

**A Focus on Interventions to Increase Rates of Genetic Services for Patients with Pancreatic  
Cancer**

by

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## **A Focus on Interventions to Increase Rates of Genetic Services for Patients with Pancreatic Cancer**

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University of Pittsburgh, 2023

Pancreatic cancer progresses rapidly and has historically been difficult to treat, with a 5-year relative survival rate of about 9-12%. Screening and early-detection are also challenging, contributing to disease morbidity. Within the past five years, a growing body of literature has demonstrated increased rates of survival and improved outcomes in individuals with germline *BRCA* pathogenic or likely pathogenic variants when offered targeted therapeutics such as PARP inhibitor maintenance therapy, showing evidence of anti-tumor activity and extended median progression-free survival.

About 5-10% of pancreatic cancer diagnoses have an underlying genetic cause. 2-5% are caused by *BRCA1/2* variants that may direct use of targeted therapies. The National Comprehensive Cancer Network (NCCN) has recognized the importance of identifying germline status in the context of pancreatic cancer treatment in addition to understanding familial health implications due to inheritance and increased cancer risks. On December 4, 2019, NCCN released Genetic/Familial High-Risk Assessment Guidelines for Breast, Ovarian, and Pancreatic cancers (Version 1.2020), recommending genetic counseling and genetic testing for every individual diagnosed with exocrine type pancreatic cancer. These rates are far lower than 100% for several reasons related to testing service access, therapeutic decision-making, and disease progression.

This quality improvement study was completed to better understand cancer genetic counseling referral and genetic testing rates in the clinical setting to identify areas that could

benefit from public health intervention strategies aimed at increasing rates of genetic services. Deidentified electronic medical record (EHR) data was collected from 449 patients diagnosed with exocrine pancreatic cancer between July 2019 and June of 2020 across three Geisinger hospital sites across central Pennsylvania. Overall, 1/5 patients (88/449) were referred to genetic counseling, and half of those referrals (44/88) were completed. In total, only 13% (59/449) underwent genetic testing. For patients completing genetic counseling appointments, 86% had testing. Comparatively, for patients that did not have genetic counseling, 5% completed testing. Understanding current gaps in clinical practice will help focus public health intervention methods aimed toward increasing overall health outcomes of pancreatic cancer patients and healthcare provider service delivery. Additionally, this study explores related interventions attempted by Geisinger and offers direction for future strategies.

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## **Preface**

Thank you, to my classmates, friends, family, and to my thesis committee.

## 1.0 Introduction and Specific Aims

### 1.1 Introduction

The National Comprehensive Cancer Network (NCCN) released guidelines on December 4<sup>th</sup>, 2019 (NCCN Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic Version 1.2020), recommending that every individual diagnosed with exocrine pancreatic cancer should be offered genetic counseling and genetic testing (Krepline, Geurts et al. 2021). The rationale behind this recommendation is to provide additional molecular information that may dictate treatment options. In a small number of cases, this may open a door for more personalized medical care. (Golan, Hammel et al. 2019). About 5-10% of total pancreatic cancer diagnoses have an underlying genetic basis. Explored further, regardless of family history of cancer or age at diagnosis, 2-5% of pathogenetic or likely pathogenetic variants are in genes *BRCA1/2*. About 1-4% of pancreatic cancer patients with a family history had germline *PALB2* mutations (Nepomuceno et al., 2017). One study performed by MAYO Clinic looked at 250 patients with pancreatic adenocarcinoma with results of about 1 out of every 6 patients having a genetic predisposition, which included also Lynch syndrome genes (For 1 in 6 patients with pancreatic cancer, pathogenic germline variants are present, 2023). While multiple factors impact survival outcomes, patients with germline variants with associated targeted therapies may potentially have extended survival rates (Uson, Samadder et al. 2021). The genes most strongly associated with hereditary pancreatic cancer are *ATM*, *BRCA1*, *BRCA2*, *CDKN2A*, *MSH2*, *MLH1*, *MSH6*, *EPCAM*, and *STK11* (Krepline, Geurts et al. 2021).

Somatic tumor testing has been recommended because it can direct treatment, and similarly patients with identified germline *BRCA1*, *BRCA2*, and *PALB2* variants may also have access to a greater selection of clinical trials. Results from these trials have demonstrated beneficially longer survival rates for individuals on treatment (Golan, Hammel et al. 2019). This parallels already clinically available Poly (adenosine diphosphate–ribose) polymerase (PARP) inhibition treatments, such as Olaparib, for individuals with an established germline *BRCA* mutation with metastatic breast or ovarian cancers (Golan, Hammel et al. 2019).

Advancement from clinical trials to clinical practice is important when considering the severity of pancreatic cancer in general, typically found to have a 5-year relative survival rate of about 9-12% (Uson, Samadder et al. 2021). From a population health perspective, pancreatic cancer rates of diagnosis and death have been increasing over the past decade, with an estimated 8% of cancer deaths due to pancreatic cancer alone in the year 2023 (SEER Cancer of the pancreas cancer stat facts, 2023). When diagnosed, these cancers are most often discovered at later stages when it is more difficult to treat, yielding less favorable health outcomes. To provide patients with the best access to clinical trials and clinical care, hospital systems and healthcare providers should adhere to these recent NCCN guidelines and refer as many eligible pancreatic cancer patients as possible for cancer genetic counseling and testing. Additionally, these genetic services provide important information regarding family members and inheritance that could influence family planning and decision-making and facilitate discussions about screening.

This study explores pancreatic cancer patient data pulled from the electronic health record (EHR) from three Geisinger clinics across central Pennsylvania using multiple variables curated through the hospital system's Cancer Registrar. Specific aims of this retrospective study will examine at the number of patients diagnosed with pancreatic cancer between July 2019 and June

2020; the rate of referral to any of three Geisinger Cancer Genetics clinics, the rate of completion of a counseling appointment, and the rate of completion of testing with or without specific counseling. Comparing these quantitative rates of genetic referrals, genetic counseling appointments, and testing completed to NCCN's recommended guideline of recommending testing for 100% of individuals with exocrine pancreatic cancer will reveal gaps in clinical practice. This study aims to identify and explore opportunities to close care gaps, increase access in practical ways, and describe barriers to access of germline testing. This review also explores implementation methods to close these gaps and improve overall health outcomes of pancreatic cancer patients and delivery of services by healthcare providers at Geisinger.

### **1.1.1 Specific Aim 1**

Quantitatively explore rates of completed cancer genetic referrals and completed genetic counseling appointments for pancreatic cancer patients diagnosed between July 2019 and June 30<sup>th</sup>, 2020, using deidentified Geisinger data from electronic medical record (EHR) patient data across three hospital branches: Geisinger Medical Center, Geisinger Wyoming Valley, and Geisinger Lewistown Hospital.

### **1.1.2 Specific Aim 2**

Quantitatively explore rates of ordered and completed germline genetic testing by genetic counselors or non-genetic providers, with or without genetic counseling, for pancreatic cancer patients diagnosed between July 2019 and June 30<sup>th</sup>, 2020, using deidentified Geisinger data from

electronic medical record (EHR) patient data across three hospital branches: Geisinger Medical Center, Geisinger Wyoming Valley, and Geisinger Lewistown Hospital.

## **2.0 Manuscript**

### **2.1 Background**

#### **2.1.1 Pancreatic Cancer**

Although lung cancer will continue to be the leading cause of cancer deaths in the United States, pancreatic cancer will soon rank second, projected to surpass breast and colon cancers in both men and women by 2030 (Rahib, Smith et al. 2014) (Loveday, Lipton et al. 2019). In Australia, pancreatic cancer has claimed its place as having the highest mortality rate among all other cancer types (Loveday, Lipton et al. 2019). According to the “Key Statistics for Pancreatic Cancer,” the American Cancer Society projects that 64,050 people will be diagnosed with pancreatic cancer in the year 2023 (Key Statistics for Pancreatic Cancer, January 12, 2023). Their statistics also predict that 50,550 of them will die from their diagnosis, 2,340 of them from the state of Pennsylvania alone (Key Statistics of Pancreatic Cancer, January 12, 2023).

#### **2.1.2 Risk Factors**

Though this study focuses on hereditary pancreatic cancer, both modifiable and unmodifiable factors impact the risk for pancreatic cancer and should be discussed. Multiple modifiable risk factors have been identified that increase risks for developing pancreatic cancer, including increased BMI (Body Mass Index), pancreatitis, diabetes, cigarette smoking, heavy alcohol consumption, and other chemical exposures. Chemical exposures and diabetes mellitus



can also increase cancer risks. Other possible risk factors consist of diet, physical activity, coffee intake, and infection (Collisson, Bailey et al. 2019). These risk factors can be mitigated to decrease risks for cancer. Factors unable to be altered include age, gender, race, high-risk benign lesions such as cysts or IPMN (intraductal papillary mucinous neoplasm), family history of pancreatic cancer, and germline mutations associated with pancreatic cancer or pancreatitis (McWilliams, Maisonneuve et al. 2016) (Dbouk et al. 2022). Among these established risk factors for pancreatic cancer, smoking, diabetes mellitus, family history, obesity, and alcohol intake are associated with EOPC (earlier onset pancreatic cancer), diagnoses under the age of 60 (McWilliams, Maisonneuve et al. 2016). This study will focus on the heritable causes of pancreatic cancer related to germline variants.

The average age of pancreatic cancer onset for the general population is about 70 years old (Petrucelli, Daly et al. 2022). About 10% of patients with pancreatic cancer have a family history of cancer, which highlights the potential value in collecting a family history to identify those at greater risk for the disease. (Collisson, Bailey et al. 2019). An earlier retrospective study identified germline mutations in 28% of 175 families that had a history of pancreatic cancer, highlighting the importance of gathering a family history further (Catts, Baig et al. 2016). Family history of at least one first-degree relative (FDR) had an OR of 2.53 for EOPC (Loveday, Lipton et al. 2016). Having two first degree relatives with pancreatic cancer can increase risks 5-10-fold (McWilliams, Maisonneuve et al. 2016). Public health efforts tend to focus on EOPC due to the higher number of years of potential life lost (McWilliams, Maisonneuve et al. 2016).

Germline mutations associated with pancreatic cancer or pancreatitis can be passed down from family member to family member, typically in an autosomal dominant fashion, increasing absolute risks of developing pancreatic adenocarcinoma for those that inherited the mutation up to

15% or more depending on the gene affected. *STK11* and *CDKN2A* both have shown increased risks of 15% or more, whereas people with a *BRCA2* pathogenic mutation can have a lifetime risk of 3-5%, and people with a *BRCA1* pathogenic mutation can have risks of 1-3% (Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic NCCN Guidelines, Version 1.2023). These risks are higher than the general population lifetime risk for pancreatic cancer, shown to be about 1.7% based on SEER (Surveillance Epidemiology, and End Result Program) data from 2017-2019 (NIH (National Institutes of Health) SEER, 2019). Germline mutations can also affect age of onset. For example, *BRCA1* and *BRCA2* pathogenic or likely pathogenic variants can decrease the average age of pancreatic cancer onset from 70 years-old to about 60 years (Petrucci, Daly et al. 2022).

Importantly, germline mutations can exist in individuals without a significant family history of cancer, creating challenges in identifying at-risk individuals, and interpreting the degree of risk even among individuals with an identified variant in the context of preventative care. (Collisson, Bailey et al. 2019). In fact, additional studies related to population genomic screening have reported that nearly 50% of individuals with identified pathogenic or likely pathogenic variants with *BRCA1* or *BRCA2* variants do not have a family history that meets NCCN's criteria for evaluation of HBOC (Hereditary Breast and Ovarian Cancer syndrome) (Guzauskas et al., 2020). This again highlights the development of guidance to recommend universal germline testing among individuals with pancreatic cancer, as family history is not a reliable factor in determining who will test positive for a *BRCA1* or *BRCA2* pathogenic or likely pathogenic variant.

### **2.1.3 Types of Pancreatic Cancer**

Historically, clinicians have used primary sites of cancer development as the basis for patient care. The idea was that, if an organ has a specific tumor in one individual, then tumors in the same organ of another individual will share more features and subsequent treatment plans than it would for an individual with the tumor located on a different organ (Collisson, Bailey et al. 2019). This outlines the importance of classifying cancer sites and subtypes, contributing to the development of treatment-based guidelines and society recommendations for initial workup of lesions, and resulting in organ-specific clinician care teams seen in hospital systems today as multidisciplinary cancer teams and one-size fits all approach to therapeutic decision-making. However, when looking at primary sites of cancer development from two separate individuals, histopathology reports can appear the same, yet have differing molecular pathways, therefore affecting their respective treatment options (Collisson, Bailey et al. 2019). While classifying tumors by cancer site is important and well established in clinical care today, understanding their molecular pathways can offer a new insight into personalized treatment options.

For pancreatic cancers, there are several histopathological subtypes that can be divided into endocrine, exocrine, or other tumor types. Pancreatic ductal adenocarcinoma (PDAC) makes up about 90% of exocrine type cancers, and it is the most common type of pancreatic cancer. In exocrine pathways, the pancreas secretes digestive enzymes into the pancreatic duct through acinar cells, and 95% of cancers arise from the pancreatic duct (Loveday, Lipton et al. 2019). Molecularly, exocrine tumor types have greater concern for genetic basis than endocrine tumor (Loveday, Lipton et al. 2019).

Endocrine pathways make up less than 5% of pancreatic tumors, where the pancreas secretes insulin and glucagon directly into the bloodstream through Islets of Langerhorn cells (Radu et al. 2018). When compared to exocrine type, the average five-year survival rate is higher, over 50%. More clinical trials and treatment options exist for neuro endocrine tumors, and the median age of onset tends to be earlier at age 60 (Philip, 2022) (Loveday, Lipton et al. 2019).

