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Original Article

Sociodemographic characteristics associated with pancreatic cancer incidence and mortality among Blacks in the United States: a SEER-based study

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Abstract: Pancreatic cancer (PC) is the third leading cause of all cancer-related fatalities and accounts for approximately 3% of cancer cases in the United States. PC survival rates are lower in Blacks compared to other races, and this has been attributed to socioeconomic and genetic factors. In this study, we evaluated sociodemographic and genetic characteristics associated with PC incidence and mortality among Blacks. Data from the SEER 22 registries (2000-2020) were used to calculate the incidence rates and relative survival. County mortality rates from 2017 to 2021 were analyzed. Incidence rate ratios based on gender, age, primary disease site, stage, level of education, and poverty were calculated. Survival analysis was conducted using the Kaplan-Meier method. Mutant gene expression was obtained from the MSK-CHORD tumor registry. Overall, 48,606 Black patients were diagnosed with malignant PC between 2000 and 2020: females (53.53%) and males (46.47%). Both males and females experienced a slight increase in Annual Percent Change (APC) of PC incidence (0.24, 95% CI, -0.02-0.53) and (0.22, 95% CI, -0.05-0.51), respectively, from 2000 to 2020. Males aged 55 to 75 years were most frequently affected. Overall incidence risk from 2000-2020 by age was higher in Black males IRR > 1 (1.18, 95% CI, 1.16-1.21). The most common primary PC site for Black males and females was the head of the pancreas, 49.06% and 49.88%, respectively. By staging, distant PC had the highest frequency in Blacks. Poverty level was associated with PC incidence among females and PC mortality among both males and females. Stage was associated with survival among males with localized and regional PC. The 5-year relative survival was less than 11% across combined PC stages for both sexes. Black males had a relatively lower 5-year survival than Black females in localized (31.7 vs. 37.2%) and distant PC (2.6% vs. 2.90%). Mutant KRAS expression was higher in Black males. PC incidence and mortality were significantly higher in Black males. Our analysis points to the importance of poverty alleviation programs that target females are likely to reduce PC incidence. Furthermore, receiving recommended screening for PC and early-stage diagnostics is important to lower PC mortality.

Keywords: Pancreatic cancer, Blacks, racial disparities, sociodemographic, incidence, mortality, genomics

Introduction

Pancreatic cancer (PC), a debilitating malignancy, is the third leading cause of all cancer-related fatalities and accounts for approximately 3% of all cancer cases in the United States [1, 2]. Currently, the yearly incidence of PC almost equals the annual mortality, according to the American Cancer Society [2]. PC has one of the lowest 5-year survival rates of all solid tumors [3]. Some implicating factors for the low survival rate include the complex nature of the tumor microenvironment, late diagnosis, as well as difficulty in performing a tissue biopsy of the pancreas, leading to poor response to chemotherapy and radiation [4]. Diagnosis of PC continues to pose a challenge to treatment and overall survival, as the symptoms are generally vague and similar to symptoms of several other conditions [5]. Furthermore, the highly aggressive nature, early metastasis, and low survival rate of PC contribute significantly to the disease burden [4, 6].

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The majority of PC cases are pancreatic ductal adenocarcinoma (PDAC), which emanates from the exocrine pancreas. However, just under a fifth of PDAC patients qualify for curative surgery after diagnosis [5, 7]. Post-surgery complications for PDAC patients coupled with low survival make resection of the primary tumor or metastatic lesions generally unsuitable when the disease has metastasized [8].

The risk of developing PC increases with age as most patients are diagnosed above 55 years [9]. The incidence of PC is higher in males compared to females, and survival is lower in African-Americans (AA)/Blacks compared to other races [10, 11]. The disparity in PC incidence and survival in AAs compared to other racial groups has been attributed to socioeconomic and genetic factors [12, 13]. Also, the underreporting of PC cases and the low representation of AAs in clinical trials play a role in the PC treatment disparities among races [14, 15]. Socioeconomic factors such as income, level of education, insurance status, etc., significantly contribute to pancreatic cancer survival among races. It has been determined that PC patients who have lower income, less education, and either no insurance or minimal insurance coverage are less likely to have surgical resections [16, 17].

Some studies have investigated how racial disparities influence PC treatment. Specifically, Riall et al. demonstrated that AAs diagnosed with locoregional PC were less likely to visit a surgeon and undergo resection after the visit compared to other racial counterparts [18]. This racial treatment bias was confirmed when a similar study by Shapiro et al. showed a similar result of AAs having a significantly lower rate of resection compared to white patients [19]. Another factor contributing to the disparity in PC incidence and survival among AAs is access to healthcare facilities [20]. It has been found that greater medical visits lead to increased diagnoses and an earlier stage of diagnosis [21]. AAs frequently face challenges related to low socioeconomic status or non-insurance, which can limit their access to healthcare and ultimately reduce their chances of survival [21].

There is generally limited research on PC trends among AAs/Blacks. This affects policymaking and treatment options, ultimately leading to low survival outcomes. Using the Surveillance, Epidemiology, and End Results (SEER) database and Memorial Sloan Kettering Cancer Center tumor registry, our study focuses on current trends in PC among Blacks. We explored the incidence and mortality based on the age, stage of diagnosis, the location of the tumor, genomics, and the impact of other socioeconomic factors on PC survival.

Methods

Data source

We used the SEER*stat software (version 8.4.3) to obtain data on PC cases diagnosed during 2000-2020 from SEER 22 registries; Incidence-SEER Research Limited Field data, Nov 2022 Sub (2000-2022) [22]. Largest geographic coverage available - approximately 47.9% of the US population (based on 2020 census). Rates are available by expanded race (white, black, AI/AN, and API) and Hispanic ethnicity (Hispanic and non-Hispanic). Includes adjustments for areas impacted by hurricanes Katrina and Rita. Two age variables are available: 19 age groups (< 1 year, 1-4 years, 5-9 years, ..., 85+ years) and single ages with 85+. Seer 22-Incidence Seer Research Plus (2000-2020) data was analyzed for county incidence rates [23]. County mortality registry data (1969-2021) was analyzed for county mortality rates among Blacks from 2017-2021 [24]. Genomic data was obtained from the Memorial Sloan Kettering Cancer Center tumor registry (MSK-CHORD (MSK, Nature 2024)) through the cBioPortal database [25].

Study population

The study included patients with PC diagnosed during 2000-2020. Site recode ICD-0-3/WHO 2008: Pancreas (ICD-0-3 site C25) was used via SEER*Stat software to select PC cases. Only malignant cases were included. We excluded patients below age 24 as previous studies excluded patients in this age group due to reportedly low incidence [9]. We analyzed the population using two main variables (sex and race), then stratified further using the following variables: age at diagnosis, stage at diagnosis (SEER combined stage 2004+), site of the

tumor within the pancreas (primary site labeled), poverty status (% of persons below poverty ACS 2017-2021) and level of education (% < HS Educ ACS 2017-2021). The primary sites were C25.0-Head of pancreas, C25.1-Body of pancreas, C25.2-Tail of pancreas, C25.9-Pancreas, NOS. We divided county incidence and mortality into five quintiles based on the total number of counties in the database. For mortality rates, we excluded cases whose diagnosis relied only on autopsy or death certificates. Genomic data of patients with only pancreatic adenocarcinoma and a primary race of Black or African American were selected. The expression of four frequently mutant PC genes (KRAS, TP53, CDKN2A, and SMAD4) were determined.

Outcomes

We calculated three main outcomes: incidence rates, mortality rates, and relative survival. All rates were adjusted to the 2000 US standard population and expressed by 100,000 person-years. These rates were calculated from 2000 to 2020 according to race and sex. County incidence and mortality rates were calculated for 2017 to 2021. Relative survival was determined for cases from 2017-2021. We calculated the Annual Percentage Changes (APCs) of incidence trends and incidence and mortality Risk Ratios (RR) with 95% confidence intervals (CIs) included over the study period. Survival rates based on the expression of PC mutant genes were determined.

Statistical analysis

The SEER*stat software (version 8.4.3) was used to calculate all incidence rates, mortality rates, and relative survival [26]. The National Cancer Institute's Joinpoint Regression software, version 5.2.0, calculated APCs [27]. Joinpoint Regression analyzed trends for significant changes in APCs (p-value < 0.05). The most suitable model with minimum join points was selected [28]. Incidence Rate Ratios (IRRs) based on gender, age, the primary site of the disease, stage, level of education, and poverty were calculated. 95% CIs for the IRRs were calculated using the Tiwari method. Survival analysis was conducted using the Kaplan-Meier method, and cumulative survival was performed using the Ederer II method [29]. Trends in 5-year relative survival rates were evaluated as percentage survival from 2017-2021 (P < 0.05) was considered statistically significant. Expression of PC mutant genes was determined using the cBioPortal, and a chi-squared test was used to determine significance [30-32]. The figures were generated using GraphPad Prism, Joinpoint, and Microsoft Excel.

