and 1/500, respectively. Based on the estimated incidence of LS and HBOC, there are approximately 1 million individuals with LS and 660,000 individuals with HBOC in the United States.[38]

Given the public health burden of LS and HBOC, and the significant potential for positive impact with evidence-based guidelines, population-based screening programs to increase identification of these hereditary cancer conditions have been proposed by various national public health organizations and initiatives. The Centers for Disease Control and Prevention (CDC) office of Public Health Genomics has classified screening for both conditions as tier one genomic applications (i.e. evidence supports implementation into medical practice and surveillance).[39,40] In 2013, the US Preventative Services Task Force (USPSTF) recommended genetic risk assessment and, if warranted, *BRCA* mutation testing in asymptomatic women with a family history of breast and ovarian cancer.[41] It is a goal of the Healthy People 2030 initiative to increase the proportion of persons with newly diagnosed CRC who receive genetic testing to identify LS. The Evaluation of Genomic Application in Practice and Prevention (EGAPP) working group has recommend that all patients receiving new colorectal cancer diagnoses should also receive genetic counseling and testing, and that their family members would benefit from knowing if the colorectal cancer in their family is a result of LS.[39,42,43] Additionally, National Comprehensive Cancer Network (NCCN) guidelines changed in 2014 to include consideration of screening unaffected relatives for LS when affected relatives are unavailable.

Despite the potential for cancer prevention with identification of LS and HBOC, especially in individuals never having been diagnosed with cancer, both conditions remain largely under-diagnosed.

Approximately 2% of individuals with LS have been diagnosed, and only 7% of those undergoing testing for LS are unaffected by cancer. Approximately 70% of *BRCA* mutation carriers with breast or ovarian cancer and 95% of unaffected *BRCA* mutation carriers remain unidentified.[39,44] Barriers to identification of hereditary cancer syndromes include genetic testing criteria that have historically focused on individuals with an existing cancer diagnosis, lower healthcare provider (HCP) awareness of genetic testing guidelines or availability of genetic counseling/testing services, and limited time for overburdened HCPs to take a detailed family history, among others.[45] Access to healthcare, including genetic counseling and testing services, is even more limited for ethnic minorities, geographically isolated individuals, and underserved patients who often encounter obstacles such as financial hardship or lack of health insurance, inability to take time off work, and lack of access to childcare or transportation.[46-53] As a result, these individuals are more likely to present with poor cancer outcomes, including advanced cancer with worse stage-specific survival, that requires significantly more costly treatment that further exacerbates their financial hardships.[54,55]

Despite calls for population-based screening for HBOC and LS, population screening outcomes data, especially in underserved communities, and studies that quantitate the reduction of cancer cases as a result of large-scale population screening for HBOC and LS are scant. The goal of population screening is not only to identify mutation carriers, but also to improve compliance with management recommendations in mutation carriers to prevent cancers. However, since compliance rates are largely unknown, so too are the benefits of screening, especially in underserved communities.

Identifying Solutions- Implementing Population Screening Programs for HBOC and LS: An Institutional Experience

Family History of Cancer Screening and Tumor Analysis: Simplified universal screening tools can increase access to genetics services on a larger scare. Particularly in non-oncology settings such as imaging centers, such tools have shown great success in increasing identification of unaffected individuals eligible for genetics services, including in underserved have populations where awareness of, and referrals for hereditary cancer are lower.[56-58] Several brief cancer family history screening tools have been developed to identify individuals at risk for HBOC, and have successfully implemented in screening mammography populations.[59-63] The genetics screening tool initially developed and then updated by the Centers for Disease Control (CDC), the Referral Screening Tool (RST) is the most thoroughly validated.[63,64] It is a simple form that uses check boxes to capture relevant personal and family history. The form takes less than a minute to complete and has a sensitivity of 81.2%, a specificity of 91.9%, and a discriminatory accuracy of 0.87 when assessed against BRCAPRO, a validated mathematical model that is too time-consuming to use for general screening.[65] In the validation study, screening in 2,464 unselected mammography participants generated genetics referrals in 6.2%.[63]

In 2010, the RST was programmed into the mammography management software used by the mobile and fixed breast imaging sites at the UT Southwestern Center for Breast Care. The tool was modified to include breast cancer patients diagnosed before the age of 45 and all ovarian cancer patients maximize identification of high-risk patients, including those who may not have previously been offered genetic services. In the first four months of operation, 8,605 women were screened and 110 (1.3%) met criteria for genetic counseling, of whom 37 (34%) had already undergone genetic testing.