#### **2.1.4 Diagnostics**

Early detection of pancreatic cancer proves difficult. Without cardinal symptoms or established screening procedures for the general population, pancreatic tumors can develop and grow undetected (Loveday, Lipton et al. 2019). Key symptoms can include weight loss, back pain, abdominal pain, nausea, vomiting, diarrhea, constipation, jaundice, or new onset of diabetes (Loveday, Lipton et al. 2019). Overall, the 5-year relative survival rate of pancreatic cancer is about 12%, but this changes drastically according to how early the tumor is detected and its treatment options. Surgical resection is an option in about 13% of pancreatic cancer cases, yielding a 5-year relative survival rate of 42%. In most cases (52%) where metastasis has occurred and surgical resection is no longer an option, the 5-year relative survival rate is merely 3% (Pancreatic Cancer Statistics, 2022), highlighting the importance of detecting pancreatic cancer as early as possible for more effective treatment. New diagnoses often at a late stage require multidisciplinary discussion and plans for swift intervention because of this. The workup of pancreatic cancer lesions via imaging has its own challenges and typically occurs in the research setting. Imaging techniques can include a combination of Endoscopic Ultrasound (EUS), Computed Tomography scans (CT),

and Magnetic Resonance Imaging (MRI) performed at regular intervals (Cancer of the pancreas screening study (CAPS) 2023).

For over 20 years, the CAPS study (Cancer of the Pancreas Screening Study) has focused research efforts on early detection for individuals at higher risk for pancreatic cancer, having risks factors of a family history of pancreatic cancer, cysts or intraductal papillary mucinous neoplasm, and/or having an identified genetic predisposition (Cancer of the pancreas screening study (CAPS) 2023). Individuals without these risk factors and having lower than 5% lifetime pancreatic cancer risk should not consider pancreatic cancer surveillance, since there are no standard screening approaches in the general population (Dbouk et al. 2022). Participants of the CAPS study, all at high-risk for pancreatic cancer whether by a suspicious lesion, genetic predisposition, or family history, have received imaging for pancreatic cancer surveillance according to current recommendations, typically in the form of recommended annual magnetic resonance imaging and endoscopic ultrasound (Dbouk et al. 2022). In a 2022 updated analysis of CAPS, not only were pancreatic adenocarcinomas detected at earlier stages more often than that of previously established data, but the 5-year overall survival rates among those that had screen-detected lesions had increased to about 73% (Dbouk et al. 2022). This not only supports the importance of imaging for high-risk individuals for early detection, but it also highlights the importance of cascade genetic testing for family members to an individual with an identified germline mutation, regardless of symptom presence or family history (Dbouk et al. 2022).

### 2.1.5 Treatment

Treatment of disease using adjuvant or neo-adjuvant therapy is dependent upon many factors including patient performance status, disease status (resectable, borderline resectable, locally advanced, and unresectable), molecular profiling of the tumor, and germline mutations status. Patients with early-stage disease can benefit from surgical intervention followed by consideration of adjuvant therapy or observation (Holter et al., 2015). Surgical resection remains the only potential curative option for pancreatic cancer diagnoses, with only 1 out of 5 cases meeting eligibility (Rahib, Smith et al. 2014).

For patients with locally advanced or metastatic disease that may not be surgically resectable, molecular profiling via somatic testing is recommended because of anti-cancer treatment options for certain mutations. For example, the drug FOLFORINOX is recommended as neoadjuvant therapy for resectable tumors with *BRCA1/2* or *PALB2* mutations (NCCN Guidelines Pancreatic Adenocarcinoma Version 2.2022). FOLFORINOX is also recommended as first-line therapy for locally advanced or metastatic tumors with established *BRCA1/2* or *PALB2* mutations. Additionally, somatic fusions (*ALK*, *NRG1*, *NTRK*, *ROS1*, *FGFR2*, *RET*) or amplifications of genes (*BRAF*, *BRCA1/2*, *KRAS*, *PALB2*), microsatellite instability, mismatch repair deficiency, and other rare somatic mutations can possibly influence treatment options (NCCN Guidelines Pancreatic Adenocarcinoma Version 2.2022). The germline status of heritable mutations can also influence treatment after a confirmed pancreatic cancer diagnosis, and it is the focus of this study (Holter et al., 2015).

Poly (adenosine diphosphate–ribose) polymerase (PARP) inhibition treatments, such as Olaparib, have shown clinical efficacy for patients that have germline *BRCA1/2* and *PALB2*

mutations and diagnoses of associated breast or ovarian cancers (Holter et al., 2015) (Tischkowitz et al., 2021). Although not yet clinically practiced, a phase two prospective clinical trial funded by AstraZeneca in 2019 showed similar results for patients having metastatic pancreatic cancer and associated germline mutations (Golan, Hammel et al. 2019). In this Pancreas Cancer Olaparib Ongoing (POLO) trial, qualifying patients with confirmed *BRCA1* and *BRCA2* germline mutations and no disease progression of their metastatic cancer for at least 16-week periods of initial platinum-based chemotherapy treatment, anti-tumor activity from Olaparib maintenance showed significantly extended survival rates when compared to patients receiving placebos, with a median progression-free survival of 7.4 months compared to 3.8 months in placebos (Golan, Hammel et al. 2019). Unfortunately, the estimated amount of time for cancer treatment clinical trials like these mentioned are lengthy, about 8 years in length (Rahib, Smith et al. 2014).

In certain circumstances, prior platinum-based maintenance therapy with the drug called Rucaparib can be useful for patients with metastatic pancreatic cancer and an established germline or somatic *BRCA1/2* or *PALB2* mutations (NCCN Guidelines Pancreatic Adenocarcinoma Version 2.2022). Additionally, germline mutations in Lynch syndrome related genes, like DNA mismatch repair (MMR) genes *MLH1*, *MSH2*, *MSH6*, have been shown to increase pancreatic cancer risks 8.6-fold, with a lifetime risk of about 4% (Bujanda & Herreros-Villanueva, 2017). Pancreatic cancer patients with defective DNA mismatch repair (MMR) or high microsatellite instability (MSI), commonly seen in patients with Lynch syndrome, may have tumors that respond well to a certain immunotherapy drug called Keytruda (Pembrolizumab), therefore supporting germline mutation status consideration (Patil & Khan, 2020). Due to the importance of somatic and germline status in the context of pancreatic cancer treatment, timing of somatic and germline testing has

been included into recommended national guidelines on pancreatic cancer treatment and diagnosis workflow (NCCN Guidelines Pancreatic Adenocarcinoma Version 2.2022).

### **2.1.6 Hereditary Pancreatic Cancer**

According to the NCCN (National Comprehensive Cancer Network) guidelines posted in late December of 2019, every patient with a confirmed exocrine pancreatic cancer diagnosis should undergo germline genetic testing for key genes associated with familial inheritance of increased risk for pancreatic cancer (NCCN Genetic/Familial High-Risk Assessment of Breast, Ovarian, and Pancreatic Cancer, Version 1.2020). Pathogenic variants in *BRCA1* and *BRCA2* genes cause cases of hereditary pancreatic cancer and have on average an earlier age of onset of about 60.3 years, when compared to the average age of onset for the general population of about 70 years (Petrucci, Daly et al. 2022). In addition to increasing pancreatic cancer risks, pathogenic or likely pathogenic variants in the *BRCA1*, *BRCA2*, and *PALB2* genes cause Hereditary Breast and Ovarian Cancer (HBOC) syndrome, which can increase breast cancer risks up to 72%, ovarian cancer risks up to 44%, and increase risks for other types of cancer like male breast cancer, prostate, and melanoma (Petrucci, Daly et al. 2022). Multi-gene panel tests for hereditary pancreatic cancer often include these three genes, among several others, that are related to inherited cancer syndromes associated with pancreatitis and other cancer types.

The “NCCN Guidelines Version 2.2021 Pancreatic Adenocarcinoma,” listed eleven genes as the most common genes having variants associated with pancreatic cancer inheritance: *ATM*, *BRCA1*, *BRCA2*, *PALB2*, *MLH1*, *MSH2*, *MSH6*, *PMS2*, *CDKN2A*, *TP53*, *STK11*, and emerging evidence to show that the following three genes *PRSS1*, *SPINK1*, and *CFTR* are associated with



familial pancreatitis, which can increase risk for pancreatic cancer in itself (Tempero, Malafa et al. 2021). On the most recent version, however, NCCN has included the gene *EPCAM* with this list and found that there is no longer enough evidence to support *PMS2* as a pancreatic cancer gene, represented in Table 1. (Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic NCCN Guidelines, 2023). Although only three of these genes affect pancreatic cancer targeted therapy options (*BRCA1*, *BRCA2*, and *PALB2*), identification of pathogenic or likely pathogenic variants in the other mentioned genes could influence screening frequency and screening start-time recommendations for other cancers, inform family members of potential risks, start cascade testing, and open risk-reduction discussions surrounding options like surgical intervention (Holter et al., 2015). Additionally, Lynch syndrome genes could influence treatment by introducing immunotherapy that has shown favorable responses to defective DNA mismatch repair (MMR) or high microsatellite instability (MSI) (Patil & Khan, 2020). Ordering providers should consider including these eleven pancreatic cancer risk genes on their panels after a diagnosis of pancreatic cancer, although the choice remains up to the patient in addition to their genetic counselor or other ordering provider. These guidelines continue to change, adding new genes as research reveals cancer associations, or sometimes removing genes as previous thoughts of association lack statistical support, exemplified by *PMS2*.

### **2.1.7 Familial Testing**

Benefits from increasing genetic services provided to pancreatic cancer patients extend to subsequent variant identification in family members. Factors such as additional family cancer history and health insurance coverage can affect genetic testing options, influencing which genes

to include on panels and at which commercial laboratory. If a pathogenic or likely pathogenic variant in one of the genes listed in Table 1 was identified in an unaffected family member, a provider may only choose to order that single gene for cascade testing, or targeted testing if the exact variant is known. If the individual being tested reports a family history of pancreatic cancer as well as other cancer types (e.g., Breast or uterine cancers) the provider may expand the panel to include genes associated with those other cancer types. Guidelines exist to help providers make those choices with this information, but panel selection ultimately remains in the hands of the ordering provider. NCCN continually monitors and updates another resource that includes genes associated with pancreatic, breast, ovarian, and other cancers to help guide providers further in their genetic testing ordering thought processes, called the “NCCN Clinical Practice Guidelines in Oncology, Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic.” In the latest version, Version 3.2023, it lists genes associated with increased risks in these cancer types in addition to similar syndromes and health conditions (Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic NCCN Guidelines, 2023). As mentioned, the eleven pancreatic genes mentioned to typically be tested for pancreatic cancer risk are organized into Table 1 according to evidence of association: *ATM*, *BRCA1*, *BRCA2*, *CDKN2A*, most Lynch syndrome genes (*MLH1*, *MSH2*, *MSH6*, and *EPCAM*, with an exception to *PMS2*), *PALB2*, *STK11*, and *TP53* (Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic NCCN Guidelines, 2023).

**Table 1: Pancreatic Cancer Associated Genes by Evidence of Association**

Evidence of Association	Genes
Very Strong	<i>BRCA2, CDKN2A</i>
Strong	<i>ATM, BRCA1, Lynch genes (MSH2, MLH1, MSH6, EPCAM), STK11</i>
Limited	<i>PALB2, TP53</i>
Insufficient	<i>PMS2*</i>
<p><i>This table was adapted from Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic, NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) Version 3.2023 — February 13, 2023. It includes genes typically tested for pancreatic cancer risk (Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic NCCN Guidelines, 2023).</i></p>	

Similarly, the American Gastroenterological Association (AGA) updates and publishes clinical guidelines for genetic testing. In their most recent published guidelines for pancreatic cancer genetic testing, the “AGA Clinical Practice Update on Pancreas Cancer Screening in High-Risk Individuals: Expert Review,” they list several hereditary conditions associated with pancreatic cancer, and the genes involved (Aslanian, Lee, & Canto, 2020), which aligns closely with NCCN’s guidance. This suggests concordance between these bodies and the reviewed evidence in developing these practice guidelines.

### **2.1.8 American College of Surgeons Commission on Cancer**

The educational association, the American College of Surgeons, was created in the early 1900s and with a purpose to improve standards and outcomes for patients by focusing on quality, research, and optimal patient care. One major function focuses on cancer care, carried out by a consortium of professional organizations called the Commission on Cancer (CoC) (Schroeder et al. 2022). Cancer institutes and programs can become accredited by the Commission on Cancer if they

continually meet specific requirements demonstrating a high quality of care. Measurements of clinical care quality were recently updated in 2020 to include delivery of genetic services for cancer patients or referral to genetic services (Schroeder et al. 2022). To monitor clinical program initiatives and compliance with practice standards, on-site visits occur every three years in addition to data assessment (Schroeder et al. 2022). The three Geisinger clinics that this study investigates are all cancer programs that have been accredited by the Commission on Cancer.

### **2.1.9 Cancer Genetic Clinics**

In the literature, before any interventions aimed at increasing genetic services were implemented, clinical genetic testing rates in the clinical setting tended to be well below NCCN recommendations. One study recorded an overall 16.5% germline genetic testing rate for pancreatic cancer patients (Chittenden et al., 2021). Another study had a slightly higher rate of 19% (Kwon et al. 2023). A study on prostate cancer germline genetic testing, a similarly time-sensitive diagnosis in terms of gathering genetic information for treatment, had rates of testing at about 9%. (cite) This demonstrates room for improvement, particularly by introducing new methods to increase germline genetic testing rates for optimal cancer treatment that challenge established referral-based genetic service delivery.