Results

Temporal trends

The SEER 22 registry consisted of 48,606 Black patients diagnosed with malignant PC between 2000 and 2020. A greater percentage of the total population were females (53.53%) compared to males (46.47%), as shown in **Table 1**. Both males and females experienced a slight increase in Annual Percent Change (APC) from 2000-2020, as shown in **Figure 1A**. However, the overall change in APC for Black males (0.24, 95% CI, -0.02-0.53) in the 20 years was slightly higher than that of females (0.22, 95% CI, -0.05-0.51). The Joinpoint model showed that for 2018-2020, there was a decrease in the incidence of PC among both Black males APC (-2.76, 95% CI, -6.83-1.04) and females APC (-3.70, 95% CI, -6.76-0.36) as shown in Table S1. This contrasts with previous years, as both sexes had increased APC in PC incidence from 2000-2017.

The incidence of PC in Black males by age showed that the most frequently affected age groups were males between 55 and 75, as shown in **Table 1** and **Figure 1B**. There was a significant change in the APC in Black males aged (60-64 and 65-69) from 2000-2020. The highest increase in APC over the 20 years in Black males was in males of ages 60-64; APC (1.19, 95% CI, 0.70-1.79, p-value < 0.05) and 65-69; APC (0.85, 95% CI, 0.23-1.61, p-value < 0.05). The Joinpoint model showed that black males over 85 had increased APC in PC incidence between 2000 and 2015. However, a decrease in APC was observed in recent years (2015-2020).

The incidence among Black females by age showed that the most frequently affected age

Table 1. Case counts and Annual Percentage Changes (APCs) for Blacks by sex, age, and primary site, SEER 22 (2000-2020)

Trends						
Overall (2000-2020)						
Sex	Male		APC (95% CI)	Female		APC (95% CI)
	Count	%Pop		Count	%Pop	
	22,589	46.47	0.24 (-0.02-0.53)	26,017	53.53	0.22 (-0.05-0.51)
Age Group						
25-29	31	0.14	~	64	0.25	~
30-34	87	0.39	~	123	0.47	~
35-39	209	0.93	0.10 (-2.52-2.85)	193	0.74	2.69 (-0.68-6.76)
40-44	496	2.20	0.64 (-1.28-2.58)	480	1.84	1.51 (-0.40-3.49)
45-49	1,110	4.91	-0.26 (-1.33-0.84)	973	3.74	0.50 (-0.62-1.71)
50-54	2,138	9.46	-0.58 (-1.58-0.47)	1,688	6.49	1.47* (0.42-2.66)
55-59	3,133	13.87	0.11 (-0.69-1.02)	2,558	9.83	1.26* (0.39-2.32)
60-64	3,701	16.38	1.19* (0.70-1.79)	3,223	12.39	1.22* (0.58-2.00)
65-69	3,537	15.66	0.85* (0.23-1.61)	3,643	14.00	0.81* (0.20-1.57)
70-74	3,099	13.72	0.02 (-0.60-0.71)	3,646	14.01	0.16 (-0.63-1.07)
75-79	2,308	10.22	-0.04 (-0.80-0.83)	3,437	13.21	-0.11 (-0.76-0.58)
80-84	1,606	7.11	-0.06 (-1.09-1.10)	2,807	10.79	-0.47 (-1.25-0.36)
85+	1,134	5.02	-0.16 (-1.45-1.34)	3,182	12.23	-1.37* (-2.25 - -0.48)
Primary Site						
Head	10,224	49.06	-0.03 (-0.54-0.55)	11,902	49.88	0.00 (-0.45-0.45)
Body	2,351	11.28	4.09* (2.84-5.46)	3,003	12.59	4.38* (3.11-6.02)
Tail	3,386	16.25	2.51* (1.43-3.83)	3,426	14.36	3.01* (2.54-3.60)
NOS	4,877	23.41	-2.36* (-3.16 - -1.52)	5,530	23.18	-2.70* (-3.74-1.85)

Cases included first primary tumors that were malignant. APC = Annual percent change; LCI, UCI = lower, upper 95% confidence interval. APCs were calculated using the weighted least squares method, based on rates per 100,000 person-years, age-adjusted to the 2000 US Standard Population (19 age groups). ~Statistic could not be calculated because at least one year had zero cases. Using SEER labeled primary site. *p-value < 0.05. Primary site represents primary site of pancreas.

groups were 55 to 85 years old, as shown in **Table 1** and **Figure 1C**. There was a statistically significant change in the APC in Black females aged (50-54, 55-59, 60-64, 65-69 and 85+ years). The most significant changes in APC over the 20 years were females aged 50-54 APC (1.47, 95% CI, 0.42-2.66, p-value < 0.05). However, a significant decline in the incidence in females above 85 years APC (-1.37, 95% CI, -2.25 - -0.48, p-value < 0.05) was observed in the 20 years. The most frequently affected PC primary site for Black males was the head of the pancreas (49.06%) and the pancreas, NOS (23.41%), as shown in **Table 1**. For Black males, there was a significant increase in the APC in the body, tail, and pancreas, NOS. The highest increase in APC was observed in the body of the pancreas, APC (4.09, 95% CI, 2.84-5.46, p-value < 0.05). For Black female PC patients, the most frequently affected sites were also the head of the pancreas (49.88%) and pancreas, NOS (23.18%). The highest increase in APC between 2000 and 2020 was observed in the cases in the body of the pancreas, APC (4.38, 95% CI, 3.11-6.02, p-value < 0.05). Black males APC (-2.36, 95% CI, -3.16 - -1.52, p-value < 0.05) and females APC (-2.70, 95% CI, -3.74 - -1.85, p-value < 0.05) with the pancreas, NOS as the primary site, had reduced incidence over the last two decades. However, the decline in incidence was more significant in Black females. The decline in PC incidence APC among Black males and females between 2018 and 2020 is shown in **Figure 2A**. The Joinpoint model further showed that women aged 50-54 had a slight increase in APC of PC incidence from 2000-2014, APC (2.85, 95% CI, -5.68-15.30), this was followed by a sharp decrease from 2014-2017 APC (-7.84, 95% CI, -13.98-12.46), then a subsequent increase

