UNIVERSITY OF MIAMI

PSYCHOLOGICAL DISTRESS IN PANCREATIC CANCER: A RETROSPECTIVE ANALYSIS WITHIN THE SCOPE OF GASTROINTESTINAL MALIGNANCIES

By

Magela Pons

A THESIS

Submitted to the Faculty
of the University of Miami
in partial fulfillment of the requirements for
the degree of Master of Science in Public Health

Coral Gables, Florida

December 2025

UNIVERSITY OF MIAMI

A thesis submitted in partial fulfillment of
the requirements for the degree of
Master of Science in Public Health

PSYCHOLOGICAL DISTRESS IN PANCREATIC CANCER: A RETROSPECTIVE ANALYSIS WITHIN THE SCOPE OF GASTROINTESTINAL MALIGNANCIES

Magela Pons

Approved:

Tulay Koru-Sengul, Ph.D., MHS Professor	Patricia Moreno, Ph.D. Assistant Professor
Frank Penedo, Ph.D. Professor	Akina Natori, MD, MSPH Research Assistant Professor
Heidy Medina, Ph.D., MPH Postdoctoral Scholar	Nicole Leeper Piquero, Ph.D. Interim Dean of the Graduate School

PONS, MAGELA (M.S.P.H., Public Health)

Psychological Distress in Pancreatic Cancer: A Cross-Sectional Analysis Within the Scope of Gastrointestinal Malignancies. (December 2025)

Abstract of a thesis at the University of Miami.

Thesis supervised by Professor Tulay Koru-Sengul.
No. of pages in text. (35)

Background: Pancreatic cancer is a highly aggressive disease with poor prognosis and burdensome treatments, leading to significant physical and emotional strain. Psychological distress – depression and anxiety – is disproportionately high in pancreatic cancer patients compared with other gastrointestinal malignancies. This study examines sociodemographic and clinical factors associated with psychological distress in a diverse cohort of patients with pancreatic and other gastrointestinal cancers.

Methods: Patient-reported outcomes were integrated with corresponding clinical and demographic patient data from ambulatory oncology records at the University of Miami Miller School of Medicine Sylvester Comprehensive Cancer Center. Descriptive statistics, group comparisons, and bivariate statistical tests were conducted. The relationships between patient characteristics and anxiety and depression T-scores were assessed using univariate and multivariate linear regression models, with separate models for the overall gastrointestinal cancer cohort and for the pancreatic cancer subgroup. R statistical software was used for both data management and statistical analysis.

Results: Among 503 cancer patients (colorectal=324, pancreas=103, liver=44, stomach=32) the mean age was 66 years; 55% were male, 58% were Hispanic/Latino, and 66% were married/living with a partner. Pancreatic cancer patients reported higher depression T-scores than other gastrointestinal cancers (49 vs 46, p=0.036); Anxiety T-

scores were higher in pancreatic cancer patients, though not statistically significant (p=0.194). In the combined cohort, anxiety was higher among patients who were female (p=0.032), were receiving chemotherapy (p=0.035), were not married/living with a partner (p=0.015), and had Medicaid insurance (p=0.037), and lower among Hispanic/Latino patients (p=0.048) and those with Stage II disease (p=0.003). Depression was significantly associated with female sex (p=0.021) and longer time since diagnosis (p<0.05). In the pancreatic cancer subgroup, no variables were statistically significant; trends indicated higher depression in non-Hispanic Black patients (p=0.055) and higher anxiety in uninsured patients (p=0.117).

Conclusions: Pancreatic cancer patients showed higher depression than other gastrointestinal cancers, largely explained by sociodemographic and clinical factors. Female sex consistently predicted psychological distress, and subgroup trends suggested potential disparities by race and insurance status. Findings support the need for early psychological screening, targeted psychosocial support, and longitudinal research to clarify depression's role as an early marker of pancreatic cancer.

Keywords: pancreatic cancer, gastrointestinal malignancies, psychological distress, electronic health records.

TABLE OF CONTENTS

Chapter 1: Introduction

Pancreatic cancer is a highly aggressive disease with one of the poorest prognoses, largely due to challenges in early detection, the pancreas' concealed anatomical location, and the lack of effective biomarkers and screening tools.[1–3] Advances in medicine and technology have highly increased survival rates for a variety of cancer types in the past years, but the mortality rate of pancreatic cancer has only marginally improved since 1975.[4] As of 2025, it is the third leading cause of cancer-related death in the United States (U.S.), despite being the 10th most prevalent type of cancer, with a 5-year survival rate of about 13%.[5–7] A diagnosis of pancreatic cancer can be highly devastating and debilitating for patients and their caregivers due to its low curability, severe symptoms, and financial strain, often leading to cognitive decline, depression, anxiety, and a reduced quality of life (QoL).[8,9] The disease and its complex treatments cause a range of negative effects, including digestive complications, multiple adverse treatment side effects, and significant emotional burden.[10,11]

Treating pancreatic cancer presents multiple challenges. The pancreas is both an endocrine (blood regulation) and exocrine (digestive enzyme production) gland[12] but 90% of pancreatic cancer diagnoses are exocrine tumors, of which 80% are diagnosed at a stage where the tumor cannot be surgically removed.[13] Even when the tumor is surgically resectable, the 5-year survival rate for patients is 39%, with poor prognosis attributed to late detection, a 75% recurrence rate, and surgical complications like acute pancreatitis, which increase morbidity.[2,3,11,14–17] Laparoscopic surgery, while reducing some complications, often fails to completely remove tumors, resulting in poorer survival outcomes.[18] Surgery is usually followed by potent adjuvant therapies, including

chemotherapy, immunotherapy, and targeted therapies.[3] Emerging treatments, such as nanotechnology and molecular targeting, also present serious adverse effects, imposing a significant burden on patients, which greatly impacts their quality of life and overall prognosis.[19] Although the cause of pancreatic cancer is unknown, occurrence, progression, and invasion of the disease is associated with both non-modifiable (e.g. age, gender, ethnicity) and modifiable (e.g. smoking, alcohol drinking, diet) risk factors.[13]

Patients with pancreatic cancer face a greater risk of psychological distress (depression and anxiety), increased suicide risk, and significantly greater levels of depression compared to those with other gastrointestinal malignancies in advanced stages.[12,20–24] Studies have shown that among several cancer types, those with pancreatic cancer exhibit the highest Global Severity Index (GSI) scores for anxiety and depression.[25,26] Data from population-based analyses show that the suicide risk is more than six times higher (standardized mortality ratio of 6.43) in pancreatic cancer compared to the U.S. general population, surpassing the risks for other gastrointestinal cancers, such as liver (SMR 2.26), gastric (SMR 4.07), and esophageal (SMR 5.45).[24,27,28] Depression affects approximately 33-50% of patients with pancreatic cancer, which is significantly higher than reported rates in other gastrointestinal cancer types such as gastric (~37%), colorectal (~23%), and liver (~21%).[24,29–32] Studies have found a prevalence of psychological distress ranging from 48 to 76%, compared to approximately 20 to 30% among patients with other gastrointestinal cancers.[29,30,33] Remarkably, multiple studies have found that anxiety and depression are prevalent even before a diagnosis is present,[34,35] with one study showing up to 50% of pancreatic cancer patients showing depressive

symptoms before their tumor was diagnosed, and sometimes preceding diagnosis by up to 43 months.[23,30,36–38]

Psychological distress has been linked to a decreased response in several of the body's physiological defense mechanisms against tumors, mediating cancer progression.[39,40] There are several mechanisms by which tumors are theorized to mediate psychological distress, including the inflammatory response triggered by pancreatic cancer in the body, which contributes to depressive and anxiety symptoms as well as insomnia; hormonal disruption in which the tumor disrupts the pancreas' secretion of mood-stabilizing hormones and neurotransmitters, leading to mood disturbances; and production of cytokines – particularly interleukin-6, a pro-inflammatory protein that has been found to mediate depression.[38,41–43] Concurrently, research continuously shows an association between greater psychological distress and lower survival rates among patients with cancer.[44,45] Depressive symptoms are linked to higher disease severity, lack of adherence to treatment, decreased engagement in physical activity and healthy eating habits, and the aforementioned increased inflammatory responses associated with higher mortality.[40,46] Stress responses have a direct impact on cancer progression and metastasis both at the psychological and at the physiological level, highlighting the need to provide patients access to specialized resources and services that address the unique challenges of their condition, and adequately manage their psychological distress.[12,47–50]

Anxiety and depression are consistent risk factors for higher mortality rates among patients with pancreatic cancer, even from pre-diagnosis and very early stages; however, very few studies have examined psychological distress in the context of pancreatic cancer in particular. Therefore, the objective of this retrospective cross-sectional study is to

characterize the psychological distress experienced by patients with pancreatic cancer, examined as part of the broader group of gastrointestinal malignancies. Specifically, this study aims to

(1) compare psychological distress levels between patients with pancreatic and other gastrointestinal cancers,

(2) evaluate demographic and clinical factors associated with psychological distress across the combined patient cohort, and

(3) identify sociodemographic and clinical factors of psychological distress in pancreatic cancer patients.