Screening colorectal and endometrial tumors for Lynch syndrome by assessing expression of the mismatch repair (MMR) genes by immunohistochemistry (IHC) has a sensitivity of 83% and a specificity 89%.[66] In 2010, the UTSW Cancer Genetics program instituted MMR gene IHC for all colorectal cancers diagnosed before age 70 at UT Southwestern Simmons Comprehensive Cancer. An audit of the first seven months of the program showed that 78 (74%) of 105 eligible colorectal cancers were tested by IHC, of which 13 (17%) exhibited abnormal IHC staining.

In 2016, the UT Southwestern Cancer Genetics program received a 3-year grant from CPRIT, *PP160103,* to expand the HBOC family history of cancer (FHOC) screening program to include screening for Lynch syndrome at UT Southwestern. The HBOC screening tool previously implemented in the mammography clinics was modified to include family history of colorectal and endometrial cancer. At the start of implementation, modified paper questionnaires were used in the mammography clinics. The questions were subsequently programmed into the mammography software to enable automation. LS FHOC screening questions were also incorporated into clinic notes within the electronic medical record system (EMR) in the gastroenterology clinics at UT Southwestern to expand the population being screened.

Expanding Population Screening Efforts to Ethnically Diverse, Underserved and Geographically Isolated Populations: In 2011, the UT Southwestern Cancer Genetics program received a 3-year grant from the Cancer Prevention and Research Institute of Texas (CPRIT), *PP110220*, to expand these programs to underserved populations. The first component of this grant-based project included systematic FHOC screening for HBOC in underserved and geographically isolated populations to increase HBOC case identification. We incorporated the paper version of the modified RST into the patient intake process of mammography clinics at two regional Texas county hospital systems in Dallas and Tarrant counties, as well as mobile mammography units serving four additional rural Texas counties. The counties addressed in *PP110220* are located in Texas Health Service Region (HSR)-03, a region with one of the highest breast cancer incidence rates in the state, and also greater than average incidences of ovarian, endometrial, and colorectal cancer.[67] The area covers 4,688 square miles, roughly the size of the state of Connecticut, and represents a population of 3,511,623. The modified screening tool was then incorporated into the mammography software at one of the two county hospital systems in 2012 to automate the screening process for increased efficiency.

The second project component included expansion of analysis of colorectal and endometrial cancer tumors using immunohistochemical (IHC) staining of the mismatch repair (MMR) proteins to include pathology departments at the same two county hospitals to increase the identification of Lynch syndrome cases in underserved populations. Grant funding was used to develop protocols for reflex IHC analysis of the MMR proteins for all colorectal cancers diagnosed before age 70 and all endometrial tumors diagnosed before age 55 at the pathology departments at the two county hospitals, and subsidize certain aspects of the protocol. IHC analysis was physically performed at UT Southwestern.

In 2014, *PP110220* was renewed for an additional 3 years and FHOC for HBOC efforts were expanded to an additional 15 rural Texas counties. In order to increase its reach, the program continued the existing partnership with the mobile mammography unit serving several of the 15 counties, and also collaborated with a community survivorship program that also provided mobile services to rural counties. The expansion area included a population increase of 1,156,449 and covered an estimated additional 13,480 square miles, more than double the size of Massachusetts.

In 2017, as part of the *PP160103* CPRIT-funded project, we used the LS FHOC screening model implemented in the UT Southwestern mammography and gastroenterology clinics as a model and translated those initiatives into a similar screening programs within the mammography and gastroenterology clinics at the Dallas County hospital.