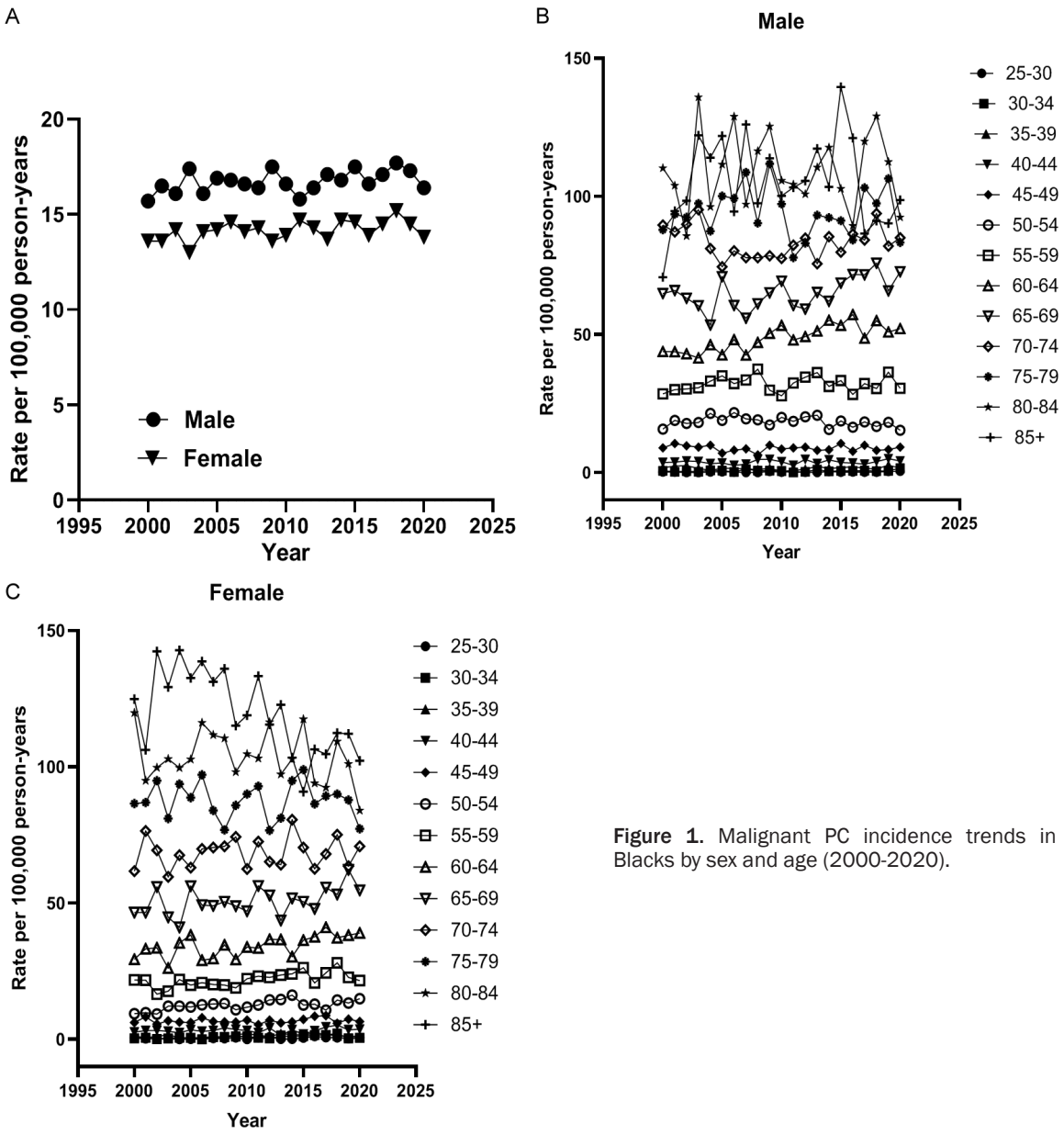
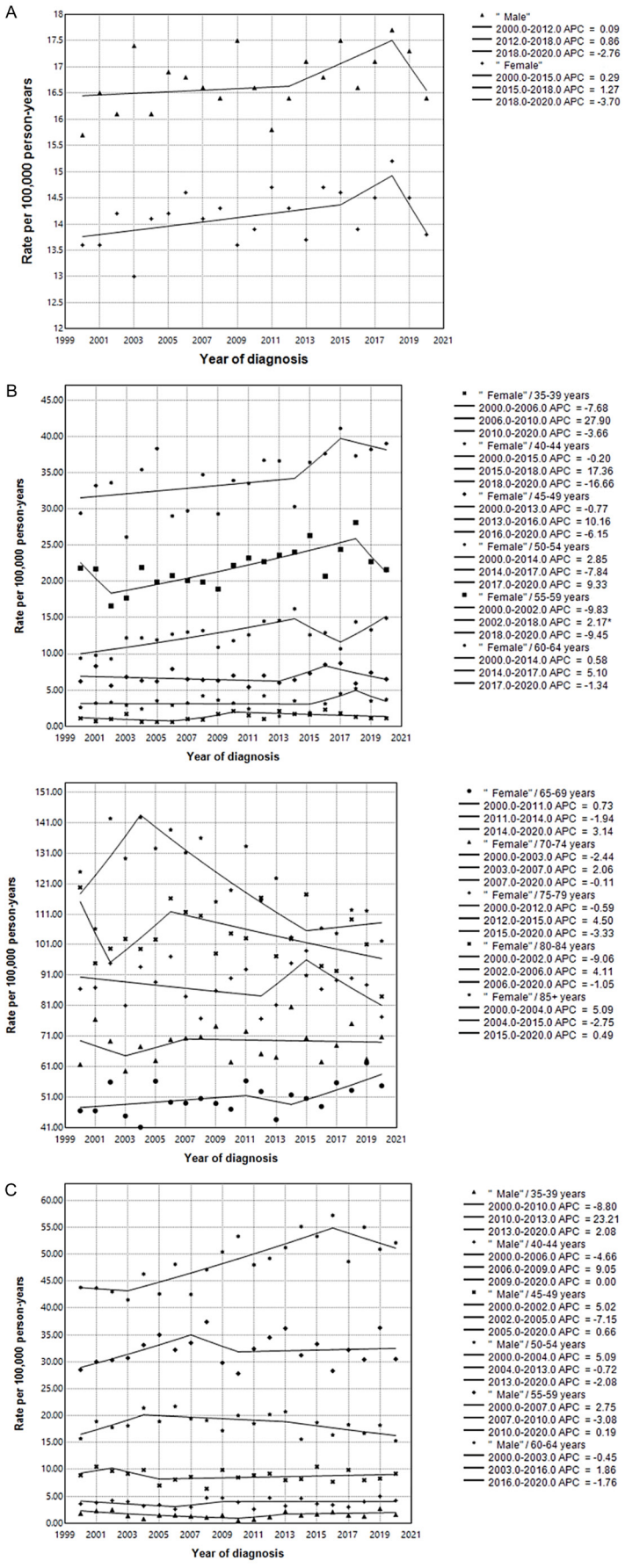


Figure 1. Malignant PC incidence trends in Blacks by sex and age (2000-2020).

form 2017-2020 APC (9.33, 95% CI, -2.48-26.25) (**Figure 2B**). Changes in PC incidence by age among Black males is shown in **Figure 2C**. The incidence of PC in the body of the pancreas is slightly higher in Black females than in Black males (**Figure 2D**). The Joinpoint model shows changes in APC at different time points in the last two decades.

Incident rates and male-to-female IRRs by age

In SEER 22 (2000-2020), the overall IRR was higher in Black males (IRR 1.18, 95% CI, 1.16-1.21) in comparison with Black females (IRR 0.85, 95% CI, 0.84-0.87) as shown in **Table 2**. Black males aged 35-84 had a higher incidence risk of PC (IRR > 1) in comparison to females of the same age group. The highest incidence risk was in black males aged 50-54 (IRR(M-F):1.45), 55-59 (IRR(M-F):1.45), and 60-64 (IRR(M-F):1.43). The age-adjusted incidence rate of PC among Blacks shows that the incidence increases with age across both sexes, as shown in **Table 2** and **Figure 3**. The highest incidence rates for males and females were recorded in patients aged 55 years and above.



Incident rates and male-to-female IRRs by stage and primary site

The incidence rate (2000-2020) based on the stage of the disease showed a significantly higher rate in regional, distant, and unstaged PC in Black males (**Figure 4A**). The highest incidence (7.6, 95% CI, 7.5-7.8, *p*-value 0.05) and risk (1.15, 95% CI, 1.12-1.18) in Black males was for distant PC. A similar trend is observed in Black females, with the highest rates observed in distant PC (5.9, 95% CI, 5.8-6, *p*-value < 0.05). Black males had a higher risk for all stages of PC in comparison with Black females, as shown in **Table 3**. The incidence rate (2000-2020) based on the PC primary site showed the highest rate in the head of the pancreas in both Black males and females (**Figure 4B**). The incidence rates for the body, tail, and pancreas NOS were significantly lower than that of the head for both sexes. The incidence risk based on all primary sites of PC in Black males was higher than in females. The RR (M-F) showed that the risk in Black males was high (IRR > 1) across all primary sites in comparison with Black females.

County-based incidence rates and IRRs by poverty level and educational level

The county-based incidence rate (2017-2021) based on the % of residents with < HS education showed that PC incidence was higher in Black males in comparison with females living in the same county. The incidence risk was, however, comparable (**Table 4**; **Figure 5A**). The county-based incidence rate (2017-2021) based on the percentage of the population living below the poverty level showed that Black males living in counties with a higher number of residents living below the poverty level had an increased risk of PC

