Research Square

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Have we gotten better at diagnosing PDAC before it is too late?: Temporal Trends in Stage at Diagnosis of Pancreatic Ductal Adenocarcinoma in the United States

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Abstract

Purpose

Pancreatic ductal adenocarcinoma (PDAC) remains one of the deadliest cancers in the United States, with most patients not being diagnosed until they present with symptomatic, advanced-stage disease. National trends in stage-specific PDAC incidence were analyzed to assess trends in stage-at-diagnosis over time and to evaluate whether advances in diagnosis and high-risk screening programs have helped shift detection towards earlier stages.

Methods

A retrospective cohort study was conducted using the Surveillance, Epidemiology, and End Results (SEER) database. Patients aged 15–84 years old diagnosed with PDAC between the years 2004 and 2022 were included. Age-adjusted incidence and mortality rates were calculated per 100,000 people. Trends were assessed using Joinpoint regression to estimate annual percent change (APC). Multivariable Poisson regression was used to estimate incidence rate ratios (IRRs), adjusting for age, sex, race/ethnicity, stage, and calendar year.

Results

Between the years 2004 and 2022, age-adjusted incidence rates of localized, regional, and distant-stage PDAC were 0.97, 1.33, and 5.62 per 100,000 population, respectively. Localized PDAC demonstrated the greatest increase over time, with an APC of 5.71% (95% CI: 4.34–7.38; $p < 0.001$), while distant staging exhibited a small increase in PDAC incidence over time (APC of 0.91% (95% CI: 0.43–1.43; $p = 0.001$). Localized-stage incidence accelerated further after approximately 2015, with APC increasing to 10.2% between 2015 and 2022. Similar localized-stage increases were observed across sex and racial/ethnic subgroups. In multivariable Poisson regression, increasing age and Non-Hispanic Black race were associated with higher PDAC incidence, while female sex was associated with lower incidence rates.

Conclusions

The findings suggest a stage shift toward increased diagnosis of localized PDAC over time. These trends may reflect improvements in imaging, surveillance of high-risk individuals, advances in endoscopic detection, and increasing diagnostic intensity, although rising underlying PDAC burden may also contribute. Further prospective studies are needed to determine whether these trends ultimately translate into meaningful improvements in survival outcomes.

Introduction

Pancreatic ductal adenocarcinoma (PDAC) is the 10th most diagnosed cancer in 2025 according to the National Cancer Institute, but accounts for the third largest share of cancer-related deaths [1]. Despite modest improvements in survival over time, the reported 5-year survival for PDAC remains between 10% and 14% [2].

One of the most reliable predictors of outcome for PDAC is the stage at diagnosis. Patients diagnosed with localized disease show significantly better survival outcomes. However, this group represents a vast minority, with most patients being diagnosed with either regional or metastatic disease. Singhi et al. note that this likely reflects both the lack of an effective screening strategy for the general population and the nonspecific setting in which early PDAC typically presents [4]. Poor outcomes are largely driven by the high proportion of patients who present with advanced-stage disease at diagnosis [3].

There have been several advancements over the past couple of decades that have improved the ability to diagnose PDAC at earlier stages. Imaging is better than it used to be, high-risk surveillance is more widely used, and endoscopic ultrasound has become more common in clinical practice. There has also been growing interest in biomarker-based detection strategies. However, there has been no definitive research confirming whether these changes have actually translated into earlier diagnosis at the population level [5–7].

Pancreatic cancer incidence and mortality continue to rise globally and are projected to become an even greater public health risk over the next several decades. Rahib et al. project that pancreatic cancer may become the second-leading cause of cancer-related death in the United States by 2030, reflecting demographic shifts as well as rising incidence rates [8]. Several factors have been implicated in these trends, including aging populations, the increasing prevalence of obesity and diabetes, and improved diagnostic detection, as described by Klein [9]. According to the CDC's Behavioral Risk Factor Surveillance System, from 2011 to 2023, the percentage of adults in the US with obesity and diabetes increased by 23% and 21%, respectively [10]. Understanding whether the increased diagnosis of localized PDAC reflects true stage migration, a rising disease burden, or both has important implications for screening and surveillance strategies.