Use of Patient Navigation and Program Automation to Reduce Disparities in Health Care Delivery:

Patient navigation is a process-based system organized to 1) identify cases, 2) identify and address barriers to care, 3) implement a specific care plan, and 4) measure effectiveness by tracking cases through to specific outcomes.[68] Patient navigation has been shown to increase screening uptake and adherence in breast[69], cervical[70], colorectal,[71] and prostate cancer[72] in disadvantaged urban populations. While data surrounding patient navigation for genetics services is scarce, a randomized trial of patient navigation to improve uptake of cancer genetic counseling services was performed in an insured patient population in Denver, Colorado, and showed that patients randomized to telephone contact by a patient navigator were more likely to undergo genetic counseling by 13%.[73]

In *PP110220* and the renewal project, *PP140182*, we were able to incorporate two bilingual (English and Spanish-speaking) patient navigators in the service delivery model at the two county hospitals to review the FHOC screening forms and determine eligibility for genetics services against national guidelines, as well as to screen IHC reports for patients with abnormal results. Both navigators completed the Cultural Competency training sections of the Genetic Counseling Cultural Competence Toolkit (http:// geneticcounselingtoolkit.com/default.htm). Navigators then contacted eligible patients via a letter and a phone call to provide education about genetic counseling and testing services. During the phone call, navigators worked to identify and address patients' barriers to care, and coordinate genetic counseling appointments. Patients were sent language-appropriate educational DVDs (UCSF DEcIEDE). Patients who did not complete their scheduled genetic counseling appointments were re-contacted by navigators to re-engage and re-schedule.

Patient contact and outcomes data was tracked by navigators using the "Navigation" console within the *CancerGene Connect* software. *CancerGene Connect* is a HIPAA compliant web-based environment that can be used for various aspects of hereditary cancer risk assessment. As part of *PP110220, CancerGene Connect* was updated to include a referral module for entering patient contact information, the results of the family history screening and IHC activities, and cancer-risk management activities (high-risk surveillance, prophylactic surgery, cascade testing) for mutation-positive patients if applicable. The program's reporting structure was enhanced to allow navigators to track patients from potential case identification through attendance at genetic counseling appointments and follow-up clinical activities based on cancer risks identified.

In *PP160103*, two bilingual (English and Spanish-speaking) navigators were used to triage LS FHOC screening reports from the mammography and gastroenterology clinics at UT Southwestern and the Dallas County hospital, and contact patients eligible for genetic counseling services. Initially, the navigators had to manually review the LS FHOC screening forms from the mammography clinics and the EMR reports generated from LS FHOC screening in the gastroeneterology clinics. These processes were later automated in 2018 and 2019 to allow for increased efficiency and sustainability. A high-risk algorithm was developed and programmed into the mammography software, allowing the software to generate reports with screen-positive patients for navigators to contact. Similarly, a high-risk algorithm was used in the gastroenterology clinics to create a high-risk registry within the EMR. This registry was

programmed to populate with patients who were eligible for navigator contact based on the algorithm. Similar to *PP110220,* navigators contacted patients to provide education about genetics services and coordinated scheduling for genetic counseling appointments. *CancerGene Connect* was used by navigators to track navigation activities and outcomes.

Use of Varying Service Delivery Models to Increase Access to Genetic Counseling and Testing: In *PP110220,* patients were primarily scheduled for in-person genetic counseling in the cancer genetics clinics established at the respective county hospitals. Telemedicine services were implemented in the four rural Texas counties in order to ensure easier access to services for patients residing in those counties. Remote genetic counseling has been associated with the same increase in knowledge, reduction in cancer-related anxiety, and overall satisfaction as traditional face-to-face counseling and has shown success in a cancer genetics setting.[74,75,76] Genetic counseling is particularly well suited to a telemedicine approach, and as such, telemedicine consultation rooms were set up at four partnering community hospitals in each of the four rural counties. A parent system was installed at UT Southwestern, where genetic counselors were housed. Telemedicine set-up required specific hardware, including computers, monitors, cameras and encryption devices. The UT Southwestern Cancer Center implemented policy changes to permit remote patient registration, with the ability for patients to complete necessary forms (Treatment Consent forms and HIPAA authorizations) online.