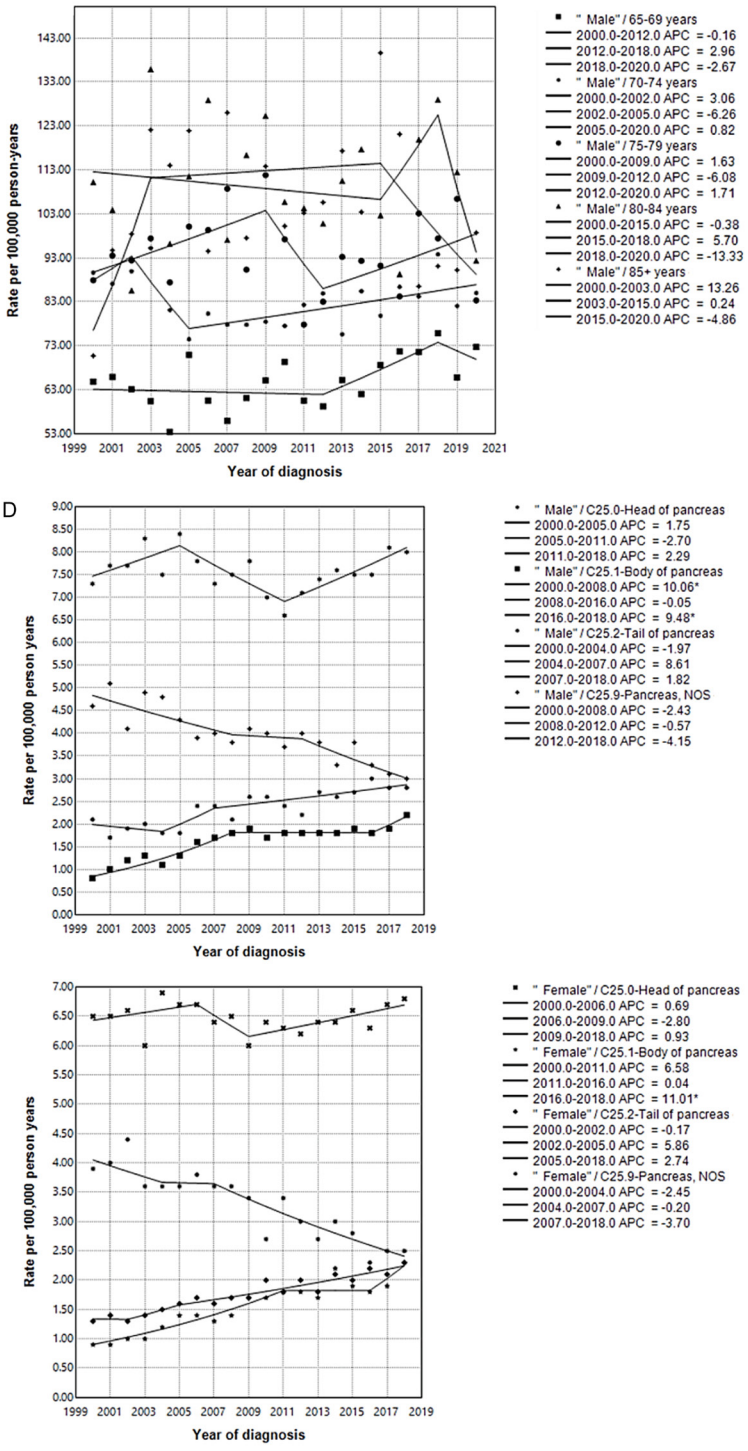


Figure 2. PC trends (Joinpoint Regression Analysis Model). A. Pancreatic cancer incidence in Blacks by sex (2000-2020). B. Pancreatic cancer incidence in Black females by age (2000-2020). C. Pancreatic cancer incidence in Black Males by age (2000-2020). D. Pancreatic cancer incidence in Blacks by primary site (2000-2020).

in comparison to females living in similar counties (**Figure 5B**).

County-based mortality rates and RRs by poverty level and educational level

The county mortality rate (2017-2021) based on level of education (% of population with < high school education) showed that Black females living in counties with < 7-9% of the residents with high school education had a slightly higher risk of PC mortality (RR 1.02, 95% CI, 0.96-1.08) in comparison with Black males (RR 0.98, 95% CI, 0.91-1.05) living in similar counties as shown in **Table 5**. The risk of PC mortality was observed to be lower in both Black males and females in counties with a higher percentage of educated residents (**Figure 6A**). The county mortality rate (2017-2021) based on the percentage of the population living below the poverty level showed that the rate of PC mortality was observed to be higher in both Black males and females in counties with a higher percentage of poor residents (**Figure 6B**). In Black males in counties with (19-59%) of poor residents, the mortality rate (15.4, 95% CI, 14.8-16, p-value < 0.05) was significantly higher than males in counties with less than 9% of the residents living in poverty (13.8, 95% CI, 13.1-14.4) as shown in **Table 5**.

Survival analysis

The relative survival by the PC stage showed that in both Black males and females, the lowest survival was observed in patients with distant PC (**Table 6**). The 12-month relative survival for all Black PC patients was lower than 60%. A further reduction in survival was observed in 5-year relative

Table 2. Case counts, rates, and male-female incidence rate ratios by age group, SEER 22 (2000-2020)

	Male					Female					IRR (M/F)	Ratio LCI	Ratio UCI
	Count	% of Pop	Rate	LCI	UCI	Count	% of Pop	Rate	LCI	UCI			
Overall	22,639	46.47	16.8*	16.6	17	26,122	53.53	14.2*	14	14.4	1.18	1.16	1.21
25-29	31	0.14	0.2	0.1	0.3	64	0.25	0.4	0.3	0.5	0.51	0.32	0.79
30-34	87	0.39	0.6	0.5	0.8	123	0.47	0.8	0.7	1	0.77	0.58	1.02
35-39	209	0.93	1.6	1.4	1.8	194	0.74	1.3	1.1	1.5	1.20	0.99	1.47
40-44	496	2.20	3.8	3.5	4.1	482	1.84	3.3	3	3.6	1.16	1.02	1.32
45-49	1,112	4.91	8.8	8.3	9.3	973	3.74	6.8	6.4	7.2	1.29	1.18	1.41
50-54	2,138	9.46	18.4	17.6	19.2	1,691	6.49	12.7	12.1	13.3	1.45	1.36	1.55
55-59	3,137	13.87	32.2	31.1	33.4	2,561	9.83	22.2	21.4	23.1	1.45	1.38	1.53
60-64	3,706	16.38	49.8	48.2	51.4	3,226	12.39	34.9	33.7	36.1	1.43	1.36	1.49
65-69	3,541	15.66	65.9	63.7	68.1	3,649	14.00	51.4	49.7	53	1.28	1.22	1.34
70-74	3,105	13.72	83.5	80.6	86.5	3,656	14.01	68.8	66.6	71.1	1.21	1.16	1.27
75-79	2,310	10.22	94.2	90.4	98.1	3,442	13.21	87.7	84.8	90.7	1.07	1.02	1.13
80-84	1,606	7.11	109.3	104	114.7	2,810	10.79	103.4	99.6	107.3	1.06	0.99	1.12
85+	1,134	5.02	104.9	98.9	111.2	3,183	12.23	118.2	114.1	122.3	0.89	0.83	0.95

Cases included first primary tumors that were malignant. Rates were calculated as the number of cases per 100,000 person-years and age-adjusted to the 2000 US standard population. Confidence intervals (Tiwari mod) are 95% for rates and ratios. IRR = Incidence Risk Ratio; LCI, UCI = lower, upper 95% confidence interval. *p-value < 0.05.

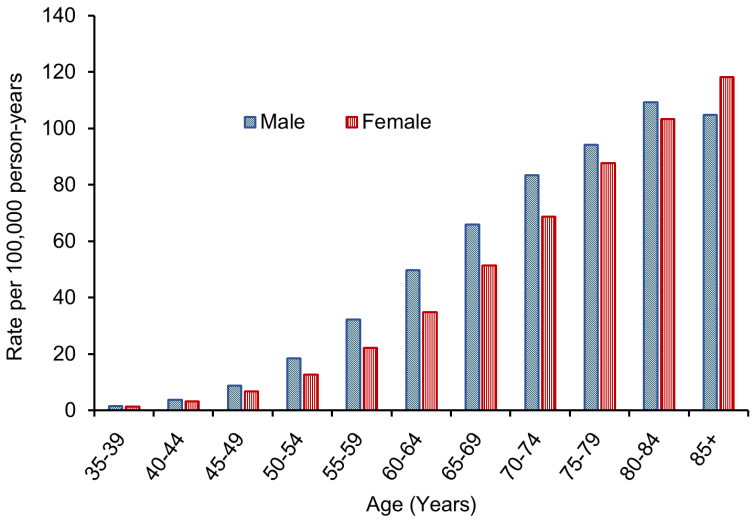


Figure 3. PC incidence rate in Blacks by age (2000-2020).

survival by stage for both sexes, less than 40% for both sexes. The 5-year relative survival in Black males with localized PC was significantly lower (31.7%, 95% CI, 28.5%-34.9%, p-value < 0.05) than that of Black females (37.20%, 95% CI, 34.60%-39.70%). We observed that Black males had relatively lower survival across all PC stages in comparison with Black females.