Currently, there is a shift from this traditional model of genetic service delivery in the context of pancreatic cancer (Crowley, Gandhi et al. 2023). Typically, providers such as oncologists or surgeons will refer patients to a cancer genetics clinic when there is clinical suspicion for a germline pathogenic or likely pathogenic variant. Historically, this was driven by family history of HBOC-related cancers. As described previously, while family history can play a

key role in identifying positive families, studies note we are missing a substantial percentage of individuals with germline variants if we are not performing universal germline testing among patients with pancreas cancer. Multiple studies, however, have also shown that these traditional methods of referral for pre-test counseling yield suboptimal genetic test completion rates. (Chittenden et al., 2021; Walker et al., 2021).

The recommendation for universal germline testing has led to various interventions, such as embedded in-clinic testing stations in the form of a kiosk for expedited pre-test counseling and sample collection, app-based consent, and automated alerts within the EHR to increase referral rates. Studies have demonstrated that these models can more than double genetic testing rates of cancer clinics when compared to their traditional referral model (Chittenden et al., 2021; Walker et al., 2021). These interventions can also decrease administrative burden, patient bills, and reduce time spent in appointments. Workflows interventions can also present barriers due to additional costs to implement tools. All considerations, including finances and reimbursement rate, are carefully considered by a clinical program prior to implementing a shift in care delivery models (Walker et al., 2021).

## **2.2 Methods**

### **2.2.1 Data Source**

Data was collected from the Geisinger EHR. Geisinger's Cancer Registrar tracks new cancer diagnoses in the system. Only pancreatic cancers diagnosed between July 2019 and June

30, 2020, were initially filtered to understand the system's baseline rate of diagnoses and referrals at the time of published guidance for offering universal germline testing.

To filter for appropriate diagnoses, we started by pulling all ICD-10 diagnosis codes for pancreatic cancer. The study population included persons with pancreatic cancer diagnosed across the Geisinger enterprise. Data on age of diagnosis, sex, ethnicity, and socioeconomic status were not collected as part of this study. Histological subtypes were reviewed for inclusion vs exclusion in the data set, described below, and included: acinar, cell carcinoma, adenocarcinoma not otherwise specified (NOS), adenosquamous carcinoma, atypical carcinoid tumor, carcinoid tumor (NOS), carcinoma, carcinoma (NOS), undifferentiated carcinoma (NOS), diffuse large B-cell lymphoma (NOS), follicular lymphoma grade 2, intraductal papillary-mucinous carcinoma non-invasive and invasive, invasive carcinoma of no special type, mixed pancreatic endocrine and exocrine malignant tumor, mucinous adenocarcinoma, non-invasive mucinous cystadenocarcinoma, malignant neoplasm, neuroendocrine carcinoma (NOS), signet ring cell carcinoma, small cell carcinoma (NOS), solid pseudopapillary carcinoma, spindle cell carcinoma, and squamous cell carcinoma. This data was deidentified before gaining access and contained a total of 636 patients pulled from the EHR.

The focus of this study was on exocrine pancreatic cancer types; therefore, data were filtered to exclude endocrine type pancreatic cancers. Histology cancer types included acinar, cell carcinoma, adenocarcinoma not otherwise specified (NOS), adenosquamous carcinoma, carcinoma, carcinoma (NOS), intraductal papillary-mucinous carcinoma non-invasive, invasive carcinoma of no special type, mixed pancreatic endocrine and exocrine malignant tumor, mucinous adenocarcinoma, malignant neoplasm, signet ring cell carcinoma. Also, the locations where each patient received chemotherapy treatment was noted to focus on patients that had continual care

through Geisinger, limited to Geisinger Medical Center (GMC), Geisinger Wyoming Valley (GWV), and Geisinger Lewistown Hospital (GLH). One patient treated at Geisinger Lewistown Hospital was referred to Penn State for genetic counseling given location. This patient was excluded from the study due to the possibility of a genetic testing result not being added to the Geisinger medical record system.

This resulted in 449 patients being used for the current data analysis, depicted in this methods section as a flowchart (Figure 1). The data included genetic counseling referrals made by any medical providers, genetic counseling appointment statuses, genetic testing ordered and by which provider, and the results of the genetic testing as either positive, negative, or variant of unknown significance (VUS) for an association with pancreatic cancer.

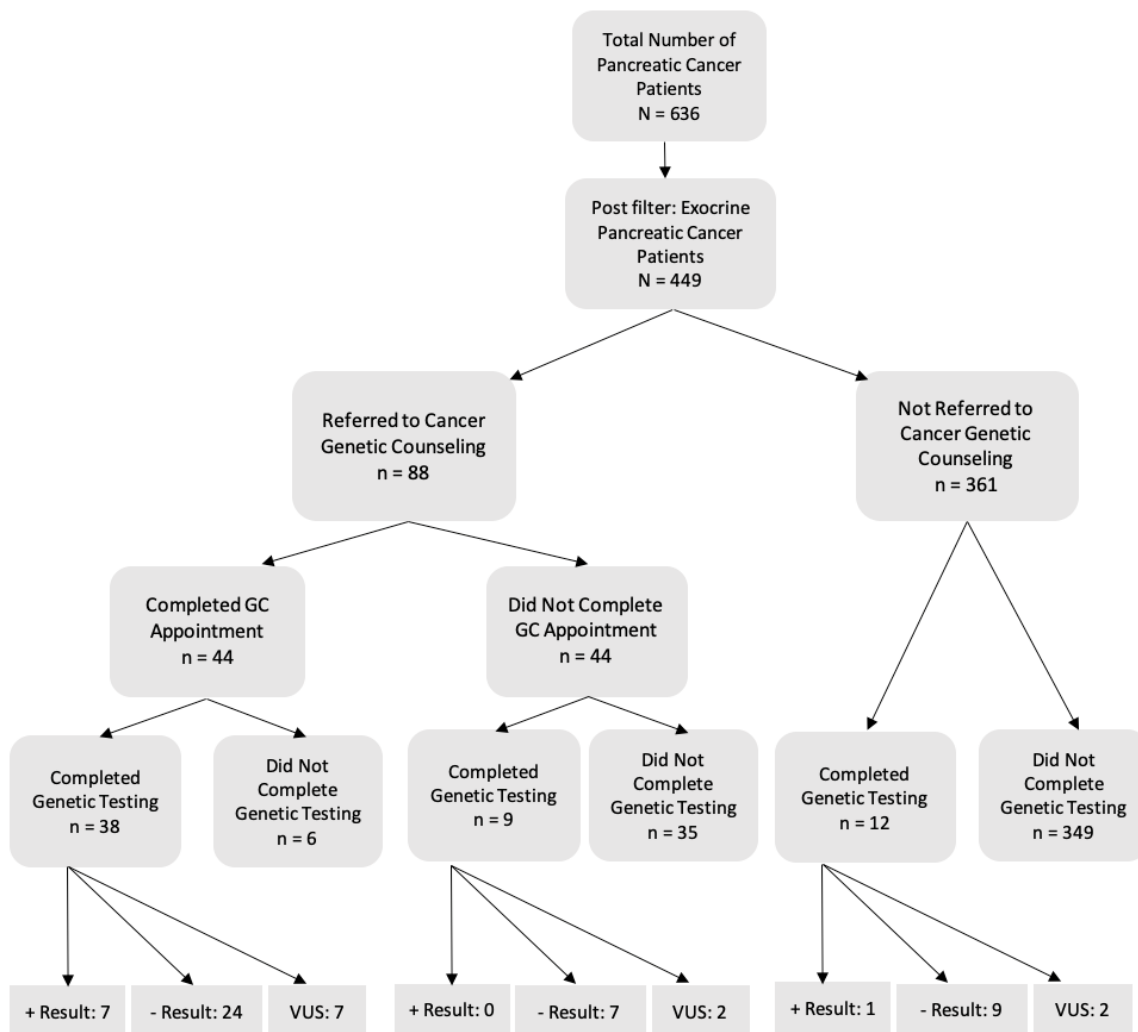
The University of Pittsburgh Institutional Review Board (IRB) and the Geisinger Institutional Review Board (IRB) both reviewed this research study, and it was deemed exempt as a quality improvement study using deidentified patient data. A “No Human Subject” Approval Letter was issued on December 7, 2021, and this study was approved as Quality Improvement under the American College of Surgeons Commission on Cancer accreditation requirements. An AAMC Uniform Clinical Training Affiliation Agreement Implementation Letter was filled out and signed, serving as a Data Use Agreement (Appendix A).

### **2.2.2 Data Analysis**

The following four data analyses were performed on the pulled and filtered data set of the 449 patients detailed above, using Excel spreadsheets and simple descriptive statistics:

- I. What are the rates of cancer genetic counseling referrals for patients diagnosed with pancreatic cancer at Geisinger across each Geisinger clinic location?
- II. What percentage of these referrals completed genetic counseling appointments across each Geisinger clinic location?
- III. What percentage of these completed referrals continued to get germline genetic testing across each Geisinger clinic location? How many genetic tests were ordered by medical professionals other than genetic counselors?
- IV. How many of those that had genetic testing, had a positive/negative/VUS result?





**Figure 1: Flowchart for Genetic Counseling Referrals and Genetic Testing**

Figure 1. visually portrays a web diagram depicting the total number of pancreatic cancer patients included in this study, broken down by referrals to genetic counseling and completion of genetic counseling appointments. These patients are broken down further to show genetic testing results for those who had genetic testing ordered, whether it was done after a completed genetic counseling appointment or not.

## 2.3 Results

To organize and summarize the overall data collection depicted in the above flowchart further, the patient data was separated by referral status across the three Geisinger clinical sites. This is depicted in Table 2 below.

**Table 2: Genetic Counseling Referrals and Genetic Testing by Clinical Site**

	<b>GMC</b>	<b>GWV</b>	<b>GLH</b>	<b>Totals</b>
<i><b>Pancreatic Cancer Diagnoses</b></i>	238	170	41	449
<i><b>Genetic Counseling Referrals</b></i>	43	43	2	88
<i><b>Completed Genetic Counseling Appointment</b></i>	18	26	0	44
<i><b>Completed Genetic Testing after Genetic Counseling</b></i>	17	21	0	38
<i><b>Completed Genetic Testing Ordered by Other Provider</b></i>	11	10	0	21
<i><b>Completed Genetic Testing, with or without Genetic Counseling</b></i>	28	31	0	59
<i><b>Contains the summarized and focused data set information for the first three data analyses after filtering out pancreatic cancer types and other Geisinger locations, all stratified by Geisinger locations [GMC (Geisinger Medical Center), GWV (Geisinger Wyoming Valley), and GLH (Geisinger Lewistown Hospital)].</b></i>				

### 2.3.1 Cancer Genetic Counseling Referral Rates by Clinical Location

The first test conducted looked at cancer genetic counseling referral rates by clinical location. Rates of genetic counseling referrals were found to vary across each Geisinger location. Shown by Table 3, 18% of patients undergoing treatment for pancreatic cancer at Geisinger Medical Center were referred to genetic counseling, whereas 25% were referred at Geisinger Wyoming Valley, and 5% for Geisinger Lewistown Hospital. About 1/5 of pancreatic cancer patients got referred in total.

**Table 3: Genetic Counseling Referrals by Clinical Site**

	<b>GMC</b>	<b>GWV</b>	<b>GLH</b>	<b>Totals</b>
<i><b>Pancreatic Cancer Diagnoses</b></i>	238	170	41	449
<i><b>Genetic Counseling Referrals</b></i>	43	43	2	88
<i><b>Percentage of Patients that were referred to Genetic Counseling Appointments</b></i>	18%	25%	5%	20%
<i><b>Contains the summarized genetic counseling referrals and referral rates for pancreatic cancer patients within the data set, all stratified by GMC (Geisinger Medical Center), GWV (Geisinger Wyoming Valley), and GLH (Geisinger Lewistown Hospital).</b></i>				

A Chi-squared test was done to analyze whether there was a significant difference of genetic counseling referrals between the three Geisinger clinical sites. The null hypothesis stated that referral status and Geisinger clinical location are independent. This null hypothesis was rejected based on the Chi statistic (9.491918626) being more than the  $\chi^2_{.050}$  Chi critical value (5.991). The p-value was statistically significant (p = 0.022020233). Therefore, this analysis

supports the alternate hypothesis that referral status and Geisinger clinical location are not independent. In conclusion, there is a relationship between referral status and Geisinger clinical location; one factor depends on the other. In other words, there is a statistical difference between referral rates across the three clinical sites.

### 2.3.2 Cancer Genetic Referral Completion Rates by Clinical Location

Rates of completed genetic counseling referrals by patients going to the appointments were highest for the Geisinger Wyoming Valley location at 60%, whereas 42% of genetic counseling referrals at Geisinger Medical Center were completed. No patients referred to the Geisinger Lewistown Hospital completed their genetic counseling appointment. In total, 50% of genetic counseling appointments from referrals were completed. These referral completion rates are depicted in Table 4 below.

**Table 4: Genetic Counseling Appointment Completions after Referrals by Site**

	<b>GMC</b>	<b>GWV</b>	<b>GLH</b>	<b>Totals</b>
<i>Genetic Counseling Referrals</i>	<b>43</b>	<b>43</b>	<b>2</b>	<b>88</b>
<i>Completed Appts</i>	<b>18</b>	<b>26</b>	<b>0</b>	<b>44</b>
<i>Percentage of Patients that were Referred and Completed their Genetic Counseling Appointments</i>	<b>42%</b>	<b>60%</b>	<b>0%</b>	<b>50%</b>
<i>Contains the summarized completed genetic counseling referrals by pancreatic cancer patients within the data set completing their appointments, all stratified by GMC (Geisinger Medical Center), GWV (Geisinger Wyoming Valley), and GLH (Geisinger Lewistown Hospital).</i>				

Due to a low number of data, a Fisher Exact test was then used to better analyze differences in variables. Results from the Fischer Exact test showed a non-significant p-value as well ( $p = 0.0799340101$ ), Based on these two analyses, there is no relationship between referral status and Geisinger clinical location, so there is not a statistical difference between genetic counseling appointment completions after referral across the various clinical sites.