Most of the existing literature has focused on incidence and overall survival. Comparatively less attention has been given to how the stage at diagnosis may have shifted over time, particularly in large, population-based datasets. Therefore, understanding whether a stage migration toward localized disease is occurring has meaningful implications for early detection strategies and future screening strategies.

In this study, we used the Surveillance, Epidemiology, and End Results (SEER) database to evaluate temporal trends in PDAC stage at diagnosis from 2004 to 2022.

Methods

Age-adjusted incidence rates for pancreatic ductal adenocarcinoma (PDAC) were calculated using SEER*Stat software (version 8.4.4; Surveillance Research Program, National Cancer Institute) [11]. Data were obtained from the Surveillance, Epidemiology, and End Results (SEER) Program [12], encompassing research data from 21 population-based cancer registries across the United States covering the period 2004–2022. The dataset included demographic variables—age, sex (male and female), and race/ethnicity (Non-Hispanic White, Non-Hispanic Black, Non-Hispanic Asian or Pacific Islander, Non-Hispanic American Indian/Alaska Native, and Hispanic of all races), as well as stage at diagnosis (in situ, localized, regional, and distant) as a clinical variable. Cases with missing or unknown race/ethnicity or staging information were excluded from all analyses. Data from 2004 onward were used to ensure completeness and consistency across registry coverage.

Age-adjusted incidence rates per 100,000 population were calculated stratified by sex, race/ethnicity, and stage at diagnosis. To assess potential effect modification by sex and race/ethnicity, rates were further examined within each demographic subgroup. Temporal trends in age-adjusted incidence rates were evaluated using Joinpoint regression, implemented in the Joinpoint Regression Program [13], which fits piecewise log-linear models to identify statistically significant inflection points in trend and to estimate annual percent changes (APCs). APCs were estimated across strata defined by sex, race/ethnicity, and stage at diagnosis; additional stratified analyses were conducted to evaluate whether temporal trends within sex and stage subgroups varied by racial/ethnic group. Multivariable Poisson regression was performed to estimate incidence rate ratios (IRRs) for demographic factors; these analyses were conducted using Stata version 18 (StataCorp, College Station, TX).

Results

Between 2004 and 2022, age-adjusted incidence rates of pancreatic ductal adenocarcinoma (PDAC) differed meaningfully by sex, race/ethnicity, and stage at diagnosis (Table 1). Males demonstrated a higher overall age-adjusted incidence rate than females (2.21 vs. 1.75 per 100,000 population). Across racial/ethnic groups, Non-Hispanic Black individuals exhibited the highest incidence rate (2.67 per 100,000), followed by Non-Hispanic White (2.16), Hispanic (1.87), Non-Hispanic American Indian/Alaska Native (1.62), and Non-Hispanic Asian or Pacific Islander (NHAPI) individuals (1.60). By stage, incidence rates increased markedly with advancing disease: localized PDAC had an age-adjusted rate of 0.97 per 100,000, regional disease 1.33 per 100,000, and distant-stage disease 5.62 per 100,000; in situ cases were too few to estimate rates reliably.

Table 1. Age-adjusted Rates	
	Incidence
Variables	Overall
	Age-Adjusted Rate (95% CI) per 100,000 people
Sex	
Male	2.21 (0.026)
Female	1.75 (0.021)
Race/Ethnicity	
Non-Hispanic White	2.16 (0.008
Non-Hispanic Black	2.67 (0.024
Non-Hispanic AI/AN	1.62 (0.075
Non-Hispanic Asian/Pacific Islander	1.60 (0.018
Hispanic	1.87 (0.018
Staging	
In Situ	N/A
Localized	0.97 (0.024)
Regional	1.33 (0.025)
Distant	5.62 (0.056)