Chapter 2: Methods

2.1 Data Source and Program Description

My Wellness Check (MWC) is an electronic health record (EHR)-integrated program at the University of Miami Miller School of Medicine Sylvester Comprehensive Cancer Center (SCCC) that monitors patient-reported outcomes (PROs) for ambulatory oncology patients. The program, available in both English and Spanish, assesses patients' specific symptoms and needs before their appointments to efficiently triage them to the appropriate supportive care services. Through the *MWC* assessments, patients complete questionnaires for depression, anxiety, fatigue, pain interference, and physical function, as well as well-validated measures that assess supportive care needs, risk of malnutrition, and overall health related QoL (HRQoL) prior to their appointment. When signs of increased psychological distress, obstacles to care or nutritional needs are detected, alerts are triggered to the corresponding team within the EHR. When moderate or severe depression and anxiety symptoms are reported (Anxiety T-score ≥ 65 or Depression T-score ≥ 60), patients are directed to social work; whereas when any unmet psychosocial, practical, or nutritional needs are endorsed in the survey, best practice alerts (BPAs) are sent to the relevant teams.[51–55] *MWC* assessments are assigned at the second clinic visit and forward, no more than once a month, and can be accessed by patients via their patient portal through a computer, smartphone or tablet 72 hours before their next appointment. Patients may also complete the assessment at the clinic during their appointment or decline to complete it altogether.

2.2 Symptom Assessment

The Patient-Reported Outcomes Measurement Information System (PROMIS®), an NIH-funded initiative, aims to develop and validate PROs for use in clinical research and practice. To administer PROMIS® measures, computerized adaptive testing (CAT) is utilized, a measurement method in which questions to individuals are based on their previous responses.[56] The algorithm adapts each question based on the patient's previous answer, starting with a question from an item bank that assesses a specific function or symptom. These questions are arranged by difficulty or severity, and the first question is typically of moderate difficulty. The CAT algorithm then estimates a person's score and selects the most appropriate next question.[56] This system is used to evaluate and monitor physical, mental, and psychosocial symptoms in individuals with chronic conditions.

The *MWC* assessment is comprised of five PROMIS CATs for anxiety, depression, pain interference, fatigue, and physical function, alongside the 7-item FACT-G7, to evaluate emotional and physical symptoms, and HRQOL in cancer patients. The two PROMIS® domains examined in this study were Anxiety and Depression[54]. PROMIS scales use a 5-point rating (1=never, 5=always), with the total raw score being the sum of all item scores. For the 28-item depression scale, raw scores range from 28 to 140, while for the 29-item anxiety scale, raw scores range from 29 to 135. These are converted into standardized T-scores (mean=50, SD=10), with higher T-scores representing greater symptom severity. T-scores under 55 are normal, 55-60 mild, 60-70 moderate, and over 70 severe. In cancer populations, a T-score of 53 or higher indicates clinically significant depressive symptoms, and 59 or higher indicates clinically significant anxiety symptoms. The standardized T-score allows for comparison across different PROMIS measures and

to population norms, with item-level analysis providing insights into the patient's psychological state.[54]

2.3 Study Population

Pancreatic, colorectal, stomach, and liver cancers were selected for analysis as they represent the most common and clinically significant gastrointestinal malignancies.[57,58] These cancers share overlapping biological, clinical, and treatment-related features (e.g., digestive complications, metabolic disturbances, and symptom burden) yet differ in prognosis, survival rates, and patterns of psychological distress.[30] Including this range of gastrointestinal cancers allows for both within-group comparisons to identify factors unique to pancreatic cancer and across-group contrasts to contextualize psychosocial outcomes within the broader landscape of gastrointestinal oncology. Our cohort included a demographically and socioeconomically diverse patient population, with a high proportion of Hispanic/Latino individuals and both English- and Spanish-speaking participants.

The inclusion criteria are the following:

(1) individuals who have been treated in ambulatory oncology clinics in Sylvester Comprehensive Cancer Center and its satellite locations,

(2) individuals who have been diagnosed with pancreatic cancer

(3) individuals who have been diagnosed with gastric, liver, and colorectal cancer (for comparison group),

(4) individuals with ICD-10 C00.xx-D47 who have completed the *MWC* questionnaire between August 2019 and September 2023

(5) English and/or Spanish speakers,

(6) patients with non-metastatic (Stage I-III) and metastatic (Stage IV) disease (i.e., patients for which cancer stage is known).

The exclusion criteria are:

(1) individuals younger than 18 years old,

(2) and individuals with unknown cancer stage.

2.4 Data Collection

The study was approved by the University of Miami Institutional Review Board (eProst #20230111). *MWC* responses were obtained through a data request form. Requested data of eligible patients and only the result of the analyses were exported to the University of Miami's approved cloud storage system, Box (https://www.box.com/). Patient data were extracted from the electronic data warehouse (EDW) by linking the *MWC* questionnaires to the patient medical record number (MRN). Reports were securely generated. The information collected included self-reported patient demographics (age, sex, language, race, ethnicity, marital status, insurance status), as well as clinical characteristics such as cancer diagnosis and stage, treatment history, comorbidities, height, and weight. PROs included PROMIS Anxiety and PROMIS Depression T-scores, along with their administration dates. Assessment responses that were taken closest after the diagnosis date were selected, and the time elapsed between diagnosis and assessment was calculated to account for variability.

2.5 Outcomes

The primary outcome variables are patient-reported measures from the PROMIS® Anxiety and PROMIS® Depression. PROMIS® Anxiety and Depression T-Scores were treated as continuous variables.

2.6 Covariates

From the data extraction, only records with complete information for each variable described below were included in the study sample.

Patients were classified by sex (male or female), marital status (partnered or not partnered), cancer site (pancreas, stomach, liver, or colorectal), language (English or Spanish), and health insurance status, which was categorized as private, Medicare, Medicaid, or uninsured (self-pay). Race data included categories for Black, White, or other, and ethnicity was classified as Hispanic/Latino or non-Hispanic/Latino. Race and ethnicity, however, were combined into a single variable categorized as non-Hispanic White, non-Hispanic Black, Hispanic/Latino, and "Other or Unknown".

Treatment information included dates in which patients received chemotherapy, radiation, and/or surgery, with missing values indicating no treatment received. Active cancer treatment was defined as having undergone chemotherapy, radiation, immunotherapy, or having had surgery within 30 days prior to completing the assessment. Tumor stage was categorized as stage I, stage II, stage III, or stage IV.[59] Comorbidities extracted from patient records were used to calculate The Charlson Comorbidity Index (CCI)[60] which was analyzed as a continuous variable, covering various conditions such as myocardial infarction, dementia, diabetes, several cancers, and HIV infection. Age (in years) and Body Mass Index (BMI, calculated from weight and height) were treated as

continuous variables. The time between a patient's cancer diagnosis and first completion of the *MWC* assessment was calculated in months and treated as a continuous variable.

Anxiety and depression severity were categorized using established thresholds, with anxiety defined as a T-score ≥65 and depression as a T-score ≥60, and patients were classified as either above or below these thresholds.[61]

2.7 Statistical Analysis

Descriptive statistics were calculated for the complete sample of cancer cases combined, as well as for patients with pancreatic cancer only, and for patients with a diagnosis of other gastrointestinal cancers (colorectal, stomach, or liver). For sociodemographic and clinical characteristics, means and standard deviations were calculated for continuous variables, and counts and percentages for categorical variables. For PROs, mean and standard deviation values were calculated for PROMIS® Anxiety and Depression T-scores. The proportion of patients meeting severity thresholds for anxiety and depression was calculated as counts and percentages for those above and below the thresholds.[61] Between-group analyses were conducted to explore the differences in anxiety and depression between patients with pancreatic cancer and those with other gastrointestinal cancers using either Chi-square tests of independence or Fisher's exact test for categorical variables, depending on cell counts, and independent samples Student's t-tests for continuous variables.

A bivariate analysis was conducted to examine the relationship between anxiety and depression T-scores and individual sociodemographic and clinical characteristics. One-way Analysis of Variance (ANOVA) was used for continuous variables to compare categorical variables with more than two groups, and Pearson correlation coefficients were

calculated for continuous variables to assess the strength and direction of associations with anxiety and depression T-scores.

To identify which sociodemographic and clinical variables were associated with higher mean levels of anxiety and depression, both univariate and multivariate linear regression models were used. Separate models were run for each outcome (anxiety and depression) in the combined gastrointestinal cancer sample, with cancer site (pancreatic vs. other gastrointestinal cancers) entered as the primary predictor variable, adjusting for all other covariates. Univariate regression models were used to assess each demographic and clinical variable individually as predictors of anxiety and depression, respectively. Variables were then entered into multivariable linear regression models to evaluate their combined effects, adjusting for potential confounders. The same approach was applied within the pancreatic cancer subgroup to identify predictors specific to this population. All categorical variables were dummy coded, with clinically relevant or most common categories serving as reference groups. Model estimates were reported as estimates of unstandardized regression coefficients (B) with its corresponding standard errors (SE) and p-values. Model fit was evaluated using the coefficient of determination (R^2).