Genomics (MSK-CHORD (MSK, Nature 2024))

Overall, there were 3,109 pancreatic cancer cases, with 2,703 cases being pancreatic adenocarcinoma. There were 144 (5.3%) patients with pancreatic adenocarcinoma and primary race of Black or African-American. Of that, there were 69 females and 55 males. The expression of four frequently mutant PC genes (KRAS, TP53, CDKN2A, and SMAD4) showed that Black males had a higher frequency of expression of the mutant genes KRAS (92.73% vs. 89.86%) and TP53 (80.00% vs. 79.71%) in comparison to Black females as shown in **Table 7**. On the other hand, Black females had a higher frequency of expression of the mutant genes CDKN2A (40.58% vs. 34.55%) and SMAD4 (26.09% vs. 23.64%) compared to Black females. **Figure 7** shows the MSK-CHORD pancreatic cancer cases by A) sex B) smoking history C) mutant gene expression

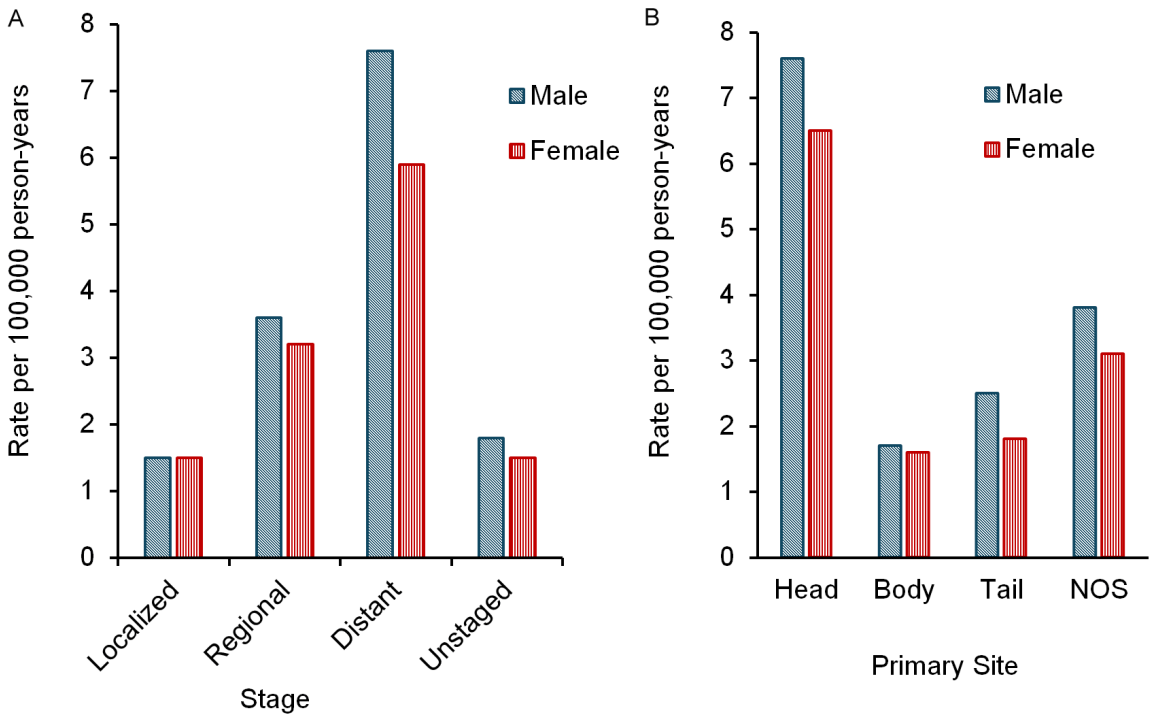


Figure 4. Pancreatic cancer incidence rate by stage and primary site (2000-2020).

Table 3. Case counts, rates, and male-female incidence rate ratios by stage and primary site (2000-2020)

	Male					Female					IRR M-F	Ratio LCI	Ratio UCI
	Count	% of Pop	Rate	LCI	UCI	Count	% of Pop	Rate	LCI	UCI			
Stage													
In situ	59	0.30	~	~	~	103	0.50	~	~	~	~	~	~
Localized	1,939	9.90	1.5	1.4	1.5	2,819	12.50	1.5	1.5	1.6	0.96	0.91	1.02
Regional	4,925	25.20	3.6*	3.5	3.7	6,093	27.10	3.2*	3.2	3.3	1.10	1.05	1.14
Distant	10,540	53.90	7.6*	7.5	7.8	10,868	48.30	5.9*	5.8	6.0	1.30	1.26	1.34
Unstaged	2,086	10.70	1.8*	1.7	1.9	2,611	11.60	1.5*	1.4	1.5	1.21	1.14	1.28
Primary Site													
Head of pancreas	10,234	49.05	7.6	7.4	7.7	11,920	49.82	6.5	6.4	6.6	1.17	1.14	1.20
Body of pancreas	2,353	11.28	1.7*	1.6	1.8	3,011	12.59	1.6*	1.6	1.7	1.05	0.99	1.11
Tail of pancreas	3,391	16.25	2.5*	2.4	2.5	3,453	14.43	1.8*	1.8	1.9	1.33	1.27	1.40
Pancreas	4,885	23.41	3.8*	3.7	3.9	5,540	23.16	3.1*	3.0	3.2	1.24	1.19	1.29
NOS													

Cases included first primary tumors that were malignant. Rates were calculated as the number of cases per 100,000 person-years and age-adjusted to the 2000 US standard population. IRR = Incidence Risk Ratio; LCI, UCI = lower, upper 95% confidence interval. Confidence intervals (Tiwari mod) are 95% for rates and ratios. *p-value < 0.05. ~Statistic could not be calculated because at least one year had zero cases.

and D) overall survival. The differences in the mutant gene expression were not statistically significant. Also, the number of Black males who were a current/former smoker was higher than that of Black females. Overall survival was less in Black males compared to Black females: median months 10.85 (95% CI; 8.42-16.34) vs. 18.08 (95% CI; 11.67-23.61).

Table 4. Case counts, rates, and incidence rate ratios by education and poverty level (quintiles) 2017-2021

Quintiles	Count	Rate	LCI	UCI	IRR	Ratio LCI	Ratio UCI
Poverty Level							
Male							
1st Quintile (1.20%-9.45%)	2,293	16.7	15.9	17.4			
2nd Quintile (9.46%-12.14%)	1,888	16.3	15.5	17.1	0.98	0.92	1.05
3rd Quintile (12.15%-14.90%)	4,509	17.3	16.8	17.9	1.04	0.98	1.10
4th Quintile (14.91%-18.78%)	2,696	17.4	16.7	18.1	1.04	0.98	1.11
5th Quintile (18.79%-59.02%)	2,581	16.5	15.8	17.2	0.99	0.93	1.05
Female							
1st Quintile (1.20%-9.45%)	2,576	14.5	14	15.1			
2nd Quintile (9.46%-12.14%)	2,038	13.6*	13	14.2	0.94	0.88	0.99
3rd Quintile (12.15%-14.90%)	5,264	14.8	14.4	15.3	1.02	0.97	1.07
4th Quintile (14.91%-18.78%)	3,039	14.6	14.1	15.2	1.01	0.95	1.06
5th Quintile (18.79%-59.02%)	2,991	13.7*	13.2	14.2	0.94	0.89	0.99
Level of Education							
Male							
First Quintile (0.60%-7.12%)	1,249	17.3	16.3	18.4			
Second Quintile (7.13%-9.5%)	1,830	17.3	16.4	18.2	1.00	0.92	1.08
Third Quintile (9.51%-12.26%)	4,205	17.2	16.7	17.8	0.99	0.93	1.07
Forth Quintile (12.27%-16.62%)	2,929	16.4	15.8	17.1	0.95	0.88	1.02
Fifth Quintile (16.63%-81.55%)	3,756	16.7	16.1	17.2	0.96	0.90	1.03
Female							
First Quintile (0.60%-7.12%)	1,370	14.7	13.9	15.5			
Second Quintile (7.13%-9.5%)	1,999	14.9	14.2	15.5	1.01	0.94	1.09
Third Quintile (9.51%-12.26%)	4,877	14.7	14.3	15.1	1.00	0.94	1.07
Forth Quintile (12.27%-16.62%)	3,456	14.0	13.5	14.5	0.96	0.90	1.02
Fifth Quintile (16.63%-81.55%)	4,206	13.9	13.5	14.4	0.95	0.89	1.01

Cases included first primary tumors that were malignant. Rates were calculated as the number of cases per 100,000 person-years and age-adjusted to the 2000 US standard population. IRR = Incidence Risk Ratio; LCI, UCI = lower, upper 95% confidence interval. Confidence intervals (Tiwari mod) are 95% for rates and ratios. *The rate ratio indicates the rate is significantly different than the rate for First Quintile (p-value < 0.05).

