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Association of Patient Activation with the Health-Related Quality of Life of Pancreatic Cancer Patients

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Association of Patient Activation with the Health-Related Quality of Life of Pancreatic Cancer Patients

by

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Dedication

I dedicate this work to my parents, Mr. Mahesh Vohra and Ms. Neelam Vohra; my sister, Ms. Nupur Vohra, and lastly, Ms. Kamayani Rai, for their unwavering support and love throughout this journey.

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Abstract

Association of Patient Activation with the Health-Related Quality of Life of Pancreatic Cancer Patients

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The study aimed to evaluate patient activation, HRQOL, and the association between these two constructs for patients with pancreatic cancer.

A cross-sectional study design was used to assess patient activation and HRQOL of locally advanced and metastatic pancreatic cancer patients. Patients undergoing chemotherapy sessions at 13 Texas Oncology clinics were approached to participate in the study via convenience sampling. Patients willing to participate were provided with a 43-item survey to complete. The survey consisted of the 13-item patient activation measure (PAM-13), the 18-item functional assessment of cancer therapy-hepatobiliary symptom index (FHSI-18), and single-item measures of clinical and demographic variables. Variables were analyzed descriptively by assessing mean, median, and frequencies. Relationships between variables were assessed using bivariate statistics.

The response rate was high (95.4%). The average age of the participants was 71.1 $\pm$ 9.5 years. The majority were females (57.1%), Caucasians (58.5%), had at least a college degree (57.2%), were married or partnered (61.9%), and had an annual household income of over $50,000 (60%). Clinically, most patients were diagnosed at stage 4 (39.0%), had no family history of the disease (87.8%), and were diagnosed less than three months prior to survey completion (46.3%). The mean patient activation score was 62.8 $\pm$ 18.5 (range 0-100), with most patients at higher patient activation levels, i.e., stage 3 or stage 4 (66.7%).

The mean HRQOL score of 42 (range: 0-72) was low. Bivariate analysis revealed significantly high patient activation scores for patients with multiple insurances and those that were married or partnered. Patients that were high school graduates or less and those that had public insurance were more likely to be at a lower activation level (stages 1 or 2). Patient activation scores had a non-significant, weak positive correlation with HRQOL scores. The predictive ability of patient activation score at predicting HRQOL score while controlling for covariates was not assessed due to the low sample size.

The results indicate a non-significant association between patient activation and HRQOL, though the study was significantly underpowered. Higher patient activation was significantly associated with having private insurance and being partnered. Research amongst larger and more diverse samples is required for conclusive evidence.

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Chapter 1: Introduction

1.1. PANCREATIC CANCER

Pancreatic cancer originates as an abnormal growth of ductal epithelium cells and evolves into invasive cancer. [1] Among the types of pancreatic cancers, the most prevalent is pancreatic ductal adenocarcinoma or PDAC, constituting more than 90 percent of all exocrine pancreatic cancers. [2] The symptoms and clinical manifestations of pancreatic cancer is location and stage dependent. Obstructive cholestasis, obstructive jaundice, pancreatic jaundice, diabetes, and pancreatitis are some of the common manifestations. [1, 2] Due to the presence of debilitating symptoms and manifestations, pancreatic cancer is often associated with high morbidity, poor prognosis, high mortality rates and decreased health-related quality of life (HRQOL). The exact etiology of pancreatic cancer is unknown, but a myriad of genetic, dietary, behavioral, and environmental factors may lead to its occurrence. [3]

Death rates for most cancers have decreased over the years, but that has not been the case for pancreatic cancer. It is still the seventh leading cause of cancer-related deaths worldwide, with 331,000 deaths among 380,000 patients diagnosed in 2012 [4] and a 5-year overall survival rate of 8.2 percent. [5] Significant geographical variations are observed in the distribution of the disease, with highest rates being observed in developed countries such as the U.S. (12 per 100,000), followed by the eastern European countries (8.7 per 100,000). Some of the developing countries of Asia and Africa have the lowest rates (<2 per 100,000). [6] Risk for cancer greatly increases with age. Two-third of the patients are above 65 years of age with an average age at diagnosis of 71 years. As per 2009-13 U.S. incidence data, cancer among white population increased from >5 per 100,000 individuals before age 45, to 30.0 per 100,000 among aged 60 to 64, and 93.7 per

100,000 in aged 80 to 84. [5] Surveillance, Epidemiology, and End Results (SEER) estimates indicate that, in 2017, there will be 53,670 new cases of pancreatic cancer and 43,090 people will die of the disease. [5] Further, rates differ by ethnicity/race such that the incidence of pancreatic cancer is relatively higher among African-Americans (17.2 per 100,000) as compared to Caucasians (14.0 per 100,000). [7]

Considering poor prognosis and shorter overall survival among pancreatic cancer patients, the economic burden is substantially high. A study, using the SEER-Medicare database, estimated that the annual mean total direct medical cost of care for a pancreatic cancer patient was $65,500 (SD: $65,400). However, the cost of care varied widely for different treatment modalities based on the bodily location and region of the pancreatic cancer. The hospitalizations, including cancer-directed procedures, accounted for a substantial share of cost per patient. [8]

1.2. HEALTH-RELATED QUALITY OF LIFE IN PANCREATIC CANCER

The treatment of pancreatic cancer patients involves surgical resection, radiation, and chemotherapy. Nearly 85 percent of the patients suffering from hepatobiliary cancers (primary site of cancer is pancreas, liver, bile duct, and gallbladder) are not candidates for surgical resection and require palliative treatment. [9] Palliative treatment includes chemotherapy, radiation, and chemoradiation. At present, these treatments marginally improve overall survival, although the toxicities due to treatment can further add to the symptom profile. [10] Due to minimal prolongation of overall survival, a broad symptom profile, and a high mortality rate, health-related quality of life (HRQOL) of a patient becomes of paramount importance. Some studies have highlighted a positive association between HRQOL and overall survival in pancreatic cancer. [11-13]

1.3. SURVIVAL IN PANCREATIC CANCER

Associated with a poor prognosis, pancreatic cancer has high correspondence between incidence and mortality. In the last 22 years, five-year overall survival has improved marginally, from 5.4 percent in 1995 to 8.2 percent in 2017. [5, 14] Overall median survival varied between 23 months among patients suitable for surgical resection with adjuvant chemotherapy, and 6 to 10 months for patients with advanced metastatic cancer requiring palliative care and systemic chemotherapy. [15] In a systematic review of HRQoL studies among all types of cancer patients, Montazeri et al., suggested that HRQOL and overall survival duration are positively associated. [16] A similar association between HRQOL and overall survival was also observed in pancreatic cancer patients in particular. [12]

1.4. PATIENT ACTIVATION

Patient's willingness and ability to manage his/her health independently has a positive association with HRQOL. The understanding of one's health care and possessing the knowledge, skills, and confidence to manage one's health is termed patient activation. Patients having these qualities are highly activated and are an effective partner in disease management. Highly activated patients have reported better health outcomes and higher HRQOL scores. [17]

According to Hibbard et al., "Patient activation is a measure of a person's knowledge, skills, and confidence for managing their health." In the year 2004, Hibbard et al. described the development of a 13-item patient activation measure (PAM). PAM is a valid, reliable, unidimensional, probabilistic, and Guttman-like scoring scale. [17, 18] Activated patients understand that their health condition relies on their own knowledge of the disease and its management, their capability to manage the disease and treatment-related symptoms, the

behavior to maintain adequate functioning and the confidence to take necessary actions. They also know how to collaborate with health care providers to access better quality healthcare apart from usual care and support. Based on the patient's score on PAM, he/she can be classified into different patient activation levels. These levels of activation follow a hierarchical order. In the first stage, patients realize the importance of self-management of their health. Patients in the second stage know their medication and lifestyle changes and have the confidence to talk to their health-care provider and take action when the need arises. The third stage involves taking action, such as maintaining lifestyle, and handling problems and symptoms by themselves. In the fourth stage, patients remain activated under the stress of their daily routine or any change in the status quo of their ailment. Knowledge of patient activation stage can assist the healthcare provider in tailoring information to an individual. For example, patients at the lowest activation levels believe that the responsibility of treating their disease solely resides with the healthcare provider. Patients with marginally high but still less than half of the total PAM score , realize the importance and have the understanding of their role in care but do not know about the disease and its management. Thus, for patients belonging to this bracket, interventions can be tailored to improve self-awareness and gain basic proficiency about their disease. Whereas, for patients in the upper end of the PAM scale, the healthcare provider can tailor their intervention to maintaining the patient's awareness of self-efficacy and sustaining behaviors. Hibbard et al., has further hypothesized that patients have to cross each stage to become effective self-managers. [18, 19]

The shorter version of the PAM was developed to improve the feasibility of assessing activation in a primary care facility. It would further be less burdensome for the patients suffering from a disease where fatigue is common. The shorter, 13-item version's reliability was similar to that of the original 22-item scale with Cronbach's alpha of 0.91

and Rasch person reliability of 0.81 and 0.88 for real and model settings, respectively. The 13-item scale has a calibrated scale with a range of 38.6 to 53.0, which is comparable to the 22-item scale range of 38.3 to 54.5. In-fit and out-fit for PAM-13 falls within the acceptable range of 0.5 to 1.5. The construct validity of the PAM-13 scale has a strong association with preventative behaviors, disease-specific behaviors, and consumeristic behaviors. [18, 19]

Several studies have examined the association between HRQOL and patient activation. One study of adults with chronic conditions reported that patients with higher PAM scores are five times more likely to report significantly higher HRQOL scores. [20] Similar results were also observed by Druss and colleagues. Their study examined the effects of a self - management intervention on the activation of patients with serious mental illness. Employment of an activation-level specific intervention improved QOL at 6-month follow-up. [21, 22] Hibbard et al. conducted a cross-sectional study to assess the association of patient activation with cancer patient's behaviors. Highly activated patients were 4.5 times more likely to manage their side-effects and 3.3 times more likely to follow healthier diets after diagnosis compared to lowly activated patients. Lower activated patients were also less likely to discuss their side-effects and follow healthcare providers' recommendations. [23] In another study, Street et al. found that breast cancer patients who perceived greater decision control reported higher HRQOL scores. [24]

1.5. STUDY SIGNIFICANCE

Studies on patient activation in chronic conditions have reported that higher activation levels are positively correlated with better health outcomes and higher HRQOL. [21] At least one study showed that cancer patients with low activation levels are poor managers of their health [24] and another among rectal and bladder cancer survivors found

a positive relationship between activation and HRQOL.[25] However, no known study has examined the association of patient activation with HRQOL, progression-free, and overall survival in patients with pancreatic cancer. If patient activation is associated with HRQOL and survival of pancreatic cancer patients, then interventions could focus on helping patients become better managers of their health, resulting in improved symptom/adverse effects management which in turn might lead to enhanced HRQOL, as well as improved progression-free and overall survival.

Thus, the purpose of this study was to evaluate the association of patient activation with HRQOL among pancreatic cancer patients.

Chapter 2: Literature Review

This chapter contains the review of literature of the relevant concepts in this study. It gives a brief overview of pancreatic cancer, its economic impact, and the current treatment modalities. Further, it introduces the concept of health-related quality of life (HRQOL) and highlights the effect of pancreatic cancer on the HRQOL of patients. It also discusses the concept of patient activation and its aim at making patients active partners in their disease management. Finally, it explains the objectives of this study, which was to assess HRQOL status, patient activation levels, and the relationship between the two concepts in pancreatic cancer patients.

2.1 PANCREATIC CANCER

Pancreatic cancer is considered a fatal disease, for which the mortality rates closely resembles the incidence rates. A majority of patients develop cancer through microscopic non-invasive epithelial proliferation within the pancreatic ducts. It is also cited as pancreatic intraepithelial neoplasia.

2.1.1. Epidemiology

The incidence and prevalence rates of pancreatic cancer are generally high in developed countries as compared to developing countries. Cases are expected to increase in North America and Europe in the coming years, indicating the global presence of the disease. In 2012, North America recorded the highest number of cases, followed by Western Europe. The increase in incidences in developed countries may also be because of the aging population and better access to health care. Compared to developed countries, the incidence is lowest among African and Southeast Asian among developing countries. It is still unclear whether the lower reported incidence of pancreatic cancer is the actual

rate or if the underdiagnosis confounds it, due to limited access to care in these developing countries. [26, 27]

As per the American Cancer Society, 2018 estimates of incidence and deaths caused by pancreatic cancer are 55,440 and 44,330, respectively. [28] Estimates for 2018 further suggest that Texas will have 3,790 incident cases out of which 2,880 will result in deaths. At present, it is the fourth and predicted to be the second leading cause of cancer-related deaths in the United States (US) by the year 2030. [29]

2.1.2. Commonly Known Risk Factors

The incidence of pancreatic cancer increases among the elderly population, particularly in those above the age of 60, indicating a positive association with increased age. In the US, incidence among Whites is as low as 5.0 per 100,000 among patients below the age of 45. Between 60 – 64 years of age, incidence increases to 30.0 per 100,000, and further increases to 93.7 per 100,000 among patients 80-84 years. [30] Pancreatic cancer cases are more common among males, with the age-adjusted incidence being 50 percent higher in men when compared to women. [15] Similar results were also reported in the United Kingdom. Similar gender disparities are also present in mortality rates. Each year worldwide, 120,000 males die of pancreatic cancer compared to 107,000 females. The cumulative risk of death in pancreatic cancer in males is 0.2 percent versus 0.1 percent in females. [31]

Like other cancers, genetic factors play a major role in predicting the risk of pancreatic cancer. These factors can be either familial or genetic mutations or a combination of the

two. Familial basis accounts for 10 percent of pancreatic cancer cases. [32] Family history of pancreatic cancer significantly increases the risk of pancreatic cancer. Findings from the case-control studies estimated that the odds of developing pancreatic cancer is 1.9 to 13 times higher in a population with a family history of pancreatic cancer than the healthier controls. [33, 34] Pooled analysis of 5 cohorts and one case-control study concluded that the odds of pancreatic cancer are 1.76 times (95% CI: 1.19-2.61) higher in individuals with at least one immediate family member with pancreatic cancer as opposed to those without the family history of the disease. The risk is much higher among individuals with two or more cases of pancreatic cancer among first degree relatives (OR = 4.26, 95% CI: 0.48-37.79). [33] At present, research is ongoing to identify genetic mutations that lead to aggregation of pancreatic cancer in families, but genes responsible for pancreatic cancer have been identified. These genetic variations for pancreatic cancer exist on a wide spectrum.[35] One end of the spectrum constitutes common genetic variations or low penetrance genes that lead to a modest or minor increase in the risk of pancreatic cancer such as ABO blood group locus (OR = 1.20; 95% CI: 1.12 – 1.28, per allele) [36] and CFTR (OR = 1.40; 95% CI)[37]. The other end of the spectrum includes rare genetic variation or high penetrance genes that can lead to a high lifetime risk of pancreatic cancer. High penetrance genes include BRCA2 (OR = 3.5; 95% CI: 1.87 – 6.58) [38], PRSS1 (SIR = 53; 95% CI: 23-105) [39] and STK11/LKB1 (SIR = 132; 95% CI: 44-261) [40].

Among modifiable risk factors, cigarette smoking is strongly related to the risk of pancreatic cancer. Many studies report that 20 percent of all pancreatic cancer cases are due to cigarette smoking. According to a meta-analysis of 82 epidemiological studies, there

is 1.74 times (95%CI: 1.61-1.87) and a 1.2 times (95% CI: 1.11-1.29) higher risk among current smokers and former smokers, respectively, when compared to non-smokers. [41] Quitting smoking reduces the risk of pancreatic cancer, although it takes 15-20 years to reduce the risk in former smokers to that of never smokers. [42, 43]

The association between diabetes and pancreatic cancer is complicated. As per the general consideration, diabetes is a risk factor of pancreatic cancer, but diabetes can also occur due to pancreatic cancer. Prevalence of diabetes among newly diagnosed pancreatic cancer shows considerable variability. Studies have reported that the prevalence of diabetes and glucose intolerance vary from 40 percent to 80 percent among pancreatic cancer patients. [44, 45] In another study, 75 percent of diabetic pancreatic cancer patients developed diabetes within two years of their pancreatic cancer diagnosis, [46] as opposed to only 1 percent of patients diagnosed with diabetes within the last three years develop pancreatic cancer. Risk of pancreatic cancer among long-standing diabetic patients is 1.5-2.4 times higher as compared to non-diabetics. [47-50] However, the association between the presence of diabetes and the occurrence of pancreatic cancer weakens as the duration of diabetes diagnosis increases.