However, PDAC incidence drastically increased over time within the localized staging (APC of 5.71% (95% CI: 4.34–7.38; p < 0.001), while distant staging exhibited a small increase in PDAC incidence over time (APC of 0.91% (95% CI: 0.43–1.43; p = 0.001) (Figure 1). Figure 2 presents sex-stratified age-adjusted PDAC incidence trends by stage from 2004 to 2022. Localized-stage incidence increased significantly and comparably for both males (APC: 5.51%; 95% CI: 3.95–7.33; p < 0.001) and females (APC: 5.76%; 3.86–7.83; p < 0.001). Regional-stage trends diverged meaningfully by sex. Males showed a non-significant overall increase (APC: 1.54%; −0.36 to 3.42; p = 0.10), with rates plateauing after an early rise and declining toward 2022. Females, by contrast, demonstrated a modest but statistically significant regional-stage increase across the study period (APC: 2.04%; 0.35–3.82; p = 0.019), with rates remaining relatively elevated through 2022. Distant-stage incidence increased slowly but significantly in both males (APC: 1.00%; 0.28–1.75; p = 0.008) and females (APC: 0.87%; 0.21–1.59; p = 0.014).

After stratification by race/ethnicity, Non-Hispanic White individuals demonstrated a sharp post-2015 acceleration (APC: 5.04%; 95% CI: 3.95–6.45; p < 0.001), with rates rising from approximately 0.85 to

over 1.50 per 100,000 by 2021. Non-Hispanic Black individuals showed a similarly steep increase (APC: 5.23%; 4.03–6.86; $p < 0.001$), with rates reaching approximately 2.0–2.2 per 100,000 by 2020–2021; the highest absolute localized-stage rates among all groups. Hispanic individuals had the steepest overall APC (6.09%; 4.68–8.28; $p < 0.001$), with rates accelerating markedly after approximately 2015. Non-Hispanic Asian or Pacific Islander individuals also showed a significant and sustained increase (APC: 5.87%; 4.42–7.87; $p < 0.001$). Non-Hispanic American Indian/Alaska Native individuals demonstrated the widest confidence intervals, reflecting a smaller population size, yet still showed a significant overall upward trend (APC: 5.41%; 1.28–12.1; $p = 0.014$) (Figure 3).

In multivariable Poisson regression adjusting for all covariates, advancing stage at diagnosis was the strongest predictor of PDAC incidence (Table 2). Compared with localized disease, regional-stage PDAC was associated with a 56% higher rate (IRR: 1.56; 95% CI: 1.53–1.59; $p < 0.001$), whereas distant-stage disease was associated with a nearly sixfold higher rate (IRR: 5.78; 5.68–5.89; $p < 0.001$). Each 5-year increment in age was associated with a 52% increase in the incidence rate (IRR: 1.52; 95% CI: 1.52–1.53; $p < 0.001$). Female sex was associated with a 25% lower incidence rate than male sex (IRR: 0.75; 0.74–0.76; $p < 0.001$). Compared with Non-Hispanic White individuals, Non-Hispanic Black individuals had a significantly elevated incidence rate (IRR: 1.27; 1.25–1.29; $p < 0.001$), whereas Non-Hispanic Asian or Pacific Islander (IRR: 0.73; 0.71–0.74), Non-Hispanic American Indian/Alaska Native (IRR: 0.78; 0.72–0.85), and Hispanic individuals (IRR: 0.84; 0.82–0.85) all had significantly lower rates (all $p < 0.001$). Each calendar year of diagnosis was associated with a 2% increase in incidence (IRR: 1.02; 95% CI: 1.02–1.02; $p < 0.001$).

Table 2. Incidence Rate Ratios to associate the rate of PDAC incidence with age, sex, race, and stage at diagnosis.