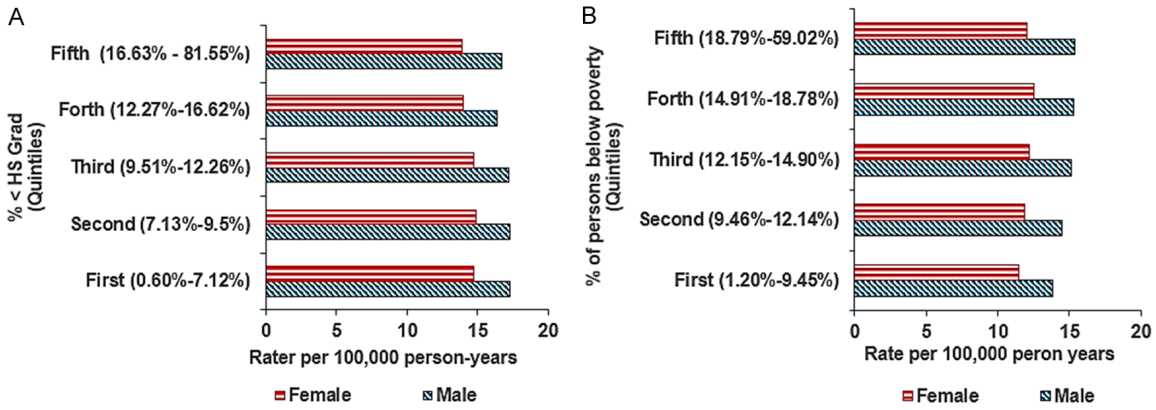


Figure 5. PC County incidence and based on level of education and persons living below the poverty level.

Table 5. Mortality case counts, rates, and rate ratios by education and poverty level (quintiles) 2017-2021

Quintile	Count	Rate	LCI	UCI	RR	Ratio LCI	Ratio UCI
Poverty level							
Male							
First Quintile (1.20%-9.45%)	2,027	13.8	13.1	14.4			
Second Quintile (9.46%-12.14%)	2,126	14.5	13.9	15.2	1.06	0.99	1.13
Third Quintile (12.15%-14.90%)	3,640	15.1*	14.6	15.6	1.10	1.03	1.16
Forth Quintile (14.91%-18.78%)	3,096	15.3*	14.8	15.9	1.11	1.05	1.19
Fifth Quintile (18.79%-59.02%)	2,788	15.4*	14.8	16	1.12	1.05	1.19
Female							
First Quintile (1.20%-9.45%)	2,214	11.5	11	12			
Second Quintile (9.46%-12.14%)	2,202	11.9	11.4	12.4	1.03	0.97	1.10
Third Quintile (12.15%-14.90%)	3,964	12.2*	11.8	12.6	1.06	1.01	1.12
Forth Quintile (14.91%-18.78%)	3,412	12.5*	12	12.9	1.08	1.03	1.15
Fifth Quintile (18.79%-59.02%)	3,044	12	11.5	12.4	1.04	0.98	1.10
Level of Education							
Male							
First Quintile (0.60%-7.12%)	1,585	15.3	14.4	16.1			
Second Quintile (7.13%-9.5%)	2,806	14.9	14.3	15.5	0.98	0.91	1.05
Third Quintile (9.51%-12.26%)	3,895	14.9	14.4	15.4	0.98	0.92	1.04
Forth Quintile (12.27%-16.62%)	3,137	14.9	14.4	15.5	0.98	0.92	1.05
Fifth Quintile (16.63%-81.55%)	2,261	14.2	13.6	14.9	0.93	0.87	1.00
Female							
First Quintile (0.60%-7.12%)	1,643	12.2	11.6	12.8			
Second Quintile (7.13%-9.5%)	3,057	12.4	11.9	12.8	1.02	0.96	1.08
Third Quintile (9.51%-12.26%)	4,252	12.2	11.8	12.6	1.00	0.95	1.07
Forth Quintile (12.27%-16.62%)	3,468	11.9	11.5	12.3	0.98	0.92	1.04
Fifth Quintile (16.63%-81.55%)	2,420	11.4	10.9	11.9	0.94	0.88	1.00

Cases included first primary malignant tumors, excluding cases identified only from autopsy records or death certificates. Rates were calculated as cases per 100,000 person-years and age-adjusted to the 2000 US standard population. RR = Risk Ratio; LCI, UCI = lower, upper 95% confidence interval. Confidence intervals (Tiwari mod) are 95% for rates and ratios. *The rate ratio indicates the rate is significantly different than the rate for First Quintile (p-value < 0.05).

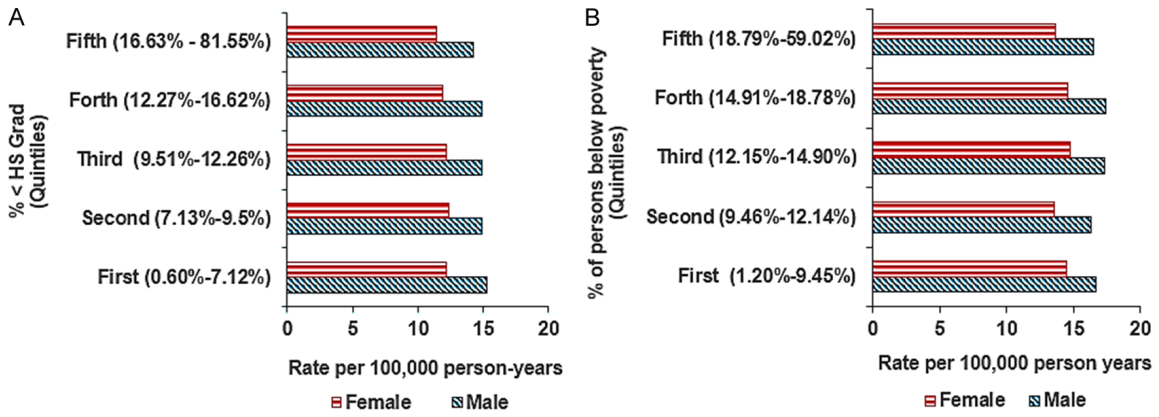


Figure 6. PC County mortality based on level of education and persons living below the poverty level.

Table 6. Case counts and 5-year relative survival by stage

Stage	Time	Male			Female		
		Relative Survival	Rel Cum LCI	Rel Cum UCI	Relative Survival	Rel Cum LCI	Rel Cum UCI
Overall	60 mo	8.8%	8.30%	9.50%	10.80%	10.20%	11.40%
Localized	12 mo	57.90%	55.00%	60.80%	57.60%	55.20%	59.90%
Localized	24 mo	43.30%	40.30%	46.30%	44.90%	42.50%	47.30%
Localized	36 mo	37.30%	34.20%	40.40%	40.70%	38.20%	43.10%
Localized	48 mo	33.60%	30.50%	36.80%	38.60%	36.10%	41.10%
Localized	60 mo	31.7%*	28.5%*	34.9%*	37.20%	34.60%	39.70%
Regional	12 mo	51.80%	50.10%	53.60%	50.70%	49.10%	52.20%
Regional	24 mo	28.00%	26.40%	29.70%	28.90%	27.40%	30.40%
Regional	36 mo	19.40%	17.90%	20.90%	20.10%	18.80%	21.50%
Regional	48 mo	15.7%*	14.3%*	17.2%*	15.50%	14.30%	16.80%
Regional	60 mo	13.60%	12.20%	15.10%	13.80%	12.60%	15.10%
Distant	12 mo	15.80%	15.00%	16.70%	17.30%	16.40%	18.10%
Distant	24 mo	6.00%	5.40%	6.60%	7.10%	6.50%	7.70%
Distant	36 mo	3.80%	3.40%	4.30%	4.60%	4.10%	5.20%
Distant	48 mo	2.90%	2.50%	3.40%	3.50%	3.00%	3.90%
Distant	60 mo	2.60%	2.10%	3.00%	2.90%	2.40%	3.30%
Unstaged	12 mo	30.40%	27.40%	33.60%	28.20%	25.70%	30.70%
Unstaged	24 mo	19.20%	16.60%	22.10%	17.90%	15.80%	20.10%
Unstaged	36 mo	14.70%	12.30%	17.30%	14.80%	12.80%	16.90%
Unstaged	48 mo	13.10%	10.80%	15.80%	13.2%*	11.2%*	15.3%*
Unstaged	60 mo	12.1%*	9.7%*	14.6%*	11.60%	9.70%	13.70%
Total Count		13,172			15,747		

Kaplan-Meier method. Ederer II method used for cumulative expected. Confidence interval: Log (-Log ()) Transformation. The level is 95%. *p-value < 0.05.

Table 7. Mutant gene expression by sex

Gene	Female	Male	p-value	Enriched In
KRAS	62 (89.86%)	51 (92.73%)	0.753	Male
TP53	55 (79.71%)	44 (80.00%)	1.00	Male
CDKN2A	28 (40.58%)	19 (34.55%)	0.577	Female
SMAD4	18 (26.09%)	13 (23.64%)	0.836	Female

Discussion

The yearly incidence and mortality of PC continues to rise among Blacks in the United States due to several socio-economic, demographic, and genetic factors [13, 33]. The 5-year survival rate of PC is meager, and this rate is even lower in Blacks [34]. Despite the high incidence and mortality of PC among Blacks, there are minimal studies on the epidemiology of PC in blacks. Some factors that may have contributed to this include the underreporting of PC cases and a small number of Blacks taking part in clinical trials, among others [15, 35]. Some studies have investigated the PC incidence and mortality in Blacks compared to other racial groups. However, our study focuses on PC incidence, mortality, and survival in Blacks. This study gives a better understanding of current trends in PC among Blacks to help identify groups at a higher risk and the impact of socio-economic factors on PC incidence and mortality to ensure better health outcomes.