Other factors that can impact the occurrence of pancreatic cancer include basal metabolic index (BMI). Individuals with a BMI of >30 kg/m2 have a relative risk of 1.72 (95% CI: 1.19-2.4) compared to those with a BMI of <23kg/m2, when controlled for age, smoking, and diabetes. [51] The relationship between alcohol and pancreatic cancer varies due to a strong link between smoking and alcohol, and hence, few studies report an association while others show no link between the two. [52] Studies report that the risk of

developing pancreatic cancer is 20-45 percent higher among the heavy drinkers (defined as three drinks/day or > 30 gm/day alcohol) when compared to the non-drinkers. [52-54]

Among the other risk factors, there is a 40 percent higher lifetime risk of pancreatic cancer among those diagnosed with hereditary pancreatitis compared to those without hereditary pancreatitis. [39] Similar to diabetes, pancreatitis can be both the risk factor and a manifestation of pancreatic cancer, which leads to difficulties in estimation of the association of the two conditions. Patients with chronic pancreatitis can lead to pancreatic cancer. However, patients who have pancreatic cancer can also develop pancreatitis due to cancer. A large case-control study by the Pancreatic Cancer Consortium revealed that the association with pancreatic cancer was higher in patients with a recent diagnosis (<1 year) of pancreatitis (OR=21.35, 95% CI: 12.03-37.86) as compared to patients with diagnosis of more than two years (OR=2.71, 95% CI: 1.96-3.74). As per the overall findings of the study, six percent of the pancreatic cancer cases reported a history of pancreatitis in contrast to one percent of cases in the control group. [55] A meta-analysis that investigated dietary factors concluded that consuming one serving of meat per day increases the risk of pancreatic cancer by 19 percent, [56] while other studies concluded that diet rich in fruit and vegetables protect against pancreatic cancer by decreasing risk by 30-40 percent. [57-59]

2.1.3. Clinical Presentation

Pancreatic adenocarcinoma often presents itself with various, nonspecific and insidious signs and symptoms. Often due to the sudden onset, early detection and diagnosis

of the carcinoma are rarely achieved. Symptoms presentation in the patient depends on the location of the tumor and the stage of the disease. A majority of the cases involve tumor formation in the head of the pancreas leading to obstructive cholestasis accompanied by abdominal discomfort and nausea. On rare occasions, this may also lead to duodenal obstruction and GI bleeding. [1]

As per a large case-control study, early pancreatic cancer patients present with 12 alarm symptoms: abdominal pain, dyspepsia, weight loss, asthenia, anorexia, new-onset diabetes, back pain, shoulder pain, lethargy, variations in bowel habits, pruritis, and jaundice. Among these, back pain, lethargy, and new onset of diabetes are uniquely associated with pancreatic cancer. [60] Uncommon symptoms may include deep and superficial venous thrombosis, panniculitis, liver-function abnormalities, increased abdominal girth, and depression. Upon conducting a physical examination, jaundice, temporal wasting, peripheral lymphadenopathy, ascites, and hepatomegaly may also be present. Abdominal pain and jaundice often manifest during the advanced stages of pancreatic cancer. [1]

2.1.4. Diagnosis

Among patients presenting with the symptoms of pancreatic cancer, a diagnostic workup is the next step. Over the years, several diagnostic modalities have been developed and used in patients with suspected pancreatic tumors. These include transcutaneous ultrasound (US), computed tomography (CT), magnetic resonance imaging (MRI), endoscopic retrograde cholangiopancreatography (ERCP), endoscopic ultrasonography (EUS) and positron emission tomography (PET).

At present, spiral CT scans are the preferred imaging diagnosis modality. Along with the diagnosis, it is also used for staging of pancreatic cancer. In addition to the evaluation of primary tumor site and size, CT scan is considered for assessing major vessels adjacent to the pancreas for any neoplastic invasion and thrombosis, hepatic and distant metastases. [61] Recent improvements in MRI suggest that it may be used in the future, but as of now, CT is less time consuming and cost effective. PET scans are conducted in cases where findings from the CT scan are ambiguous. [62] A diagnosis of cancer is rarely conducted using ERCP. The endoscopic stenting of the ampulla is often performed in patients with jaundice in order to relieve the obstruction. [63]

Serum tumor biomarkers are used in pancreatic cancer for diagnosing and monitoring disease progression along with treatment uptake. Carbohydrate antigen (CA19-9) marker is useful in therapeutic monitoring and early detection of recurrent pancreatic cancer. A significant limitation of CA19-9 is the lack of specificity. Levels of CA19-9 may increase in the presence of other conditions such as cholestasis. As CA19-9 is not a specific biomarker for pancreatic cancer, it is not used as a screening tool. To increase the specificity of diagnosis, a combination of serum CA 19-9 and carcinoembryonic antigen (CEA) is preferred. The evidence has indicated that the combination of CEA and CA19-9 can increase the specificity of detection by 84 percent in opposition to CA19-9 alone. Patients with large tumors mainly present in the body and tail of the pancreas, show indications of weight loss, elevated antigen CA 19-9 levels, and ascites along with CT findings. Stage determination can be obtained through laparoscopy to determine metastatic and vascular involvement. [64]

2.1.5. Staging

Staging in pancreatic cancer is judged based on tumor size, the location of a tumor within the pancreas, the spread of a tumor in the surrounding vessels, and the spread of a tumor to other body organs or metastasis. [65] Recent staging criteria followed by physicians are those of the American Joint Committee on Cancer (AJCC) and the National Comprehensive Cancer Network (NCCN). AJCC criteria for cancer staging is based on the TNM staging. The T stage here refers to the size of the tumor and the extent of spread of the tumor to other organs and vessels around the organ. The N stage refers to the presence of the tumor in the regional lymph nodes, and the M stage refers to the presence in the distant sites. [66] Using imaging techniques as mentioned above and the staging criteria, pancreatic cancer can be characterized as clearly resectable, borderline resectable, locally advanced or metastatic disease. In terms of tumor grade, T1, T2, and T3 tumors are potentially resectable. Unresectable T4 tumors involve the mesenteric artery or celiac axis. [65] In terms of cancer stage, stage I and II are resectable as the tumor has not spread to the adjacent celiac trunk, hepatic artery, superior mesenteric artery, superior mesenteric vein (SMV), and portal vein. In stage III, the tumor is still localized but involves major vessels. Stage IV is the distant metastatic stage. [66]

Table 2.1: Stages of Pancreatic Cancer

Stage	Tumor Grade	Nodal Status	Distant Metastases	Median Survival (*months)*	Characteristics
IA	T1	N0	M0	24.1	Tumor restricted to pancreas, $\leq$ 2 cm in longest dimension.
IB	T2	N0	M0	20.6	Tumor restricted to the pancreas, >2 cm in the longest dimension.
IIA	T3	N0	M0	15.4	The tumor is not restricted to the pancreas but is not extended to the celiac axis or superior mesenteric artery (SMA).
IIB	T1, T2, or T3	N1	M0	12.7	Regional lymph node metastasis
III	T4	N0 or N1	M0	10.6	Tumor involves the celiac axis or the superior mesenteric artery (SMA).
IV	T1, T2, T3, or T4	N0 or N1	M1	4.5	Distant metastasis

*N denotes regional lymph nodes, M distant metastases, and T primary tumor.
De Braud, F., Cascinu, S., & Gatta, G. (2004). Cancer of pancreas. *Critical reviews in oncology/hematology*, *50*(2), 147-155.

2.1.6. Treatment

Treatment modalities for pancreatic cancer patients depend on the classification of the tumor as surgically resectable, borderline resectable, locally advanced and unresectable, or metastatic. Patients may undergo one or a multidisciplinary approach of

the following treatment modalities: a) surgery, b) chemotherapy, c) radiation therapy, and d) palliative care.

a) Surgery

Surgery leads to significantly longer survival in comparison to other treatment options. Therefore, it remains the primary treatment of choice for patients with the resectable tumor. Approximately 15-20 percent of pancreatic cancer patients have resectable tumors. [67] Based on the extent of tumor spread, a resectable tumor is further classified as surgically resectable and borderline resectable. The primary determinant of the surgical procedure is the location of the tumor. The procedures are categorized as a) Cephalic Pancreatoduodenectomy (the Whipple procedure), b) Distal Pancreatectomy with splenectomy, and c) Total Pancreatectomy. [15] The main aim of these surgical procedures is to obtain the tumor-free margin. Prognosis of the procedure depends on surgical margin status, nodal involvement status, tumor size, tumor grade and postoperative levels of the CA19-9. The lymph-node metastasis, high-levels of CA19-9 post operation, positive margin-status and high-tumor grade are indicative of poor prognosis. [3]

Several randomized clinical trials suggest that an extended resection procedure does not improve survival, reduce the quality of life due to refractory diarrhea or increase postoperative morbidity. The extended resection refers to wide resection of the para-aortic lymph nodes and the nerve plexus. [68] The use of minimally invasive surgery (MIS) options such as the laparoscopic approach is also being investigated. Retrospectively performed cohort studies have indicated that the laparoscopic distal pancreatectomy is not

subordinate to open surgery. Additionally, a patient undergoing a laparoscopic procedure returned to a regular diet earlier and had a shorter hospital stay. [69] Even though some of the patient outcomes are better in this procedure, the laparoscopic procedure requires hospitals to have highly trained surgeons and therefore can increase the operational cost of the hospital without significant clinical improvement in the outcomes among pancreatic cancer patients. [70] Postoperative outcomes for resection surgery are mortality, complications, length of hospital stay, margin status, survival, and the total cost. These outcomes are associated with hospital volume. [71, 72] Therefore, specialized centers with more than 15-20 annual procedures should be preferred over other healthcare facilities for better post-operative outcomes. [72]

b) Chemotherapy

Adjuvant Chemotherapy for resected pancreatic cancer

Even after undergoing a resection, the results of the surgery can be dissatisfying. Various studies have highlighted the importance of postoperative treatments for patients undergoing resection surgery. The general practice of adjuvant therapy includes the use of gemcitabine after the surgery when the patient is in the position to tolerate the chemotherapy. [1] Several trials have investigated the role of adjuvant chemotherapy in patients who have undergone resection surgery. In the CONKO-001 trial, the patients who were in the adjuvant chemotherapy group were given six cycles of gemcitabine. These patients had improved in terms of disease-free and overall survival as compared to the group of patients not on adjuvant chemotherapy after the surgery. [73] In another trial

named the ESPAC-01, the adjuvant chemotherapy with folinic acid (leucovorin) and fluorouracil improved survival significantly as compared to chemotherapy alone. In another study by the Radiation Therapy Oncology group, highlighted that the combination of fluorouracil and gemcitabine administered via an infusion therapy and a radiation therapy improved overall survival. [74] These trials have demonstrated that gemcitabine alone or a combination of gemcitabine and fluorouracil-based chemoradiation therapy improves the outcomes in patients and can be considered a standard of care.

First-line chemotherapy for metastatic patients

Majority of the pancreatic cancer patients are diagnosed in the metastatic stage. The metastatic spread of the disease is mainly present in the liver and the peritoneal cavity. [1] A meta-analysis of the published results from clinical trials suggest that the overall survival was higher among metastatic cancer patients on chemotherapy. [75] Gemcitabine is considered as the mainstay of the chemotherapeutic regimen in metastatic pancreatic cancer. The drug acts by inhibiting ribonucleotide reductase and eroding the pool of deoxynucleotide triphosphate, thereby decreasing DNA synthesis. [67] In a head to head trial conducted in 1997, patients on gemcitabine chemotherapy had improved in terms of median survival (5.65 months vs. 4.41 months) than patients on fluorouracil. [76] After this landmark trial, gemcitabine became the conventional drug for chemotherapy in metastatic pancreatic cancer patients. [15]

Over the next few years, several trials were conducted to compare the novel regimens with gemcitabine. In phase 3 trials with erlotinib in addition to gemcitabine, improved progression-free survival in comparison to gemcitabine alone. Upon the sub-group

analyses, the patients who had developed grade 2 or higher skin rash had significantly better survival. In terms of the GI-related toxicities relative to gemcitabine alone, a combination of erlotinib plus gemcitabine caused more gastrointestinal discomfort. [77]

In another phase 3 ACCORD-11 trial, the combination treatment FOLFIRINOX regimen (oxaliplatin 85 mg/m^2, folinic acid 400 mg/m^2, irinotecan 180 mg/m^2, bolus fluorouracil 400 mg/m^2, infusional fluorouracil 2400 mg/m^2 over 46 hours every 14 days) was superior to gemcitabine with respect to response, progression-free survival, and overall survival in patients. The trial followed a strict inclusion/exclusion criterion with patients that are 75 years or younger and have a good Eastern Cooperative Oncology Group (ECOG) performance status were selected. Although the FOLFIRINOX was beneficial in improving survival, it increased the risk of febrile neutropenia, sensory neuropathy, and gastrointestinal toxicities. Due to the high toxicity profile of the FOLFIRINOX regimen and strict selection criteria of the clinical trial, it is recommended only for patients with good performance status, age 75 years or younger and without the risk of cholestasis. [78]

The MPACT phase 3 trial compared gemcitabine together with nanosized albumin-bound paclitaxel (nab-paclitaxel) to gemcitabine alone. The results of the clinical trial indicated that the combination of gemcitabine and nab-paclitaxel is superior to gemcitabine alone. Cancer-related health outcomes such as response, progression-free survival, and overall survival are better in the gemcitabine plus nab-paclitaxel group. The trial included patients aged 75 years or above and with the ECOG performance status 2. Hence, this regimen can be used in a wide variety of patients. Adverse effects due to the gemcitabine

plus nab-paclitaxel regimen were easier to manage as compared to the FOLFIRINOX regimen. [79]

The current evidence suggests that FOLFIRINOX and gemcitabine plus nab-paclitaxel are prescribed to patients that can tolerate the regimen-related toxicities. Gemcitabine plus erlotinib can be given to patients with skin rashes. Patients with low scores on ECOG performance status may be indicated gemcitabine alone. Further disease progression reduces treatment options as patients are too sick at this point. Few patients that are ambulatory and have minimal symptoms can be prescribed second-line chemotherapy drugs. At this point, there is a lack of consensus among oncologists on the standard of care for the second line of drugs. [80]

Table 2.2: Findings of Phase-3 Chemotherapy Trials for Metastatic Pancreatic Cancer

	Number of Patients	**Disease-free Survival, months (95% CI)**	**HR (95% CI) ***	**Median Overall Survival, months (95% CI)**	**HR (95% CI) ***
Moore et al.					
Gemcitabine	284	3.55 (NR)	..	5.91 (NR)	..
Gemcitabine plus erlotinib	285	3.75 (NR)	0.77 (0.64-0.92)	6.24 (NR)	0·82 (0·69-0·99)
Conroy et al. (ACCORD11)					
Gemcitabine	171	3·3 (2·2 - 3·6)	..	6·8 (5·5–7·6)	..
FOLFIRINOX	171	6·4 (5·5–7·2)	0·47 (0·37–0·59)	11·1 (9·0–13·1)	0·57 (0·45–0·73)

Von Hoeff et al. (MPACT)					
Gemcitabine	430	3·7 (3·6–4·0)		6·7 (6·0–7·2)	
Gemcitabine plus nab-paclitaxel	431	5·5 (4·5–5·9)	0·69 (0·581–0·821)	8·5 (7·9–9·5)	0·72 (0·617–0·835)