Variables	Overall					
	IRR (95% CI)[1]	p-value				
Staging						
Localized	REF					
Regional	1.56 (1.53, 1.59)	< 0.001				
Distant	5.78 (5.68, 5.89)	< 0.001				
Age (per 5-year increase)	1.52 (1.52, 1.53)	< 0.001				
Sex						
Male	REF					
Female	0.75 (0.74, 0.76)	< 0.001				
Race						
Non-Hispanic White	REF					
Non-Hispanic Black	1.27 (1.25, 1.29)	< 0.001				
Non-Hispanic AI/AN	0.78 (0.72, 0.85)	< 0.001				
Non-Hispanic Asian/PI	0.73 (0.71, 0.74)	< 0.001				
Hispanic	0.84 (0.82, 0.85)	< 0.001				
Year of Diagnosis	1.02 (1.02, 1.02)	< 0.001				
	Localized Only		Regional Only		Distant Only	
	IRR (95% CI)	p-value	IRR (95% CI)	p-value	IRR (95% CI)	p-value
Age (per 5-year increase)	1.59 (1.58, 1.60)	< 0.001	1.49 (1.48, 1.50)	< 0.001	1.52 (1.51, 1.53)	< 0.001
Sex						
Male	REF		REF		REF	

Female	0.90 (0.87, 0.93)	< 0.001	0.78 (0.76, 0.81)	< 0.001	0.72 (0.71, 0.73)	< 0.001
Race						
Non-Hispanic White	REF		REF		REF	
Non-Hispanic Black	1.32 (1.25, 1.39)	< 0.001	0.98 (0.94, 1.04)	0.067	1.35 (1.32, 1.38)	< 0.001
Non-Hispanic AI/AN	0.82 (0.63, 1.03)	0.009	0.64 (0.52, 0.78)	< 0.001	0.82 (0.74, 0.90)	< 0.001
Non-Hispanic Asian/PI	0.76 (0.71, 0.81)	< 0.001	0.69 (0.65, 0.72)	< 0.001	0.73 (0.71, 0.75)	< 0.001
Hispanic	0.89 (0.84, 0.93)	< 0.001	0.74 (0.71, 0.77)	< 0.001	0.85 (0.84, 0.87)	< 0.001
Year of Diagnosis	1.05 (1.05, 1.06)	< 0.001	1.01 (1.00, 1.01)	< 0.001	1.01 (1.01, 1.01)	< 0.001

[1] Poisson Regression adjusting for all other variables.

[2] Poisson Regression adjusting for all other variables following the stratification of Stage Status.

Stage-stratified Poisson models yielded broadly consistent racial/ethnic findings. Non-Hispanic Black individuals had significantly elevated rates across localized (IRR: 1.32; 1.25–1.39) and distant stages (IRR: 1.35; 1.32–1.38), though not at the regional stage (IRR: 0.98; 0.94–1.04; p = 0.067). The protective effect of female sex was present at all stages but was most pronounced for distant disease (IRR: 0.72; 0.71–0.73).

Discussion

The overall incidence of PDAC is increasing in the United States. The diagnosis of localized PDAC increased over time, with a more pronounced rise beginning around 2015 [6, 7, 14]. At the same time, distant-stage disease remained by far the most common presentation, underscoring the persistent challenges in early diagnosis (Figs. 1–4) [3].

There are several likely explanations for the observed increase in localized PDAC diagnoses. First, both the frequency and the quality of imaging have increased substantially over time. According to Shiang et al., between 2013 and 2023, the number of CT scans performed in the US increased by 19.2%, and the number of MRIs increased by 21.4% [15]. Second, improvements in cross-sectional imaging, MRI, and endoscopic ultrasound (EUS) have increased the ability to detect smaller pancreatic abnormalities that may have gone undetected previously [7]. Third, surveillance programs for high-risk patients with genetic or familial predisposition have become more common. Increased recognition of hereditary pancreatic cancer syndromes, including BRCA1/2, PALB2, Lynch syndrome, hereditary pancreatitis, and familial

pancreatic cancer syndromes, has contributed to broader implementation of targeted surveillance strategies utilizing MRI and EUS in high-risk individuals [16]. This increase in imaging frequency, paired with the ever-improving quality and new targeted surveillance strategies, has led to greater incidental detection of pancreatic lesions.