At the time of appointment scheduling, patients were sent log-in information for *CancerGene Connect*, which allowed them to enter their family history and other risk factor information online using the patient portal prior to the telemedicine visit. The *CancerGene Connect* software is a freely available, HIPAA-compliant online platform that can be used to record patient health information, family history of cancer, and genetic test results; calculate mutation and cancer risks using risk assessment models (BRCApro, MMRpro, Pancpro, Melapro, Claus, Gail, and Tyrer-Cuzick); generate pedigrees; document risk assessments and clinical risk-management recommendations; track data; and generate reports. The software includes patient and provider portals. For the purpose of the telemedicine set-up, the system was configured so that the patient and genetic counselor could see each other while simultaneously viewing *CancerGene Connect* screens during the appointment. Patients electing to proceed with genetic testing were able to have their samples collected at the telemedicine sites, each responsible for then sending samples to the respective testing laboratories. Each of the expansion counties in the renewal, *PP140182,* was within an hour's drive of one of the original telemedicine sites, which allowed for increased access to genetic counseling/testing to a larger population of patients.

In *PP160103*, telephone genetic counseling and at-home saliva testing were used to further reduce access-related barriers for underserved patients. Studies comparing telephone genetic counseling to in-person consultation have revealed that telephone genetic counseling is not inferior to in-person genetic counseling in knowledge, satisfaction, decision-making, distress or quality of life.[77-85] At the beginning of the project, saliva test kits were mailed directly by the cancer genetics program to patients electing to pursue genetic testing, along with necessary paperwork such as laboratory test consent forms or financial assistance paperwork for testing, and instructions for saliva sample collection and send-out. This process was later updated with the testing laboratories sending saliva kits to patients and/or coordinating mobile phlebotomy. The program also then incorporated use of an online signature platform to send necessary documents and enable patients to sign necessary paperwork electronically. Patients who had not sent a sample to the testing laboratory were sent periodic reminders either via telephone or by mail. A systematic reminder process with two separate reminders was later

implemented for patients with pending samples. Patients with valid e-mail addresses were sent an electronic reminder via the online signature platform, with a follow-up telephone reminder as needed. Patients without valid e-mail addresses received two separate telephone reminders. Internal review of data showed that implementation of the systematic reminder process significantly increased test completion rates. With *PP160103*, for patients who had a sample failure or logistical issues with the sample that was sent to the laboratory for testing (i.e., mislabeled tubes, leaking sample, etc), collection of a subsequent sample for testing was coordinated.

Testing costs for underserved patients across all projects were covered using a combination of CPRIT grant funding and funding through laboratory financial assistance programs. Genetic testing for patients undergoing evaluation as part of *PP110220* was limited to either HBOC or LS, and this continued into part of *PP140182.* However, a subset of patients seen as part of *PP140182* did receive next-generation sequencing, an emerging technology at the time. All patients seen through *PP160103* were offered next-generation panel testing. Use of panel testing allowed for identification of actionable mutations in other hereditary cancer genes that may not have otherwise been identified.

Use of Patient Navigators to Increase Compliance to Cancer Risk-Management Recommendations in Mutation-Positive Patients: Data about compliance to recommended cancer risk-management in underserved patients with hereditary cancer is scarce. In *PP110220*, a baseline of patient compliance with the evidence-based National Comprehensive Cancer Network (NCCN) management recommendations in the underserved population was established. This data showed significant differences in compliance rates between underserved and insured patient populations, and further highlighted disparities in care between underserved and insured patients, and the need for interventions. Barriers to care that were identified included lapsed care coverage within hospital systems due to inability to navigate health care systems or insurance plans; lack of transportation to appointments; minimal time or means to obtain care; and inaccurate understanding of cancer risks.