### 2.3.3 Completed Genetic Testing Rates with or without Completing Referrals

This analysis explored genetic testing completed overall within the dataset. Among those that completed their scheduled genetic counseling appointments after a referral, 86% (38/44 patients) underwent genetic testing. This contrasts with those patients that received a genetic testing result without having a genetic counseling appointment, only showing a total of 5% (21/405 patients). Of everyone diagnosed with pancreatic cancer, about 13% (59/449 patients) underwent genetic testing regardless of genetic counseling appointment completion status. This includes any provider ordering testing: Oncologists, Surgeons, Genetic Counselors, and Primary Care Physicians. These results are summarized in Table 5.

**Table 5: Genetic Testing According to Genetic Counseling Appointment Status**

	GMC	GWV	GLH	Totals
<i>Patients that Completed GC (Genetic Counselor) Appt</i>	18	26	0	44
<i>Patients that had a Genetic Testing Result after Completing GC Appt</i>	17	21	0	38

<i>Percentage of Patients that had a Genetic Testing Result after Completing GC Appt</i>	<b>94%</b>	<b>81%</b>	<b>0%</b>	<b>86%</b>
<i>Patients that did not Complete GC Appt</i>	<b>220</b>	<b>144</b>	<b>41</b>	<b>405</b>
<i>Patients that had a Genetic Testing Result without Completing a GC Appt</i>	<b>11</b>	<b>10</b>	<b>0</b>	<b>21</b>
<i>Percentage of Patients that had a Genetic Testing Result without Completing a GC Appt</i>	<b>5%</b>	<b>7%</b>	<b>0%</b>	<b>5%</b>
<i>Total Pancreatic Cancer Diagnoses</i>	<b>238</b>	<b>170</b>	<b>41</b>	<b>449</b>
<i>Patients that Completed Genetic Testing, with or without Genetic Counseling Appt</i>	<b>28</b>	<b>31</b>	<b>0</b>	<b>59</b>
<i>Percentage of Patients with a Genetic Testing Result</i>	<b>12%</b>	<b>18%</b>	<b>0%</b>	<b>13%</b>
<i>Table 5 details the summarized genetic testing rates for pancreatic cancer patients within the data set, divided into three sections for those that had genetic counseling appointments completed, those that had no genetic counseling appointments, and all patients that had genetic testing results regardless of their appointment completion status, all stratified by GMC (Geisinger Medical Center), GWV (Geisinger Wyoming Valley), and GLH (Geisinger Lewistown Hospital).</i>				

### 2.3.4 Genetic Testing Results by Clinical Location and Referral Completion

Looking at the overall genetic testing results for patients within this data set, Table 6 depicts overall genetic testing results for the patients that had genetic testing done. About 14% were positive, 68% were negative, and 19% were variants of unknown significance. Table 7 separates patients that had genetic testing done after having a genetic counseling appointment. After a genetic counselor ordered testing for these patients, about 18% were positive, 63% were negative, and 18% were variants of unknown significance. Table 8 separates patients that had genetic testing

done without having a genetic counseling appointment. After other medical providers like Primary Care Physicians or Oncologists ordered their testing, about 5% were positive, 76% were negative, and 19% were variants of unknown significance. Types of ordered genetic tests included panels and single gene testing from various laboratories, including Ambry, Baylor, Invitae, Myriad, unknown labs, and MyCode, which is a population-based genomic screening research study offered to all patients across the Geisinger enterprise.

**Table 6: Total Genetic Results by Clinical Site**

<b><i>Total Genetic Testing Results</i></b>	<b>GMC</b>	<b>GWV</b>	<b>GLH</b>	<b>Totals</b>
<b><i>Positive</i></b>	4	4	0	8 (13.6%)
<b><i>Negative</i></b>	19	21	0	40 (67.8%)
<b><i>VUS</i></b>	5	6	0	11 (18.6%)
<b><i>Total</i></b>	28	31	0	59 (100%)

***Depicts the genetic testing results stratified by clinical location for all patients that underwent genetic testing, regardless of who ordered it and whether genetic counseling appointments were completed (N= 59). GMC (Geisinger Medical Center), GWV (Geisinger Wyoming Valley), and GLH (Geisinger Lewistown Hospital); VUS (Variant of Unknown Significance).***

**Table 7: Genetic Testing Results after Completing Genetic Counseling Appointments**

<i>Total Genetic Testing Results After GC Appointment</i>	<b>GMC</b>	<b>GWV</b>	<b>GLH</b>	<b>Totals</b>
<i>Positive</i>	3	4	0	7 (18.4%)
<i>Negative</i>	11	13	0	24 (63.2%)
<i>VUS</i>	3	4	0	7 (18.4%)
<i>Total</i>	17	21	0	38 (100%)

*Depicts the genetic testing results stratified by clinical location for patients that underwent genetic testing by genetic counselors after their genetic counseling appointments were completed (N= 38). GMC (Geisinger Medical Center), GWV (Geisinger Wyoming Valley), and GLH (Geisinger Lewistown Hospital); VUS (Variant of Unknown Significance).*

**Table 8: Genetic Testing Results without Completing Genetic Counseling Appointments**

<i>Total Genetic Testing Results Without GC Appointment</i>	<b>GMC</b>	<b>GWV</b>	<b>GLH</b>	<b>Totals</b>
<i>Positive</i>	1	0	0	1 (4.8%)
<i>Negative</i>	8	8	0	16 (76.2%)
<i>VUS</i>	2	2	0	4 (19.0%)
<i>Total</i>	11	10	0	21 (100%)

*Depicts the genetic testing results stratified by clinical location for all patients that underwent genetic testing without genetic counseling appointments, ordered by providers other than genetic counselors (N= 21). GMC (Geisinger Medical Center), GWV (Geisinger Wyoming Valley), and GLH (Geisinger Lewistown Hospital); VUS (Variant of Unknown Significance).*



## 2.4 Conclusions and Implications

### 2.4.1 Genetic Counseling Referral Rates

Overall, about 1 out of 5 people diagnosed with pancreatic cancer and treated at any of the three different Geisinger locations were referred to their respective cancer genetics clinic for genetic counseling. This is lower than the NCCN recommended rate of 100% of patients. Geisinger Wyoming Valley had the highest genetic counseling referral rates of about 25%. This was surprising, because Geisinger Medical Center is the hub and the largest hospital of all site locations, but there was only approximately an 18% referral rate. A Chi-square analysis was performed, and the result was statistically significant, showing that referral status and Geisinger clinical location are not independent. In other words, depending on where a patient is diagnosed, they will have a higher or lower chance to be referred to genetic counseling. Geisinger Wyoming Valley does have an older population, however, which may have influenced these results. The Geisinger Wyoming Valley clinic resides in Wilke-Barre of Luzerne County, which is considered part of the Northeast Region of Pennsylvania. According to the “*Geisinger Community Health Needs Assessment 2021*,” the Northeast Region is aging at a faster rate than the Pennsylvania state average (Geisinger Community Health Needs Assessment, 2021). Although younger cancer patients tend to be referred to genetics more often due to increased suspicions of hereditary syndromes, perhaps a clinic with an established older population has more resources geared toward treatment and management of older-onset diseases like cancer, increasing their referral rates (Wurtmann et al. 2022). It is difficult to draw any conclusions, however, given the lack of demographic data from this study. Geisinger Lewistown Hospital had the lowest genetic

counseling referral rate, at only 5%. Regardless of the demographics for each clinical site, these rates need improved to meet recent NCCN Guidelines to refer all patients with exocrine pancreatic cancer diagnoses to genetic counseling (NCCN Guidelines for Patients Pancreatic Cancer, 2021).

Many studies focus on interventions that recognize at-risk individuals for hereditary causes of cancer, then provide genetic counseling referrals. One such intervention is the Genetic Cancer Screening Tool (GCST), an Electronic Health Record (EHR) integrated tool with the goal of increasing genetic counseling referral rates for primary care patients at risk by screening family histories of different cancers, including pancreatic (Wurtmann et al. 2022). After implementing this screening tool, the researchers measured success of increasing referrals, resulting in genetic counseling referral orders placed for 13% of their study population that screened positive for being “at-risk” after using their GCST (Wurtmann et al. 2022). In comparison, this percentage is lower than Geisinger’s overall referral rates for pancreatic cancer patients of 20%. Though this study focuses on a different population, particularly an undiagnosed population, it may provide an additional opportunity for patients to address care gaps outside of their oncology visits. Most patients with pancreatic cancer will still see their primary care doctor for other needs, and this could be a value-add for services.

One study focused on the implementation of an automated genetic referral workflow for pancreatic cancer patients in a single medical institution, specifically for pancreatic ductal adenocarcinoma (Chittenden et al., 2021). About ¼ of the automated referrals ended up in a genetic counseling appointment the same day of meeting with the oncologist, which may not be feasible for every department. Regardless, this automated referral system more than doubled their germline genetic testing rates (from 16.5% to 38.0%) when compared to their previous model of genetic testing rates from provider choice only (Chittenden et al., 2021). This strategy demonstrates that

on-demand services may increase both referral rates as well as germline genetic testing (Chittenden et al., 2021). An intervention that allows a provider to refer to a genetics program for coordination of testing to handle collection of family history, discussion of insurance coverage, and logistics of test completion may be more appealing to oncologists working in a high-volume clinical setting.

Future studies should examine further and focus on how hospital systems can increase these rates effectively. Interventions could focus on educating providers on genetic resources and information or exploring difficulties with contacting local cancer genetics clinics for the referral process. One thing the GCST did well was increase the amount of primary care physicians that ordered at least one referral from 1/26 to 11/26 providers in their study (Wurtmann et al. 2022). Interventions like this can help clinics place referrals by targeting providers that do not typically place them and reduce the mental burden of referring providers to remember all extra items outside the primary reason for the visit to the clinic that day.

#### **2.4.2 Genetic Counseling Appointment Completion**

Overall, the appointments completed for referred Geisinger patients was 50%. According to clinical sites, Geisinger Wyoming Valley had 60%, Geisinger Medical Center had 42%, and Geisinger Lewistown had 0%. Fischer Exact Test results were not statistically significant for genetic counseling appointment completion status across the three different clinical sites, though there was a limited amount of data. Exploring the reasoning behind the differences in these rates could be beneficial toward improving Geisinger Lewistown Hospital. For instance, if the cancer genetics clinic is scheduling genetic counseling appointments weeks or months in advance, that may deter patients from scheduling or attending their appointments to begin with. Reasons for

patients not attending their genetic counseling appointments are also important factors to consider. Poor survival rates with pancreatic cancer could affect referral rate and test completion decision-making. Referred patients may have had intentions to attend their scheduled appointments but may have been admitted due to complications from treatment, passed away, or been too ill to complete a telehealth visit. Other patients may have elected into hospice or palliative care, and decided with their oncologist to forego treatments that would not impact their immediate quality of life. At Geisinger, the genetics team prioritizes pancreatic cancer cases, but sample collection and test completion can be delayed if a patient isn't on site for the genetics visit. In the literature, bad timing (or too much stress), not wanting to know results, and financial concerns ranked among the top three reasons for patients not completing genetic counseling appointments for newly diagnosed breast cancer patients (Hafertepen et al., 2017).

Offering telemedicine or telephone appointments may help these patients, allowing patients to easily meet with a genetic provider in addition to their other cancer diagnosis follow-up appointments. One study explored the effectiveness of a telehealth genetic intervention for male patients diagnosed with prostate cancer, in the form of meeting a medical oncologist and genetic counselor to facilitate germline genetic testing in a timely manner (Kwon et al. 2023). Originally, this intervention was in-person and imbedded into their clinics, but the pandemic forced them to adapt with remote access. They found that the success of their intervention model did not statistically differ from in-person to telemedicine, and that their rates of germline testing were at about 83% overall after the intervention was implemented (Kwon et al. 2023). When comparing pre-intervention clinical germline genetic testing rates of the clinic to post-intervention, the study found that testing rates increased from 9% to 53% within a 60-day window of having their oncology appointment (Kwon et al. 2023). This is especially interesting considering the current

study focuses on a population where time is of the essence. Focusing interventions on effectiveness and capacity of these cancer genetics clinics could improve genetic counseling appointment completion rates, and therefore genetic testing rates. At Geisinger, "...genetic counseling services transitioned to more than 95% telehealth as of March 2020, to adapt to the pandemic and improve accessibility" (Heather M. Rocha, LGC, personal communication, April 12, 2023).

The University of California in San Francisco implemented an in-clinic genetic testing station to expedite genetic counseling appointment referrals, decrease appointment attrition rates, and increase genetic testing completion rates for patients with pancreatic cancer (Walker et al., 2021). A post-implementation study revealed that not only did it increase genetic testing rates from 19% to 71%, but it also decreased attrition rates for genetic counseling from 36% to 3% (Walker et al., 2021). These results are promising and could serve as an example for Geisinger or other clinics to streamline care effectively. To do so, UCSF placed a multidisciplinary team within the Gastrointestinal Medical Oncology clinic, including a Nurse Navigator, New Patient Coordinator, Genetic Counseling Assistant that works a kiosk that provides pre-test counseling and additional information, and a supervising Genetic Counselor also available for further pre-test counseling and follow-up (Walker et al., 2021). Heather M. Rocha, LGC explained that "Geisinger has entertained this idea in the form of a tablet device rather than a kiosk, available for providers to hand directly to patients" (personal communication, April 12, 2023).