Emerging biomarker-based approaches in the diagnosis and monitoring of pancreatic lesions are also being explored. Current candidates include protein markers, autoantibodies, circulating tumor DNA, microRNAs, methylated DNA, and exosome-based assays. However, most research in this field has focused on symptomatic patients rather than on asymptomatic surveillance cohorts. In patients with pancreatic cysts, cyst-fluid biomarkers such as CEA, KRAS, and GNAS mutations, as well as alterations in TP53, SMAD4, PIK3CA, PTEN, and AKT1, may help risk-stratify mucinous cysts, but these tests remain adjunctive and require further validation before widespread clinical use [4]. Collectively, these developments may contribute to the earlier diagnosis of PDAC.

Notably, the observed increase in early-stage PDAC does not occur in isolation, as incidence across all stages has also risen over time. This raises the possibility that the findings observed in this study also reflect a broader increase in PDAC burden nationally. Rahib et al. previously projected that pancreatic cancer may become the second leading cause of cancer-related death in the United States by 2030 [8].

Several established risk factors may contribute to the rising incidence of PDAC. Increasing prevalence of obesity, metabolic diseases, diabetes mellitus, chronic pancreatitis, and aging populations are important contributors to increasing pancreatic cancer incidence worldwide, including in the United States [9, 10].

Racial disparities in PDAC incidence were also observed in this study, with non-Hispanic Black patients demonstrating higher incidence rates compared with White patients. These findings are consistent with prior epidemiologic studies demonstrating significantly higher pancreatic cancer incidence and mortality among Black individuals in the United States, with some studies reporting up to 32% higher pancreatic cancer mortality rates in Black individuals compared with White individuals, although currently recognized risk factors alone did not fully explain this disparity [17]. Differences in smoking prevalence, obesity, diabetes, socioeconomic disparities, delayed diagnosis, differences in healthcare access, and biological and environmental factors all likely play a role, although the contribution of each of these factors remains incompletely understood.

This study has several limitations. This study was a retrospective analysis of SEER data, and the SEER database does not provide information on screening or diagnostic pathways, which limits what we can infer about the underlying causes of these patterns. Further, changes in staging definitions or reporting over time could have influenced the results. However, the dataset's size and national scope certainly allow for a broad view of trends over a relatively long period.

Conclusion

In recent years, the data reflect a shift towards earlier detection of PDAC. Incidence of localized disease has increased, while regional and distant-stage disease has shown comparatively smaller increases over time. This shift likely reflects advancements in imaging, leading to increased rates of incidental findings, better surveillance programs for high-risk patients, improved techniques such as endoscopic ultrasound for detecting smaller lesions, and perhaps even emerging biomarker-based approaches. Regardless, most patients are still diagnosed with advanced-stage disease. Further research is needed to determine whether the increasing proportion of PDAC being diagnosed with only localized disease reflects real earlier detection, greater diagnostic intensity, an increasing underlying disease burden, or a combination of these factors.

Future prospective multicenter investigations and randomized trials evaluating targeted screening and surveillance strategies will be critical to determine whether these trends translate into meaningful improvements in early detection and survival outcomes in PDAC.

Declarations

Competing Interests:

The authors have no relevant financial or non-financial interests to disclose.

Data Availability

The datasets generated during and/or analyzed during the current study are available in the Surveillance, Epidemiology, and End Results (SEER) Program repository, www.seer.cancer.gov.