*HR denotes Hazard Ratio and NR - Not reported
Kamisawa, T., et al., *Pancreatic cancer.* The Lancet, 2016. **388**(10039): p. 73-85.

c) Radiation Therapy

Radiation therapy has been studied exhaustively in locally advanced pancreatic cancer. The head to head ECOG trial compared gemcitabine chemotherapy and chemoradiotherapy in patients with locally advanced pancreatic cancer. The median survival in the gemcitabine group was 9.2 months versus 11.1 months in the chemoradiotherapy group. Even though the median survival was higher in the chemoradiation group, it is difficult to draw a definitive conclusion as the power of the study was low. At this point, further studies are required to highlight the possible benefits of chemoradiation therapy. [81]

d) Palliative Care

Pancreatic cancer is associated with low mean overall survival and poor response to treatment/therapy, especially at the metastatic stage. Palliative care is of particular importance in pancreatic cancer as majority patients require it at some point in time. Palliative care in pancreatic cancer is centered around controlling the disease and the therapy-related symptoms to improve the HRQOL of patients. Surgical and radiological interventions can correct obstructive jaundice and obstruction of the duodenum. [15] With

the advancement in endoscopic techniques over the years, endoscopic stenting has replaced percutaneous biliary drainage. Large diameter metallic stents are preferred over plastic stents due longer latency period (time to occlusion) and lower incidence of cholangitis. [82, 83] Pain in patients can be relieved by using analgesics and performing pancreatic ductal decompression with surgery or endoscopy. Another method used for pain relief is external-beam radiotherapy. [2]

2.1.7. Economic Burden of Systemic Therapies

The economic burden of cancer is anticipated to increase in the coming years due to improvement in survival and the aging population. [84] A retrospective database analysis of the Medicare beneficiaries using SEER-Medicare claims data estimated that the mean total direct medical costs of care were $65,500 and mean incremental costs were $61,700. Mean total cost for surgically resectable locoregional disease ($134,700) is higher than unresectable disease ($65,300) or distant disease ($49,900). Hospitalization contributed to the largest portion of health care costs in patients with unresectable locoregional and distant disease. Cancer-directed surgical procedures constituted the largest fraction of total costs in patients with surgically resectable disease. The percentage of cancer-directed procedure costs were 38 percent, 19 percent and 14 percent for locoregional resectable, unresectable and distant diseases, respectively. As discussed above, specialized centers with high volume had better postoperative outcomes. A decision model that compared different treatment strategies also concurred that the specialized centers with high volume [$5991/quality-adjusted life-months (QALMs)] had better incremental cost-effectiveness

ratio (ICER) than low volume centers ($9144/QALMs). The SEER-Medicare study also assessed chemotherapies and radiation through cohort analysis. Chemotherapy and radiation therapy constituted a greater proportion of mean direct costs in patients with a diagnosis of unresectable locoregional disease and distant disease. Whereas, mean direct costs are much lower in cases with a diagnosis of resectable locoregional disease. The percentage of chemo/radiotherapy was 19 percent, 14 percent and 10 percent of the direct cost for unresectable locoregional, distant disease, and resectable locoregional, respectively. [8]

Head to head economic analyses for gemcitabine and 5- fluorouracil (5-FU) therapies was conducted by the National Health Service, UK. The results showed that gemcitabine therapy was more cost-effective than 5-FU, with an incremental cost per life year of £ 12,206 and cost per progression-free life-year of £ 19, 888. [85] Recent chemotherapy treatment options such as gemcitabine and capecitabine (gem-cap), gemcitabine and erlotinib (gem-e), and FOLFIRINOX were analyzed for cost-effectiveness using Markov modeling. The model was developed using Canadian costing data (2010 dollars), efficacy data from published literature and utilities from surveying Canadian oncologists. The most cost-effective treatment varied as per the societal willingness to pay (WTP) threshold. ICER for gem-cap, gem-e, FOLFIRINOX when compared to gemcitabine were CA$ 84, 299, CA$ 153,631, and CA$ 133,184 per QALY. FOLFIRINOX was cost-effective only if patients WTP is high or the cost of the drug is reduced. [86]

2.2 HEALTH-RELATED QUALITY OF LIFE

2.2.1. The Concept

According to the CDC, "Quality of Life (QOL) is a broad multidimensional concept that usually includes subjective evaluations of both negative and positive aspects of life." Health-related quality of life (HRQOL) as a concept has expanded to include all those facets of quality of life that reflect health conditions. HRQOL addresses subjective perception by measuring the impact of symptoms, that includes physical, emotional, social and cognitive functions. Further, it also captures the influence of disease symptoms and side effects of the treatment on the patient. [87] Physiologic markers provide information about the disease to the clinician but make little sense to the patients. Patients are more interested in the areas of functional capacity and overall well-being with which physiologic markers are poorly correlated. [88] For example, in chronic heart disease patients, exercise capacity in the laboratory is poorly correlated with the exercise capacity in daily life. [89]

HRQOL measure can consist of a single measure or multiple measures that combine to form a domain or dimension. A domain refers to an area of behavior, experience or health that we are trying measure. For instance, the physical domain can include mobility, self-care, fatigue, etc. and on the other hand, the emotional domain can include depression, anxiety, and well-being. Psychometrists and behavioral scientists perform studies to determine weights for each domain or item based on the importance of each item relative to the other. [90]

HRQOL tools are categorized as generic or disease-specific. Generic tools further include single indicator measures, health profiles, and utility measures. A health profile considers all the important aspects of HRQOL. An example of a health profile is the sickness impact profile (SIP) and includes a physical domain consisting of items on ambulation, mobility, body care and movement, and a psychosocial domain with items on social interaction, alert behavior, communication, and emotional behavior. Further, SIP can also consist of domains on eating, work, sleep, and home management. Advantages of a generic HRQOL tool are that it can be used for any population irrespective of the disease condition and enables researchers to make a general comparison; for example, using generic tool to estimate the relative impact of different health care programs among different sections of the populations. A major disadvantage of the generic tools is that they might be unresponsive or inflate the scores due to lack of sensitivity. [90, 91]

Disease-specific tools are focused on the areas that are of main concern for a patient in a disease condition. This approach improves the responsiveness of the tool. Several disease-specific tools exist for various conditions. Hence, it is important for researchers to make an evidence-driven decision while making their choice. Apart from higher responsiveness, disease-specific tools are related closely to the areas that are assessed by the clinicians on a routine basis. [91]

In recent years, the paradigm of health is shifting towards a more patient-centric approach. Self-reported HRQOL assessment is considered as a critical predictor of morbidity, mortality, and treatment effectiveness. As more tools for measuring HRQOL are validated, there are sustained efforts to include these tools as a measure of the quality

of care, clinical effectiveness, and reimbursement decision-making. [16] Similarly, many studies suggest that HRQOL tools used among cancer patients provide critical information that helps in clinical decision making and patient management in a better way. Over the last decade, survival among cancer patients has lengthened. Several oncology-related studies suggest that survival is associated with HRQOL. Therefore, several oncologists have started accepting HRQOL as an important aspect of cancer care. [92]

2.2.2. Health-Related Quality of Life in Cancer

Cancer is characterized by disease and treatment-related psychosocial consequences that include psychological, physical, functional, social, sexual, and occupational effects. [93] HRQOL is considered as an important end-point in oncology-related outcomes studies. Studies following correct methodologies can provide critical insights which could be of prognostic value for the oncologists to further improve the treatment efficiency and effectiveness. [94] The evidence from the recent studies among cancer patients suggests that the patient-reported data on QOL measures could also be helpful in clinical decision making and patient management. A systematic review assessing the relationship between health-related quality of life (HRQOL) and survival in cancer patients provided evidence that there is a positive relationship between QOL scores and survival duration. This justifies the collection of HRQOL information to assess survival in cancer patients. [16]

Oncology has several validated tools such as European Organization for Research and Treatment of Cancer and Quality of Life Questionnaire Core 30 (EORTC QLQ C30) [95]

and Functional Assessment of Cancer Therapy-General (FACT-G). [96] Both tools have been translated into 24 languages and are often used in clinical trials for cross-population comparisons. These instruments have been developed with a core module and a treatment or a symptom-specific module. For example, FACT-G determines the overall QOL and FACT-Anemia module measures the impact of anemia and fatigue on the patients. FACT-G development and validation were completed over the four phases- item generation, item reduction, scale construction, and psychometric evaluation. After several modifications and improvements, the current version includes 27 items. [93] FACT-G assesses HRQOL across four dimensions; physical well-being (PWB) – seven items, social/family well-being (SWB) – seven items, emotional well-being (EWB) – six items and functional well-being (FWB) seven items. [96]

Measurement of general HRQOL in oncology by reliable and validated tools has proliferated in the present. [95, 96] Despite the uptake, many researchers have expressed their concerns about the interpretation of multi-dimensional tools. [97] Following FACT-G development, several site-specific, treatment-specific, symptom-specific, and non-cancer subscales were developed using the same four-phase development process. [93] Many experts in oncology have highlighted the need for HRQOL assessment tools in a disease such as hepatobiliary cancers which are highly symptomatic and are marked by rapid deterioration of the overall health. For example, in hepatobiliary cancers, 18 questions pertaining to the assessment of the effects of cancer and treatment-related symptoms on HRQOL were added to the FACT-G tool. This approach enables oncologists

and researchers to make treatment adjustments or file regulatory claims for the drugs in an informed way. [98]

2.2.3. Health-Related Quality of Life (HRQOL) of Pancreatic Cancer Patients

Pancreatic cancer is the fourth leading cause of cancer-related deaths across genders. Majority of pancreatic cancer patients are diagnosed at an advanced stage. [26, 99] The disease at this stage is marked with multiple symptoms along with the brisk deterioration of HRQOL and functional status. Current treatment modalities available increase post-treatment morbidities and symptom burden with minimal or negligible improvement in survival. [100]

Crippa et al. assessed the HRQOL of pancreatic cancer patients across all the stages undergoing surgical and medical treatment. The assessment was carried out using the FACT tools at baseline and follow-up at three and six months. Based on the diagnosis, patients were divided into three groups: 30.5 percent had localized disease (group 1), 37 percent had locally advanced (group 2), and 32.5 percent had metastatic disease (group 3). As per the baseline assessment of the HRQOL in patients, there was no statistical difference between the three groups. Patients who had stent placement saw a deterioration in HRQOL at three months, but the scores were improved significantly at the six-month assessment. On the contrary, HRQOL scores of the patients on chemotherapy significantly decreased at three months, and no significant changes were observed at six months. The patients that were prescribed chemoradiation therapy reported no significant changes in HRQOL scores at both time points. HRQOL scores improved from baseline evaluation to follow-up only

for patients that underwent the surgical resection. Authors of the study concluded that for pancreatic cancer, the patient's palliation of symptoms remains the main goal of therapy. Further, metastatic disease significantly decreases HRQOL at the time of follow-up, which may be attributed to both therapy and progression of the disease. [11]

In the last few years, several studies compared various chemotherapeutic agents on HRQOL outcomes among the metastatic cancer patient population. For instance, ACCORD 11 randomized controlled trial (RCT) compared the two first-line chemotherapy agents, FOLFIRINOX and gemcitabine, among metastatic cancer patients with good performance status. [78] The study findings highlighted the contrast on HRQOL between the two regimens. The HRQOL assessment was carried out using the EORTC-C 30 tool. The FOLFIRINOX arm had significantly less HRQOL impairment as compared to the gemcitabine arm as patients' conditions deteriorated throughout the disease. FOLFIRNOX also demonstrated better results in terms of overall survival and pain outcomes. Therefore, FOLFIRINOX is considered a standard of treatment for patients with good performance status. [101]

In a systematic review of the effect of chemotherapy on the HRQOL of advanced pancreatic cancer patients, 36 articles stemming from 30 RCTs were evaluated. Out of 23 studies that evaluated HRQOL, 14 studies reported a change in scores from baseline. Four studies concluded improvement in HRQOL scores in at least one treatment arm, and three studies reported a decrease. Remaining studies reported stable scores. Four studies that reported an increase in HRQOL scores compared following pairs of regimens: gemcitabine versus BAY12-9566, gemcitabine plus placebo versus gemcitabine plus marimastat,

FOLIFIRINOX versus gemcitabine and fluorouracil plus cisplatin with fluorouracil alone. Gemcitabine was better than BAY12-9566 in terms of global health status, physical, functional, and pain scores of the EORTC-C 30 tool. The gemcitabine combination with placebo yielded higher scores for the FACT-Pancreas tool when compared with the gemcitabine combination with marimastat. The combination of fluorouracil with cisplatin also slowed down the decrease in HRQOL as compared to fluorouracil alone. Gemcitabine is considered as the standard of care for treatment in advanced pancreatic cancer patients but can be substituted with FOLIFIRINOX in patients with good performance status. The study concluded that chemotherapy could stabilize HRQOL in metastatic pancreatic cancer patients. It further highlighted that since survival is positively associated with HRQOL for current chemotherapy modalities, improvement in survival may not lead to deterioration in HRQOL. [102]

2.2.4. Health-Related Quality of Life (HRQOL) Measures in Pancreatic Cancer

Along with general cancer tools such as FACT-G and EORTC QLQ-C 30 that exist for measuring HRQOL in pancreatic cancer, commonly used condition-specific tools are the Functional Assessment of Cancer Therapy-Hepatobiliary Questionnaire (FACT-Hep), and the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Pancreatic Cancer (EORTC QLQ-PAN26).

EORTC QLQ-PAN 26 questionnaire is designed specifically for pancreatic cancer. The tool can only be used when combined with EORTC-QLQ C30. The combination of both measures increases the total number of items to 56. [103] Along with a high number of

items, the survey has not been validated in metastatic pancreatic cancer patients. Even though the tool is commonly used in pancreatic cancer, the lack of information on the reliability and validity of the tool raises uncertainties on the results. [104]

FACT-Hep was developed to assess the HRQOL of patients suffering from liver cancer, hepatobiliary -pancreatic cancer, and metastatic pancreatic cancer. It comprises of 27 core items of FACT-G and 18 items that specifically assess the effect of hepatobiliary cancer. [9] Hepatobiliary cancer subscale (HCS) consists of items that assess the effects of back and stomach pain, gastrointestinal symptoms, anorexia, weight loss, and jaundice in patients. FACT-HEP in total consists of five subscales and an overall HRQOL scale, with higher scores indicating better HRQOL. The scale is rated on a four-point Likert-type scale, which ranges from 0 (not at all) to 4 (very much). [104]

A study conducted by Heffernan et al. tested the psychometric properties of the FACT-HEP tool. The study reported that FACT-Hep has high internal consistency with Cronbach's alpha value of 0.94. Test-retest reliability was also high, with a spearmen correlation value of 0.91. The scale also demonstrated convergent and divergent validity when tested among a group of hepatobiliary cancer patients that included metastatic colorectal cancer, hepatocellular carcinoma, gall bladder cancer, and pancreatic cancer. [9] In another study, Cella et al. conducted a psychometric assessment of FACT-Hep in metastatic pancreatic cancer patients. The scale reported good internal consistency, content validity, and responsiveness. [104]

The shorter versions derived from FACT-Hep include FACT Hepatobiliary Symptom Index (FHSI)-18, an 18-item symptom index and FHSI-8, an 8-item symptom index. Aim

for the FHSI-18 is to assess HRQOL by adopting a rapid and symptom-focused approach. [98, 105] In a study conducted to assess the psychometric properties among hepatobiliary cancers, the FHSI-18 scale performed well. The scale showed high internal consistency, good test-retest reliability and strong association with other similar scales such as ECOG performance status and treatment status of the patients. [98] Similar study was also conducted in metastatic pancreatic cancer patients. Considering 0.70 as the threshold, the FHSI-18 demonstrated good internal consistency with standardized Cronbach's alpha of 0.89. FSHI-18 also has high convergent and divergent internal consistency. The FHSI-18 scores were significantly different for a group of patients with the ECOG performance status of 0 when compared with the other group with ECOG performance status of 1, indicating high construct validity of the FHSI-18. The FHSI-18 tool was also responsive to change in tumor response. Patients that had progressive disease scored lower than the stable patients. The difference between the scores for the two group of patients was statistically significant ($p<0.05$). The authors further indicated that the FHSI-18 tool demonstrated strong psychometric properties; the FHSI-18 may be useful in assessing HRQOL of patients with significant disease burden. [104] One of the key predictors of HRQOL in patients with chronic conditions is the patient's ability to manage his/her own health. [20, 21, 106, 107] In a study conducted among breast cancer patients, patients who perceived greater decision control reported higher QOL scores. [24]

2.3 PATIENT ACTIVATION

In recent years, there are two emerging policies to enable patients to become a key influencer of their health care quality and costs. First, consumer-directed health insurance plans that aim to lower the cost and enhance the quality of care. Second, the Chronic Illness Care model which aims at the patient-oriented care by involving patients and family members as part of the health care team. The model is driven by enabling patients with skills, knowledge, and motivation to make them an activated and effective member. [108] Past research has provided us with the evidence that patients are more likely to make better decisions and take better care of their health if they are more involved, informed and confident to take care of themselves. [108, 109]

In 2004, Hibbard and colleagues developed Patient Activation Measure (PAM) to assess the broader concept of "activation" that includes patient's knowledge, skills, confidence, and beliefs about managing a chronic illness.