Given that patient navigators have focused training in certain health conditions and can provide education and social support, make referrals, and schedule appointments, they have been shown to promote adherence to recommended cancer screenings and appointment attendance, and increase patient satisfaction and healthcare knowledge. [86-90] The literature on use of patient navigators in the genetics setting is scarce, and baseline values for patient outcomes in this setting is not well-established. In *PP140182,* program navigators attempted to re-contact underserved LS and HBOC patients to increase compliance within this population, as feasible between other navigation duties, and data demonstrating improved outcomes paved the way for a more robust navigation program for mutation-positive patients. In 2016, we received a CPRIT grant to create the role of a genetic patient navigator (GPN) to assist in increasing compliance within the LS/HBOC patient populations. An oncology nurse navigator was hired for this role, and re-contacted LS/HBOC mutation positive patients previously seen in the program's various clinics to assess compliance to NCCN risk-management recommendations; identify and address barriers to care; provide counseling on healthy lifestyle options; help coordinate cascade testing for at-risk relatives; and assist individuals with enrollment in survivorship programs. While the GPN did re-contact insured patients, the primary focus was on underserved populations. Due to the significant amount of time it took for the GPN to re-contact individual patients via phone and address patient needs, we eventually developed an electronic survey that was sent to all patients with listed valid email addresses. This survey was meant to efficiently assess patient compliance and needs,

thereby allowing the GPN to determine which patients had the greatest needs, and thus prioritize those contacts. Navigation activities and patient outcomes were tracked using *CancerGene Connect*.

Demonstrating Impactful Outcomes:

Population-based screening protocols can significantly increase identification of individuals with hereditary cancer, especially in underserved and geographically isolated populations. Between *PP110220* and *PP140182,* 209,156 underserved women were screened for HBOC using the family history of cancer screening tool incorporated into the mammography clinics and mammography/survivorship mobile units across 21 counties in Texas. Additionally, 1,381 colorectal and endometrial tumors were screened using IHC staining. A total of 144 mutations associated with hereditary breast cancer were identified through population-based HBOC FHOC screening; 121 mutations associated with hereditary colorectal cancer were identified through IHC tumor analysis; and an additional 12 mutations associated with other hereditary cancer syndromes were incidentally identified through screening efforts with the use of next-generation panel testing. In the *PP160103* project, 212,827 individuals were screened for LS using the family history of cancer screening tools used in the mammography and gastroenterology clinics at UT Southwestern and the Dallas county hospital system. A total of 83 mutations associated with hereditary colorectal cancer were identified and an additional 52 actionable mutations associated with other hereditary cancer syndromes were identified.

Across the different grant-based projects, approximately 4-5% of those undergoing screening with the FHOC screening tools were identified as being eligible for hereditary cancer risk assessment based on family history. Data from our *PP110220* and *PP140182* population screening projects shows that involvement of patient navigators led to higher genetic counseling appointment attendance- approximately 50%-59% of patients scheduled for genetic counseling services completed their appointments. This is compared to a genetic counseling appointment attendance rate of 26-31% that has been reported in the literature.[91,92,93] Data from *PP160103* shows a 73% appointment attendance rate, demonstrating that in addition to incorporation of patient navigators, use of various service delivery models such as a robust remote genetic counseling and testing program can help further increase access to services by addressing certain known healthcare barriers. The outcomes data from our various programs shows that using alternate service delivery models and incorporation of patient navigators to engage patients can increase uptake of genetic counseling services by as much as 19-47%.

Data analysis and chart review for the first 20 months of *PP110220* was used to establish baseline compliance to cancer risk-management recommendations in the underserved population. This data showed 81% of underserved Lynch syndrome patients were in compliance with NCCN colorectal cancer surveillance guidelines, compared with 90% of the insured population. The differences in compliance between underserved and insured patients was more pronounced in the HBOC population. Approximately 25% and 40% of underserved HBOC patients underwent prophylactic bilateral mastectomy and prophylactic bilateral oophorectomy respectively, compared to 41% and 71% of insured patients; and approximately 39% of HBOC underserved patients were compliant with breast surveillance recommendations compared to 72% of their insured counterparts. Data from *PP140182* showed a 13% increase in bilateral mastectomy rates, 24% increase in bilateral salpingo-oophorectomy rates, and 29% increase in breast surveillance among underserved HBOC patients.