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Author Contribution

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by D.H. and P.K.. The first draft of the manuscript was written by D.H. and P.K., and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Figures

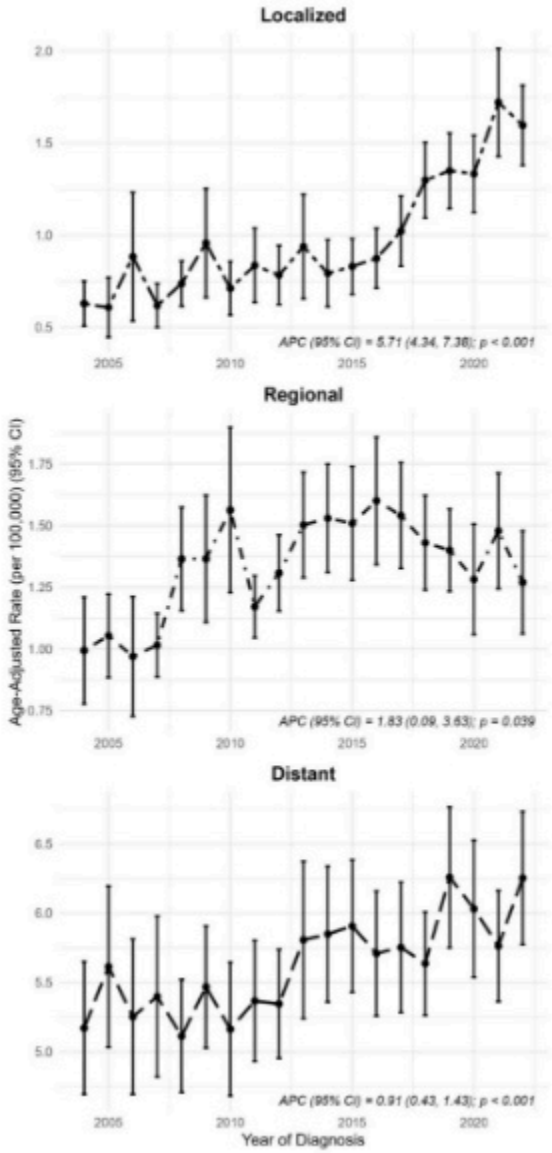


Figure 1

Annual Percent Change in Age-Adjusted Incidence Rates of PDAC by Diagnosis.