### **2.4.3 Genetic Testing Completion**

Once a patient was referred and completed their genetic counseling appointments, an overall rate of 86% (38/44) underwent testing. Geisinger Medical Center had the highest success

for genetic testing rates after completing an appointment, at about 94% (17/18). Geisinger Wyoming Valley had a genetic testing rate of 81% (21/26) after meeting with a genetic counselor, and Geisinger Lewistown Hospital had 0% (0/0). For context, after implementation of the prostate cancer genetic testing intervention mentioned above, genetic testing rates were measured at 83% (Kwon et al. 2023). For this study, when comparing the overall rate of genetic testing done without having genetic counseling, there was a stark difference. Data showed that only 5% of patients had genetic testing done when ordered through a different medical provider, not having completed a genetic counseling appointment. This shows that having genetic counselors involved in the germline genetic testing process positively impacts test recommendation and completion rates. Therefore, interventions that facilitate referral to cancer genetic counselors, increasing appointment completion rates, and hiring more genetic counselors to handle these increases in referrals could improve overall genetic testing rates, which was about 14% for this data set, regardless of genetic counseling referral or appointment completion status. Implementing streamlined genetic testing services after a cancer diagnosis, like the telemedicine model from the Kwon et al. study, could help increase appointment completion rates, but it may not be successful without enough medical staff to train and facilitate the intervention. This was listed in their discussion section for future concerns (Kwon et al. 2023).

Since NCCN Guidelines recommend universal germline testing for patients with exocrine pancreatic cancer diagnosis, the identification process for those who are eligible for such testing is simplified, as compared to other cancer sites with more complex criteria involving age at diagnosis with or without additional family cancer history. Pathologists, oncologists and surgeons can easily identify appropriate candidates for germline studies at the time of diagnosis and make

determinations about the timing and necessity of testing. Interventions, therefore, could focus on genetic test ordering and logistics rather than facilitating referrals.

One recent study analyzed their germline genetic testing rates across a hospital system without an automated system and genetic test ordering under each provider's discretion alone between 2019 and 2021 (Crowley, Gandhi et al. 2023). Genetic referrals were made primarily after a germline mutation was established, which is also a more effective use of genetic services if test selection is simplified. Their genetic testing rates for patients with exocrine pancreatic cancer increased each year, averaging 44% from 2019 to 2021 and having about 61% in 2021. These results are lower than rates of genetic testing seen for cancer patients that met with genetic counseling in this Geisinger study (86%), but when compared to overall testing rates, it is nearly four times higher (13%). Looking at this study's referral and genetic testing rates across each year could reveal improvements in genetic testing rates like the Crowley et al study did, as provider awareness of guidelines, comfort with germline testing, and education is likely to improve over time as these guidelines becomes more familiar (Crowley, Gandhi et al. 2023). Given the structure of their clinic, they did not analyze referral rates, but they did point out the lack of genetic professionals in the workforce and the need to keep up with increasing recommendations for referrals and genetic testing (Crowley, Gandhi et al. 2023).

#### **2.4.4 Genetic Testing Results**

When analyzing the types of genetic testing results across the three Geisinger locations, about 14% of patients diagnosed with pancreatic cancer that underwent testing yielded positive results. These study results show higher positive rates than the average 5-10% found in the general

population in previous studies (Uson, Samadder et al. 2021). Future studies on why these results are higher may be warranted to set an example for other health institutions on how to test their patients more effectively, though the difference could be due to the small sample size represented in this study. One other explanation could reside in the context of the study population. Patients through the Geisinger Medical Institute can take part in a populational research study called MyCode, which analyzes genomic information and returns medically actionable results, like pathogenic variants in cancer susceptibility genes. In addition to this, there are many staffed genetic counselors at Geisinger Medical Center and Geisinger Wyoming Valley, which might contrast other clinics across the country. Geisinger Lewistown Hospital is not as well staffed, which may be reflected in their lower genetic counseling referral rates and limited genetic testing.

Furthermore, when ordered by a genetic counselor, rates of a positive result were higher (18%) when compared to positive results when ordered from a different medical provider, not having a genetic counseling appointment (5%). We suspect this may be because providers may be referring patients with more complex family history where the standard germline panel may not feel like appropriate coverage for all cancer types reported in the family. This study did not collect or address family history information, however. In addition, there are known test ordering differences. The current workflow recommends a 20 gene hereditary pancreatic cancer panel that does not include limited evidence genes or genes involved in hereditary pancreatitis. Because genetic counselors are comfortable ordering larger panels, this may contribute to the increased rate of positive results. Looking at the data this was unclear, showing 31/38 tests ordered by Genetic Counselors as panels with the remaining 7 tests not specified, and 19/21 tests ordered by providers other than Genetic Counselors were larger panels (2/21 were Baylor: BRCA1/2 and Myriad: MLH1/MSH2 testing).



#### **2.4.5 Geisinger Interventions**

After performing this data analysis, an exploration of existing interventions at Geisinger revealed that they have attempted to implement four separate public health interventions to increase genetic counseling referral rates and genetic testing rates, which included: clear EHR documentation of recommendations, flagging pathology reports, educating the nursing staff, and paired tumor testing.

One of these four interventions was implemented and established, in the form of clear EHR documentation provided to medical providers during tumor board meetings. This documentation clearly outlines recommendations made by genetic counselors for medical oncologists to order genetic testing for their pancreatic cancer patients, through a panel offered by a contracted, commercial laboratory (Pancreatic Cancer Panel) following tumor board discussion. This document clearly dictates responsibility to the treating provider, whether it be the surgeon or oncologist depending upon staging and immediate management recommends, along with the option to either refer the patient for full family history evaluation, education, and coordination of testing, or for the presenting provider to order testing with recommendation for follow up by Cancer Genetics, only if a positive result is found. This intervention has been well accepted by Geisinger medical providers involved in tumor board meetings, and the process has continued (Heather M. Rocha, LGC, personal communication, April 12, 2023). The impact of this intervention is currently under investigation and is not reported in this study.

The other three interventions were not as fruitful. One intervention involved flagging pathology reports with pancreatic adenocarcinoma results by adding “consider referral to genetics” at the bottom of the pathology report. This plan was initially declined by laboratory medical

leadership given their unfamiliarity with the recommendation and reservations about dictating necessity of germline testing versus tumor testing.

Another intervention involved teaching the nursing staff involved with pancreatic cancer patient treatment across four clinical sites, Geisinger Wyoming Valley, Geisinger Medical Center, Selinsgrove, and West Clinic. Unfortunately, after starting this program, staffing turnover and re-training overburdened and overworked support staff created barriers to success related to the pandemic. With high rates of support staff turnover, it became burdensome to train and re-train nursing staff for testing that was ordered infrequently and didn't fall within their typical or accustomed workflows. This workflow was attempted for 18 months and continues on a case-by-case basis.

The last intervention focused on increasing genetic testing rates by sending paired tumor-testing with germline testing to an outside laboratory. This intervention was started and only used for a handful of patients, and it ceased once Geisinger started ordering in-house tumor testing only two months after initiating the workflow. The starting and stopping periods of each intervention were not identified.

#### **2.4.6 Limitations**

Limitations for this study include the dates of which these data were collected. Retrospectively, these data were collected for patients diagnosed between July of 2019 to June of 2020. The shortened timeline of 1 year presents challenges in studying the impact of interventions that were initiated during the study period. There were also challenges in gathering additional data from each patient and this resulted in excluding some patients for missing data, exemplified by

patients referred to other clinics that may or may not have had genetic counseling or testing. Additionally, this timeline does not allow for the assessment of referral rates over time, as referrals may have increased as provider knowledge about the guidelines increased. Additional patient data collected at least until 2021 could have allowed a further analysis of the interventions that Geisinger has already implemented or attempted to implement. Data from this study was collected on patients before and during the COVID-19 pandemic, with lockdowns starting in March 2020. This may have affected the study results, though Geisinger's transition to remote genetic counseling was smooth with patient adherence to adapted telemedicine and telephone visits (Heather M. Rocha, LGC, personal communication, April 12, 2023).

A second limitation was the lack of demographic information contained in the original data set. Attempts to collect additional demographic data, including age of onset, race, sex, and zip-codes for all patients, were made but not able to be achieved. This information, however, could be important for future directions since past studies have shown disparities in genetic counseling referral rates and germline genetic testing for cancer patients of minority populations (Dharwadkar et al. 2022). Revealing gaps in quality of healthcare can help focus public health interventions on helping subgroups more equitably. For example, another possible limitation of this study, regarding the higher rates of positive genetic testing results from ordering genetic counselors, could be associated with socioeconomic status and family history. Without this data, however, we cannot make these conclusions. This data can be collected for future analyses to facilitate more equitable analyses and subsequent policy creation.

Additionally, as mentioned above, survival rates are poor for pancreatic cancer patients. Patients dying prior to their scheduled genetic counseling appointments will affect these results more so than other illnesses that patients survive longer. We are aware of at least two patients who

died before an appointment could be completed, which indicates very advanced stage at diagnosis given the Cancer Genetics program workflow to schedule these patients within a week of referral. Some treating providers may elect not to refer to genetics or complete germline testing if the patient has declined further follow up, chemotherapy, or other interventions. This limitation can be accounted for in future analyses as vital status was collected, but date of death was not. The filtering of pancreatic cancer histologic subtypes that have a less degree of concern for a genetic underlying basis were excluded, but mixed histologies were included if any portion of the tumor was reported as an adenocarcinoma. Carcinoid, neuroendocrine tumors, and lymphoma in the pancreas were excluded.

Later in 2022, there was an attempt to collect additional data for further analysis. Initially, the collection of zip-code data was discussed to collect information and reflect on socioeconomic status regarding genetic counseling referrals and genetic testing rates. This was denied since this additional data would be Protected Health Information (PHI) and the data would no longer be de-identified, remarkably changing the established IRB approval terms. Age of diagnosis, sex, race, and extending the original data timeline from 2019-2020 to 2019-2021 for patient information was also discussed in greater detail. This separate proposal for pulling additional deidentified data was taken through the IRB adjustment and approval process. Unfortunately, IRB approval could not be granted within a reasonable time of completing this research project, due to extenuating circumstances with Geisinger's IRB, so additional PHI was not available for review and comment as part of this study.

### **3.0 Research Significance to Genetic Counseling and Public Health**

In the realm of cancer management, genetic counselors and other medical providers use established guidelines to provide consistent care options to patients. As this study has pointed out, guidelines have already recommended that pancreatic cancer patients should receive genetic services through means of genetic counseling and genetic testing (Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic NCCN Guidelines, 2023). Converting these guidelines into practice, however, is neither immediate nor straightforward.

Applying a public health lens can help address systematic issues in the field of genetic counseling. The three core functions of public health created in 1994 provide a useful framework and should be addressed: assessment, policy development, and assurance (Castrucci, 2021). According to “The Futures Initiative: the 10 Essential Public Health Services, the de Beaumont Foundation,” recent revisions were made to the framework in 2020, focusing core functions and services through the lens of health equity. This study primarily focuses on the first major function of public health: assessing, investigating, and discussing public health in the context of genetic service delivery in the clinical setting.

Before exploring any public health issue further, every interested party should first be considered. For instance, a goal of this research project was to explore strategies put in place to increase rates of delivering genetic services, which would impact the patient population, their families and loved ones, the hospital system, medical oncology team and clinic, Cancer Genetic Counselors and genetics clinic, and others. Each stakeholder will have an impact on public health interventions and their effectiveness in practice. Through a scope of health equity, research like

this study and others before it, remains at the heart of public health intervention, providing information to lay the groundwork for creating, evaluating, and optimizing programs and strategies.

This research project assesses information on how genetic services are being provided and utilized at three specific Geisinger cancer clinics. To increase provision of genetic services to meet recommended national guideline standards, understanding the status of the service delivery is the first step. Specifically, this study assessed genetic counseling referral rates for pancreatic cancer patients, genetic counseling appointment completion rates if referred, and genetic testing rates across all pancreatic cancer patients with or without having met with a genetic counselor. From a health equity perspective, prior studies have shown under-referral and lower genetic testing rates for individuals in minority populations (Singh et al. 2022). These gaps prevent people of certain races and ethnicities from accessing important healthcare opportunities like targeted therapies. Before starting this study, it was mentioned that ethnic and race data may not have been accurately collected or input from providers, pointing out a flaw in data collection and missing opportunities to investigate vital statistics and possible disparities that should be addressed. Although everyone with an exocrine pancreatic cancer diagnosis should be referred to genetic counseling and have the option for testing, gaps could exist for minority groups of this study population consistent with previous literature.

Existing interventions and their examples of successes can direct policy development. Geisinger has developed, implemented, and continues to use clear documentation for cancer genetic referrals and genetic testing panel recommendations given to providers during tumor board meetings. Geisinger's paired tumor testing intervention mentioned in this study was short-lasting due to a shift in ordering genetic testing via outside establishments to an in-house laboratory. A

similar intervention, as outlined by a previous study, describes an automated referral system that was implemented for colorectal cancer patients, showing increased rates in referrals to appropriate patients as well as showing no statistical differences in referrals made to minority populations when compared to Non-Hispanic Whites (Singh et al. 2022). Knowing this, Geisinger's paired tumor testing intervention could be worth re-exploring to not only improve referral rates but improve referral rates equitably.

Lastly, although the data did not compare genetic service rates before and after an intervention, this research study revealed aspects of the third core function of public health; assurance. One key stakeholder includes the hospital system itself and the quality of their cancer clinics. Different associations exist to help maintain the quality of these different programs. For example, the American College of Surgeons has many roles and functions. One function focuses on improving standards and outcomes for patients with cancer, such as increasing access to genetic services, and it is carried out by a consortium of professional organizations called the Commission on Cancer (CoC) (Schroeder et al. 2022). The Commission on Cancer can grant hospital systems and branches with accreditation by sending on-site visits every three years to review clinical activity, address standards of care, and ensure compliance. This is one way to have a third-party check on the quality of care distributed by Geisinger cancer clinics. It is important to keep in mind that these quality improvement and evaluations are not perfect, as one study points out the lack of data on non-accredited cancer clinics in rural areas which could contribute to disparities in cancer treatment and outcomes between rural and urban patients (Schroeder et al. 2022). Other evaluations should then be in place, for instance, studying the effectiveness of the clear documentation intervention at Geisinger in addition to collecting and evaluating racial data to see if there are any differences in referral rates, completion rates, and genetic testing rates that should

be addressed. In addition to patient-facing duties, Genetic Counselors may be involved with CoC evaluations or other measures of intervention successes, and therefore should familiarize themselves.