All p-values were two-sided, with statistical significance defined as p-value < 0.05. All analyses were conducted using RStudio 2023.12.1+402 (© 2009-2024, Posit team (2025). RStudio: Integrated Development Environment for R. Posit Software, PBC, Boston, MA. URL http://www.posit.co/).

Chapter 3: Results

3.1 Participant Characteristics

The study sample included n=503 patients diagnosed with a gastrointestinal malignancy with known staging, who were treated in the ambulatory oncology clinics in Sylvester Comprehensive Cancer Center and its satellite locations, and completed the *MWC* questionnaire between August 2019 and September 2023. Of these, n=103 (20.5%) patients had pancreatic cancer, n=32 (6.4%) had stomach cancer, n=44 (8.7%) had liver cancer, and n=324 (64.4%) participants had colorectal cancer. The 503 patients had a mean age of 66 (Standard Deviation = 12) years and were primarily male (55%), Hispanic/Latino (58%), partnered (66%), reported English as their preferred language (59%), and had private insurance (68%) according to their patient records, summarized in Table 1. On average, patients had been diagnosed 37 months earlier (SD = 36), with the majority presenting with stage III disease (36%), a mean body mass index (BMI) of 27.0 (SD=5.4), and mean CCI score of 8 (SD = 4). At the time of their *MWC* assessment, the majority of patients (95%) were not receiving active treatment. The proportion of patients exceeding severity thresholds was 5.6% for anxiety (T-score ≥ 65) and 5.6% for depression (T-score ≥ 60), with mean scores of 51 (SD = 10) and 47 (SD = 10), respectively.

The 103 patients with pancreatic cancer had a mean age of 73 years (SD = 10) and were mostly female (52%), partnered (67%, i.e. married or living with a partner), non-Hispanic White (53%), reported English as their preferred language (81%), and had private insurance (54%). On average, patients had a BMI of 24.8 (SD = 4.6) and a CCI score of 9 (SD = 3). The mean time since diagnosis was 37 months (SD = 42), with the largest proportion presenting with stage II (29%) disease. Most patients (98%) were not receiving

active treatment at the time of their *MWC* assessment. The proportion of patients exceeding severity thresholds was 7% for anxiety (T-score ≥ 65) and 9% for depression (T-score ≥ 60), with mean T scores of 53 (SD = 10) and 49 (SD = 10), respectively.

Statistically significant differences between patients with pancreatic cancer and other gastrointestinal cancers were observed for age ($p < 0.001$), language ($p < 0.001$), insurance ($p = 0.003$), race/ethnicity ($p < 0.001$), BMI ($p < 0.001$), tumor stage ($p = 0.001$), CCI ($p < 0.001$), and depression T scores ($p = 0.036$).

Figure 1 presents adjusted regression coefficients for demographic and clinical factors associated with anxiety and depression T-scores among patients with gastrointestinal cancers. Each point represents the estimated β coefficient with corresponding 95% confidence intervals. Overall, the figure shows that higher scores were more common among patients who were uninsured or covered by Medicaid, those identifying as Hispanic/Latino, and those who were not partnered, whereas patients receiving chemotherapy or radiation tended to report lower anxiety and depression scores.

Table 1. Demographic and Clinical Characteristics among Patients with Pancreatic Cancer vs Other Gastrointestinal Cancer

Characteristics	**Overall**	**Other GI[a]**	**Pancreas**	***p*[b]**
	N = 503	**N = 400 (80%)**	**N = 103 (20%)**	
Age in years, mean (SD)	66 (12)	64 (12)	73 (10)	<0.001*
Sex, No. (%)				0.119
Male	276 (55%)	227 (57%)	49 (48%)	
Female	227 (45%)	173 (43%)	54 (52%)	
Language, No. (%)				<0.001*
English	299 (59%)	216 (54%)	83 (81%)	
Spanish	204 (41%)	184 (46%)	20 (19%)	
Marital Status, No. (%)				0.867
Partnered	331 (66%)	262 (66%)	69 (67%)	
Not Partnered	172 (34%)	138 (35%)	34 (33%)	
Insurance, No. (%)				0.003*
Private	342 (68%)	286 (72%)	56 (54%)	
Medicare	137 (27%)	94 (24%)	43 (42%)	
Medicaid	11 (2%)	--	--	
Uninsured	13 (3%)	--	--	
Race/Ethnicity, No. (%)				<0.001*
Non-Hispanic White	150 (30%)	95 (24%)	55 (53%)	
Hispanic or Latino	294 (58%)	254 (64%)	40 (39%)	
Non-Hispanic Black	38 (8%)	32 (8%)	--	
Other or Unknown	21 (4%)	19 (4.8%)	--	
Body Mass Index, mean (SD)	27.0 (5.4)	27.7 (5.5)	24.8 (4.6)	<0.001*
Tumor Stage				0.001*
Stage I	84 (17%)	60 (15%)	24 (23%)	
Stage II	127 (25%)	97 (24%)	30 (29%)	
Stage III	179 (36%)	159 (40%)	20 (19%)	
Stage IV	113 (22%)	84 (21%)	29 (28%)	
Charlson Comorbidity Index, mean (SD)	8 (4)	8 (4)	9 (3)	<0.001*
Time Since Cancer Diagnosis in Months, mean (SD)	37 (36)	37 (35)	37 (42)	0.961
Active Treatment[c]				0.053
None[d]	478 (95%)	377 (94%)	101 (98%)	0.183
Surgery[d]	11 (2.2%)	11 (3%)	--	0.186
Radiation[d]	10 (2.0%)	10 (2%)	--	0.221
Chemotherapy[d]	--	--	--	0.596
Anxiety T Score, mean (SD)	51 (10)	51 (10)	53 (10)	0.194
Depression T Score, mean (SD)	47 (10)	46 (10)	49 (10)	0.036*
Anxiety Threshold of 65, No. (%)				0.712
Above	28 (5.6%)	21 (5.3%)	7(7%)	
Below	475 (94%)	379 (95%)	96 (93%)	
Depression Threshold of 60, No. (%)				0.182
Above	28 (5.6%)	19 (4.8%)	9(9%)	
Below	475 (94%)	381 (95%)	94 (91%)	

-- Note: Not reported; observations fewer than 10

[a] Other Gastrointestinal cancers include Colorectal: 324 (64.4%); Liver: 44 (8.7%); Stomach: 32 (6.4%)

[b] Welch Two Sample t-test; Pearson's Chi-squared test; Fisher's exact test (insurance only due to sparse categories)

[c] p-value reflects a comparison of Anxiety and Depression T scores across multiple treatment categories

[d] p-values represent comparisons in Anxiety and Depression T scores between patients who did and did not receive the specified treatment (Yes vs. No)

*p<0.05

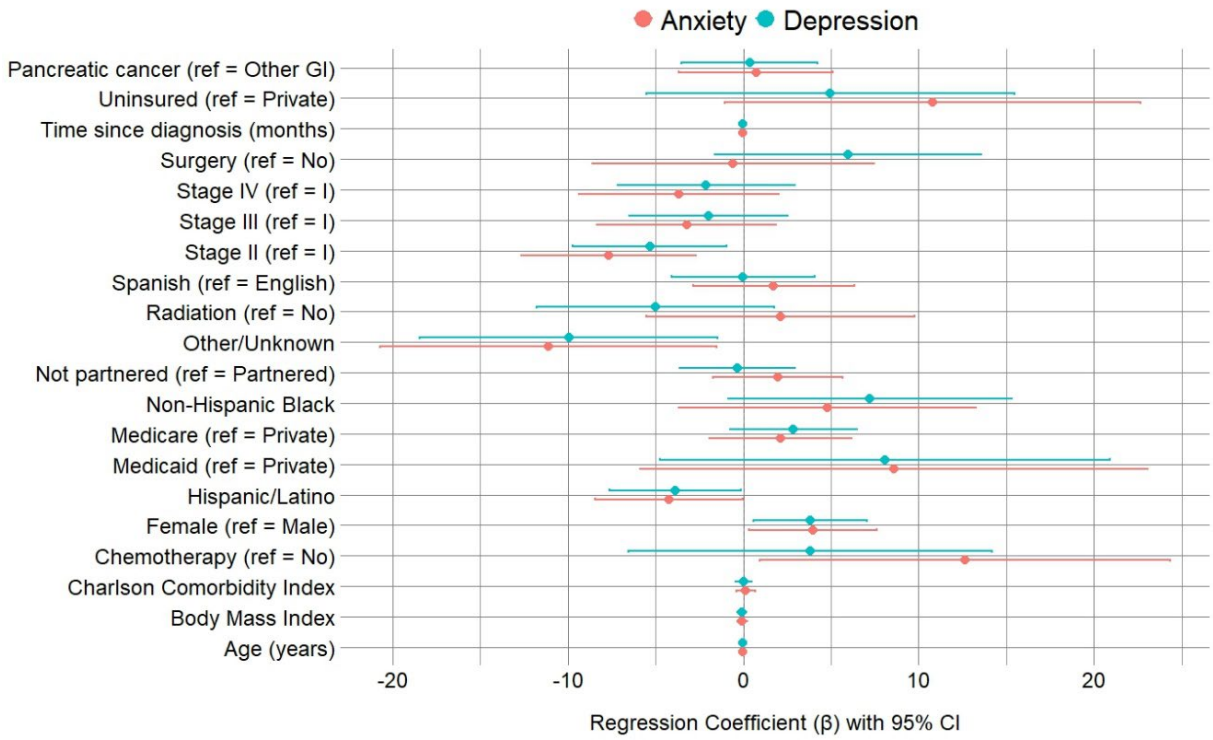

Figure 1 *Multivariate Linear Regression Coefficients for Anxiety and Depression Scores by Clinical and Demographic Factors*