2.3.1. Patient Activation Measure

Patient activation measure (PAM) is developed as a probabilistic Guttman-like scale that segregates patients with a varying level of activation among four stages. PAM evaluates activation on a continuous scale. The continuous scale enables evaluation of the varying level of patients' activation. The measure evaluates a broad range of dimensions that include knowledge, skills, belief, and behavior of the patients. In the first stage, patients should possess the belief that they have an essential role to play in their health care. This stage further does not require them to act towards their disease management. Patients in the second stage are required to have the necessary knowledge and confidence

to take steps towards disease management. The “knowledge” is not limited to the disease area but also medications and lifestyle changes. In the third stage, patients are involved proactively in disease management. This includes maintaining a required lifestyle and managing disease and treatment-related symptoms. The fourth stage requires patients to be partners in health, address their health problems and maintain their lifestyle even under stress.

The PAM tool development process comprised of four stages. In stage 1, literature review and consultations with experts using ‘consensus method’ was carried out. Stage 2 comprised of preliminary survey implementation and conducting a psychometric assessment using Rasch methodology. Rasch methodology is a technique that was developed to assess and improve the precision of the instrument. It uses respondents raw test scores to generate its performance on a linear scale while accounting for varying difficulty across items on a survey. [110] Stage 3 aimed at increasing the range of measurement and testing the feasibility of using the tool in conditions other than chronic illnesses. Stage 4 involved the assessment of construct validity of the tool in different subsamples of the population. [18]

A study assessing the psychometric properties of the tool was conducted among a convenience sample of 486 patients, out of which 118 were suffering from chronic illnesses. Item selection for the tool was conducted using the fit statistics, which measures the deviation of the item responses from the model expectations. [18] The infit value is most sensitive to the fit of an item when its scale location is close to the respondent’s scale location. Whereas the outfit value is most sensitive when the item’s scale location is distant

from the respondent's scale location. Smith et al. suggest that the fit values that are between 0.5 and 1.5 generate a tool with sufficient unidimensionality and variability. [111]

Rasch analysis generated a 22-item tool with an item-hierarchical order of knowledge, belief, and skill, which suggests that activation is developmental. The items have infit values between 0.76-1.32, which are indicative of unidimensionality. Rasch person reliability estimates were between 0.85 (real) and 0.88 (model). Cronbach's alpha for the was 0.91. The tool was further evaluated with a national probability sample to measure the performance in a heterogeneous group of patients and estimate the construct validity. The PAM performed identically with the national sample data. The Rasch person reliability estimates range for the infit value was from 0.71-1.44 and outfit value was from 0.80-1.34 (except for one). The PAM also had a high degree of construct and criterion validity. [18] Hibbard et al. designed a 13-item shorter version to reduce patient burden and implementation cost. The shorter version would also be easier to implement in a clinical setting. The psychometric properties of the 13-item scale were comparable to the 22-item scale. The range of scores on the shorter version was between 38.6-53.0 on a theoretical scale of 0-100-point scale. In terms of the infit and the outfit values, they ranged between 0.5-1.5. The scale had lower reliability leading to some loss of precision in individuals without chronic diseases, those that belong to lower socio-economic class, aged above 85 years, and rated their health as poor. [19]

As per a study conducted among chronically ill patients, those with higher PAM scores had significantly higher patient outcomes such as quality of life, physical and mental functional status, and patient satisfaction. Patients with the lowest PAM scores reported

very low scores on the physical functional scales. Hence, the authors suggested that PAM can help identify patients with the low physical functional status that may need tailored management and further follow-ups. [18]

In another study examining the relationships between patient activation and health outcomes, cost of care and patient experience results indicated that the patients with higher activation scores utilized less health care resources scored higher on clinical and behavioral outcomes scales and had better patient-care experience. [22]

The relationship between patient activation and health-related quality of life has been studied in many chronic conditions. In a study conducted by Magnezi et al., researchers evaluated the association of patient activation, depressive symptoms and quality of life in a primary care setting. The cross-sectional study was conducted among 278 patients using PAM-13 to measure patients' activation levels, and SF-12 to measure HRQOL. PAM scores and SF-12 scores were positively correlated ($r = 0.39$, $p<0.0001$). Physical health composite (PHC) and mental health composite (MHC) subscales also showed a positive correlation with the PAM scores ($p < 0.0001$). Analysis of covariance (ANCOVA) identified that the SF-12 scores were also significant predictors of the PAM scores (F value = 38.2). [112]

2.3.2. Patient Activation in Cancer

The PAM has shown a positive correlation with health outcomes in several cancer disease states. Some examples of studies are summarized below:

In a study conducted by Hay et al. in 2016, researchers investigated the relationship between cancer risk beliefs, language preferences, and patient activation in a multilingual urban primary care setting. The cross-sectional study was carried out in a sample of 460 patients. The sample comprised of Haitian-Creole speakers, Spanish speakers, and English speakers admitted at New York's queen hospital center. The cancer risk beliefs and patient activation using PAM-13 were measured for the patients across different languages. Patients with greater beliefs in the role of wishful thinking and avoiding too much thought about the risk of cancer demonstrated higher patient activation scores ($b = 0.07$, $SE(b) = 0.4$, $P = .046$ and $b = 0.12$, $SE(b) = 0.03$, $P<0.01$, respectively). Similar results were obtained upon multivariate analysis while controlling for language preferences and other covariates. [113]

In another study, O'Malley et al. estimated the levels of patient activation in breast and prostate cancer survivors and explored the factors associated with patient activation. The cross-sectional study was conducted among 325 patients across four community hospital sites in New Jersey. PAM-13 measure was used to assess patient activation levels, where higher composite scores refer to higher levels of activation. Cancer-site was found to be correlated to the patients' activation levels with marginally higher mean patient activation scores among breast cancer ($M + SD = 3.34 + 0.37$) survivors versus prostate cancer survivors ($M + SD = 3.25 + 0.38$). Among breast cancer survivors, none of the patients' demographics were related to patient activation. Prostate cancer survivors of Caucasian background reported higher patient activation scores when compared to other races/ethnicities. Further, prostate cancer survivors with unemployment status reported the

lowest activation scores. Similar trends were observed in prostate cancer survivors with annual incomes less than 20k with mean activation scores of 3.07 + 0.38. Access to an oncology team and primary care physicians ($p < .001$) and perception of time spent with oncologists ($p < .01$) were both positive predictors of activation among both groups. [114]

Hibbard et al. investigated the impact of patient activation on the cancer patient journey. The study aimed at understanding the relationship between behavior, decision-making, communication with providers, and adhering to medicines among cancer patients. The 41-item survey collected responses on patient activation using PAM-13, patient behavior, and experiences at different phases of cancer. The data was collected from 500 patients diagnosed with common cancers (lung, breast, colorectal, or prostate). The results of the multivariate analysis conducted indicate that the while controlling for demographics and health status, activated patients are 4.7 times more likely to begin exercises and 3.33 times more likely to initiate healthy eating than the patients with low activation levels. In terms of voicing concerns, activated patients are 10 percent more likely to raise concerns or provide suggestions than others. Activated patients were also 4.5 times more likely to manage side-effects and 45 percent more likely to adhere to medications than less-activated patients. In other matrices such as satisfaction with care, understanding the diagnosis, following doctor recommendation, and discussing side-effects with health care providers (HCPs), highly activated patients were significantly better than their counterparts. Overall findings indicate that highly activated patients are more likely to communicate concerns to providers, more likely to adopt healthy lifestyles, less likely to be ill-informed about their

condition, more confident at managing their symptoms and more likely to follow HCPs directions. [23]

A study published by Schneeberger and colleagues in 2019 evaluated the effectiveness of a lifestyle medicine intervention on the quality of life of breast cancer survivors. The retrospective review of the intervention program included 31 breast cancer patients that completed the therapy or were on hormonal therapy. The intervention consisted of education and experience in nutrition, culinary medicine, physical activity, and stress relief practices. Validated questionnaires were employed over seven weeks to estimate perceived stress, depression, patient activation, and quality of life at each visit. Although not statistically significant, respondents reported changes in the positive direction in patient activation and HRQOL throughout seven weeks. [115]

In a study conducted by Jansen et al., researchers aimed at understanding the relationships between patient activation, total cost, and HRQOL in cancer patients treated with total laryngectomy. The cross-sectional study was conducted in the Netherlands among 248 patients. Total costs were calculated using medical consumption and productivity cost questionnaire; patient activation and HRQOL were assessed using PAM and EQ-5D, respectively. The mean PAM score for 248 patients was 59 (SD =17). The majority of patients belonged to patient activation level – 3 and had a total score ranging from 55.2 to 67.0. Fifty-six patients had the lowest PAM scores (level – 1). Forty-three patients with slightly higher PAM scores belong to level – 2. Remaining 45 patients reported higher scores indicative of patient activation level – 4. Patients with activation level – 4 had the highest EQ-5 D scores, indicating a positive correlation between the two

measures. While controlling for other clinical and demographic characteristics in a multivariate analysis, patients at different activation levels differed significantly on EQ-5D status. [116]

2.4 SUMMARY

Pancreatic cancer is associated with a poor prognosis and a high mortality rate; thus, care management should include palliation of debilitating symptoms such as pain, fatigue, malabsorption, thromboembolism, obstruction of biliary and intestinal tracts and cachexia. [7, 28] Risk for cancer dramatically increases as age increases. Two-thirds of the pancreatic cancer patients are ≥65 years of age with an average age at diagnosis of 71 years. The treatment of pancreatic cancer with surgery, radiation, and chemotherapy can marginally improve survival, although the toxicities of the treatment can further add to the patient symptom profile. [10] As current treatment options have resulted in only minimal prolongation of survival and disease mortality rate is still high, health-related quality of life (HRQOL) has become of paramount importance. Several studies have shown that baseline QOL measures are associated with survival in pancreatic cancer. [12] In chronic conditions including cancer, one of the important predictors of HRQOL is a patient's ability to manage his/her own health (specifically, patient activation in this study), with increasing evidence of a positive association between the two. [20, 21, 24, 115, 116]

A cross-sectional survey conducted to measure activation level across a broad range of cancer patients gave insights that less activated patients are likely to be ill-informed about their disease, less effective at management of their symptoms and side effects, more

hesitant to adopt a healthy lifestyle and less inclined to follow doctor recommendations. [23] A study conducted in adults with chronic conditions, reported that patients with higher patient activation measure (PAM) scores are 5 times more likely to report significantly higher QOL scores. [20] Similar results were observed in a study conducted among sixty stage 1 and stage 2 breast cancer patients to assess patient activation and quality of life scores; patients who perceived greater decision control reported higher QOL scores. [24] However, no known study has examined the association of patient activation levels with the HRQOL scores of pancreatic cancer patients, which could yield important information for health care and outcomes of pancreatic patients.

Chapter 3: Methodology

Patient activation is an important concept that is related to HRQOL of patients. Activated patients are better able to regulate their own care by becoming partners in disease management, which is essential in treating diseases such as cancer. The patient activation is a variable concept that can be altered with time. This study aimed at understanding the relationship between patient activation and HRQOL in patients diagnosed with metastatic pancreatic cancer. We collaborated with Texas Oncology clinics in Texas, where patients were recruited at their multiple care sites. Texas Oncology is a participant in the oncology care model (OCM). The OCM is a program initiated by the Centers for Medicare and Medicaid Services that focuses on high quality patient care and treatment experience.

The chapter is sub-divided into eight sections: Study Design, Study Objectives and Hypotheses, Study Instruments, Study Variables, Study Sample and Selection Criteria, IRB Procedure, Data Collection Procedure, and Statistical Analysis.

3.1. STUDY DESIGN

The research study employed a non-experimental, cross-sectional survey design. A self-reported questionnaire was to collect the data from locally advanced or stage IV or recurrent pancreatic cancer patients selected through convenience sampling. Locally advanced, stage IV and recurrent pancreatic cancer patients were considered as a target population of this study as they visited clinics frequently for chemotherapy treatment. Patient completed surveys during their visits. The survey instrument first measured patient activation or the ability of the patient to take their own care. Second, the HRQOL of the patient was assessed. Finally, we measured several patient demographics/personal factors. Also, before rolling out the survey instrument was pre-tested by five pancreatic cancer

patients from one of the oncology clinics on readability, relevance, format, and time to complete.

3.2. STUDY OBJECTIVES AND HYPOTHESES

The study objectives and corresponding hypotheses are as follows:

Objective 1: To describe patient activation, HRQOL, clinical (stage of pancreatic cancer at diagnosis, comorbidities, time since diagnosis, and treatment history) and demographic (age, gender, education level, ethnicity, household income, insurance status, marital status) characteristics of the pancreatic cancer patient population.

Objective 2: To examine the relationships between HRQOL and clinical and demographic characteristics among the pancreatic cancer patient population.

Objective 3: To examine the relationships between patient activation and clinical and demographic characteristics in the pancreatic cancer patient population.

Objective 4: To determine the direction and the predictive strength of patient activation in predicting the HRQOL of pancreatic cancer patients while controlling for clinical and demographic characteristics.

> **H1:** Patient activation will be the significant positive predictor for HRQOL scores of pancreatic cancer patients while controlling for other covariates.

Objective 5: To determine if patient activation is a significant predictor of HRQOL subdomains.

H2: Patient activation will be a significant positive predictor of disease-related – physical HRQOL scores.

H3: Patient activation will be a significant positive predictor of disease-related – emotional HRQOL scores.

H4: Patient activation will be a significant positive predictor of disease-related – functional well-being HRQOL scores.

3.3. STUDY INSTRUMENT

The 38- item cross-sectional study instrument was subdivided into three sections. Section 1 consisted of the Patient Activation Measure – 13 items (PAM-13), section 2 was the functional assessment of cancer therapy – Hepatobiliary cancer symptom index – 18 items (FHSI-18), and section 3 consisted of 12 items that include measures of patient demographics and disease characteristics. The survey responses for this study were collected as a paper survey from different oncology clinic sites. The operationalization of study variables is discussed below.

3.4. STUDY VARIABLES

The dependent variable in this study was HRQOL, and the independent variable was the patient activation level. Table 3.1 describes all study variables, followed by their operational definitions, and the number of items that measure each variable.