In summary, this study can serve as a reference for future researchers that want to compare delivery and effectiveness of genetic services provided to pancreatic cancer patients before and after Geisinger interventions. It outlines the need for attention to health equity data input, collection, and analysis to create more equitable strategies. Simple standardized data collection that includes demographics could also save time for those analyzing the data and provide clarity in results. Looking toward the future, assuring the quality and accessibility of these services could be done by expanding data to measure successes of the various interventions that Geisinger has implemented, starting with the ongoing clear documentation presented to oncology providers at tumor board meetings. Additionally, knowing the successes of previous studies with increasing cancer genetic referral rates in a health equitable fashion, a discussion on revisiting the intervention of paired-tumor testing after a pancreatic cancer diagnosis is recommended. The intervention that educated oncology nurses about appropriate cancer genetic referrals was not successful at Geisinger due to workload and employee turnover. This is a public health issue that should be addressed. Perhaps this issue has been resolved with recent hires and clinic stability, in which case revisiting this intervention might be worthwhile. Revisiting the intervention that was turned down by leadership, adding notes with clear referral instructions to the bottom of pancreatic adenocarcinoma pathology reports, could help bypass an overworked nursing staff and increase referral rates. Lastly, increasing genetic referrals would increase workload for the genetic counselors, and to prevent this same type of burnout from occurring, focusing on the capacity of these cancer clinics should also be explored.



## **4.0 MPH Chapter: Intervention Analysis**

### **4.1 Intro**

Genetic counselors effectively recognize people with higher chances for a genetic condition that could benefit from genetic testing. If a genetic condition is identified, clinical management for these individuals can be altered to monitor their health more closely or prevent serious disease. Since genetic conditions can be passed down through families, preventative and predictive testing can impact family members as well. Genetic counseling and genetic testing in the sphere of cancer genetics can reveal increased chances to develop cancers over the lifespan, provide cancer patients with a genetic cause for their diagnosis, and sometimes alter cancer treatment toward a more targeted and effective approach.

Oncologists and other physicians can order genetic testing directly, without referring their patients to genetic counseling for pre-test education and consent. Genetic counselors are trained medical professionals through ACGC-approved master's degree programs to better explain the nuances surrounding genetic testing, which can include genetic risk assessment, inheritance patterns, genetic testing and its effects on insurance policies and employment, clinical management, and psychosocial impacts. Additionally, genetic counselors can save institutions and patients money by ordering the most appropriate genetic test (Kotzer et al. 2013). Physicians do not typically undergo this specialized genetic training throughout medical school, though about 60% report having ordered testing in the past (Kotzer et al. 2013). In one study on Primary Care Physicians (PCPs) ordering genetic testing for their patients, these physicians reported several

barriers toward properly achieving one of the first steps in genetic counseling, a comprehensive risk assessment (Wurtmann, Baldinger et al. 2022). These barriers included self-reported lack of knowledge, lack of confidence discussing genetic testing with patients, challenges gathering family history information from patients, and time constraints (Wurtmann, Baldinger et al. 2022). Genetic counselors can help identify which patients would benefit the most from genetic testing through the development of clinical support tools and provide more comprehensive discussions surrounding the nuances mentioned above.

The National Comprehensive Cancer Network (NCCN) is viewed as an authoritative resource for evidence-based treatment recommendations per cancer site. Current guidelines recommend that all patients with exocrine type pancreatic cancer should have genetic services offered to them, because germline status could affect treatment options (NCCN Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic Version 1.2020). Clinics have shown pre-intervention rates of genetic testing far lower than the recommended guidelines, though these rates remain variable due to clinical differences like medical provider staffing, location, patient demographics, and financial implications (Walker et al., 2021). This thesis study analyzed de-identified patient data gathered from three specific cancer clinics that diagnosed patients with exocrine pancreatic cancer between the years 2019-2020, across three satellite hospitals from Geisinger in Central Pennsylvania. Results showed that overall genetic testing rates were lower than the NCCN recommended 100%, with a baseline of around 13% at the time of recommendation update. Another finding showed that when these genetic tests were ordered by genetic counselors, they ordered genetic testing at a much higher rate than physicians, shown as 86% compared to 5%. One similar study measured genetic testing success of a cancer clinic without interventions, from 2019 until 2021 (Crowley, 2023). This clinic showed that rates of genetic testing for exocrine

pancreatic cancer increased each year, without intervention. This clinic was based on the same model of provider discretion-based referrals and yielded overall about 44% genetic testing rates, well above Geisinger's 13% reported in this thesis study (Crowley, 2023). This shows that rates of genetic testing had increased after NCCN guidelines have been established in 2019, yet they still remain suboptimal (Crowley, 2023).

Based on the findings of these studies, there is a need to increase genetic testing rates for pancreatic cancer patients to meet the recommended national cancer guidelines and improve overall patient outcomes. Additionally, increasing referrals to genetic counselors has been shown to be an effective method toward increasing genetic test ordering and completion rates. This literature review analyzed existing clinical interventions aimed at increasing cancer genetic counseling referrals and/or cancer genetic testing rates in the context of this quality improvement thesis study. By looking at the successes of existing interventions unspecific to cancer sites, this literature review provides insight on which strategies could be most effective for improving pancreatic cancer patient care by increasing rates of genetic services.

## **4.2 Methods**

This literature search was performed using the following two databases, PubMed and primarily OVID MedLine. The search was intended to target and analyze existing public health interventions that focused on increasing cancer genetic counseling referral rates and/or genetic testing rates for individuals with a concern for cancer predisposition, whether affected or not. This essay focused on the interventions themselves in addition to measures of success after

implementation. First, a basic PubMed search was made, including terms: cancer genetic referrals, genetic counseling referrals, clinical interventions, increase genetic testing rates, increase genetic referral rates. To pull more articles of relevance, another more thorough literature search was made through OVID on February 17, 2023. To assess the most current information, English-language articles published from within a period of 2020-2023 were pulled, totaling 149 results. Among these results, 9 articles were reviewed to inform this essay, having chosen 3 articles for each of three categorized intervention models represented in the literature search. Appendix B depicts the second OVID literature search with each term included, showing line 30 as the final search resulting in 149 resources.

### **4.3 Results**

The articles with the most applicable discussions and interventions surrounding increasing genetic services in the cancer setting were analyzed in this literature review. In total, about 9 articles were reviewed, summarized below (Table 9). Interventions outlined by these articles spanned a number of different strategies to increase genetic services, either by increasing referral rates or genetic testing directly. These interventions were organized into separate categories, including family history assessment, referral systems, and point-of-care models.

Family history assessment interventions tended to focus on increasing referral rates for persons at high-risk for cancer syndromes. Referral system interventions also focused on increasing referral rates for persons at higher risk for cancer syndromes, and they tended to be more specific than the family history assessment interventions. Point-of-care models interventions

tended to focus on increasing genetic testing rates directly. These interventions had higher success rates in terms of increasing genetic testing, and they tended to bypass referrals.

**Table 9: Cancer Genetic Service Intervention Models and Examples in Literature**

Intervention Model	Article	Intervention	Setting	Results
Family History Assessment	<p><a href="#">“An Electronic Health Record Tool Increases Genetic Counseling Referral of Individuals at Hereditary Cancer Risk: An Intervention Study.”</a></p> <p>Wurtmann, Elisabeth J., et al. “An Electronic Health Record Tool Increases Genetic Counseling Referral of Individuals at Hereditary Cancer Risk: An Intervention Study.” <i>Public Health Genomics</i>, vol. 25, no. 5-6, 2022, pp. 134–140., <a href="https://doi.org/10.1159/000525447">https://doi.org/10.1159/000525447</a>.</p>	Genetic Cancer Screening Tool (GCST) via EHR	2 PCP Clinics in Minnesota, (one rural, one urban), for unaffected patients at-risk for cancer syndromes.	<p>Increased cancer genetic counseling referrals after wellness visits from 0.1% (1 of 1,086) to 2.1% (22 of 1,062).</p> <p>Increased proportion of referring providers from 3.8% (1 of 26) to 42.3% (11 of 26).</p>
	<p><a href="#">“Implementation-effectiveness trial of systematic family health history-based risk assessment and impact on clinical disease prevention</a></p>	Family health history-based health risk assessment (HRA) via EHR	19 PCP clinics in 4 diverse population/locations across 4 different	Genetic counseling referral rates of 9.4% (51 of 543) after PCP visit for positive screened patients (no pre-intervention rate measured).

	<p><a href="#">and surveillance activities”</a></p> <p>Wu, R. R., Myers, R. A., Neuner, J., McCarty, C., Haller, I. V., Harry, M., Fulda, K. G., Dimmock, D., Rakhra-Burris, T., Buchanan, A., Ginsburg, G. S., &amp; Orlando, L. A. (2022). Implementation-effectiveness trial of systematic family health history based risk assessment and impact on clinical disease prevention and surveillance activities. <i>BMC health services research</i>, 22(1), 1486. <a href="https://doi-org.pitt.idm.oclc.org/10.1186/s12913-022-08879-2">https://doi-org.pitt.idm.oclc.org/10.1186/s12913-022-08879-2</a></p>		<p>institutions, for unaffected patients at-risk for genetic syndromes.</p>	<p>Of the referred, 66.6% (34/51) attended their genetic counseling appointment.</p>
	<p><a href="#">“A Cluster Randomized Trial of a Family Health History Platform to Identify and Manage Patients at Increased Risk for Colorectal Cancer”</a></p> <p>Voils, C. I., Coffman, C. J., Wu, R. R., Grubber, J. M., Fisher, D. A., Strawbridge, E. M., Sperber, N., Wang,</p>	<p>Comprehensive family health history (FHH) patient-facing web-based platform followed by clinical decision support (CDS)</p>	<p>2 urban PCP clinics in VA hospitals (Durham, NC and Madison, WI) with 17 PCPs total, for unaffected patients at high-risk for colorectal cancer.</p>	<p>9.9% (50/505) patients with no history of disease were flagged at increased risk for CRC based on the FHH platform.</p> <p>4% (2/50) were referred to cancer genetic counseling by their PCP, despite having CDS recommendations.</p>

	V., Scheuner, M. T., Provenzale, D., Nelson, R. E., Hauser, E., Orlando, L. A., & Goldstein, K. M. (2022). A Cluster Randomized Trial of a Family Health History Platform to Identify and Manage Patients at Increased Risk for Colorectal Cancer. <i>Journal of general internal medicine</i> , 10.1007/s11606-022-07787-9. Advance online publication. <a href="https://doi.org/10.1007/s11606-022-07787-9">https://doi.org/10.1007/s11606-022-07787-9</a>			
Referral Systems	<a href="#">“A Systems Approach to Enhance Lynch Syndrome Diagnosis through Tumor Testing.”</a> Singh, Vinit, et al. “A Systems Approach to Enhance Lynch Syndrome Diagnosis through Tumor Testing.” 2022, <a href="https://doi.org/10.1101/2022.06.13.22276231">https://doi.org/10.1101/2022.06.13.22276231</a> .	Closed Loop Enhancement Assessment and Referral for Lynch Syndrome (CLEAR LS)	1 hospital (Yale New Haven Hospital), for 1,541 patients diagnosed with colorectal cancer with somatic testing results.	Rate of referral to cancer genetic counseling increased from 27.58% (pre-intervention) to 92.1% (post-intervention).  After referred, rate of genetic counseling appointment completion increased from 27.58% (pre-intervention) to 74.3% (post-intervention).
	<a href="#">“Programmatic Efforts Increase</a>	Multidisciplinary Precision	1 tertiary referral	11.2% of patients with somatic results

	<p><a href="#">Adoption of Genomic Precision Medicine in Cancer Care in a Community Cancer Center”</a></p> <p>Darabi, S., Braxton, D., Homer, J., Brodie, T., Holnagel, D., Eisenberg, B., &amp; Demeure, M. J. (2022). Programmatic efforts increase adoption of genomic precision medicine in cancer care in a community cancer center. <i>JCO Precision Oncology</i>, (6). doi:10.1200/po.22.00090</p>	<p>Medicine program</p>	<p>community cancer center, with in-house somatic testing (3,131 large somatic panels), for affected patients with tumors.</p>	<p>suspicious of a germline mutation underwent immediate genetic counseling referrals.</p> <p>32% increase in hereditary cancer program referrals for germline testing from baseline in 2017.</p>
	<p><a href="#">“Increasing referral of at-risk women for genetic counseling and BRCA testing using a screening tool in a community breast imaging center”</a></p> <p>Arun, B. K., Peterson, S. K., Sweeney, L. E., Bluebond, R. D., Tidwell, R. S., Makhnoon, S., &amp; Kushwaha, A. C. (2021). Increasing referral of at-risk women for</p>	<p>1-page, self-administered screening tool to assess BRCA1/2 mutation risk prior to breast screening, plus staffed Genetic Counselor</p>	<p>34,851 patients screened by mammogram at one community breast imaging center, 1,246 were eligible for genetic counseling.</p>	<p>19.7% (245/1246) made a genetic counseling appointment, 58.0% (142/245) completed the appointment.</p> <p>13% of all referral-eligible women directly attended an on-site genetic counseling session.</p>



	genetic counseling and BRCA testing using a screening tool in a Community Breast Imaging Center. <i>Cancer</i> , 128(1), 94-102. doi:10.1002/cncr.33866			
Point-of-Care	<p><a href="#">“Implementation of a Telehealth Genetic Testing Station to Deliver Germline Testing for Men With Prostate Cancer”</a></p> <p>Kwon, Daniel H., et al. “Implementation of a Telehealth Genetic Testing Station to Deliver Germline Testing for Men with Prostate Cancer.” <i>JCO Oncology Practice</i>, 2023, <a href="https://doi.org/10.1200/op.22.00638">https://doi.org/10.1200/op.22.00638</a>.</p>	Hybrid Oncologist/Genetic Counselor delivered genetic testing station (GTS)	Single-institution, four clinics, for affected men with prostate cancer (906 patients).	<p>83% (592/713) patients that were eligible for GTS completed germline genetic testing.</p> <p>White patient genetic testing completion rates were highest (85%), compared to Black patients with the lowest rates (70%).</p>
	<p><a href="#">“Implementation of an Embedded In-Clinic Genetic Testing Station to Optimize Germline Testing for Patients with Pancreatic Adenocarcinoma”</a></p> <p>Walker, E. J., Goldberg, D., Gordon, K. M., Pedley, C., Carnevale, J., Cinar,</p>	In-clinic genetic testing station (GTS)	Single clinic, University of California San Francisco (UCSF) GI Medical Oncology, for newly diagnosed pancreatic adenocarcinoma patients.	<p>Increased germline genetic testing rates from pre-intervention (19%) to post GTS intervention (71%).</p> <p>Patient attrition of genetic counseling appointment after referral decreased from 36% to 3%.</p>