3.2 Group Differences in Psychological Distress

Bivariate comparisons of anxiety and depression T scores across sociodemographic and clinical characteristics for the combined gastrointestinal cancer sample are presented in Table 2. Patients who were female, indicated Spanish as their preferred language, were not partnered, had a stage I cancer diagnosis, had Medicaid insurance, and identified as non-Hispanic White, had higher mean anxiety and depression T scores compared to their counterparts. Higher anxiety T scores were observed among individuals with stomach cancer and among those receiving chemotherapy, whereas higher depression T scores were observed among individuals with pancreatic cancer and among those who had undergone surgery. CCI showed positive correlations with anxiety and depression, whereas age, BMI, and time since cancer diagnosis showed negative correlations.

Table 2. Anxiety and Depression T Scores by Characteristics among All Gastrointestinal Cancer Cases Combined[a]

Characteristic, mean (SD)	Anxiety T Score	*p or r*[b]	Depression T Score	*p or r*[b]
Cancer Site		0.376		0.112
Colorectal	50.63 (10.46)		46.30 (10.04)	
Liver	49.32 (10.69)		44.15 (8.61)	
Pancreas	52.67 (10.05)		49.36 (10.15)	
Stomach	53.11 (9.66)		47.47 (10.28)	
Age	66.06 (12.09)	r = -0.05, p = 0.381	66.06 (12.09)	r = -0.02, p = 0.711
Sex		0.044*		0.067
Male	49.83 (10.20)		45.67 (9.91)	
Female	52.31 (10.40)		47.91 (10.02)	
Language		0.059		0.334
English	50.28 (10.36)		46.41 (9.27)	
Spanish	52.80 (10.19)		47.70 (11.52)	
Marital Status		0.015*		0.067
Partnered	50.03 (10.52)		46.03 (9.70)	
Not partnered	53.26 (9.69)		48.43 (10.50)	
Insurance		0.099		0.487
Private	51.21 (10.44)		46.87 (10.59)	
Medicare	49.71 (9.90)		46.21 (8.32)	
Medicaid	60.17 (11.75)		53.40 (12.95)	
Uninsured	53.14 (9.12)		46.17 (6.46)	
Race/Ethnicity		0.650		0.186
Non-Hispanic White	51.98 (10.25)		48.31 (8.36)	
Hispanic or Latino	50.73 (10.53)		46.34 (10.93)	
Non-Hispanic Black	49.18 (9.74)		43.71 (11.17)	
Other or Unknown	49.92 (10.53)		43.82 (7.61)	
Body Mass Index	27.03 (5.40)	r = -0.08, p = 0.303	27.03 (5.40)	r = -0.09, p = 0.252
Tumor Stage		0.161		0.521
Stage I	53.05 (9.89)		48.20 (10.58)	
Stage II	48.83 (10.95)		45.40 (9.81)	
Stage III	51.29 (10.72)		47.04 (10.24)	
Stage IV	51.68 (9.25)		46.93 (9.44)	
Charlson Comorbidity Index	7.79 (3.85)	r = 0.01, p = 0.825	7.79 (3.85)	r = 0.03, p = 0.665
Time Since Cancer Diagnosis	36.92 (36.25)	r = -0.13, p = 0.038*	36.92 (36.25)	r = -0.13, p =0.035*
Active Treatment[c]		0.538		0.514
None[d]	50.96 (10.42)	0.659	46.77 (10.04)	0.853
Chemotherapy[d]	57.40 (13.05)	0.167	47.60 (12.86)	0.858
Surgery[d]	48.64 (8.00)	0.432	49.20 (7.86)	0.442
Radiation[d]	54.30 (10.19)	0.313	43.60 (10.82)	0.303

[a] Gastrointestinal cancers include: Colorectal: 324 (64.4%); Pancreas: 103 (20.5%) Liver: 44 (8.7%); Stomach: 32 (6.4%)

[b] One-way ANOVA; Pearson Correlation (r)

[c] p-value reflects a comparison of Anxiety and Depression T scores across multiple treatment categories

[d] p-values represent comparisons in Anxiety and Depression T scores between patients who did and did not receive the specified treatment (Yes vs. No)

*p<0.05

3.3 Factors Associated with Anxiety and Depression in Gastrointestinal Cancer

Univariate and multivariate linear regression analyses were conducted separately for anxiety and depression T scores in the gastrointestinal cancer cohort. Univariate analyses (Table 3) revealed that being female (estimated $\beta = 2.48$, Standard Error= 1.23, $p = 0.044$), not partnered ($\beta = 3.23$, SE = 1.32, $p = 0.015$), and having Medicaid insurance ($\beta = 8.95$, SE = 4.27, $p = 0.037$) was associated with higher anxiety scores on average compared to those who are male, partnered, and have private insurance. Patients with Stage II disease had significantly lower anxiety scores on average compared to those with Stage I ($\beta = –4.21$, SE = 1.99, $p = 0.035$), while longer time since diagnosis was associated with lower anxiety ($\beta = –0.04$, SE = 0.02, $p = 0.038$) and depression ($\beta = -0.04$, SE = 0.02, $p = 0.035$). Pancreatic cancer patients reported higher depression scores on average than patients with other gastrointestinal cancers ($\beta = 3.23$, SE = 1.49, $p = 0.032$).

Multivariate linear regression analyses (Table 4) identified several factors independently associated with anxiety and depression T scores after adjusting for all covariates. Higher anxiety scores were observed among females compared with males ($\beta = 3.98$, SE = 1.84, $p = 0.032$), and among patients receiving chemotherapy compared with no active treatment ($\beta = 12.64$, SE = 5.91, $p = 0.035$). Hispanic/Latino patients ($\beta = –4.25$, SE = 2.12, $p = 0.048$) and those categorized as Other/Unknown race/ethnicity ($\beta = –11.12$, SE = 4.86, $p = 0.024$) had significantly lower anxiety scores compared with non-Hispanic White patients. Stage II disease was associated with lower anxiety scores relative to Stage I ($\beta = –7.69$, SE = 2.51, $p = 0.003$).

For depression, higher scores were observed among females compared with males ($\beta = 3.83$, SE = 1.63, $p = 0.021$), whereas Hispanic/Latino ($\beta = –3.88$, SE = 1.89, $p = 0.042$)

and Other/Unknown race/ethnicity (β = –9.96, SE = 4.30, p = 0.022) patients had lower scores compared with non-Hispanic White patients. Stage II disease was also associated with lower depression scores compared with Stage I (β = –5.34, SE = 2.21, p = 0.017), and longer time since diagnosis was associated with lower depression scores (β = –0.05, SE = 0.02, p = 0.033). The models explained 26.0% of the variance in anxiety and 27.7% of the variance in depression scores, respectively.