3.4.1. Independent Variable

a) Patient activation

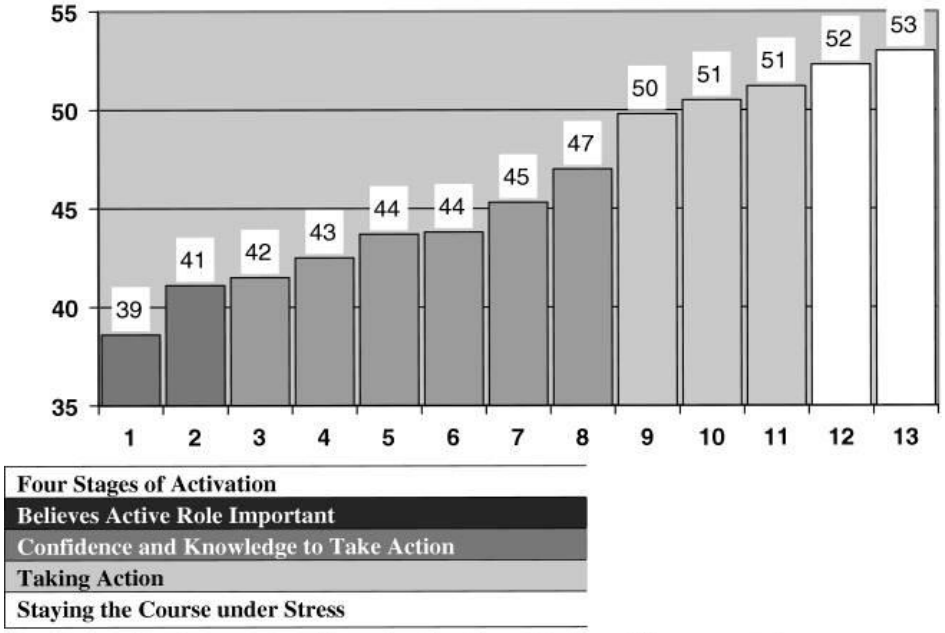
Patient activation as a concept is defined as the confidence, skill, and knowledge that a patient possesses for managing their own disease or healthcare condition. The construct was measured using patient activation measure (PAM) that segregates patients with a varying level of activation among four stages.

The PAM is an interval level, unidimensional, Guttman-like measure developed using Rasch's methodology. Rasch's analysis of the 22-item original scale has the infit values (0.71 to 1.44) and the outfit values (0.80 to 1.34) within the normal range of 0.5 to 1.5. The Rasch person reliability estimates of the measure are between .85 (real) and .88 (model). Cronbach's alpha for the measure was 0.91. The shorter 13-item version has psychometric properties comparable to the longer version. The calibrated range of PAM-13 is 38.6 to 53.0 on a 0-100-point scale. The range of the scale is comparable to PAM-22 range of 38.3 to 54.5. The infit and the outfit statistics were also within the acceptable range of 0.5 to 1.5. The PAM-13 scores were significantly related ($p<0.01$) to the constructs, for example, preventative behaviors, disease-specific self-management behavior, and consumeristic behaviors. This indicates high construct validity of the scale.

Patient activation involves four progressive stages of activation (Figure 3.1). The patients in stage 1 understand the importance of playing an active role in managing their disease condition. In addition to realizing the importance, patients in the second stage possess the confidence as well as knowledge to manage the disease condition and the side-

effects that may arise during the period of treatment. Patients in stage 3 are involved in taking action that includes following the recommended lifestyle, managing symptoms by themselves, and knowing ways to prevent future problems that may occur due to the disease condition. Stage 4 patients are activated even when under a daily-life or a disease-related stress. The item scale locations on the original scale can be converted to a 0-100-point theoretical scale. This can be achieved using the PAM-13 scoring spreadsheet (Figure 3.2). The scores range from 38.6 to 53.0 with a greater score indicating higher activation levels. See Appendix 2 for the 13-items scale.

Figure 3.1: Patient Activation Measure with Item Calibrations and the Four Stages Identified



Key: Item calibrations are the calibrated scale value of the item. This represents how much activation is required to endorse the item.

Figure 3.2: PAM-13 Score Spreadsheet

	A	B	C	D	E	F
1	Member/Patient ID	Spreadsheet ID	PAM score	PAM leve	PAM Type	Survey date
2	731-001	6F539244-280D-5043-BCC4-98676EFE9F38	55.6	3	13	2/24/202(
3	217-001	89976E78-FF01-FC40-A609-DA83CA89A41C	77.7	4	13	2/26/202(
4	032-001	86E3F272-F0B3-904C-9C87-9A7B1E150C3D	60.6	3	13	3/11/202(
5	702-001	7C0FEE34-DEED-FF48-B56C-C383326D8138	60.6	3	13	3/6/202(
6	231-001	AB98003C-C467-0E49-9DC5-1717058ABA77	60.6	3	13	3/2/202(
7	231-002	0F05FEC5-0865-D444-8F2F-69931BA606EA	48.9	2	13	3/4/202(
8	231-003	FD4FB344-9490-7142-AA08-DD50ECD3CCC0	48.9	2	13	3/10/202(
9	231-004	4490730A-19C3-8B49-B1FB-247C00F770AD	100	4	13	9/13/202(

b) Patient demographics and clinical characteristics

Patients demographics and clinical characteristics information were collected using single item measures. Patients' responses regarding the following variables were collected: Age, race/ethnicity, gender, education level, family history of pancreatic cancer, household income, insurance status, marital status, time since cancer diagnosis, tumor stage at diagnosis, treatment history, and co-morbidities.

3.4.2. Primary Dependent Variable

a) Health-related quality of life (HRQOL)

The multidimensional concept of HRQOL includes subjective evaluations of both negative and positive aspects of life. It measures the impact of the disease and symptoms, that includes physical, emotional, social, and cognitive functions. The HRQOL in pancreatic cancer patients was measured using the 18-item version of the FACT-Hep tool, named FACT Hepatobiliary Symptom Index – 18 (FHSI-18).

The shorter FHSI-18 version was derived from the FACT-HEP. The FACT-HEP, FHSI-18, and FHSI-8 were developed as an initiative of creating a set of brief symptom

indexes for nine cancer sites. The process involved interviewing clinicians and nurses (N=455) at the National Comprehensive Care Network (NCCN). The FHSI-18 is rated on a range of 0-72. It has three subscales: Disease-Related Symptoms- Physical (FHSI-DRS-P-12) scale with a range of 0-48, Disease-Related Symptoms- Emotional (FHS-DRS-E) scale with a range of 0-8, Functional Well-being (FHSI-FWB-3) scale with a range of 0-12, and Treatment Side Effects (FHSI-TSE-1) scale with a range of 0-4. Each item on the scale is rated on 5-point Likert type scale with 0 referring to "Not at All" to 4 referring to "Very Much." Patients with higher scores reflect better symptom control and a higher quality of life.

The longer FACT-HEP tool has demonstrated excellent psychometric properties among patients suffering from hepatobiliary cancers that included patients with pancreatic cancer. Similarly, excellent psychometric properties were also demonstrated by the shorter versions among metastatic pancreatic cancer patients. The FHSI-18 reported high internal consistency reliability. The standardized Cronbach's alpha value for the scale was 0.89. Convergent and discriminant validity for the scale was also significantly high ($p < 0.05$). The scale showed good discriminant properties for patients whose baseline performance status (PS) was 0 versus those patients whose PS was 1. In terms of responsiveness, the FHSI-18 tool demonstrated high responsiveness. This was measured using Guyatt's statistic with absolute values of >1.0 for both ECOG performance status response and tumor response. The minimally important difference (MID) for the scale is a change of 3 points on FHSI-18 for every unit change on PS.

Table 3.1: Constructs and Operational Definitions

Construct	Operational Definition	Item(s)	Levels/Categories
Independent Variable			
Patient Activation	Self-reported measure of knowledge, skill, and confidence for self-management of one's health. The 13-item patient activation measure (PAM) will be used to measure patient activation. Total score ranges from 0 to 100, with higher scores indicating greater patient activation. Patients will be grouped into four stages of activation based on the scores.	PAM-13	Patient Activation Score; Total Range = 0-100 *Stage 1*- $\leq$ 41 coded as 1 *Stage 2*- $\geq$ 42 but <50 coded as 2 *Stage 3*- 50-51 coded as 3 *Stage 4*- $\geq$ 52 coded as 4
Dependent Variable			
Health-Related Quality of Life (HRQOL)	Self-reported, subjective and multi-dimensional concept, which includes physical and occupational function, psychological state, social interaction, and somatic sensation. FHSI-18 (18-items) [18] 1. Disease-related symptoms-Physical: 12-items 2. Disease-related symptoms- Emotional: 2 items 3. Treatment Side Effects: 1 item 4. Functional Well-being: 3 items	FHSI-18	Higher scores = Higher QOL Total score range = 0-72
Covariates			
Age	Age at the time of the study Year of birth (subtracted from 2019)	1	Years

	In what year were you born?		
Race/Ethnicity	Self-identified racial/ethnic background One question with six nominal responses will be used to measure the construct: **Which of the following options best describes your race/ethnicity?**	1	1 = African American or Non-Hispanic Black 2 = American Indian or Alaska Native 3 = Asian-American or Pacific Islander 4 = Caucasian or Non-Hispanic White 5 = Mexican American or Hispanic 6 = Other (please specify)
Gender	Self-identified gender One question with four nominal responses will be used to measure this construct: **What is your gender?**	1	1 = Male 2 = Female 3 = Transgender 4 = Other (please specify)
Education Level	The highest level of education One question with four ordinal response options will be used to measure this construct: **Which option describes your highest education level?**	1	1= Less than high school 2 = High school graduate or GED 3 = College Graduate 4 = Postgraduate (e.g., MD, MS, Ph.D.) 5 = Other (please specify) Higher numbers will indicate a higher educational level.
Household Income	An option which defines household income. One question with five ordinal response options will be used to measure this construct: **Which of the following options best describes your household income?**	1	1 = Less than $25,000 2 = $25,000 to $50,000 3 = >$50,000 to $75,000 4 = >75,000 to $100,000 5 = >$100,000 Higher numbers indicate a higher household income.
Insurance Status	An option that describes the insurance they currently have. One question with four nominal response options will be used to measure this construct: **Which of the following types of health**	1	1 = None 2 = Private Insurance 3 = Public Insurance (Medicare, Medicaid) 4 = Other

	insurance do you currently have (Check all that apply)?		
Marital Status	An option that describes patients' current marital status. One item with six nominal response options will be used to measure this construct: **What is your current marital status?**	1	1= Single, in a relationship 2 = Single, not in a relationship 3 = Married 4 = Partner/Living together 5 = Divorced/Separated 6 = Widowed
A family history of pancreatic cancer	**Has anyone ever been diagnosed with pancreatic in your immediate family?**	1	Yes/No
Time since pancreatic cancer diagnosis	A single item with five response options will be used to measure the length of time that each patient had the disease. **How long ago you were diagnosed with pancreatic cancer?**	1	1 = 3 months ago or less 2 = greater than 3 to 6 months 3 = greater than 6 months to 1 year 4 = greater than 1 to 1.5 years 5 = greater than 1.5 to 3 years
Tumor stage at diagnosis	An option that describes patients' tumor stage at the time of diagnosis. A single item with five response options will be used to measure this construct. **What was the tumor stage when you were first diagnosed with pancreatic cancer?**	1	1 = Stage 1 2 = Stage 2 3 = Stage 3 4 = Stage 4 5 = Missing
Treatment history	An option that describes patients' treatment history. A single item with two response option will be used to measure this construct. **Which option best describes your treatment history?**	1	1 = Newly diagnosed 2 = Prior treatment history
Co-morbidities	An option that describes other comorbid conditions patients' have along with pancreatic cancer. One item with ten nominal responses and converted to number of comorbidities on an	1	Number of comorbidities Types of comorbidities □ Asthma □ Arthritis □ Diabetes □ Hypertension

	interval scale will be used to measure this construct. **In addition to pancreatic cancer, what other illnesses do you have? Check all that apply.**		□Hypercholesterolemia □ Kidney problems □ Heart disease □ Anxiety □ Liver disease □ Pancreatitis □ Depression □ Other

3.5. STUDY SAMPLE AND SAMPLE SELECTION

3.5.1. Inclusion and Exclusion Criteria

The study population consisted of patients from different sites of Texas Oncology clinics in Texas. To be eligible for the study, patients must meet all of the inclusion criteria: (1) Adults (18 years or older) receiving care at the study clinic site, (2) Able to read and write in English, (3) Diagnosed with locally advanced (unresectable), stage IV or recurrent pancreatic cancer, (4) Being treated with first line or second line chemotherapy, and (5) Expressing willingness and consent to participate.

The study was approved by the Institutional Review Board of the University of Texas at Austin (IRB Study Number- 2018-09-0042). All responses collected were anonymous, and any patient identifiers were not collected. Patient-level data for the study was kept confidential and in a secure environment.

3.5.2. Sampling Method

The study was conducted at thirteen Texas Oncology clinics at multiple sites in Texas. The contact person for the patients was Dr. Wilfong (Co-investigator) at Texas

Oncology. The clinic provided a letter of support for the study to be conducted at the Texas Oncology sites. (Appendix-4)

Patients meeting the inclusion criteria were enrolled on a continuous basis via convenience sampling by the clinical research staff at the Texas Oncology clinic during their routine clinic visit. Texas Oncology research staff members have received human subjects training. Further, the clinical research staff were trained on the procedures of patient recruitment before the beginning of the enrollment. The clinic research staff members screened the patients as per the inclusion/exclusion criteria, and those who qualified were asked if they would like to participate in a UT College of Pharmacy Survey. The cover letter along with the survey included information on the purpose of the study, voluntary nature of the study participants, the importance of the respondents' participation, the approximate time to complete the study, assurance of confidentiality of responses as well as the contact information of the primary investigator. The patients who were approached but did not provide consent to enroll in the study were logged by research staff in the informed consent tracking log (Appendix - 03).

3.5.3. Sample Size

It is crucial to estimate sample size for multivariate regression analysis. Sample size calculation ensures enough power to reduce the probability of incorrectly accepting the null hypothesis. G-power was used to calculate the appropriate sample size. The sample size calculation is based on the effect size, alpha level, power level, and the number of

predictors. Assuming a medium effect size of 0.5, an alpha level of 0.05 and the power of the study as 0.80, and 13 predictors, the sample size required for this study was 131.

3.6. Data Collection Procedures

The prospective, non-experimental, cross-sectional survey study design was used to achieve the study objectives. At their regular clinic visit, patients were approached by the clinical research staff and offered participation in the study. Clinic research staff were trained on study protocols through virtual training sessions organized for each clinical site. Patients who expressed willingness to participate in the study received a cover letter (Appendix 01) describing the study as well as a self-reported survey (Appendix 02) to complete. The data obtained using patient-reported outcomes on self-administered surveys was assessed to estimate patient activation and HRQOL of pancreatic cancer patients. No Texas Oncology PHI or other EHR data was accessed or used at any point during this study.

3.7. IRB Procedures

The study was conducted as per the most recent directions issued by the University of Texas Institutional Review Board (IRB). The IRB application for the study has been approved.

3.8. Statistical Analysis

The data analysis was conducted using R Studio version 1.1.463. The a priori level of significance for all statistical comparisons was set at $p<0.05$. Responses were analyzed with both descriptive and inferential statistics. Descriptive statistics included means, standard deviation, frequencies, and percentages.

T-test and analysis of variance (ANOVA) tests were conducted to assess the differences in means for all variables: independent, dependent, and covariables. Chi-square tests/fisher's exact test were used to assess the association between categorical variables. Due to low sample size, multiple linear regression could not be used to predict the effect of patient activation levels on the HRQOL of pancreatic cancer patients, while controlling for other covariates. Further, multiple regression models also could not be used to predict the effect of patient activation levels on the HRQOL scores of each of the three domains of FHSI-18: physical, emotional, and functional well-being.

Statistical Assumptions

While conducting statistical analysis, the assumption for the tests should be fulfilled. The assumptions for t-tests for normality and independence of observation, and equality of variance were assessed. As per the linearity assumption, there was a linear relationship between the dependent and the independent variable. This was assessed by observing bivariate scatter plots. Normality assumption was assessed by examining skewness (symmetry) and kurtosis (peakedness) of the distribution of the variables. Distribution was normal as skewness was within the range of ± 2 and kurtosis was within the range of ± 7. Further, the assumption of the equal variance in error or homoscedasticity across all the levels of the independent variable was also assessed by visually inspecting residual scatter plots. The variance of error was equal across all levels of the independent variable. The chi-square test assumption of independence and percentage of expected cell counts were assessed prior to running any analysis. If the expected cell count was less than 5, Fisher's exact test was used instead of chi-square test.