	<p>P., . . . Dhawan, M. (2021). Implementation of an embedded in-clinic genetic testing station to optimize germline testing for patients with pancreatic adenocarcinoma. <i>The Oncologist</i>, 26(11). doi:10.1002/onco.13968</p>			
	<p><a href="#">“Implementing digital systems to facilitate genetic testing for hereditary cancer syndromes: An observational study of 4 clinical workflows”</a></p> <p>Wang, C., Lu, H., Bowen, D. J., &amp; Xuan, Z. (2023). Implementing Digital Systems to facilitate genetic testing for hereditary cancer syndromes: An observational study of 4 clinical workflows. <i>Genetics in Medicine</i>, 25(5), 100802. doi:10.1016/j.gim.2023.100802</p>	<p>Four different digital point-of-care clinical workflows: referral-based, scheduling-based, counseling and/or telegenetics, and point-of-care genetic testing</p>	<p>27 cancer clinics (15 breast/colon health centers, 3 primary care sites, 7 other clinical specialty sites), for unaffected patients at-risk for HBOC and/or Lynch syndrome.</p>	<p>16% (5147/102,542) of patients identified to be at high-risk for HBOC and/or Lynch syndrome received germline genetic testing.</p> <p>Point-of-care genetic testing had the highest rate of completed genetic testing, at 35%.</p>

***Depicts nine examples of interventions aimed to increase cancer genetic services, including referral and/or genetic testing rates, selected from the OVID search on February 17, 2023.***

## 4.4 Discussion

### 4.4.1 Family History Assessment

One study focused on increasing genetic counseling referrals for individuals at hereditary cancer risk made by 26 PCPs across two clinics (one rural and one urban) in Minneapolis, MN, using a Genetic Cancer Screening Tool (GCST) (Wurtmann, Baldinger et al. 2022). Barriers to genetic counseling referrals were identified by surveying PCPs, and they included limited cancer risk assessment skills, lack of genetic testing knowledge and topic confidence, family history gathering challenges, and time limitations (Wurtmann, Baldinger et al. 2022). Genetic Cancer Screening Tool (GCST) was developed and implemented into these clinics for PCPs to help mitigate these barriers and increase genetic counseling referral rates for patients at higher risks of hereditary cancer conditions like HBOC (Hereditary Breast and Ovarian Cancer), Lynch, and other cancer syndromes. The GCST consisted of an EPIC EHR clinical decision support tool, initially pre-screening patients by identifying family histories or suspicious questionnaire results, which flagged and prompting PCPs to complete the GCST with the patient, based on NCCN guidelines. If the patient met any criteria, there was an option for the PCP to refer to cancer genetics or indicate reasons for non-referral. Pre-implementation, the number of patients being referred to genetic counseling increased 20-fold, starting at 0.1% of wellness visits and increasing to 2.1% (Wurtmann, Baldinger et al. 2022).

Though this intervention increased genetic referrals made by PCPs, it might not be as effective for exocrine pancreatic cancer specifically since the at-risk population is already identified as individuals with a diagnosis and the time sensitivity surrounding that diagnosis.

Clinics could prioritize these referrals as Geisinger did, attempting to have patients seen within one week of their diagnosis. One interesting finding from this study included its success at increasing the number of PCPs making referrals. Additionally, it explored reasons for why referrals were not made, with action not taken by the provider ranking the most common at 61% (Wurtmann, Baldinger et al. 2022). The results of this thesis study on Geisinger referrals showed that only ½ of the pancreatic cancer patients were being referred to cancer genetic counseling, when they all should have been. Exploring reasons for no referrals at Geisinger could prove beneficial to increase those referral rates, and implementing a tool like the GCST could encourage other medical providers that do not typically place referrals. A family history assessment tool could help clinics screen for at-risk patients with a family history of pancreatic or other cancers, prompting PCPs to refer to cancer genetics and reducing their work-burden.

A similar study focused on a risk assessment tool for patients, prior to attending their PCP appointment across four separate hospital institutions at 19 clinics with diverse populations and locations (Wu et al. 2022). This family health history-based health risk assessment (HRA) via electronic health records (EHR) took form of a family history questionnaire for patients to fill out, and the PCP could then discuss their results with them during the appointment, having recommendations flagged for the PCP like referring to genetic counseling or to increase/start health screenings like colonoscopies. This study looked at 1,829 patients total, 543 of which were flagged for a genetic counseling referral recommendation unspecific to cancer (Wu et al. 2022). Though cancer genetic counseling was not the only genetic department receiving these patient referrals, as the assessment was not limited to cancer family history, they did make up most indications for the referred at 74% (364/543) (Wu et al. 2022). Overall, 9.4% (51/543) of patients flagged for a genetic counseling recommendation were referred to genetic counseling, though for

those with a cancer indication the referral rate was higher at about 14.5% when compared to genetic counseling referrals unrelated cancer at about 6.6% (Wu et al. 2022). Of the total 51 patients being referred to genetic counseling, 34 (66.6%) completed their appointment, which was higher than Geisinger cancer genetic counseling appointment completion rates of 50% (Wu et al. 2022). This study did not measure genetic counseling referral rates prior to the HRA intervention, though it does provide an example of how prior risk assessment and subsequent discussions with a PCP can assist with generating appropriate genetic counseling referrals.

Specific to colorectal cancer (CRC), one study implemented a comprehensive family health history (FHH) patient-facing web-based platform that provided risk assessment to help PCPs with decisions based on care for unaffected patients between the ages of 40 and 64 with CRC risk (Voils et al. 2022). Clinical decision support (CDS) was given to one group with colonoscopy guidelines and genetic assessment guidelines provided by NCCN, while the second (control) group had no decisional support nor FHH prior to the PCP appointment, with the goal to measure tool effectiveness via a two-arm cluster-randomized design when compared to standard risk assessment of electronic medical records without the platform. 50 out of the total 505 patients in this study were flagged as high-risk for CRC, though only 2 of these patients were referred by their PCP to genetic counseling (Voils et al. 2022). For the control group, only 1 patient was referred to genetic counseling by their PCP, though 78.6% (22/28) were flagged at increased risk for CRC based on the platform in addition to referral recommendations by the CDS (Voils et al. 2022). For the intervention group, only 1 patient was referred by their PCP as well, with 68.2% (15/22) flagging at increased risk for CRC based on the platform after their PCP appointment (Voils et al. 2022). This platform intervention established at-risk patients for CRC and provided support recommendations in their electronic medical records, although it fell short with significantly

increasing rates of referrals. The authors explained that the reasoning behind the lack provider concordance with CDS recommendations needs explored further but that workforce sufficiency needs to meet genetic service demands, as most VA clinics do not have on-site genetic counselors, which influenced reasons for non-referrals in this study (Voils et al. 2022). Other clinics, such as VA clinics, looking to increase genetic service rates may want to focus on other methods like provider education, genetic counseling resources to locate genetic counselors in the area, or simply hiring on-site genetic counselors to meet these demands.

#### **4.4.2 Referral Systems**

Lynch syndrome increases risks for pancreatic cancer in addition to many other cancers, causing about 3-5% of all colorectal cancers (Singh, et al. 2022). Identifying a pathogenic variant that causes Lynch syndrome can influence clinical management by increasing cancer screening and open discussions with family members about heredity. Universal tumor testing on colorectal samples acts as a screen for Lynch syndrome, though the positive predictive value for a germline finding in a patient with abnormal IHC is around 20-30%. Studies of Universal Lynch Syndrome screening (ULS) implementation through the LS Screening Network (LSSN) have identified multiple steps in the screening algorithm where cases should be flagged for referrals but may be overlooked due to the manual nature of implementation of this screening program. (Singh, et al. 2022). One study focused on this oversight and established an automated cancer genetic referral system using a computer algorithm called the Closed Loop Enhancement Assessment and Referral for Lynch Syndrome (CLEAR LS), which recognized colorectal cancer patients with tumor testing results concerning for Lynch syndrome through the EHR (Electronic Health Record System)

(Singh, et al. 2022). This intervention successfully tripled referral rates of at-risk cancer patients, and they also tripled their diagnoses of Lynch syndrome after implementing CLEAR LS (Singh, et al. 2022). This automated referral process was able to recognize at-risk patients effectively, using already existing electronic health records, refer more patients to cancer genetics, and ultimately increase overall genetic testing rates and improving patient care. Additionally, it cut hospital systems costs in half, from about \$170,000 to about \$90,000 per Lynch syndrome diagnosis (Singh, et al. 2022).

In the context of exocrine pancreatic cancer, this intervention strategy could reduce the burden on other ordering providers like surgeons or oncologists, and it could facilitate referrals to genetic counseling, all while improving patient care and saving money. Like colorectal cancer, molecular profiling of pancreatic tumors can inform treatment decisions as well, which could allow for streamlined germline testing in addition to somatic. Also, this intervention did not statistically differ in referral rates across race/ethnicity. An intervention like this could be favorable, having seen successes regarding equitable genetic service delivery, though demographic data should be addressed in future studies regardless.

Another study implemented a coordinated multi-disciplinary precision medicine clinic to assist Medical Oncologists with understanding somatic test results and identifying candidates for clinical trials across all types of cancer (Darabi et al. 2022). This multidisciplinary clinic consisted of a physician lead, molecular pathologist, clinical genomic scientist, medical geneticist, and multiple licensed genetic counselors (Darabi et al. 2022). Of all the in-house tumor panels in the study that were tested (3,131 tumor samples total) and flagged as a somatic result suspicious of a germline mutation, 11.2% underwent immediate genetic counseling referrals for germline testing discussions (Darabi et al. 2022). This intervention resulted in a rate increase of 32% for germline

genetic testing from the baseline in 2017 (Darabi et al. 2022). Although the focus of this multi-disciplinary precision medicine clinic was to assist physician understanding of somatic testing for treatment purposes, having genetic professionals like genetic counselors enabled easy access to appointments and increased overall germline testing rates for this clinic. Worth noting, this intervention was established at a community cancer center that performed their own in-house somatic testing, which may not be feasible for smaller clinics hoping to replicate these increased rates (Darabi et al. 2022). Also, ongoing education on understanding molecular profiling and clinical trial availability was requested by members of the multi-disciplinary clinic (Darabi et al. 2022). In the context of pancreatic cancer, discussions of exocrine type pancreatic cancer diagnoses in multi-disciplinary meetings would help direct appropriate patients toward receiving cancer genetics and increase referral rates, having more knowledgeable providers and other genetic counselors attending meetings.

One other study on 34,851 individuals focused on increasing referral rates for patients at risk for HBOC at the Memorial Hermann Breast Imaging Center at time of imaging. By giving patients that were already scheduled to have a mammogram a one-paged self-administered questionnaire, this screening tool assessed BRCA1/2 mutation risk before their breast screening (Arun et al. 2021). Patients that flagged risk for HBOC were referred to genetic counseling while at the community breast imaging center, resulting in 19.7% (245/1246) that made a genetic counseling appointment, and 58.0% (142/245) that completed their appointment (Arun et al. 2021). This screening tool expedited referral rates for individuals already seeking healthcare in the form of breast cancer screening and would have a Genetic Counselor on site to see patients after their imaging was finished (Arun et al. 2021). Only 13% of all referral-eligible women directly attended an on-site genetic counseling session (Henderson et al. 2021). This referral system intervention



also touches on another intervention method discussed in detail below, the point-of-care method, since there was an on-site genetic counselor available directly after mammography.

#### **4.4.3 Point-of-Care**

Point-of-care methods involve interventions at the treating medical team level, often right after a diagnosis. One study focused on implementing a Telehealth Genetic Station (GTS) that involved both Oncologists and Genetic Counselors to increase genetic testing rates for men diagnosed with prostate cancer, which can be time-sensitive due to treatment implications like pancreatic cancer (Kwon et al. 2023). The GTS was implemented in-person at first in 2019, but due to the pandemic they transitioned to remote, having no statistical effect on genetic testing completion rates (Kwon et al. 2023). Before the intervention only 9% of eligible patients completed genetic testing within two months of their initial Oncology appointment, compared to an increased 53% after GTS implementation (Kwon et al. 2023). Although these genetic testing rates increased favorably, minority disparities persisted with Black and Hispanic/Latinx patients having 70% test completion rates compared to 85% for White patients. Additionally, this intervention requires extra dedicated work time from GCAs (Genetic Counseling Assistants) which takes them away from assisting Genetic Counselors. In the workflow, the GCA triages prostate cancer patients after a Medical Oncologist refers them to GTS, schedules appropriate patients for telephone intakes where they gather family histories, consent patients, and handle sample collection, and then they assisted with initiating orders for genetic testing. The authors proposed methods to reduce this burden, shifting workload toward pre-test counseling via electronic methods.