Table 3. Univariate Linear Regression Models for Anxiety and Depression among All Gastrointestinal Cancer Cases Combined

Predictor	**Anxiety β (SE)**	***p***	**Depression β (SE)**	***p***
Cancer Site				
Pancreas vs Other Gastrointestinal (ref)	2.00 (1.56)	0.202	3.23 (1.49)	0.032*
Age	-0.04 (0.05)	0.381	-0.02 (0.05)	0.711
Sex				
Female vs Male (ref)	2.48 (1.23)	0.044*	2.24 (1.22)	0.068
Language				
Spanish vs English (ref)	2.53 (1.33)	0.059	1.28 (1.32)	0.334
Marital Status				
Not Partnered vs Partnered (ref)	3.23 (1.32)	0.015*	2.40 (1.30)	0.067
Insurance				
Medicaid vs Private (ref)	8.95 (4.27)	0.037*	6.53 (4.54)	0.152
Medicare vs Private (ref)	-1.50 (1.39)	0.282	-0.66 (1.40)	0.641
Uninsured vs Private (ref)	1.93 (3.96)	0.626	-0.70 (4.16)	0.866
Race/Ethnicity				
Hispanic/Latino vs Non-Hispanic White (ref)	-1.25 (1.34)	0.351	-1.98 (1.31)	0.133
Non-Hispanic Black vs Non-Hispanic White (ref)	-2.80 (2.72)	0.304	-4.60 (2.85)	0.108
Other or Unknown vs Non-Hispanic White (ref)	-2.06 (3.17)	0.516	-4.49 (3.18)	0.158
Body Mass Index	-0.15 (0.14)	0.303	-0.15 (0.13)	0.252
Tumor Stage				
Stage II vs Stage I (ref)	-4.21 (1.99)	0.035*	-2.79 (1.92)	0.147
Stage III vs Stage I (ref)	-1.76 (1.87)	0.348	-1.15 (1.80)	0.522
Stage IV vs Stage I (ref)	-1.37 (2.00)	0.493	-1.26 (1.97)	0.522
Charlson Comorbidity Index	0.04 (0.17)	0.825	0.07 (0.16)	0.665
Time Since Cancer Diagnosis	-0.04 (0.02)	0.038*	-0.04 (0.02)	0.035
Active Treatment				
In Chemotherapy vs No Treatment (ref)	6.47 (4.67)	0.167	0.81 (4.53)	0.858
Had Surgery vs No Treatment (ref)	-2.51 (3.19)	0.432	2.49 (3.23)	0.442
In Radiation vs No Treatment (ref)	3.37 (3.34)	0.313	-3.33 (3.23)	0.303

β: estimated β

3.4 Factors Associated with Anxiety and Depression in Pancreatic Cancer

Table 4. Multivariate Linear Regression Models for Anxiety and Depression among All Gastrointestinal Cancer Cases Combined

Predictor	**Anxiety β (SE)**[a]	***p***	**Depression β (SE)**[a]	***p***
Cancer site				
Pancreatic vs other gastrointestinal (ref)	0.72 (2.22)	0.747	0.36 (1.95)	0.856
Age	-0.05 (0.08)	0.553	-0.01 (0.07)	0.883
Sex				
Female vs male (ref)	3.98 (1.84)	0.032*	3.83 (1.63)	0.021*
Language				
Spanish vs English (ref)	1.73 (2.33)	0.459	-0.01 (2.06)	0.994
Marital status				
Not Partnered vs Partnered (ref)	1.98 (1.87)	0.291	-0.34 (1.66)	0.838
Insurance				
Medicare vs Private (ref)	2.13 (2.05)	0.301	2.86 (1.83)	0.122
Medicaid vs Private (ref)	8.58 (7.3)	0.242	8.08 (6.48)	0.215
Uninsured vs Private (ref)	10.81 (5.99)	0.074	4.97 (5.3)	0.35
Race/ethnicity				
Hispanic/Latino vs Non-Hispanic White (ref)	-4.25 (2.12)	0.048*	-3.88 (1.89)	0.042*
Non-Hispanic Black vs Non-Hispanic White (ref)	4.78 (4.27)	0.265	7.23 (4.08)	0.079
Other or Unknown vs Non-Hispanic White (ref)	-11.12 (4.86)	0.024*	-9.96 (4.3)	0.022*
Body Mass Index	-0.07 (0.15)	0.623	-0.09 (0.13)	0.483
Tumor Stage	-0.31 (0.91)	0.736	-0.26 (0.8)	0.749
Stage II vs Stage I (ref)	-7.69 (2.51)	0.003*	-5.34 (2.21)	0.017*
Stage III vs Stage I (ref)	-3.23 (2.59)	0.214	-1.99 (2.28)	0.384
Stage IV vs Stage I (ref)	-3.67 (2.89)	0.206	-2.12 (2.55)	0.408
Charlson Comorbidity Index	0.13 (0.27)	0.633	0.02 (0.24)	0.924
Time since cancer diagnosis	-0.05 (0.03)	0.055	-0.05 (0.02)	0.033*
Active Treatment				
Chemotherapy vs none (ref)	12.64 (5.91)	0.035*	3.82 (5.23)	0.466
Surgery vs none (ref)	-0.58 (4.06)	0.887	5.97 (3.83)	0.122
Radiation vs none (ref)	2.13 (3.87)	0.582	-5.03 (3.42)	0.144

[a]Anxiety $R^2 = 0.26$; Depression $R^2 = 0.277$
*$p<0.05$

Univariate linear regression analyses for the pancreatic cancer subgroup revealed no statistically significant associations between sociodemographic or clinical variables and anxiety or depression T scores (all $p > 0.05$). Marginally higher depression scores were observed among patients with Medicare insurance compared to private insurance (β = –

4.86, SE = 2.77, p = 0.08) and among non-Hispanic Black patients compared to non-Hispanic White patients (β = 11.06, SE = 7.20, p = 0.13). Longer time since cancer diagnosis showed a non-significant trend toward lower anxiety (β = –0.05, SE = 0.03, p = 0.12) and depression (β = –0.06, SE = 0.04, p = 0.12) scores.

Similarly, multivariate linear regression models (Table 5) showed no statistically significant variables associated with anxiety or depression within this subgroup. For anxiety, a trend toward higher levels was observed among uninsured patients compared with those with private insurance (β = 20.00, SE = 12.15, p = 0.117) and for non-Hispanic Black patients compared to non-Hispanic White patients (β = 9.02, SE = 9.18, p = 0.339). For depression, higher scores were most notably observed among non-Hispanic Black patients compared to non-Hispanic White patients (β = 16.21, SE = 7.92, p = 0.055) and uninsured patients compared to privately insured patients (β = 12.83, SE = 10.46, p = 0.235). The overall model fit was R^2 = 0.446 for anxiety and R^2 = 0.587 for depression.

Table 5. Multivariate Linear Regression Models for Anxiety and Depression among Pancreatic Cancer Patients				
Predictors	**Anxiety β (SE)[a]**	***p***	**Depression β (SE)[a]**	***p***
Age	0.13 (0.21)	0.556	0.35 (0.18)	0.071
Sex				
Female vs male (ref)	1.17 (4.63)	0.804	1.40 (3.62)	0.703
Language				
Spanish vs English (ref)	-16.68 (12.19)	0.188	6.41 (7.73)	0.417
Marital Status				
Not partnered vs partnered (ref)	1.15 (5.22)	0.829	-2.58 (4.11)	0.537
Insurance				
Medicare vs Private (ref)	-0.30 (5)	0.953	-1.41 (4.29)	0.747
Uninsured vs Private (ref)	20 (12.15)	0.117	12.83 (10.46)	0.235
Race/Ethnicity				
Hispanic/Latino vs Non-Hispanic White (ref)	-3.99 (6.8)	0.564	-8.86 (5.73)	0.139
Non-Hispanic Black vs Non-Hispanic White (ref)	9.02 (9.18)	0.339	16.21 (7.92)	0.055
Other or Unknown vs Non-Hispanic White (ref)	-7.42 (12.01)	0.544	-11.69 (10.12)	0.262
Body Mass Index (BMI)	0.01 (0.46)	0.975	-0.44 (0.39)	0.284
Tumor Stage				
Stage II vs stage I (ref)	2.28 (6.88)	0.744	-4.72 (5.75)	0.421
Stage III vs stage I (ref)	1.51 (6.61)	0.822	5.34 (5.67)	0.358
Stage IV vs stage I (ref)	7.39 (6.43)	0.265	3.15 (5.54)	0.576
Charlson Comorbidity Index (CCI)	0.24 (0.66)	0.717	0.34 (0.56)	0.549
Time Since Cancer Diagnosis (months)	-0.06 (0.06)	0.333	-0.06 (0.05)	0.245
[a] Anxiety $R^2 = 0.446$; Depression $R^2 = 0.587$				

Chapter 4: Discussion

The present study integrates patient-reported outcomes with demographic and clinical indicators to provide a comprehensive assessment of psychological distress among patients with pancreatic cancer and other gastrointestinal malignancies. By situating these findings within the broader context of gastrointestinal cancers, this analysis offers insight into the unique challenges faced by pancreatic cancer patients and highlights opportunities for targeted interventions. Pancreatic cancer represents a complex population with distinct supportive care needs. Despite its poor prognosis and high symptom burden, few studies have examined psychological distress specifically in this group. Notably, the study sample was diverse, with a majority (58%) of Hispanic/Latino patients, and all participants had completed their assessments.