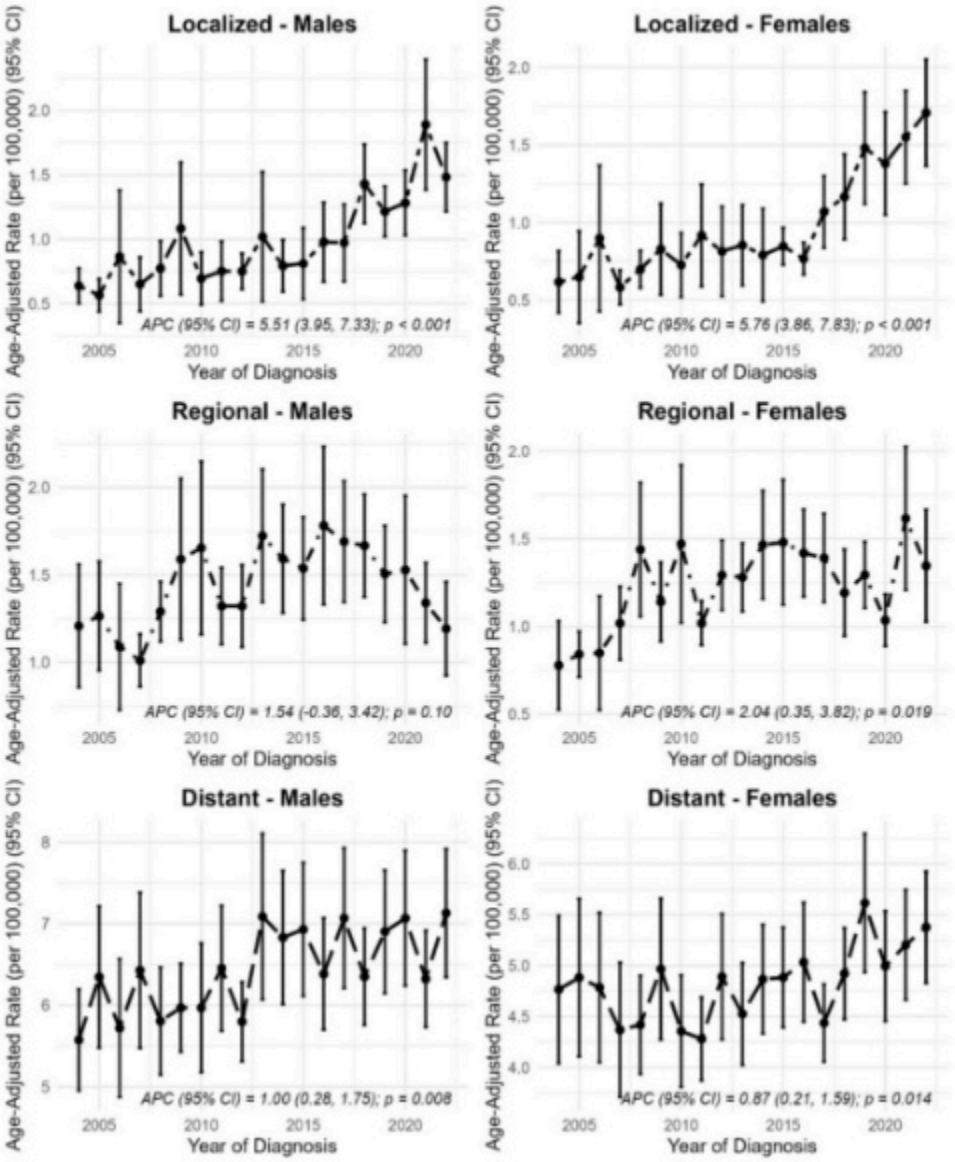


Figure 2

Annual Percent Change in Age-Adjusted Incidence Rates of PDAC by Diagnosis stratified by sex.