Our analysis of the SEER 22 data showed a higher number of malignant PC cases in Black females in comparison with Black males, as there was a greater number of females in the population covered. However, evaluating incidence trends over the last two decades showed a slightly higher incidence in Black males based on APC. APC analysis is valuable as it helps characterize cancer incidence and mortality trends over specified periods [36]. There was

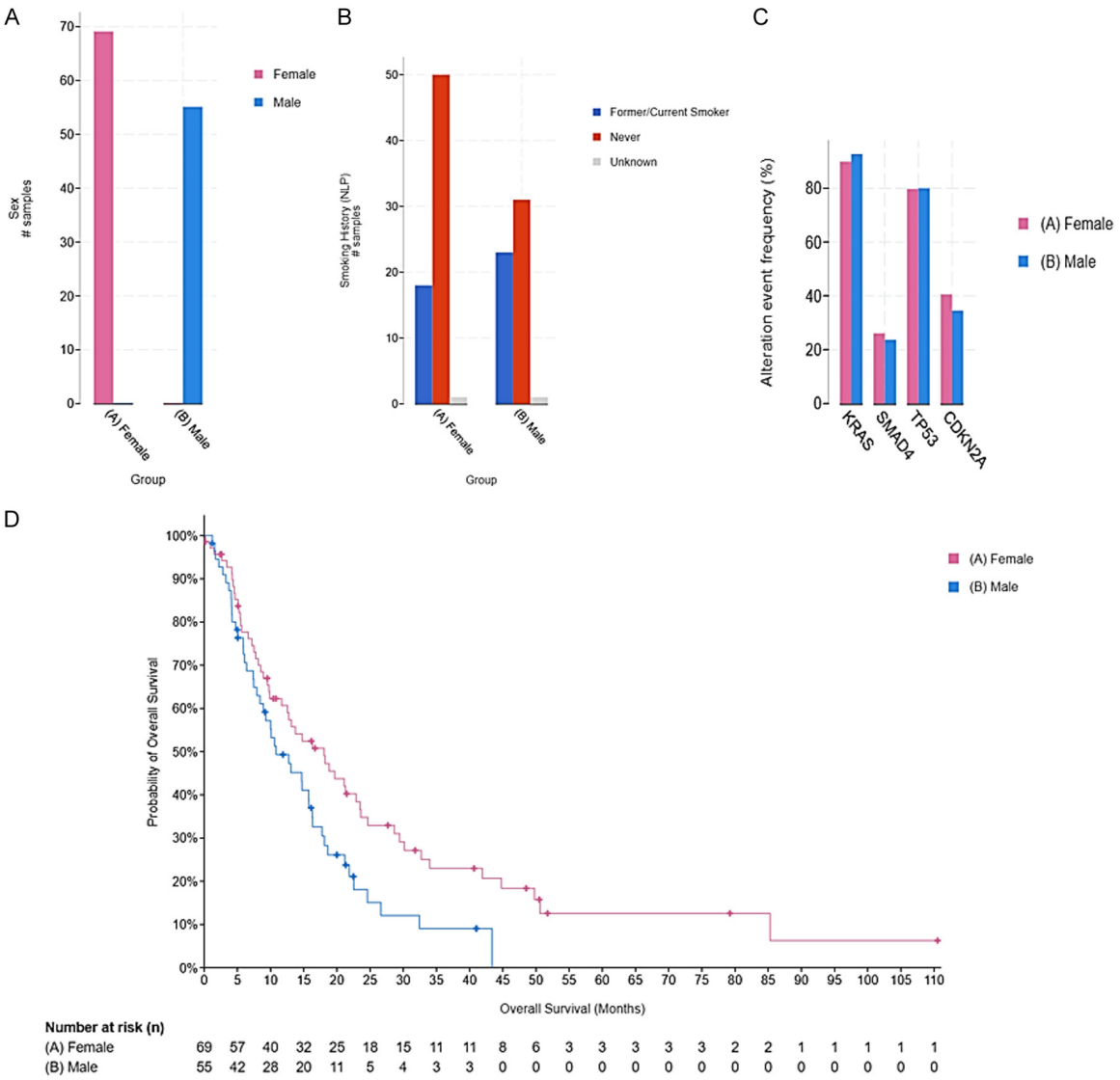


Figure 7. Mutant gene expression by sex, smoking history, and overall survival.

an increase in APC of PC incidence among both male and female populations between 2000 and 2017, as similarly reported in previous studies [37]. However, the Joinpoint model showed decreased APC between 2018 and 2020 for both sexes. The cause of the decrease is not precisely known but may be due to increased PC risk awareness programs in recent years. The American Society of Clinical Oncology (ASCO) new treatment guidelines and Pancreatic Cancer Action Network action statements may have contributed to the decline in incidence [38].

Our study showed that the most frequently affected age group in both sexes for PC was 55 years and above, consistent with previous study's results [11, 39]. The risk of PC increases with age, as shown in a previous study conducted by Samaan et al. comparing the incidence rate of PC in persons above 55 to those younger than 55 [40]. Interestingly, Black males aged 50-70 significantly had a higher increase in APC of PC incidence in comparison with Black females of the same age group. This supports the evidence that the PC rate in males is higher and more heightened in older males. PC trends based on the primary site of the disease showed the most frequently affected primary site being the head of the pancreas in both males (49.1%) and females (49.8%), similar to results from previous studies [41, 42].

However, a review of the APC shows the most significant increase in the incidence of Blacks in the body of the pancreas over the last 20 years. Interestingly, the incidence of PC in the pancreas NOS decreased in both sexes from 2000-2020. The exact cause of the reduction is unknown and could be investigated in future studies.

Our study showed that the incidence rate (per 100,000 person-years) of PC was higher in Black males than in females. Analysis of the incidence risk ratio showed a similar trend where the risk of PC in males was higher in Black males than females. Also, Black males over the age of 35 had a higher risk (> 1) of PC compared to females of the same age. Programs promoting lifestyle changes, such as a reduction in smoking and red meat consumption, should be encouraged in Black males to help ensure better health outcomes. County attributes are essential as social determinants of health. Socioeconomic factors such as education, employment, insurance status, income, etc., are vital in PC incidence and survival [43]. We found that the incidence rate of PC by level of education (% of persons with < high school education) was slightly higher in counties with less educated people than in counties with a more significant portion of their residents being educated. We suggest that increased awareness of the modifiable risk factors for PC plays a role in reducing the incidence in the more educated counties. The county-based mortality data from our study also showed a slightly higher mortality rate in counties with fewer educated people than in counties with more educated residents, emphasizing the role of education in PC mortality. The county mortality rate based on the percentage of the residents living below the poverty level showed a higher PC mortality rate and risk in both sexes in counties with more poor residents. Income is vital in ensuring better health outcomes as it allows access to the proper treatment facilities, ensures insurance, and affords treatment. The impact of poverty is evident in our findings, and it significantly impacts mortality and overall survival for PC patients. A more significant portion of Black males and females were diagnosed at an advanced stage of the disease. The PC rates at regional and distant stages were significantly higher than in situ and localized stages for both sexes. This trend is to be expected as Blacks have been previously reported to report at clinics at the advanced stage of the disease and have lower access to treatment facilities, leading ultimately to high mortality rates [44].

PC has one of the lowest 5-year survival rates of all solid tumors [2]. This low survival rate has been attributed to the aggressive nature of the malignancy, difficulty in diagnosis, late diagnosis due to the symptoms being vague, and limited treatment options [34]. The tumor microenvironment of PC consists of a dense desmoplasia that reduces the penetration of anticancer agents [45]. The current treatment options for PC have had limited benefits for Black PC patients due to treatment delays and reduced chemosensitivity [46, 47]. Black patients have historically not taken part in clinical trials; thereby, variations in treatment response that can be exposed during clinical trials have been missed. These have contributed to significantly low survival of Black PC patients.