This study found that patients with pancreatic cancer reported significantly higher depression scores on average compared with patients with other gastrointestinal malignancies. Specifically, 9% of pancreatic cancer patients met the threshold for depression compared with 4.8% of patients with other gastrointestinal cancers, with average depression scores nearly 2 points higher in the pancreatic cancer group. Univariate linear regression analyses confirmed higher depression scores among pancreatic cancer patients relative to other gastrointestinal cancers. However, in multivariate linear regression analyses, cancer type was no longer independently associated with depression after adjusting for sociodemographic and clinical factors, indicating that the apparent association was largely explained by differences in patient characteristics rather than cancer type alone. This distinction is important, as it suggests that the higher psychological burden observed in pancreatic cancer may be driven by the clinical and demographic

profile of this population, which together contribute to worse outcomes. In contrast, for anxiety, neither univariate nor multivariate analyses demonstrated significant differences between pancreatic and other gastrointestinal cancers, highlighting that anxiety may be less influenced by cancer type and more evenly distributed across gastrointestinal malignancies.

In line with previous work, our findings reinforce the observation that pancreatic cancer patients carry a disproportionate psychological burden.[12,22,23] Although multivariate models showed cancer type was not independently associated with depression after adjustment, the elevated rates observed in pancreatic cancer likely reflect the unique combination of characteristics defining this population. Even so, the clinical realities unique to pancreatic cancer (e.g., poor prognosis, aggressive progression, heavy symptom burden, and nutritional complications) likely contribute to heightened psychological distress.[2,3,11,15,17,30] Proposed biological mechanisms, including tumor-related cytokine activity and neuroendocrine dysregulation, also provide a plausible pathway linking the disease process itself to vulnerability to depression.[33,36,38] The fact that depression and related symptoms have been documented to precede a pancreatic cancer diagnosis[20,33,36,38] further supports the possibility that these associations are not incidental, but may be integral to the disease course.

Beyond psychological outcomes, significant demographic and clinical differences were also observed between patients with pancreatic cancer and those with other gastrointestinal cancers, including age, language, insurance type, race/ethnicity, BMI, tumor stage, and CCI. While univariate analyses confirmed these contrasts, several associations diminished in multivariate models, suggesting that the differences are shaped

by patient characteristics common in pancreatic cancer rather than the diagnosis itself. This helps explain why the pancreatic cancer population carries a heavier clinical burden and ultimately worse outcomes. These patterns are consistent with prior literature showing pancreatic cancer's higher prevalence among older adults, non-Hispanic Whites, and females, in contrast to cancers like colorectal, which tend to affect younger populations and comprised a large portion of the "other gastrointestinal" group in our study.[62–64] Greater comorbidity burden among pancreatic cancer patients aligns with evidence linking the disease to multiple metabolic and inflammatory conditions, including hypertension, metabolic syndrome, pancreatitis, and diabetes.[65,66] Although its impact on survival remains debated, with studies showing conflicting results,[67–69] the observed association between lower BMI and higher psychological distress likely reflects unintentional cancer-related weight loss, often due to anorexia, malabsorption, or cachexia.[70] Both groups followed similar psychological distress trajectories over time, with greater variability and symptom severity soon after diagnosis, supporting evidence that psychological distress often peaks at diagnosis and treatment initiation, then decreases as patients adjust to the illness and treatment course.[36,71,72]

Within the pancreatic cancer subgroup, neither univariate nor multivariate analyses identified statistically significant predictors of anxiety or depression, although several variables approached significance. Univariate results suggested possible trends toward higher depression among uninsured and non-Hispanic Black patients, and lower depression among Medicare recipients. In adjusted models, non-Hispanic Black race was slightly associated with higher depression scores, age showed a borderline association with higher

depression, and Spanish language preference was linked to substantially lower anxiety, though not statistically significant.

These findings indicate that while clear independent predictors were not confirmed, there may be meaningful sociodemographic patterns in psychological distress among pancreatic cancer patients that need further investigation. The absence of statistically significant predictors could be due to the smaller sample size in the pancreatic subgroup, limiting statistical power. However, the magnitude of some associations, such as the large positive coefficient for non-Hispanic Black race/ethnicity and depression, suggests potentially important disparities that may emerge in larger studies.

Sociodemographic disparities in psychological distress were evident across the cohort, underscoring the importance of social context in shaping anxiety and depression outcomes. Consistent with prior research, females reported higher levels of both depression and anxiety, highlighting a gendered vulnerability to psychological burden among cancer patients.[73] Greater psychological distress among Medicaid patients likely reflects socioeconomic disadvantage and barriers to healthcare access[74,75] while Spanish language preference and lack of a partner may exacerbate emotional burden through communication challenges and reduced social support. Treatment factors also showed distinct patterns, with chemotherapy linked to heightened anxiety and surgery associated with greater depression, suggesting that different treatment modalities carry unique emotional responses.

Univariate models identified multiple factors linked to elevated anxiety, including female sex, lack of a partner, Medicaid insurance, Stage I disease, and shorter time since diagnosis. However, multivariate models confirmed only female sex as an independent

predictor of both anxiety and depression. Hispanic/Latino and "Other or Unknown" patients reported lower levels of psychological distress than non-Hispanic Whites. This finding contrasts with prior evidence showing higher psychological distress among minority groups facing language and access barriers. Given that Hispanic/Latino patients comprised the majority of our sample, this association may reflect protective cultural or community factors. These findings suggest that psychological distress is shaped by an interplay of medical, demographic, and social factors.

The finding of higher depression among pancreatic cancer patients adds to growing evidence that depression may represent a distinguishing psychosocial feature of this disease and underscores the need to examine its role in screening and prevention, particularly in the absence of a gold standard. Sociodemographic disparities observed in the broader cohort highlight the importance of early psychological distress screening and psychosocial support at diagnosis, when variability and symptom severity are greatest[76] with special attention to high-risk groups such as females, Spanish speakers, individuals without partners, and those with Medicaid insurance. Tailored interventions should also be integrated into supportive care pathways for patients undergoing intensive treatments like chemotherapy or surgery. Although no independent predictors emerged within the pancreatic cancer subgroup, potential influences of race, insurance status, and age underscore the importance of larger studies to clarify these associations. Pending confirmation, targeted psychosocial interventions for uninsured patients and racial/ethnic minorities may help address emerging inequities in psychological outcomes in this high-risk population.

A major strength of this study is the use of EMR-integrated patient-reported outcome data, which enabled the simultaneous examination of clinical characteristics (e.g., stage, treatment, procedures) alongside psychosocial factors (e.g., anxiety and depression). This integration provided a more comprehensive picture of patient experiences than would be possible using clinical data alone.

Several limitations should also be acknowledged. Excluding patients with missing stage information may have introduced selection bias if these patients differed systematically from those included. Similarly, “unknown” race/ethnicity values were treated as missing, and blank treatment fields may reflect care received outside of Sylvester Comprehensive Cancer Center, limiting the completeness of treatment history. The cross-sectional design prevents conclusions about causality, and psychological distress was measured at a single time point, which may not capture its variability over the disease course. Finally, small sample sizes in some subgroups, such as uninsured patients and certain racial/ethnic minorities, may have reduced statistical power to detect significant differences.

Chapter 5: Conclusion

This study contributes to the understanding of psychological distress in pancreatic cancer by comparing distress levels and associated factors across gastrointestinal malignancies in a large, diverse, real-world sample. Patients with pancreatic cancer reported higher depression scores compared with those with other gastrointestinal cancers; however, these differences were largely explained by sociodemographic and clinical characteristics. Across the full cohort, disparities by sex, insurance status, language, and social support highlight the importance of social determinants in shaping psychological outcomes. Although independent predictors were not confirmed within the pancreatic cancer subgroup, trends by race, insurance, and age suggest potential disparities that warrant further study with larger samples.

These findings underscore the need for longitudinal research to monitor changes in psychological distress across the disease trajectory, identify critical timepoints for intervention, and evaluate the role of depression as a possible early marker of pancreatic cancer. Integrating validated psychological distress screening measures, such as anxiety and depression scales, into both oncology and primary care could facilitate earlier identification of psychological burden and, in certain contexts, prompt further medical evaluation. Embedding early, targeted psychosocial interventions within cancer care pathways has the potential to improve quality of life, enhance treatment adherence, and reduce inequities in outcomes for patients with gastrointestinal cancers, particularly those with pancreatic cancer.