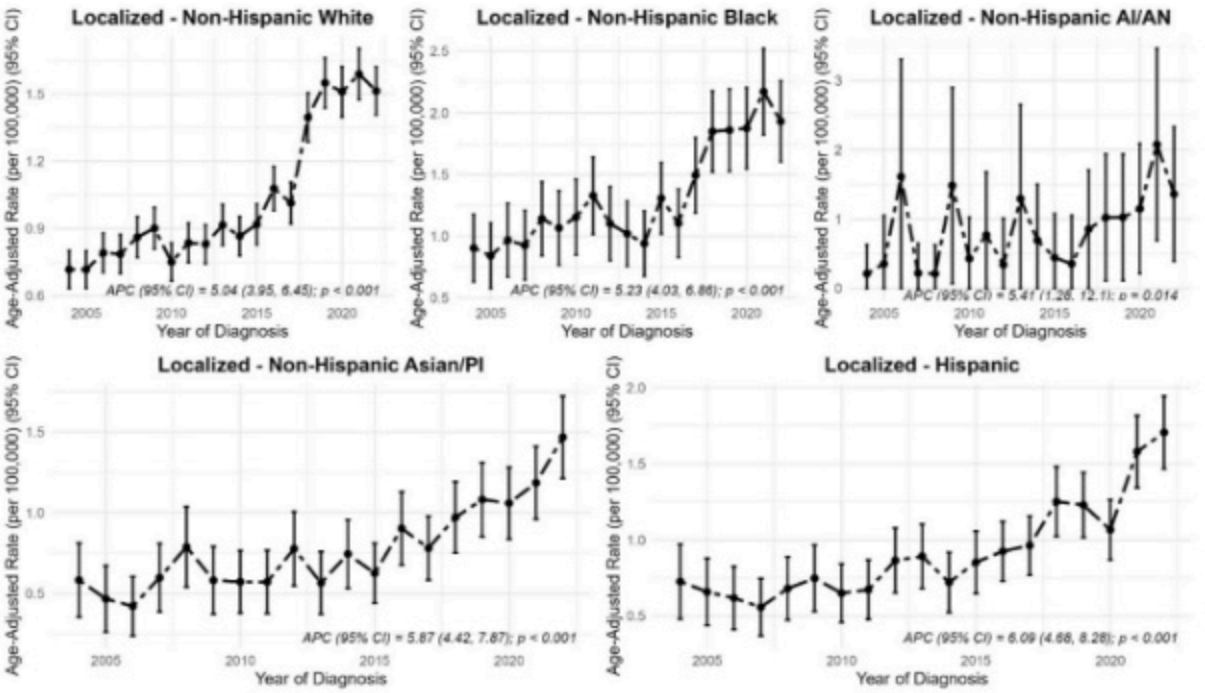


Figure 3

Annual Percent Change in Age-Adjusted Incidence Rates of Localized PDAC stratified by Race/Ethnicity.

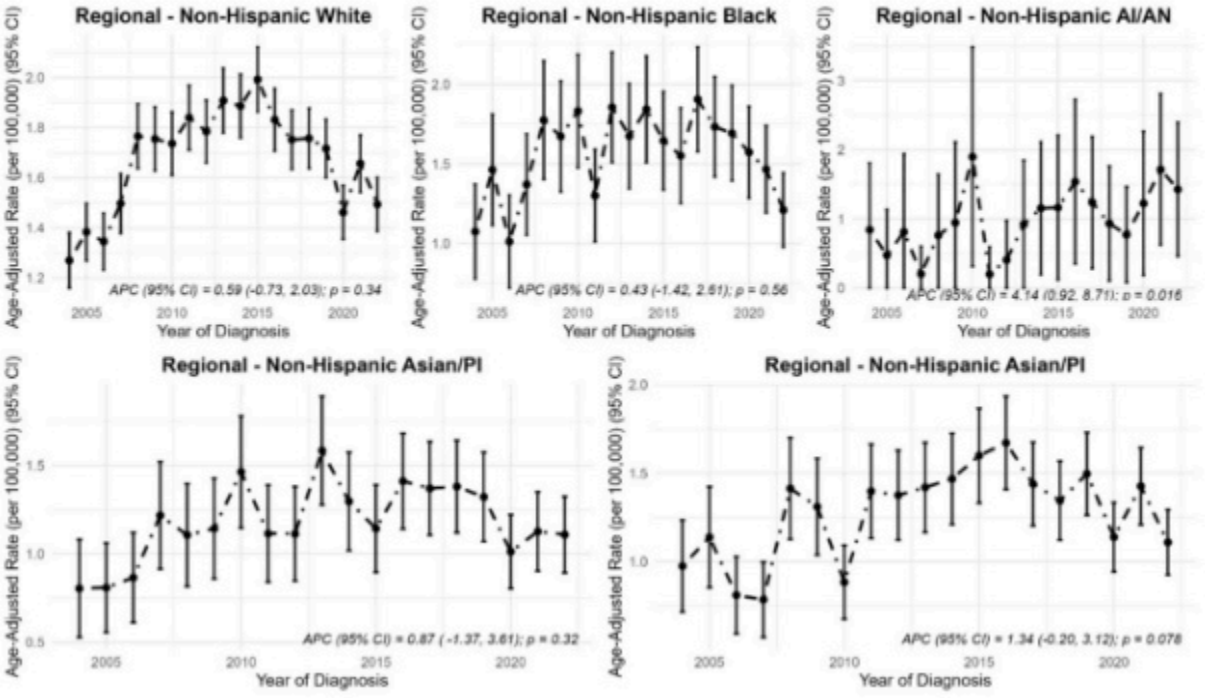


Figure 4

Annual Percent Change in Age-Adjusted Incidence Rates of Regional PDAC stratified by Race/Ethnicity.