Another point-of-care intervention took place at the University of California San Francisco (Walker et al., 2021). This intervention took the form of an in-clinic genetic testing station (GTS), where exocrine pancreatic cancer patients could use a kiosk directly after their initial Oncology appointment (Walker et al., 2021). Like the previously mentioned GTS intervention, a GCA had many duties within the workflow, including assisting patients with education, consent, family history gathering, sample collection, send out of the sample, and scheduling an appointment for follow-up with the Genetic Counselor (Walker et al., 2021). This intervention was more successful, having increased genetic testing rates from pre-intervention (19%) to post-intervention (71%) (Walker et al., 2021). This was the highest reported rate of genetic testing when it came to pancreatic cancer (Walker et al., 2021).

One large study evaluated genetic referral and testing rates across 27 separate cancer clinics, each with four different point-of-care clinical workflows: referral-based, scheduling-based, counseling and/or telegenetics, and point-of-care genetic testing (Wang et al. 2023). Overall, 16% (5147/102,542) of patients identified to be at high-risk for HBOC and/or Lynch syndrome received genetic testing, though they differed across clinics according to each workflow type (Wang et al. 2023). Point-of-care genetic testing had the highest rates of genetic testing completed at 35%, followed by point-of-care genetic counseling (14%), schedule (10%), and referral only (5%) (Wang et al. 2023). Though these models all utilized digital point-of-care interventions, the differences in functions and focus of each model resulted in varying genetic testing rates. The Walker et al. 2021 study represented the highest achieving genetic testing rates by using a point-of-care kiosk after a patient's oncology visit, and this Wang et al. 2023 study supports other studies with similar models in the context of risk for HBOC and Lynch syndrome (Walker et al., 2021) (Wang et al. 2023).

#### **4.4.4 Recommendations for Pancreatic Cancer Genetic Service Intervention**

Among the three methods of intervention, the point-of-care method has shown the highest rates of success in terms of increasing genetic testing rates, and it has the capability of reducing the need for interventions focusing on increasing referrals by utilizing in-clinic stations and directly targeting genetic testing rates. Point-of-care interventions could also help increase rates of genetic testing in a timely manner from receiving a diagnosis, which is especially important for pancreatic cancer due to its severity and influence on treatment planning. Drawbacks include the staffing requirements to maintain point-of-care models, which could consist of Genetic Counseling Assistants, Genetic Counselors, collaborating Medical Oncologists, and trained nursing staff.

Referral systems could also increase referral rates to genetic counseling, but it can increase the work burden on referring providers and result in higher rates of non-referrals due to workload and other reasons like a limited education about appropriate genetic referrals. Referral systems have the benefit of taking advantage of already ordered somatic testing or scheduled screening, which could be easily implemented in clinics with regimented services like mammography or tumor testing. For pancreatic cancer diagnoses, tumor testing regularly occurs, so adding an intervention to the workflow of somatic testing might be a smooth transition and result in a boost of germline genetic testing rates. For clinics that have or want to start multi-disciplinary tumor boards, this intervention could be an easy transition as well. Hiring and having Genetic Counselors to be present at these meetings to help direct questions and referrals to cancer genetics would increase genetic service rates and improve patient health outcomes.

The family risk assessment method showed the lowest rates of cancer genetic referrals and was mostly focused on unaffected patients with the goal of identifying at-risk individuals for

hereditary cancer. This would be a great option to explore for clinics with an overall goal of increasing genetic referral rates, but not particularly for clinics geared toward improving genetic services for pancreatic cancer patients. Worth noting, it could help identify families with a history of pancreatic cancer and inform them of their risks and options. This could improve cascade testing and overall genetic testing rates.

In summary, the point-of-care model type seems to be the most beneficial regarding increasing genetic services for pancreatic cancer. However, for clinics interested in improving their genetic testing rates, it would be important to establish methods to decrease the burden on providers involved in upkeep, perhaps by hiring more Genetic Counseling Assistants or creating pre-test counseling education materials. A kiosk located outside of the Oncology exam room or an electronic tablet that is distributed to patients directly proceeding a pancreatic cancer diagnosis are two exemplified forms of point-of-care. Also important for any method type, clinics should develop ways to navigate gaps in genetic testing among minority groups and mitigate these disparities before program development and throughout implementation. Referral systems can be implemented into clinics that cannot sustain point-of-care models and have an established in-house somatic testing workflow, pancreatic cancer screening for high-risk individuals, or multi-disciplinary tumor board meetings. Family risk assessment interventions can be utilized by any clinic to increase overall genetic counseling referral rates, regardless of cancer indication, though it may not help pancreatic cancer indications specifically due to the severe nature of the condition. Every clinic will differ in size, demographics, location, resources, age, cancer indication, and many other factors, so one intervention will not fit all models. It will be important to weigh these factors while deciding on which interventions to implement, and how these factors will affect patient health outcomes.

#### **4.4.5 Limitations**

Limitations for this literature search include the number of articles read and evaluated. Nine articles do not represent the multitude of interventions that have been implemented to increase access to cancer genetic services, exemplified by the vast 149 results. Three examples for each of the categorized intervention methods, therefore, cannot accurately portray their clinical successes. Additionally, though this literature search was restricted to articles published between 2020-2023, interventions covered by these studies may have started earlier than that, resulting in less than current evaluations as suggested. This literature review serves as a starting point to understand the recent climate of cancer genetic counseling referral and germline genetic testing rates across clinics, and what interventions exist to increase those rates. Before any motivated cancer clinic thinks about implementing an intervention geared toward increasing cancer genetic services, further analysis should be conducted.

## Appendix A

**AAMC UNIFORM CLINICAL TRAINING AFFILIATION AGREEMENT IMPLEMENTATION LETTER (Page 1 of 2)**

The purpose of this letter is to provide a record of the AAMC Uniform Clinical Training Affiliation Agreement (formerly the Universal Student Affiliation agreement) between the SCHOOL and the HOST AGENCY with respect to a clinical training experience for one of the SCHOOL's students, and faculty if applicable, (identified below) and the agreement of the parties to abide by all terms and conditions of the AAMC Uniform Clinical Training Affiliation Agreement, which is hereby incorporated by reference, without modification or exception except as specified below.

**Modifications or Exceptions (if none, please indicate by writing "NONE"):**

The following criteria must be met for each Student, and faculty if applicable, performing SCHOOL's duties set forth in the AAMC Uniform Clinical Training Affiliation Agreement prior to performing such duties, and: (i) SCHOOL shall provide, or (ii) SCHOOL shall inform the Student that the Student must provide evidence of such to Geisinger [HOST AGENCY] immediately upon request:

- A. (i) Mandatory vaccinations pursuant to HOST AGENCY's Mandatory Vaccine Policy, which is expressly incorporated herein by reference and can be accessed at <https://www.geisinger.org/about-geisinger/Corporate/vendor-relations>; (ii) Two-Step Tuberculosis Skin Test or TB lab test (negative, or positive with documented follow-up chest x-ray) done within one year prior to the start; (iii) completed Hepatitis B Vaccination [or declination]; and (iv) physical showing the individual is medically clear of communicable diseases if duties will be performed at a Life Geisinger facility; Additionally, the following vaccines are recommended: (i) Rubeola, (ii) Mumps, (iii) Rubella, and (iv) Varicella;
- B. Successfully passing a minimum 7 panel drug screen testing for (i) Amphetamines; (ii) Benzodiazepines; (iii) Cannabinoids; (iv) Cocaine; (v) Opiates; (vi) Oxycodone; and (vii) Heroin [6-Acetylmor] done within 1 year prior to the start;
- C. Criminal history record check through PATCH (PA Access to Criminal History), showing no relevant criminal history, done within 1 year prior to the start;  
<https://epatch.state.pa.us/Home.jsp>
- D. PA Child Abuse History Clearance Form (Website Check) (CT-113), showing no relevant criminal history, done within 1 year prior to the start; and  
[http://keepkidssafe.pa.gov/cs/groups/webcontent/documents/form/s\\_001762.pdf](http://keepkidssafe.pa.gov/cs/groups/webcontent/documents/form/s_001762.pdf) - Direct Link to the CY 113 Form
- E. Fingerprint-based Federal Criminal History Records Check, in compliance with Pennsylvania Act 73 of 2007, showing no relevant criminal history, done within 1 year prior to the start  
<https://www.dhs.pa.gov/providers/Clearances-and-Licensing/Pages/default.aspx>  
<https://enroll.identogo.com> - Website where Student must register for this service (utilize code: 1KG756)

For additional information, please refer to <http://keepkidssafe.pa.gov/resources/clearances/index.htm>

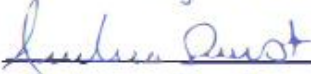
All fees incurred in obtaining these screening requirements are the responsibility of the student and/or his/her institution. All background checks noted above must be performed every three years.

Student Name and Profession: Daniel Brennstainer, Genetic Counseling Student  
Clinical Training Experience (Type, Location and Preceptor): Thesis data use, Andrea Durst through Univ of Pittsburgh; Heather Rocha and Alanna Rahon from Geisinger  
Dates of Clinical Training Experience: 12/1/2023 - 5/1/2023

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This IMPLEMENTATION LETTER is effective when signed by all parties. The individuals executing this IMPLEMENTATION LETTER are authorized to sign on behalf of their institutions and certify that their institutions have accepted the terms of the AAMC Uniform Clinical Training Affiliation Agreement and further agree to comply with its terms except as noted above.

**SCHOOL**

Name of School: University of Pittsburgh  
Signature:   
Name: Andrea Durst  
Title: Associate Program Director  
Date: 12/21/22  
Address: 3129 Public Health  
Pittsburgh, PA 15213

**HOST AGENCY**

**Geisinger Medical Center on behalf of itself  
and its affiliated entities**

Signature:   
Name: Brad Crossin  
Title: Authorized Signer  
Date: 12/21/22



## Appendix B

### Search Term Collective for Ovid MedLine Literature Search

Database: Ovid MEDLINE(R) ALL <1946 to February 17, 2023>	
Search Strategy:	
1	genetic services/ or genetic counseling/ or genetic testing/ or pharmacogenomic testing/ (56360)
2	Counseling/ (39346)
3	exp "Diagnostic Techniques and Procedures"/ (7808134)
4	(counsel* or diagnostic* or screen* or test*).ti,ab,kf. (5238176)
5	2 or 3 or 4 (11340113)
6	Genetic Predisposition to Disease/ (155718)
7	((genetic adj2 predispos*) or hereditary).ti,ab,kf. (101714)
8	6 or 7 (245120)
9	5 and 8 (100897)
10	(genetic* adj4 (counsel* or service* or test*).ti,ab,kf. (66443)
11	1 or 9 or 10 (181193)
12	exp neoplasms/ (3795854)
13	(cancer* or carcinoma* or leukemia* or lymphoma* or melanoma* or neoplasm* or sarcoma*).ti,ab,kf. (3263568)
14	12 or 13 (4620967)
15	11 and 14 (42172)
16	"referral and consultation"/ or ethics consultation/ or remote consultation/ or distance counseling/ or secondary care/ (82687)
17	(consult* or refer*).ti,ab,kf. (1144830)
18	16 or 17 (1175239)
19	15 and 18 (3602)
20	limit 19 to (english language and yr="2020 - 2023") (852)
21	intervention*.ti,ab,kf. (1286620)
22	20 and 21 (87)
23	evaluation studies/ or "evaluation studies as topic".pt. or program evaluation/ or validation studies/ or "validation studies as topic".pt. or (effectiveness or intervention or (pre- adj5 post-) or (pretest adj5 posttest) or (program* adj6 (evaluate or evaluated or evaluates or evaluating or evaluation or evaluations or evaluator or evaluators)) or (quasi adj1 experimental)).ti,ab,kf. (1761307)
24	20 and 23 (95)
25	("adaptive clinical trial" or "clinical trial" or "clinical trial, phase i" or "clinical trial, phase ii" or "clinical trial, phase iii" or "clinical trial, phase iv" or "controlled clinical trial" or "equivalence trial" or "multicenter study" or "pragmatic clinical trial" or "randomized controlled trial").pt. or double-blind method/ or "adaptive clinical trials as topic" or "clinical trials as topic" or "clinical trials, phase i as topic" or "clinical trials, phase ii as topic" or "clinical trials, phase iii as topic" or "clinical trials, phase iv as topic" or "controlled clinical trials as topic" or "equivalence trials as topic" or "intention to treat analysis" or "non-randomized controlled trials as topic" or "pragmatic clinical trials as topic" or "randomized controlled trials as topic" or "multicenter studies as topic" or (phase adj1 ("I" or "II" or "III" or "IV" or "1" or "2" or "3" or "4")).ti,ab,kf. or ((randomi?ed adj7 trial*) or (controlled adj3 trial*) or ((clinical or pragmatic) adj2 trial*) or ((single or doubl* or tripl* or treb*) adj4 (blind* or mask*))).ti,ab,kf. or (("4" or four adj arm).ti,ab,kf. (1963504)
26	23 or 25 (3354608)

27	20 and 26 (148)
28	22 or 27 (179)
29	28 not ((exp africa/ or exp asia/ or exp australia/ or exp canada/ or exp central america/ or exp europe/ or exp south america/) not (north america/ or exp united states/)) (152)
30	29 not protocol.ti. (149)
<b>Lists the combination of 30 search terms used in the MedLine Ovid literature search resulting in 149 published articles that were pulled, performed on February 17, 2023.</b>	

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