References

1. Pancreatic Cancer Stages | Staging Pancreatic Cancer. Accessed July 24, 2023. https://www.cancer.org/cancer/types/pancreatic-cancer/detection-diagnosis-staging/staging.html

2. Oberstein PE, Olive KP. Pancreatic cancer: why is it so hard to treat? *Therap Adv Gastroenterol*. 2013;6(4):321-337. doi:10.1177/1756283X13478680

3. Tonini V, Zanni M. Pancreatic cancer in 2021: What you need to know to win. *World J Gastroenterol*. 2021;27(35):5851-5889. doi:10.3748/wjg.v27.i35.5851

4. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer Statistics, 2021. *CA: A Cancer Journal for Clinicians*. 2021;71(1):7-33. doi:10.3322/caac.21654

5. Siegel RL, Giaquinto AN, Jemal A. Cancer statistics, 2024. *CA: A Cancer Journal for Clinicians*. 2024;74(1):12-49. doi:10.3322/caac.21820

6. Survival Rates for Pancreatic Cancer. Accessed September 6, 2024. https://www.cancer.org/cancer/types/pancreatic-cancer/detection-diagnosis-staging/survival-rates.html

7. Cancer Facts & Figures 2025. Published online 1930.

8. Cipora E, Czerw A, Partyka O, et al. Quality of Life in Patients with Pancreatic Cancer—A Literature Review. *Int J Environ Res Public Health*. 2023;20(6):4895. doi:10.3390/ijerph20064895

9. Bauer MR, Bright EE, MacDonald JJ, Cleary EH, Hines OJ, Stanton AL. Quality of Life in Patients With Pancreatic Cancer and Their Caregivers: A Systematic Review. *Pancreas*. 2018;47(4):368-375. doi:10.1097/MPA.0000000000001025

10. Schepis T, De Lucia SS, Pellegrino A, et al. State-of-the-Art and Upcoming Innovations in Pancreatic Cancer Care: A Step Forward to Precision Medicine. *Cancers (Basel)*. 2023;15(13):3423. doi:10.3390/cancers15133423

11. McGuigan A, Kelly P, Turkington RC, Jones C, Coleman HG, McCain RS. Pancreatic cancer: A review of clinical diagnosis, epidemiology, treatment and outcomes. *World J Gastroenterol*. 2018;24(43):4846-4861. doi:10.3748/wjg.v24.i43.4846

12. Mazzella Ebstein AM, Joseph SJ, Hernandez M. Psychological stress and pancreatic cancer patients: a qualitative systematic review protocol. *JBI Evidence Synthesis*. 2020;18(3):576. doi:10.11124/JBISRIR-D-18-00006

13. Hu JX, Zhao CF, Chen WB, et al. Pancreatic cancer: A review of epidemiology, trend, and risk factors. *World J Gastroenterol*. 2021;27(27):4298-4321. doi:10.3748/wjg.v27.i27.4298

14. Karim SAM, Abdulla KS, Abdulkarim QH, Rahim FH. The outcomes and complications of pancreaticoduodenectomy (Whipple procedure): Cross sectional study. *Int J Surg*. 2018;52:383-387. doi:10.1016/j.ijsu.2018.01.041

15. Noda Y, Tomita H, Ishihara T, et al. Prediction of overall survival in patients with pancreatic ductal adenocarcinoma: histogram analysis of ADC value and correlation with pathological intratumoral necrosis. *BMC Medical Imaging*. 2022;22(1):23. doi:10.1186/s12880-022-00751-3

16. Feng Q, Li C, Zhang S, et al. Recurrence and survival after surgery for pancreatic cancer with or without acute pancreatitis. *World J Gastroenterol*. 2019;25(39):6006-6015. doi:10.3748/wjg.v25.i39.6006

17. Puckett Y, Garfield K. Pancreatic Cancer. In: *StatPearls*. StatPearls Publishing; 2024. Accessed September 6, 2024. http://www.ncbi.nlm.nih.gov/books/NBK518996/

18. Badger S, Brant J, Jones C, et al. The role of surgery for pancreatic cancer: a 12-year review of patient outcome. *Ulster Med J*. 2010;79(2):70-75.

19. Duan H, Li L, He S. Advances and Prospects in the Treatment of Pancreatic Cancer. *Int J Nanomedicine*. 2023;18:3973-3988. doi:10.2147/IJN.S413496

20. PhD AR. It Starts with Someone: Barbara Kenner, PhD. Pancreatic Cancer Action Network. February 13, 2019. Accessed July 15, 2023. https://pancan.org/stories/life-after-loss/it-starts-with-someone-barbara-kenner-phd/

21. Park SA, Chung SH, Lee Y. Factors Associated with Suicide Risk in Advanced Cancer Patients: A Cross-Sectional Study. *Asian Pac J Cancer Prev*. 2016;17(11):4831-4836. doi:10.22034/APJCP.2016.17.11.4831

22. Batty GD, Russ TC, Stamatakis E, Kivimäki M. Psychological distress in relation to site specific cancer mortality: pooling of unpublished data from 16 prospective cohort studies. *BMJ*. Published online January 25, 2017:j108. doi:10.1136/bmj.j108

23. Michoglou K, Ravinthiranathan A, San Ti S, Dolly S, Thillai K. Pancreatic cancer and depression. *World J Clin Cases*. 2023;11(12):2631-2636. doi:10.12998/wjcc.v11.i12.2631

24. Ma Y, Lyu J, Yang B, et al. Incidence and risk factors of suicide among patients with pancreatic cancer: A population-based analysis from 2000 to 2018. *Front Oncol*. 2022;12:972908. doi:10.3389/fonc.2022.972908

25. Zabora J, Brintzenhofeszoc K, Curbow B, Hooker CM, Piantadosi S. The prevalence of psychological distress by cancer site. *Psycho-oncology*. 2001;10(1):19-28. doi:10.1002/1099-1611(200101/02)10:1<19::AID-PON501>3.0.CO;2-6

26. Schuller HM, Al-Wadei HAN, Ullah MF, Plummer HK. Regulation of pancreatic cancer by neuropsychological stress responses: a novel target for intervention. *Carcinogenesis*. 2012;33(1):191-196. doi:10.1093/carcin/bgr251

27. Hu X, Ma J, Jemal A, et al. Suicide Risk Among Individuals Diagnosed With Cancer in the US, 2000-2016. *JAMA Network Open*. 2023;6(1):e2251863. doi:10.1001/jamanetworkopen.2022.51863

28. Turaga KK, Malafa MP, Jacobsen PB, Schell MJ, Sarr MG. Suicide In Patients With Pancreatic Cancer. *Cancer*. 2011;117(3):642-647. doi:10.1002/cncr.25428

29. Zamani M, Alizadeh-Tabari S. Anxiety and depression prevalence in digestive cancers: a systematic review and meta-analysis. *BMJ Support Palliat Care*. 2023;13(e2):e235-e243. doi:10.1136/bmjspcare-2021-003275

30. Mayr M, Schmid RM. Pancreatic cancer and depression: myth and truth. *BMC Cancer*. 2010;10:569. doi:10.1186/1471-2407-10-569

31. Kouhestani M, Ahmadi Gharaei H, Fararouei M, Hosienpour Ghahremanloo H, Ghaiasvand R, Dianatinasab M. Global and regional geographical prevalence of depression in gastric cancer: a systematic review and meta-analysis. *BMJ Support Palliat Care*. 2022;12(e4):e526-e536. doi:10.1136/bmjspcare-2019-002050

32. Tan DJH, Quek SXZ, Yong JN, et al. Global prevalence of depression and anxiety in patients with hepatocellular carcinoma: Systematic review and meta-analysis. *Clin Mol Hepatol*. 2022;28(4):864-875. doi:10.3350/cmh.2022.0136

33. Fras I, Litin EM, Bartholomew LG. Mental Symptoms as an Aid in the Early Diagnosis of Carcinoma of the Pancreas. *Gastroenterology*. 1968;55(2):191-198. doi:10.1016/S0016-5085(19)34069-7

34. Kuczmarski TM, Jaung T, Mancuso CE, et al. Precancer and cancer-associated depression and anxiety among older adults with blood cancers in the United States. *Blood Adv*. 2022;6(4):1126-1136. doi:10.1182/bloodadvances.2021005862

35. Tastula A, Jukkola A, Alakokkare AE, et al. Depression and Anxiety Symptoms Before and After Breast-Cancer Diagnosis Among Young Women in the Northern Finland Birth Cohort 1966. *European Journal of Breast Health*. Published online September 26, 2024. doi:10.4274/ejbh.galenos.2024.2024-7-1

36. Passik SD, Roth AJ. Anxiety symptoms and panic attacks preceding pancreatic cancer diagnosis. *Psychooncology*. 1999;8(3):268-272. doi:10.1002/(SICI)1099-1611(199905/06)8:3<268::AID-PON369>3.0.CO;2-W

37. Pitman A, Suleman S, Hyde N, Hodgkiss A. Depression and anxiety in patients with cancer. *BMJ*. 2018;361:k1415. doi:10.1136/bmj.k1415

38. Kenner BJ. Early Detection of Pancreatic Cancer: The Role of Depression and Anxiety as a Precursor for Disease. *Pancreas*. 2018;47(4):363. doi:10.1097/MPA.0000000000001024

39. Kiecolt-Glaser JK, Robles TF, Heffner KL, Loving TJ, Glaser R. Psycho-oncology and cancer: psychoneuroimmunology and cancer. *Ann Oncol*. 2002;13 Suppl 4:165-169. doi:10.1093/annonc/mdf655

40. Spiegel D, Giese-Davis J. Depression and cancer: mechanisms and disease progression. *Biol Psychiatry*. 2003;54(3):269-282. doi:10.1016/s0006-3223(03)00566-3

41. Musselman DL, Miller AH, Porter MR, et al. Higher than normal plasma interleukin-6 concentrations in cancer patients with depression: preliminary findings. *Am J Psychiatry*. 2001;158(8):1252-1257. doi:10.1176/appi.ajp.158.8.1252