Relative survival is an estimate of the percentage of patients who would be expected to survive the effects of their cancer, excluding the risk of dying from other causes [48]. The 5-year survival rate of PCs across all stages combined is about 13% in the United States [2]. Considering that the most frequently occurring stages of PC in both sexes were regional and distant PC, then the results of our study show an alarming survival rate. Our study highlights the disparity in PC survival among Black men and women, as the 5-year relative survival across all stages was 8.8% and 10.8%, respectively. For localized PC, the 5-year relative survival was about 32% in Black males and 37% in Black females. However, for regional and distant PC, the relative survival was just under 14% and 3%, respectively, for both sexes. The low relative survival in Blacks is very alarming and demonstrates the impact of health disparities and genetics on health outcomes. Interestingly, the relative survival from year 1 to year 5 was consistently lower in Black males than females, supporting the evidence from other analyses in this study. Policies to increase access to health facilities and improve insurance among Blacks could be instituted to improve survival and enhance health outcomes in Black PC patients.

Genetics has been implicated as a contributing factor to the high PC incidence [49, 50]. The most frequently mutated gene in PC patients is KRAS, with other genes being TP53, CDKN2A, and SMAD4 [51, 52]. Our analysis of genomic data from the cBioPortal showed that Black males had a higher frequency of expression of KRAS and TP53 in comparison with Black females. These 2 mutant genes were the most common in the sample population. Hence, a higher expression in Black males could contribute to the higher PC incidence in Black males. Also, the number of Black males who were smokers and had been smokers was higher than black females. Since smoking leads to the release of toxins that lead to genetic mutations, the higher expression of mutant genes in Black males was expected [53]. Overall survival in black males was significantly lower than in Black females. However, due to the limited sample size, the differences in mutant gene expression between Black males and females were not statistically significant. We cannot state the definite impact of genomics on PC incidence and mortality among Blacks. Further studies on the genetic linkage between Black males and PC incidence with a larger sample size could be explored.

Conclusion

PC incidence and mortality are significantly higher in Black males. Our analysis points to the importance of poverty alleviation programs that target females are likely to reduce PC incidence. Furthermore, receiving recommended screening for PC and early-stage diagnostics is important to lower PC mortality. Advocacy groups should organize health outreach programs highlighting the modifiable and non-modifiable risk factors of PC to increase awareness among Black communities. These programs should also educate residents on PC symptoms to encourage early reporting and facilitate early diagnosis.

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Disclosure of conflict of interest

None.

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Table S1. Case Counts and Annual Percentage Changes (APCs) for Blacks by sex, age, and primary site, SEER 22 (2000-2020)

		1		2		3	
		Year	APC (95% CI)	Year	APC (95% CI)	Year	APC (95% CI)
Sex	Count						
Male	22,589	2000-2012	0.09 (-3.65-4.92)	2012-2018	0.86 (-1.92-3.47)	2018-2020	-2.76 (-6.83-1.04)
Female	26,017	2000-2015	0.29 (-3.03-4.56)	2015-2018	1.27 (-0.85-3.16)	2018-2020	-3.70 (-6.76-0.36)
Age Group							
Male							
25-29	31	~	~	~	~	~	~
30-34	87	~	~	~	~	~	~
35-39	209	2000-2010	-8.80 (-32.98-35.06)	2010-2013	23.21 (28.88-51.77)	2013-2020	2.08 (-32.90-29.26)
40-44	496	2000-2006	-4.66 (-26.93-30.80)	2006-2009	9.05 (-17.11-27.53)	2009-2020	0.00 (-25.66-30.41)
45-49	1,110	2000-2002	5.02 (-10.68-26.60)	2002-2005	-7.15 (-13.21-11.47)	2005-2020	0.66 (-14.01-13.70)
50-54	2,138	2000-2004	5.09 (-7.78-28.59)	2004-2013	-0.72 (-11.15-12.23)	2013-2020	-2.08 (-16.22-10.68)
55-59	3,133	2000-2007	2.75 (-10.14-19.83)	2007-2010	-3.08 (-7.98-10.68)	2010-2020	0.19 (-8.78-9.60)
60-64	3,701	2000-2003	-0.45 (-9.00-10.31)	2003-2016	1.86 (-3.73-9.50)	2016-2020	-1.76 (-9.33-3.82)
65-69	3,537	2000-2012	-0.16 (-7.50-10.87)	2012-2018	2.96 (-5.58-8.50)	2018-2020	-2.67 (-9.47-3.51)
70-74	3,099	2000-2002	3.06 (-5.97-12.65)	2002-2005	-6.26 (-9.48-6.00)	2005-2020	0.82 (-4.56-4.93)
75-79	2,308	2000-2009	1.63 (-5.76-13.57)	2009-2012	-6.08 (-10.36-6.39)	2012-2020	1.71 (-2.83-9.83)
80-84	1,606	2000-2015	-0.38 (-12.28-15.40)	2015-2018	5.70 (-7.17-12.66)	2018-2020	-13.33 (-24.57-2.48)
85+	1,134	2000-2003	13.26 (-6.51-59.64)	2003-2015	0.24 (-15.71-17.71)	2015-2020	-4.86 (-22.38-13.33)
Female							
25-29	64	~	~	~	~	~	~
30-34	123	~	~	~	~	~	~
35-39	193	2000-2006	-7.68 (-38.84-11.96)	2006-2010	27.90 (-20.08-70.65)	2010-2020	-3.66 (-27.04-24.06)
40-44	480	2000-2015	-0.2 (-18.75-32.18)	2015-2028	17.37 (-14.66-31.97)	2018-2020	-16.66 (-35.52-12.27)
45-49	973	2000-2013	-0.77 (-9.54-10.08)	2013-2016	10.16 (-6.76-17.32)	2016-2020	-6.15 (-20.46-2.62)
50-54	1688	2000-2014	2.85 (-5.68-15.30)	2014-2017	-7.84 (-13.98-12.46)	2017-2020	9.33 (-2.48-26.25)
55-59	2558	2000-2002	-9.83 (-18.02-1.81)	2002-2018	2.17* (1.63-10.40)	2018-2020	-9.45 (-17.85-0.85)
60-64	3223	2000-2014	0.58 (-14.10-25.23)	2014-2017	5.10 (-7.48-12.62)	2017-2020	-1.34 (-14.37-8.15)
65-69	3643	2000-2011	0.73 (-14.01-26.54)	2011-2014	-1.94 (-9.76-12.29)	2014-2020	3.14 (-10.28-16.44)
70-74	3646	2000-2003	-2.44 (-18.89-20.49)	2003-2007	2.06 (-9.86-14.73)	2007-2020	-0.11 (-13.89-13.81)
75-79	3437	2000-2012	-0.59 (-10.17-13.46)	2012-2015	4.50 (-6.38-9.86)	2015-2020	-3.33 (-14.61-4.90)
80-84	2807	2000-2002	-9.06 (-18.57-3.21)	2002-2006	4.11 (-6.82-12.11)	2006-2020	-1.05 (-8.64-7.06)
85+	3182	2000-2004	5.09 (-1.40-21.85)	2004-2015	-2.75 (-10.29-1.62)	2015-2020	0.49 (-6.72-10.36)
Primary Site							
Male							
Head	10,224	2000-2005	1.75 (-1.08-13.97)	2005-2011	-2.70 (-8.16-3.09)	2011-2018	2.29 (-0.35-8.28)
Body	2,351	2000-2008	10.06* (0.43-18.03)	2008-2016	-0.05 (-7.09-18.32)	2016-2018	9.48* (0.15-17.49)
Tail	3,386	2000-2004	-1.97 (-16.54-10.05)	2004-2007	8.61 (-6.04-18.88)	2007-2018	1.82 (-9.98-12.54)
NOS	4,877	2000-2008	-2.44 (-11.09-8.72)	2008-2012	-0.57 (-9.55-6.34)	2012-2018	-4.15 (-14.74-5.58)
Female							
Head	11,902	2000-2006	0.69 (-0.91-5.91)	2006-2009	-2.80 (-4.59-2.38)	2009-2018	0.93 (-3.20-4.33)
Body	3,003	2000-2011	6.58 (-8.31-34.42)	2011-2016	0.04 (-8.61-20.64)	2016-2018	11.01* (0.45-22.51)
Tail	3,426	2000-2002	-0.17 (-9.57-12.62)	2002-2005	5.86 (-2.56-12.51)	2005-2018	2.74 (-4.34-9.56)
NOS	5,530	2000-2004	-2.45 (-9.98-4.60)	2004-2007	-0.20 (-10.19-4.58)	2007-2018	-3.70 (-13.45-6.72)

Cases included first primary tumors that were malignant. APC = Annual percent change; LCI, UCI = lower, upper 95% confidence interval. APCs were calculated using the weighted least squares method, based on rates per 100,000 person-years, age-adjusted to the 2000 US Standard Population (19 age groups). ~Statistic could not be calculated because at least one year had zero cases. Using SEER labeled primary site. *p-value < 0.05.