Based on data collected from the first 20 months of *PP110220*, we developed a statistical model to calculate the long-term impact of population screening on cancer incidence in HBOC populations, based on patient compliance with NCCN guidelines and the uptake of prophylactic surgery. This model predicted the reduction in both breast and ovarian cancer in our underserved population to be 9% for over 30 years. As a comparison in this study, we looked at the compliance and uptake of surgery in our insured population. We found a 57% reduction in breast cancer and 51% reduction in ovarian cancer over 30 years, highlighting a significant disparity for the underserved. The initial data indicated that compliance with both guidelines and recommendation of prophylactic oophorectomy reduced the projected cancer risk in this population. Based on updated compliance data from *PP140182*, we saw a projected decrease of the 30-year breast and ovarian cancer rates in the underserved population from 9% to 64% and 54% over the course of three years, respectively. We also examined this for LS, showing 46% decrease in colon cancer incidence over 30 years in the underserved population compared to a 51% decrease in the insured population. We anticipate these projections (and continued increases in cancer prevention) will lead to significant healthcare dollars saved, which will benefit the population and healthcare systems in the state.

Use of a dedicated genetic patient navigator (GPN) for follow up of mutation-positive patients led to further improved patient outcomes. In the underserved HBOC population, compliance to breast cancer risk-management and ovarian cancer risk management recommendations increased by 33% and 32% respectively. Given the relatively high colon cancer surveillance compliance in the underserved Lynch syndrome population compared to the insured population (81% vs. 90%), GPN intervention led to marginally increased compliance of 1.5%. Observed cascade testing rates increased by 230% over three years and smoking cessation rates increased by 11%. Prior to the GPN, no HBOC/LS patients had been enrolled in the survivorship program, but over 3 years, 86 patients were patients were enrolled, of whom 51 were previvors.

Conclusions:

Implementing a population screening program is not without its challenges. Some significant challenges encountered by our program included, but were not limited to changing genetic testing/evaluation criteria over time which necessitated re-evaluation of our screening protocols and re-education of clinicians using these tools; tracking down tumor samples and/or medical records for patients receiving care at outside institutions to ensure standard of care was provided, and led to significant issues in assessing compliance to for some patients; institutional administrative barriers and priorities that led to significant delays in planned implementation of certain initiatives. Navigators also observed that compared to what had initially been anticipated, significantly more time was required to re-contact patients via telephone and address barriers to care, especially in underserved populations.

Despite growing pains, we were able to implement successful population screening programs for hereditary cancer across multiple clinical settings and hospital systems. Review of internal data showed the CancerGene Connect program reduced the amount of time genetic counselors spend on each case by 46%. Use of the versatile platform allowed our cancer genetics program to be more efficient and absorb the increase in patient volume as a result of populations screening programs. Furthermore, automation of screening protocols enhanced the efficiency of our navigators. We observed that use of navigators in a genetics clinic setting helped to boost uptake of genetic counseling services, and improved other patient outcomes such as compliance to cancer risk-management recommendations

and health-related behavior modifications, and cascade testing. We also observed that use of remote genetic counseling and genetic testing service delivery models helped address access barriers, particularly in underserved patient populations and led to higher uptake of services. A combination of these initiatives led to increased identification of hereditary cancer, and thereby more opportunities for cancer prevention, which subsequently led to more healthcare dollars saved.

With the continued growth of our program, we aim to explore other opportunities for population screening for hereditary cancer, focusing on alternate service delivery models, and expanding screening initiatives to other medical specialties and clinics that have synergy with cancer genetics, as well as other cancer programs in Texas. We are also working to disseminate the resources we have used and developed through our programmatic experience with others in Texas and nationally via a free, online toolkit (available at www.utswmed.org/geneticstoolkit) and look forward to collaborating with programs or clinics interested in implementation of one or more aspects of our previous initiatives.

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