42. Holland JC, Korzun AH, Tross S, et al. Comparative psychological disturbance in patients with pancreatic and gastric cancer. *Am J Psychiatry*. 1986;143(8):982-986. doi:10.1176/ajp.143.8.982

43. krysti. The Link Between Depression and Pancreatic Cancer. Let's Win Pancreatic Cancer. July 18, 2019. Accessed August 27, 2024. https://letswinpc.org/research/depression-and-pancreatic-cancer-link/

44. Wang YH, Li JQ, Shi JF, et al. Depression and anxiety in relation to cancer incidence and mortality: a systematic review and meta-analysis of cohort studies. *Mol Psychiatry*. 2020;25(7):1487-1499. doi:10.1038/s41380-019-0595-x

45. Hamer M, Chida Y, Molloy GJ. Psychological distress and cancer mortality. *J Psychosom Res*. 2009;66(3):255-258. doi:10.1016/j.jpsychores.2008.11.002

46. Pinquart M, Duberstein PR. Depression and cancer mortality: a meta-analysis. *Psychol Med*. 2010;40(11):1797-1810. doi:10.1017/S0033291709992285

47. McDonald PG, Antoni MH, Lutgendorf SK, et al. A biobehavioral perspective of tumor biology. *Discov Med*. 2005;5(30):520-526.

48. Moreno-Smith M, Lutgendorf SK, Sood AK. Impact of stress on cancer metastasis. *Future Oncol*. 2010;6(12):1863-1881. doi:10.2217/fon.10.142

49. Pyter LM. The influence of cancer on endocrine, immune, and behavioral stress responses. *Physiol Behav*. 2016;166:4-13. doi:10.1016/j.physbeh.2015.09.031

50. Bettison TM, Nahm CB, Gill AJ, Mittal A, Malhi GS, Samra JS. Understanding the Pathophysiology of Psychological Distress and Pancreatic Cancer: A Systematic Review. *Pancreas*. 2018;47(4):376-381. doi:10.1097/MPA.0000000000001016

51. Amtmann D, Cook KF, Jensen MP, et al. Development of a PROMIS item bank to measure pain interference. *PAIN*. 2010;150(1):173. doi:10.1016/j.pain.2010.04.025

52. Rose M, Bjorner JB, Becker J, Fries JF, Ware JE. Evaluation of a preliminary physical function item bank supported the expected advantages of the Patient-Reported Outcomes Measurement Information System (PROMIS). *J Clin Epidemiol*. 2008;61(1):17-33. doi:10.1016/j.jclinepi.2006.06.025

53. Lai JS, Cella D, Choi S, et al. How item banks and their application can influence measurement practice in rehabilitation medicine: a PROMIS fatigue item bank example. *Arch Phys Med Rehabil*. 2011;92(10 Suppl):S20-27. doi:10.1016/j.apmr.2010.08.033

54. Pilkonis PA, Choi SW, Reise SP, Stover AM, Riley WT, Cella D. Item Banks for Measuring Emotional Distress From the Patient-Reported Outcomes Measurement Information System (PROMIS®): Depression, Anxiety, and Anger. *Assessment*. 2011;18(3):263-283. doi:10.1177/1073191111411667

55. Penedo F, Medina H, Moreno P, et al. Implementation and Feasibility of an Electronic Health Record–Integrated Patient-Reported Outcomes Symptom and Needs Monitoring Pilot in Ambulatory Oncology. *JCO Oncology Practice*. Published online March 15, 2022. doi:10.1200/OP.21.00706

56. Cella D, Gershon R, Lai JS, Choi S. The future of outcomes measurement: item banking, tailored short-forms, and computerized adaptive assessment. *Qual Life Res*. 2007;16(1):133-141. doi:10.1007/s11136-007-9204-6

57. Arnold M, Abnet CC, Neale RE, et al. Global Burden of 5 Major Types Of Gastrointestinal Cancer. *Gastroenterology*. 2020;159(1):335-349.e15. doi:10.1053/j.gastro.2020.02.068

58. Li M, Cao S, Xu RH. Global trends and epidemiological shifts in gastrointestinal cancers: insights from the past four decades. *Cancer Communications*. 2025;45(7):774-788. doi:10.1002/cac2.70017

59. AJCC Version 9 Cancer Staging System. ACS. Accessed August 15, 2025. https://www.facs.org/quality-programs/cancer-programs/american-joint-committee-on-cancer/version-9/

60. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40(5):373-383. doi:10.1016/0021-9681(87)90171-8

61. Natori A, Sookdeo VD, Koru-Sengul T, et al. Symptoms and Needs Monitoring in Diverse Ambulatory Oncology Patients: Usage Characteristics and Impact on Emergency Room Visits and Hospitalization. *J Clin Oncol*. 2023;41(2):285-294. doi:10.1200/JCO.22.01038

62. Colorectal Cancer Rising among Young Adults - NCI. November 5, 2020. Accessed August 10, 2025. https://www.cancer.gov/news-events/cancer-currents-blog/2020/colorectal-cancer-rising-younger-adults

63. Guillot Morales M, Visa L, Brozos Vázquez E, et al. Update on the management of older patients with pancreatic adenocarcinoma: a perspective from medical oncology. *Clin Transl Oncol*. 2024;26(7):1570-1583. doi:10.1007/s12094-024-03386-8

64. Samaan JS, Abboud Y, Oh J, et al. Pancreatic Cancer Incidence Trends by Race, Ethnicity, Age and Sex in the United States: A Population-Based Study, 2000–2018. *Cancers (Basel)*. 2023;15(3):870. doi:10.3390/cancers15030870

65. Powers BD, Allenson K, Perone JA, et al. The impact of age and comorbidity on localized pancreatic cancer outcomes: A US retrospective cohort analysis with implications for surgical centralization. *Surg Open Sci*. 2023;12:14-21. doi:10.1016/j.sopen.2023.02.001

66. Merza N, Rutledge BP, Kiwan W, Mohamad B. S3225 The Most Common Presentations and Comorbidities of Pancreatic Cancer: Nationwide Cohort Study. *Official journal of the American College of Gastroenterology | ACG*. 2021;116:S1329. doi:10.14309/01.ajg.0000786432.37524.44

67. Higher body mass index indicated better overall survival in pancreatic ductal adenocarcinoma patients: a real-world study of 2010 patients | BMC Cancer | Full Text. Accessed August 11, 2025. https://bmccancer.biomedcentral.com/articles/10.1186/s12885-021-09056-0

68. Arslan AA, Helzlsouer KJ, Kooperberg C, et al. Anthropometric Measures, Body Mass Index, and Pancreatic Cancer: A Pooled Analysis From the Pancreatic Cancer Cohort Consortium (PanScan). *Arch Intern Med*. 2010;170(9):791-802. doi:10.1001/archinternmed.2010.63

69. Shi YQ, Yang J, Du P, et al. Effect of Body Mass Index on Overall Survival of Pancreatic Cancer. *Medicine (Baltimore)*. 2016;95(14):e3305. doi:10.1097/MD.0000000000003305

70. Hendifar AE, Petzel MQB, Zimmers TA, et al. Pancreas Cancer-Associated Weight Loss. *Oncologist*. 2019;24(5):691-701. doi:10.1634/theoncologist.2018-0266

71. Kant J, Czisch A, Schott S, Siewerdt-Werner D, Birkenfeld F, Keller M. Identifying and predicting distinct distress trajectories following a breast cancer diagnosis - from treatment into early survival. *Journal of Psychosomatic Research*. 2018;115:6-13. doi:10.1016/j.jpsychores.2018.09.012

72. Shahsavar Y, Choudhury A. Examining influential factors in newly diagnosed cancer patients and survivors: Emphasizing distress, self-care ability, peer support, health perception, daily life activity, and the role of time since diagnosis. *PLoS One*. 2023;18(9):e0291064. doi:10.1371/journal.pone.0291064

73. Vitale E, Halemani K, Shetty A, et al. Sex Differences in Anxiety and Depression Conditions among Cancer Patients: A Systematic Review and Meta-Analysis. *Cancers (Basel)*. 2024;16(11):1969. doi:10.3390/cancers16111969

74. Cancer Disparities - NCI. August 4, 2016. Accessed August 11, 2025. https://www.cancer.gov/about-cancer/understanding/disparities

75. Cheng E, Soulos PR, Irwin ML, et al. Neighborhood and Individual Socioeconomic Disadvantage and Survival Among Patients With Nonmetastatic Common Cancers. *JAMA Netw Open*. 2021;4(12):e2139593. doi:10.1001/jamanetworkopen.2021.39593

76. Cook SA, Salmon P, Hayes G, Byrne A, Fisher PL. Predictors of emotional distress a year or more after diagnosis of cancer: A systematic review of the literature. *Psychooncology*. 2018;27(3):791-801. doi:10.1002/pon.4601