Table 3.2 provides an outline of the objectives, hypotheses, and respective statistical tests that were conducted for the study. Table 3.3 contains the measurement level for each variable.

Table 3.2: Study Objectives, Hypotheses, and Corresponding Statistical Tests

Objectives/Hypotheses	Dependent Variable	Independent Variables	Statistical Tests
Objective 1: To describe patient activation, health-related quality of life (HRQOL), clinical (stage of pancreatic cancer at diagnosis, comorbidities, time since diagnosis, and treatment history) and demographic (age, gender, education level, ethnicity, household income, insurance status, marital status) characteristics of pancreatic cancer patient population.			Mean, Standard Deviation, and Frequency
Objective 2: To examine the relationships between HRQOL and clinical and demographic characteristics among the pancreatic cancer patient population.			
	HRQOL Score	Age	Correlation
		Number of Comorbidities	Correlation
		Race/Ethnicity	One-way ANOVA
		Gender	T-Test
		Education Level	One-way ANOVA
		Household Income	One-way ANOVA
		Insurance Status	One-way ANOVA
		Marital Status	One-way ANOVA
		Family History of Pancreatic cancer	T-Test
		Time since pancreatic cancer diagnosis	One-way ANOVA

		Tumor stage at diagnosis	One-way ANOVA
		Treatment History	T-Test
Objective 3: To examine the relationships between patient activation and clinical and demographic characteristics in the pancreatic cancer patient population.			
	Patient Activation Score, Patient Activation Stage	Age	Correlation, T-Test
		Number of comorbidities	Correlation, T-Test
		Race/Ethnicity	ANOVA, Fisher Exact Test
		Gender	T-Test, Chi-Square Test
		Education Level	ANOVA, Fisher Exact Test
		Household Income	ANOVA, Fisher Exact Test
		Insurance Status	ANOVA, Fisher Exact Test
		Marital Status	ANOVA, Fisher Exact Test
		Family History of Pancreatic cancer	T-Test, Fisher Exact Test
		Time since pancreatic cancer diagnosis	ANOVA, Fisher Exact Test
		Tumor stage at diagnosis	ANOVA, Fisher Exact Test
		Treatment History	T-Test, Chi-Square Test

Objective 4: To determine the direction and the predictive strength of patient activation in predicting HRQOL of pancreatic cancer patients while controlling for clinical and demographic characteristics.			
H1: Patient activation will be the significant positive predictor for HRQOL scores of pancreatic cancer patients while controlling for other covariates.	HRQOL score	Patient activation score, Clinical and demographic covariates	Multiple linear regression: R^2, F-statistic
Objective 5: To determine if patient activation is a significant predictor of HRQOL subdomains.			
H2: Patient activation will be a significant positive predictor of disease-related - physical HRQOL scores.	Physical domain HRQOL score	Patient activation score, Clinical and demographic covariates	Multiple linear regression: R^2, F-statistic
H3: Patient activation will be a significant positive predictor of disease-related – emotional HRQOL scores.	Emotional domain HRQOL score	Patient activation score, Clinical and demographic covariates	Multiple linear regression: R^2, F-statistic
H4: Patient activation will be a significant positive predictor of disease-related – functional well-being HRQOL scores	Functional well-being domain HRQOL score	Patient activation score, Clinical and demographic covariates	Multiple linear regression: R^2, F-statistic

Table 3.3: Study Variables and Measurement Levels

Study Variable	**Measurement Level**
Dependent Variable	
Patient Activation Score	Interval
HRQOL Score	Interval
Patient Activation Stage	Ordinal
Independent Variable	

Patient Activation Score	Interval
Age	Interval
Race/Ethnicity	Nominal
Gender	Nominal
Education Level	Ordinal
Household Income	Nominal
Insurance Status	Nominal
Marital Status	Nominal
Family History of Pancreatic cancer	Nominal
Time since pancreatic cancer diagnosis	Nominal
Tumor stage at diagnosis	Nominal
Treatment History	Nominal
Co-morbidities	Nominal
Number of Co-morbidities	Interval

3.9. STUDY TIMELINE

The study took nine months to complete. Patient enrollment began in February 2020 and continued until August 2020. Patients completed the survey while waiting for their appointments with the physician/healthcare provider. Data analysis and thesis write up were completed over the next two months. Table 3.4 describe the details of the timeline.

Table 3.4: Timeline of study

Activity Name	Start Date	End Date	Duration	Feb' 20	Mar' 20	Apr' 20	May' 20	Jun' 20	Jul' 20	Aug' 20	Sept' 20	Oct' 20
Project Duration	02/20	10/20	9 months									
Recruiting patient, obtaining consent, and administering survey	02/20	08/20	7 months									
Data analysis and write-up	09/20	10/20	2 months									

Chapter 4: Results

The results of the study are presented in depth in this chapter. Firstly, the pretest results, followed by the steps for data preparation and cleaning process, and preliminary data analysis results are discussed. Next, the demographics of the participants are stated. Finally, the bivariate analyses results are reported.

4.1 Pretest Results

Five pancreatic cancer patients who satisfied the inclusion/exclusion criteria assessed the study survey. The assessment was completed using a survey evaluation form (Appendix 05). The evaluation form consisted of questions to assess the following parameters: a) readability of the survey item, b) relevance of the survey item, c) survey format, and d) time required to complete the survey.

The five study participants completed the survey within 8-10 minutes. In terms of readability of the survey items, the patients responded that all the items were clear and easy to understand. Further, all the patients agreed that the items in the survey were relevant. Finally, all of them concurred that the survey format was easy to read and user-friendly.

4.2 Data Preparation and Cleaning

Forty-four patients who met the study's inclusion and exclusion criteria were approached by the clinical research staff in 13 Texas Oncology clinics and offered participation in the study. The response rate for the study was high (95.4%) as 42 patients gave consent to participate in the study and completed the survey. Table 4.1 contains details of study participation by clinic.

Table 4.1: Study Participation by Clinics

Subject/Number	Site Name	Completed	Declined	Total
1.	Austin Central	1	0	1
2.	Dallas Presbyterian	14	0	14
3.	Longview	1	0	1
4.	Plano East	4	0	4
5.	Plano East (Prestonwood)	2	0	2
6.	Rockwall	2	0	2
7.	San Antonio (Downtown)	2	1	3
8.	San Antonio (North East)	6	1	7
9.	San Antonio (Stone Oak)	1	0	1
10.	Tyler	9	0	9
		42	**2**	**44**

4.3 PRELIMINARY DATA ANALYSIS

The interval level variables were assessed for normality by assessing the symmetry and kurtosis of the distributions. The kurtosis (|7|) and skewness (|2|) of the interval variables were not an issue as both were within the threshold values (Table 4.2).

Table 4.2: Skewness and Kurtosis Values of Interval Level Variables

Variable	Skewness	Kurtosis
Age	-0.23	2.44
PAM Scores	-0.49	4.79
FHSI-18 Total Score	-0.14	2.35
Number of Comorbidities	0.86	2.88

4.4 DESCRIPTIVE STATISTICS RESULTS

The average age of the study participants was 71.1(9.5) years. The majority were females (42.9%), Caucasian (58.5%), married or living with partner (61.9%), and college graduates or higher (57.2%). Most study participants had an annual household income of more than $50,000 (60%) and had multiple insurances (38.1%). Clinically most participants were diagnosed less than three months ago (46.3%), and the stage of cancer at diagnosis was stage 4 (39.0%). The majority of patients had two comorbidities or less (66.3%), with hypertension (HTN) being the most common comorbidity (45.2%) followed by diabetes (38.1%) (Table 4.3).

Table 4.3: Demographic and Clinical Characteristics of Study Participants

Variable	**Mean (SD)**
Age (n = 40)	71.1 (9.5)
Number of comorbidities (n=42)	3.2 (1.8)
	Frequency (%)
Gender (n = 42)	
Male	18 (42.9%)
Female	24 (57.1%)
Race/Ethnicity (n = 41)	
African American or non-Hispanic black	11 (26.8%)
Asian-American or Pacific Islander	2 (4.9%)
Caucasian or non-Hispanic white	24 (58.5%)
Mexican American or Hispanic	4 (9.8%)
Education Level (n = 42)	
Less than high school/ High school graduate	18 (42.9%)
College graduate	18 (42.9%)
Postgraduate	6 (14.3%)
Household Income (n = 40)	
Less than $25,000	11 (27.5%)
$25,000-50,000	5 (12.5%)
$50,000-75,000	7 (17.5%)

$75,000-100,000	7 (17.5%)
Greater than $100,000	10 (25.0%)
Health Insurance Status (n = 41)	
Private Insurance Only	10 (23.8%)
Public Insurance Only (Medicare/ Medicaid/ Tricare)	15 (35.7%)
Multiple	16 (38.1%)
Marital Status (n = 42)	
Single (in a relationship/not in a relationship)	6 (14.3%)
Married/ Partner/ Living Together	26 (61.9%)
Divorced/ Separated/ Widowed	10 (23.8%)
History of Pancreatic Cancer in Immediate Family (n = 41)	
Yes	5 (12.2%)
No	36 (87.8%)
Time since Initial Pancreatic Diagnosis (n = 41)	
Less than 3 months	19 (46.3%)
3 months to 1 year ago	10 (24.4%)
More than 1 year ago	12 (29.3%)
Stage of Pancreatic Cancer at the Time of Initial Diagnosis (n = 41)	
Stage 1	2 (4.9%)
Stage 2	6 (14.6%)
Stage 3	10 (24.4%)
Stage 4	16 (39.0%)
Not Sure	7 (17.1%)
Description of Treatment History (n = 42)	
Newly Diagnosed	27 (64.3%)
Prior Treatment History	15 (35.7%)
Number of Comorbidities	
0	6 (14.3%)

1	13 (31%)
2	9 (21%)
3	4 (9.5%)
4	4 (9.5%)
5 +	6 (14.2%)
Comorbidity Type (n = 42) *	
HTN	19 (45.2%)
Diabetes	16 (38.1%)
Arthritis	13 (30.1%)
Hypercholesterolemia	12 (28.6%)
Anxiety	14 (33.2%)
Depression	7 (16.6%)
Pancreatitis	5 (11.9%)
Kidney Problem	5 (11.9%)
Heart Disease	3 (7.1%)
Asthma	3 (7.1%)
Other	4 (9.5%)

* Variable percentages may exceed 100% for questions with multiple responses

The FHSI-18 score was low with the average score of 42 $\pm$ 12.4 (range 12-66.7). The average domain specific scores were Disease Related Symptoms - Physical 28.9 $\pm$ 9.1 (range 8-44.7), Disease Related Symptoms – Emotional 4.3 $\pm$ 2.3 (range 0-8), Treatment Side Effects (TSE) 2.7 $\pm$ 1.16 (range 0-4), and Functional Well-being 6.2 $\pm$ 3.3 (range 0-12). The overall Cronbach's alpha indicated high internal consistency (0.87). The internal consistency values for the FHSI domain scales were also high. (Table 4.4)

Table 4.4: FHSI-18 Scores and Scale Reliability (N=42)

FHSI-18 Domain	Number of items (Possible Range)	Mean (SD)	Range	Reliability
FHSI-DRS-P (Disease Related Symptoms-Physical)	12 (0-48)	28.9 (9.1)	8-44.7	0.84
FHSI-DRS-E (Disease Related Symptoms-Emotional)	2 (0-8)	4.3 (2.3)	0-8	0.77
FHSI-TSE (Treatment Side Effects)	1 (0-4)	2.7 (1.16)	0-4	N/A*
FHSI-F/WB (Functional/Well-Being)	3 (0-12)	6.2 (3.3)	0-12	0.84
FHSI-18 Total	18 (0-72)	42 (12.4)	12-66.7	0.87

*single item measure

The mean patient activation score for the study participants was 62.82 $\pm$ 18.52 (range 0.0-100.0). Most patients (66.7%, N=28) had higher levels of patient activation (level 3 or 4). The Cronbach's coefficient for PAM was 0.94, indicating high internal consistency for the measure (Table 4.5).

Table 4.5: The Distribution of Patients by Patient Activation Levels (N=42)

Patient Activation Level (n = 42)	Frequency (%)
Level 1	5 (11.9%)
Level 2	9 (21.4%)
Level 3	15 (35.7%)
Level 4	13 (31.0%)

4.5 BIVARIATE ANALYSIS RESULTS

Data was analyzed to assess bivariate relationships using t-tests, correlations, and ANOVA for the following objectives:

4.5.1 To examine the relationships between HRQOL and clinical and demographic characteristics among the pancreatic cancer patient population.

Results in Table 4.6 show no significant relationships between the HRQOL (total FHSI-18 score) scores and any of the clinical/demographic variables.

Table 4.6: Relationships between Health-Related Quality of Life (FHSI-Total) and Clinical/Demographic Variables

Variable	**Correlation**		**P Value**
Age (N=40)	-0.04		0.78
Number of Comorbidities (N=42)	-0.03		0.87
	Mean FHSI-Score (SD)	**T Value**	**P Value**
Gender (N=42)		0.08	0.936
Male	42.2 (11.4)		
Female	41.9 (13.5)		
History of Pancreatic Cancer in Immediate Family (N= 41)		0.23	0.82
Yes	43 (12.7)		
No	41.6 (12.7)		
Description of Treatment History (n = 42)		-0.06	0.94
Newly Diagnosed	41.9 (13.1)		
Prior Treatment History	42.2 (11.8)		
	Mean FHSI-18 Score (SD)	**F Value**	**P Value**
Race (N=41)		0.048	0.996
African American	41.3 (13.5)		
Asian American or Pacific Islander	43.0 (18.4)		
Caucasian or Non-Hispanic White	42.1 (12.7)		
Mexican American or Hispanic White	41.8 (12.8)		
Education Level (N=42)		1.50	0.23

Less than high school/ High school graduate	44 (13.8)		
College graduate	38.4 (12)		
Postgraduate	47 (7)		
Household Income (N=40)		0.70	0.623
Less than $25,000	40.3 (13.5)		
$25,000-50,000	35.0 (16.6)		
$50,000-75,000	41.1 (9.5)		
$75,000-100,000	42.4 (10.1)		
Greater than $100,000	47.2 (11.6)		
Health Insurance Status (n = 41)		1.95	0.15
Private Insurance Only	44.7 (13.1)		
Public Insurance Only (Medicare/ Medicaid/ Tricare)	36.8 (11.8)		
Multiple	44.6 (12.0)		
Marital Status (n = 42)		0.29	0.748
Single (in a relationship/not in a relationship)	38.5 (9.8)		
Married/ Partner/ Living Together	42.8 (13.1)		
Divorced/ Separated/ Widowed	42.0 (12.8)		
Time since Initial Pancreatic Diagnosis (n = 41)		0.017	0.98
Less than 3 months	41.9 (13.2)		
3 months to 1 year ago	42.2 (14.9)		
More than 1 year ago	41.3 (10.1)		
Stage of Pancreatic Cancer at the Time of Initial Diagnosis (n = 41)		0.20	0.93
Stage 1	47.0 (1.41)		
Stage 2	43.1 (14.7)		
Stage 3	42.1 (10.5)		
Stage 4	39.7 (13.6)		
Not Sure	42.1 (12.9)		

4.5.2 To examine the relationships between patient activation and clinical and demographic characteristics in the pancreatic cancer patient population.

Results in Table 4.7 show statistically significant differences in patient activation scores for health insurance status ($F = 7.26$, $df = 2, 38$, $p = 0.0021$) and marital status ($F = 3.41$, $df = 2, 39$, $p = 0.04$). A Tukey's HSD post-hoc test for pairwise comparisons revealed that for health insurance status, the mean patient activation score for public insurance only

(50.6 ± 18.2) was significantly lower than private insurance only (67.3 ± 14.4) and multiple insurance (72.2 ± 15.4) ($p < 0.05$). For marital status, the mean patient activation score for married/living (68.3 ± 15.8) with partner was higher than divorced/separated/widowed (53.2 ± 23.6) ($p < 0.05$). Bivariate analysis was conducted between patient activation levels and clinical/demographic variables. Patient activation levels were significantly associated with education levels ($X^2 = 7$, p value = 0.03) and health insurance status ($X^2 = 8.90$, p value = 0.01). Patients with low PAM levels (level 1 or 2) were mostly high school graduates or less (N = 10, 71.4%) and had public insurance (N = 9, 69.2%), while many patients that were on a higher PAM level (level 3 or 4) were college graduates (N = 15, 53.5%) and had multiple insurances (N = 14, 50%).

Table 4.7: Relationship between Patient Activation Score (PAM-13) and Clinical/Demographic Variables

Variable	**Correlation**		**P Value**
Age (N=40)	-0.07		0.68
Number of Comorbidities (N=42)	0.68		0.07
	Mean PAM Score (SD)	**T Value**	**P Value**
Gender (N=42)		1.06	0.29
Male	66.2 (14.8)		
Female	60.3 (20.8)		
History of Pancreatic Cancer in Immediate Family (n = 41)		0.23	0.82
Yes	65.3 (17.5)		
No	62.8 (18.9)		
Description of Treatment History (n = 42)		0.24	0.81
Newly Diagnosed	63.3 (18.9)		
Prior Treatment History	61.8 (18.4)		
	Mean PAM Score (SD)	**F Value**	**P Value**

Race (N=41)		2.06	0.12
African American	57.9 (12.7)		
Asian American or Pacific Islander	65.9 (21.4)		
Caucasian or Non-Hispanic White	67.5 (17.5)		
Mexican American or Hispanic White	45.4 (31.1)		
Education Level (N=42)		2.7	0.07
Less than high school/ High school graduate	55.5 (18.8)		
College graduate	68.8 (16.3)		
Postgraduate	67.05 (19.3)		
Household Income (N=40)		2.23	0.08
Less than $25,000	51.9 (21.8)		
$25,000-50,000	57.2 (7.7)		
$50,000-75,000	68.2 (15.1)		
$75,000-100,000	60.8 (13.1)		
Greater than $100,000	73.2 (19.4)		
Health Insurance Status (n = 41)		7.26	**0.0021**[α]
Private Insurance Only	67.3 (14.4))		
Public Insurance Only (Medicare/ Medicaid/ Tricare)	50.6 (18.2)		
Multiple	72.2 (15.4)		
Marital Status (n = 42)		3.41	**0.04** [α]
Single (in a relationship/not in a relationship)	54.8 (11.7)		
Married/ Partner/ Living Together	68.3 (15.8)		
Divorced/ Separated/ Widowed	53.2 (23.6)		
Time since Initial Pancreatic Diagnosis (n = 41)		0.94	0.39
Less than 3 months	62.5 (21.5)		
3 months to 1 year ago	69.05 (13.6)		
More than 1 year ago	58.0 (17.5)		
Stage of Pancreatic Cancer at the Time of Initial Diagnosis (n = 41)		0.94	0.44
Stage 1	65.4 (17.3)		
Stage 2	65.1 (17.1)		
Stage 3	69.6 (22.7)		
Stage 4	55.7 (19.3)		
Not Sure	63.3 (6.8)		

[α] Statistically significant

Table 4.8: Relationship between Patient Activation Level (PAM-13) and Clinical/Demographic Variable

Variable	Low PAM (Level 1 & 2)	High PAM (Level 3 & 4)	T/ X^2 Value	P Value
	Mean (SD)		T Value	
Age (N=40)	71.76 (9.3)	70.70 (9.7)	0.33	0.74
Number of Comorbidities (N=42)	2.78 (2.3)	1.92 (1.5)	1.26	0.22
	Frequency (%)		X^2 Value	P Value
Gender (n = 42)				
Male	4 (28.5)	14 (50)	0.98	0.32
Female	10 (71.4)	14 (50)		
Race (N=41) *				
African American	4 (28.5)	7 (25)	0.95	0.81
Asian American or Pacific Islander	1 (7.1)	1 (3.5)		
Caucasian or Non-Hispanic White	7 (50)	17 (60.7)		
Mexican American or Hispanic White	2 (14.2)	2 (7.1)		
Education Level (n = 42) *				
Less than high school/ High school graduate	10 (71.4)	8 (28.5)	7	**0.03** [α]
College graduate	3 (21.4)	15 (53.5)		
Postgraduate	1 (7.1)	5 (17.8)		
Household Income (n = 40) *				
Less than $25,000	6 (42.8)	5 (17.8)	5.65	0.27
$25,000-50,000	3 (21.4)	2 (7.1)		
$50,000-75,000	1 (7.1)	6 (21.4)		
$75,000-100,000	2 (14.2)	5 (17.8)		
Greater than $100,000	2 (14.2)	8 (28.5)		
Health Insurance Status (n = 41) *				
Private Insurance Only	2 (15.3)	8 (28.5)	8.90	**0.01** [α]
Public Insurance Only (Medicare/ Medicaid/ Tricare)	9 (69.2)	6 (21.4)		
Multiple	2 15.3)	14 (50)		

Marital Status (n = 42) *				
Single (in a relationship/not in a relationship)	2 (14.2)	4 (14.2)	4.43	0.10
Married/ Partner/ Living Together	6 (42.8)	20 (71.4)		
Divorced/ Separated/ Widowed	6 (42.8)	4 (14.2)		
History of Pancreatic Cancer in Immediate Family (n = 41) *				
Yes	2 (15.3)	3 (10.7)	0.002	0.64
No	11 (84.6)	25 (89.2)		
Description of Treatment History (n = 42)				
Newly Diagnosed	8 (57.1)	19 (67.8)	0.11	0.73
Prior Treatment History	6 (42.8)	9 (32.1)		
Time since Initial Pancreatic Diagnosis (n = 41) *				
Less than 3 months	6 (42.8)	13 (48.1)	2.28	0.36
3 months to 1 year ago	2 (14.2)	8 (29.6)		
More than 1 year ago	6 (42.8)	6 (22.2)		
Stage of Pancreatic Cancer at the Time of Initial Diagnosis (n = 41) *				
Stage 1	1 (7.1)	1 (3.7)	2.18	0.70
Stage 2	2 (14.2)	4 (14.8)		
Stage 3	3 (21.4)	7 (25.9)		
Stage 4	7 (50)	9 (33.3)		
Not Sure	1 (7.1)	6 (22.2)		

α: Statistically significant; * Fisher Exact Test

4.6 SUMMARY OF STUDY FINDINGS

Two out of five study objectives were dropped. The two objectives aimed at understanding the predictive strength of patient activation score for predicting total HRQOL and subdomain scores while controlling for covariates were not achieved because of insufficient sample size. However, the relationship between patient activation (PAM score and PAM level) and HRQOL (FHSI-18 total) was assessed using correlation and

ANOVA. The correlation test indicated a non-significant weak correlation of 0.2 between the two variables (Table 4.9).

Table 4.9: Relationship between patient activation score (PAM-13) and Health Related Quality of Life (FHSI-18)

Variable	**Correlation**		**P Value**
PAM -13 Score (N=42)	0.21		0.19
	Mean FHSI-18 Score (SD)	F Value	P Value
PAM-13 Level (N=42)		1.9	0.16
Level 1	43.6 (6.5)		
Level 2	35.5 (14.3)		
Level 3	40.8 (10.8)		
Level 4	47.2 (13.4)		

Table 4.10 summarizes the study objectives and corresponding statistical tests and results.

Table 4.10: Summary of Study Objectives and Test Results

Objectives/Hypotheses	**Statistical Tests**	**Results**
Objective 1: To describe patient activation, health-related quality of life (HRQOL), clinical (stage of pancreatic cancer at diagnosis, comorbidities, time since diagnosis, and treatment history) and demographic (age, gender, education level, ethnicity, household	Mean, Standard Deviation, and Frequency	• Average Age- 71.1 $\pm$ 9.5 years • 57.1% female • 58.5% Caucasians • 57.2% had at least a college degree • 60% had annual household income over $50,000 • 38.1% had multiple insurances

income, insurance status, marital status) characteristics of pancreatic cancer patient population.		• 61.9% married or are in relationship • 87.8% had no h/o pancreatic cancer in immediate family • 46.3% had diagnosis less than 3 mo. ago. • 39.0% had stage 4 cancer at diagnosis • 66.7% had higher levels of activation (Level 3 or 4) • 42 was the mean HRQOL score
Objective 2: To examine the relationships between HRQOL and clinical and demographic characteristics among the pancreatic cancer patient population.	Correlation, T-Test, ANOVA	• No significant relationships
Objective 3: To examine the relationships between patient activation (score and level) and clinical and demographic characteristics in the pancreatic cancer patient population.	Correlation, T-Test, ANOVA, Chi-Square/Fisher-Exact Test	• Significant relationships between patient activation score with health insurance and marital status • Significant relationship between patient activation level with health insurance status and education level
Objective 4: To determine the direction and the predictive strength of patient activation in predicting HRQOL of pancreatic cancer patients while controlling for clinical and demographic characteristics. **H1:** Patient activation will be the significant positive predictor for HRQOL scores of pancreatic cancer patients while controlling for other covariates.	Multiple linear regression: R^2, F- statistic	• **Hypothesis H1 not tested**
Objective 5: To determine if patient activation is a significant predictor of HRQOL subdomains.	Multiple linear	• **Hypotheses (H2, H3 & H4) not tested**

H2: Patient activation will be a significant positive predictor of disease-related - physical HRQOL scores. **H3**: Patient activation will be a significant positive predictor of disease-related – emotional HRQOL scores. **H4**: Patient activation will be a significant positive predictor of disease-related – functional wellbeing HRQOL scores	regression: R^2, F- statistic	

Chapter 5: Discussion and Conclusion

This study aimed to understand the association between patient activation and HRQOL of pancreatic cancer patients. This chapter presents the discussion and conclusion of the study results. In the first section, study findings are discussed, and possible implications are offered. The second section discussed the study limitations. The last two sections explore future research suggestions and present the conclusion.

5.1 Study Findings

5.1.1 Study Sample Characteristics

The response rate for the study was considerably high (95.4%). Almost all the participants (42 out of 44) approached by the clinical research staff agreed to participate in the study and completed the survey. The high participation rate in the study may be attributed to the patient's willingness to contribute to research aiming at potentially improving the pancreatic cancer care experience. Also, clinical research staff followed the convenience sampling method for patient enrollment. It is likely that clinic staff approached patients they deemed as more likely to participate in the study. This could have further inflated the response rate.

Initially, this study aimed to enroll 131 study participants across 13 participating clinics, but eventually, 42 participants were enrolled across ten clinics. Low patient enrollment could be due to the low prevalence of pancreatic cancer, which accounts for 3% of all cancer cases in the US. [117] In addition, the COVID

(Corona Virus Disease) pandemic at the time of data collection impacted patient enrollment. Patients were asked to reschedule their routine appointments as cancer patients are at increased risk of severe COVID. [118]

The average age of the study participants was 71.1 (9.5) years, which is consistent with the average age of pancreatic cancer patients in the US. The majority of participants were females (57.1%), which is contrary to the national estimates. [15] Higher female participation could be due to willingness among female participants to contribute to a study that can potentially impact the care of pancreatic cancer patients. Further, most participants were Caucasians (58.5%), married/living with a partner (61.9%), college graduates or higher (57.2%), with an annual household income of more than $50,000 (60%), and multiple health insurance coverages (38.1%). Descriptive data suggest that the study participants were mostly from an advantaged socio-economic background.

In terms of clinical characteristics of the study participants, most were diagnosed less than three months ago (46.3%), with the majority diagnosed at stage 4 (39.0%) cancer. Pancreatic cancer poses challenges in early diagnosis. Often the disease is silent in the early stages and gets diagnosed as distant or stage 4 pancreatic cancer. [119] Besides, more than 85% of patients have at least one comorbidity. This is consistent with the findings of Wong et al. study that showed the mean total number of comorbidities among pancreatic cancer patients is 2.4 $\pm$ 1.7. [120] Twelve percent of the study participants had a family history of

pancreatic cancer, which is in line with the extant research which indicates that the familial basis accounts for 10 percent of pancreatic cancer cases. [32]

5.2 Primary Study Variables

Patient Activation in Pancreatic Cancer Patients

Patient activation, the primary independent variable, had a relatively high score with a mean value of 62.82 ± 18.52. In terms of categorical PAM levels, more than half of the study participants had higher activation levels (level 3 or level 4). Patient activation has not been assessed among pancreatic cancer patients; however, studies have been conducted among other cancers. In a study conducted by Hay et al. among cancer patients admitted at New York's Queen hospital center, mean PAM score (64.4 ± 16.7) was comparable to the mean score in our population. [113]

Patient activation was significantly lower for patients with public insurance (50.6 ± 18.2) as compared to those with private insurance (67.3 ± 14.4) or multiple insurances (72.2 ± 15.4). Results reported in other studies suggest mean patient activation scores were higher for patients with private health insurance versus those on public health insurance. [121, 122] This could be attributed to the fact that private insurance is often purchased through an employer. Study participants that were employed might gain more confidence in taking managing their health due to financial security provided through jobs. The relationship between the employment status and PAM scores was explored by O'Malley et al. and colleagues. They found

that among prostate cancer patients, unemployment status was associated with lower PAM scores. [114] Even though the clinical sites included in this study were high functioning sites, the finding highlights that the patients from low socio-economic status (SES) often ended up demonstrating low patient activation. With the evolving delivery and payor systems, it is important to support patients with low SES as the opportunity to improve patient activation within this subgroup is huge. This can be achieved by promoting patient-provider communication, working on patient's question asking skills and imparting patient focused communication training to oncologists that are treating patients from low SES backgrounds. [17, 123, 124]

Further, patient activation scores were significantly higher for study participants that were married/living (68.3 $\pm$ 15.8) with a partner than those that were divorced/separated/widowed (53.2 $\pm$ 23.6). In a study conducted among prostate cancer survivors, Hibbard et al. [107] found that married participants had higher patient activation levels as compared to the unmarried counterparts ($p < 0.001$). [114] Further, a study conducted by Parker et al., using the Medicare Beneficiary Survey, indicated similar findings. The odds of low patient activation level were associated with marital status of unmarried (OR = 1.72, $p < 0.001$) or widowed (OR = 2.2, $p < 0.001$). [125] Increased confidence due to constant support provided by a spouse or partner could attribute to higher patient activation levels among participants who are married/living with a partner. Couples are also more likely to have a better social support system as compared to those who are single/unmarried,

which can further improve confidence and self-efficacy. [126, 127] . Also, previous research has shown that a spouse can be beneficial in providing economic stability through better access to housing, food, and healthcare. [127] In addition to the economic safety net, a spouse's presence can lead to positive health behaviors such as participating in regular health screenings and adhering to diet and exercise routines. Being partnered may also lead to earlier detection of life-threatening disease-related symptoms or treatment-related toxicities. [128, 129] Therefore, patients that are married or are living with a partner tend to have a better survival rate with pancreatic cancer, [130] and health in general. [131] Patients that are unmarried or widowed can specifically be targeted for enhanced services involving patient-provider communication, education on treatment / side effects, and financial impact of pancreatic cancer treatment. These holistic approaches may improve activation of the patients that are suffering from this deadly disease and needing additional support.

Patients with high activation are far more likely to participate in clinical decision-making, communicate with health care providers, and adopt healthy lifestyles. [23, 122] On the contrary, patients with low activation are more prone to having delayed medical care, increased emergency care visits or hospitalization, and poor medication adherence. [132, 133]

Pancreatic cancer is most prevalent in the elderly population and often presents itself as late-stage cancer. The factors above, coupled with low patient activation, can affect a patient's care-seeking behaviors. Further, such patients might also find

it challenging to identify and manage a worsening health condition. Subsequently, this discussion highlights the inherent effect of socio-economic determinants on patient activation, hence their ability to manage health. Interventions being designed to improve patient-provider communications and patient's decision-making should consider the effects of these socio-economic determinants to meet patients where they are on their cancer care continuum.

Health-Related Quality of Life in Pancreatic Cancer Patients

The health-related quality of life of pancreatic cancer patients was evaluated using the FHSI-18 tool. The average FHSI-18 score of study participants was 42 $\pm$ 12.4, with an internal consistency of 0.87. The HRQOL score for our study is low. These are comparable to the scores reported by Cella et al., among metastatic pancreatic cancer patients with ECOG PS (Eastern Cooperative Oncology Group Performance Status) of 1. The study reported mean FHSI-18 score of 42.2 + 12 with an internal consistency of 0.89. Patients with ECOG PS of 1 are usually restricted with physically strenuous activity but can carry out light house/office work. [104]

However, the results are relatively lower to one reported in a validation study of FHSI-18 conducted by Butt et al. The study enrolled stage III and IV pancreatic cancer patients with at least one cycle of chemotherapy, reported mean FHSI-18 score of 45.7 $\pm$ 12.8, with an internal consistency of 0.89. Further, the domain-specific scores reported by Butt et al. were also similar to our study. [134]

In a systematic review focused on understanding the HRQOL of pancreatic cancer patients, the authors highlight the lack of evidence on the topic as compared to HRQOL of adults with other cancers. However, limited literature suggests that the psychological HRQOL of pancreatic cancer patients is comparatively low than patients with other cancers. Psychological HRQOL in our study, using the FHSI-DRS-E (Disease-Related Symptoms-Emotional) domain, was 4.3 $\pm$ 2.3 on a scale of 0-8. Possible causes of low psychological QOL among pancreatic cancer patients could be poor prognosis, treatment-related side effects, grueling treatment regimen, and dysregulation of immune and endocrine systems. [135]

Health-Related Quality of Life and Patient Activation of Pancreatic Cancer Patients

The relationship between patient activation and HRQOL was assessed using bivariate analysis. No significant association between HRQOL and PAM scores/levels of the participants, which could have been a result of the small sample size. Participants with higher activation levels (level 3 or level 4) had higher HRQOL scores than those on lower activation levels (level 1 or level 2). Though not significant in this study, the positive trend corroborates findings from other research studies conducted among patients with other cancers. Evidence suggests that participants with high PAM scores or activation levels tend to have higher HRQOL. A study conducted by Jansen et al. among patients who had undergone laryngectomy suggested a significant positive correlation between PAM and HRQOL scores. [116] A positive association between patient activation and HROQL was also observed by Magnezi et al. and Schneeberger et al. in their

studies among patients with depression and breast cancer survivors, respectively. [112, 115] The predictive strength of patient activation in predicting HRQOL while controlling for clinical and demographic characteristics could not be ascertained due to low patient enrollment in the study.

Considering the high prevalence of pancreatic cancer among elderly patients, minimal prolongation of survival with current chemotherapy regimens, and high disease mortality rate, efforts should be made to measure and improve patient activation scores, leading to better HRQOL. One program that have been studied extensively is Nurse Case Management or NCM. This includes assigning a dedicated nurse or healthcare worker as an educator, counselor, and advocate of care for 12 months. The interaction with the patient either during or outside the visit led to a better perception of the provider's role. Further, the intervention improved patient's confidence to adapt to challenges that arise due to the diagnosis and treatment. [136] Similarly, the telephone-based-care coordination or CONNECT program conducted among elderly colorectal patients over six months also led to decreased stress and improved psychological QOL. [137] Other studies analyzing the effects of patient activation interventions among elderly cancer patients also improved overall and/or domain specific QOL. [138, 139]

5.3 STUDY LIMITATIONS

Various oncology clinics across Texas recruited patients for the study. However, some study limitations should be considered before interpreting the results.

First, due to the low enrollment of the participants, the study is not adequately powered. Forty-two participants were successfully recruited in the study compared to a total of 131 planned initially. Therefore objectives 4 and 5 focused on prediction were not tested. Second, the data collected in this study was self-reported by the study participants. Therefore, data is prone to self-reporting biases (social desirability and recall bias). A third limitation arises due to the method of recruiting patients. The study employed convenience sampling, which may result in selection bias. There is a possibility that the participants that agreed to complete the survey were more activated and were inclined to participate in the study.

Fourth, due to the cross-sectional nature of the study and the sample size, the results were descriptive rather than inferential. Hence, the causality of the relationships could not be inferred. A final limitation is that all participating sites were from the Texas Oncology group. Therefore, the findings might not be representative of the pancreatic cancer patient population in the state of Texas or the US. Relatedly, the sites implement OCM (Oncology Care Model) to improve patient care experience, therefore, the findings may be more representative of individuals treated in clinical sites that implement similar value-based care models.

5.4 Suggestions for Future Research

This study can be expanded to include more diverse patients and different clinical practices, especially those that do not implement value-based care models. As per the health literacy skill (HLS) framework, one of the predictors of HRQOL is health literacy levels. The effects of general & cancer health literacy on HRQOL while controlling for patient activation is yet to be studied among pancreatic cancer patients. Future research could also consider conducting randomized control trials (RCT) that research the impact of behavioral interventions on improving patient activation levels. The interventions for improving patient activation could be designed to specifically target vulnerable populations (low SES, unmarried and those without the college degree). Also, there is a lack of research on patient activation and HROQL in patients with a less prevalent form of neuroendocrine pancreatic cancer. However, the sample size could be an issue with this patient population.

5.5 Conclusion

The study aimed to understand the association between patient activation and HRQOL of pancreatic cancer patients. The results indicate a non-significant association between patient activation and HRQOL of pancreatic cancer patients being treated with chemotherapy, though the study was significantly underpowered. However, higher patient activation was significantly associated with having private insurance and being partnered. Research amongst a larger

sample and more diverse pancreatic cancer population is required for conclusive evidence.

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Appendix 01: Cover Letter

Dear Patient,

You are invited to participate in a study titled "Association of Patient Activation with the Health-Related Quality of Life of Patients with Pancreatic Cancer" The study is being conducted by Yogesh Vohra, Pharm.D, for his master's thesis along with Carolyn Brown, Ph.D., College of Pharmacy of the University of Texas at Austin, and Dr. Lalan Wilfong of Texas Oncology, Austin, Texas. Kindly read the information below carefully before deciding whether or not to take part. Completing the survey will be taken as evidence of your consent to participate in the study.

The purpose of this research is to help us understand your ability to manage your own health, as well as how these self-management abilities affect your quality of life. You will be required to complete one survey during the clinic visit which should take no more than 10 minutes to complete. The study will include 150 patients with pancreatic cancer.

Your participation in the study will help us understand patients' activation level. This will help us to better serve the patients by designing appropriate information for pancreatic cancer thereby improving patient's ability to be involved in self-managing their health and quality of life.

If you agree to participate:

- The survey will take approximately 10 minutes of your time.

Benefits/Risks/Confidentiality of Data

There are no direct benefits from participating in this study. However, the findings of this study could help better serve our patients by improving pancreatic cancer patients' involvement in managing their own health. Also, the risk of participating in this study is considered minimal by the University of Texas at Austin Institutional Review Board. Your privacy and confidentiality will be protected by having clinic research staff assign unique numbers to each study participant. Consequently, no individual responses will be linked back to you. Also, all completed surveys will be permanently deleted upon completion of the study and acceptance of manuscript(s).

If it becomes necessary for the Institutional Review Board to review the study records, information that can be linked to you will be protected to the extent permitted by law. Your research records will not be released without your consent unless required by law or court order.

Participation or Withdrawal

Your participation in this study is voluntary and free of charge. You may decline to answer any question, and you have the right to withdraw from participation at any time. Withdrawal will not affect your medical care or your relationship with The University of Texas at Austin in any way. If you do not wish to participate, simply stop answering the survey questions. You will be given the survey to complete by clinic research staff at this clinic appointment.

Contact Information

Prior, during, or after your participation in this study, you can contact Yogesh Vohra at 737-333-7673 or send an email to yogeshvohrayv@utexas.edu if you encounter any problems or have any questions regarding the survey.

Question about your rights as a research participant

If you have a question about your rights or are dissatisfied at any time with any part of this study, you can contact, anonymously if you wish, the University of Texas at Austin Institutional Review Board by phone at (512)471-8871 or email at orsc@uts.cc.utexas.edu.

Thank you for your participation.

Appendix 02: Survey Instrument

Section 1: This set of questions asks about your involvement in managing your pancreatic cancer. Please check the option that best corresponds to your response in each question.					
	Strongly Disagree	**Disagree**	**Agree**	**Strongly Agree**	**N/A**
1. When all is said and done. I am the person who is responsible for managing my health.	□	□	□	□	□
2. Taking an active role in my own health care is the most important factor in determining my health and ability to function.	□	□	□	□	□
3. I am confident that I can take actions that will help prevent or minimize some symptoms or problems associated with my health.	□	□	□	□	□
4. I know what each of my prescribed medication does.	□	□	□	□	□
5. I am confident that I can tell when I need to go get medical care and when I can handle a health problem myself.	□	□	□	□	□
6. I am confident I can tell a doctor concerns I have even when he or she does not ask.	□	□	□	□	□
7. I am confident that I can follow through on medical treatments I may need to do at home.	□	□	□	□	□
8. I understand my health problems and what causes them.	□	□	□	□	□
9. I know what treatments are available for my health problems.	□	□	□	□	□
10. I have been able to maintain (keep up with) lifestyle changes, like eating right or exercising.	□	□	□	□	□
11. I know how to prevent problems with my health.	□	□	□	□	□
12. I am confident I can figure out solutions when new problems arise with my health.	□	□	□	□	□
13. I am confident that I can maintain lifestyle changes, like eating right and exercising, even during times of stress.	□	□	□	□	□

Section 2: Below is a list of statements that other people with pancreatic cancer have said are important. Please circle or mark one number per line to indicate your response as it applies to the past 7 days.					
	Not at all	**A little bit**	**Somewhat**	**Quite a but**	**Very much**
Disease-related symptoms - Physical					
14. I have a lack of energy.	0	1	2	3	4
15. I have pain.	0	1	2	3	4
16. I am losing weight.	0	1	2	3	4
17. I feel fatigued.	0	1	2	3	4
18. I have pain in my back.	0	1	2	3	4
19. I am bothered by jaundice or yellow color to my skin.	0	1	2	3	4
20. I feel ill.	0	1	2	3	4
21. I have discomfort or pain in my stomach area.	0	1	2	3	4
22. I have nausea.	0	1	2	3	4
23. Because of my physical condition, I have trouble meeting the needs of my family.	0	1	2	3	4
24. I have a good appetite.	0	1	2	3	4
25. I am sleeping well.	0	1	2	3	4
Disease-related symptoms - Emotional					
26. I worry that my condition will get worse.	0	1	2	3	4
27. I feel sad.	0	1	2	3	4
Treatment side-effects					
28. I am bothered by side effects of treatment.	0	1	2	3	4
Function and Well-Being					

29. I am able to do my usual activities.	0	1	2	3	4
30. I am able to enjoy life.	0	1	2	3	4
31. I am content with the quality of my life right now.	0	1	2	3	4

Section 3: In the end, we would like to learn a little about you and the current state of your pancreatic cancer. Please fill in your response or select the option that best corresponds to your answer for each question.

32. In what year were you born? 19____

33. Which of the following options best describes your race/ethnicity?
- □ African-American or non-Hispanic black
- □ American Indian or Alaska Native
- □ Asian-American or Pacific Islander
- □ Caucasian or non-Hispanic white
- □ Mexican-American or Hispanic
- □ Other (please specify) _____

34. What is your gender?
- □ Male
- □ Female
- □ Transgender
- □ Other

35. Which of the options describes your highest education levels?
- □ Less than High School
- □ High School Graduate or GED
- □ College graduate
- □ Postgraduate (e.g., MD, MS, PhD)
- □ Other (please specify) _____

36. Which of the following options best describes your household income?
- □ Less than $25,000
- □ $25,000 to $50,000
- □ > $50,000 to $75,000
- □ > $75,000 to $100,000
- □ >$100,000

37. Which of the following type of health insurance do you currently have? (Check all that apply)
- □ No insurance/Self-pay
- □ Private insurance
- □ Public Insurance (Medicare/Medicaid)
- □ Other (please specify) _____

38. What is your current marital status?
- □ Single, in a relationship
- □ Single, not in a relationship
- □ Married

□ Partner/Living together
□ Divorced/Separated
□ Widowed

39. Has anyone ever been diagnosed with pancreatic in your immediate family?
□ Yes
□ No

40. How long ago you were diagnosed with pancreatic cancer?
□ Less than 3 months ago
□ More than 3 to 6 months ago
□ More than 6 months to 1 year ago
□ More than 1 to 1.5 years ago
□ More than 1.5 to 3 years ago
□ More than 3 years ago
□ Not sure

41. What was the tumor stage when you were first diagnosed with pancreatic cancer?
□ Stage 1
□ Stage 2
□ Stage 3
□ Stage 4
□ Not Sure

42. Which option best describes your treatment history?
□ Newly diagnosed
□ Prior treatment history

43. In addition to pancreatic cancer, what other illness do you have? Check all that apply
□ Asthma
□ Arthritis
□ Diabetes
□ Hypertension
□ Hypercholesterolemia
□ Kidney problems
□ Heart disease
□ Anxiety
□ Liver disease
□ Pancreatitis
□ Depression
□ Other (please specify) _____

Thank you for your response.

Appendix 03: Informed Consent Tracking Log

STUDY TITLE: Association between Patient Activation and Health-Related Quality of Life of Pancreatic Cancer Patients		
PROTOCOL NO.:	**TEXAS ONCOLOGY CO-INVESTIGATOR:** Lalan S. Wilfong, MD	**SITE NAME:**
Date	Patient Study ID Number	Informed Consent Given? Y/N

Appendix 04: Site Support Letter

TEXAS ONCOLOGY

More breakthroughs. More victories.

January 29, 2019

Carolyn Brown, Ph.D.
The University of Texas at Austin
College of Pharmacy
Health Outcomes Division
1 University Station A1930
Austin, TX 78712-0120

Dear Dr. Brown:

I am pleased to provide support for the proposed study titled: "Association of Patient Activation with the Health-Related Quality of Life of Pancreatic Cancer Patients" which will be conducted in our clinics. Here at Texas Oncology, we are constantly looking for innovative ways to provide the best medical care for our patients with pancreatic cancer. Consequently, we are pleased to confirm that we will partner with you to ensure the successful execution of the proposed project.

We will work with your team, including Yogesh Vohra, and have our clinic research staff identify and obtain consent from eligible patients to be included in the study. We will also assist you with data collection by giving out the surveys to patients who give their consent to participate in the study during clinic visits. I have participated in the development of the proposed study protocol and I will ensure that the research protocol is followed in conducting the study. In addition, I will contribute to the dissemination of the study findings. My contribution to this study is free of charge because it is an unfunded study.

Sincerely,

Lalan Wilfong, M.D.

Vice President, Quality Programs Department

12221 Merit Dr., Suite 500 • Dallas, TX 75251 • T: 1-888-864-4226 • www.TexasOncology.com

Appendix 05: Survey Evaluation Form

Please evaluate the attached survey based on your experiences with pancreatic cancer. After taking the survey, please respond to the following questions and note which questions were problematic in the boxes below

Readability of the statements – Is each statement clear and understandable?
Relevance of statements – Is each statement relevant to experiences pancreatic cancer? Are any important issues missing?
Format of survey – Is the format user-friendly? Did you find it hard to follow? Any suggestions for improvement?
Time to complete the survey – Please record the time (in minutes) that it took to complete the survey.
Additional Comments – Anything else we need to know?