Original Article

Pancreatic cancer mortality trends in the United States: how much have we moved the needle?

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Background: Despite advances made in pancreatic cancer treatment, the extent of progress made in pancreatic cancer mortality at the population level remains unclear. Our cross-sectional study sought to measure trends in pancreatic cancer mortality in the United States in the last 2 decades.

Methods: Patients with pancreatic cancer mortality from 1999 to 2020 were analyzed from the Centers for Disease Control and Prevention's Wide-Ranging Online Data for Epidemiologic Research (CDC WONDER). Age-adjusted mortality rates (AAMRs) per 100,000 individuals were measured. We used joinpoint trend analysis to determine average annual percent change (AAPC) in AAMR trends.

Results: From 1999 to 2020, pancreatic cancer accounted for 809,197 deaths. Overall, the AAMRs of pancreatic cancer increased from 20.74 per 100,000 individuals in 1999 to 21.60 per 100,000 individuals in 2020. The highest AAMR was recorded in non-Hispanic Black males (30.11 per 100,000 individuals), and the lowest, in non-Hispanic White females (18.51 per 100,000 individuals). Patients aged 75–84 years had the highest AAMR (6.87 per 100,000 individuals) compared to the younger patients. The highest AAMR was observed in the Northeast region (22.07 per 100,000 individuals) and rural regions (21.29 per 100,000 individuals).

Conclusions: There was no improvement in pancreatic cancer mortality in the last two decades. These findings emphasize the importance of efforts to increase access to multidisciplinary cancer care with the realization that without it, improvements in treatment standards will not translate to lower cancer mortality at the population level.

Keywords: Pancreatic cancer; gastroenterology; oncology; cancer; epidemiology

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Introduction

Pancreatic cancer is the third leading cause of cancer death in the United States (U.S.). It is known as one of the most fatal types of cancer for its low 5-year survival rate ranging from 2–9% (1), which can be attributed to its inherent aggressive biology, late-stage at diagnosis, and limited efficacy of treatment options (2). While there have seemingly been advances in the treatment of pancreatic cancer through improved chemotherapeutics and better sequencing of therapies (3,4), it is not well-established if pancreatic cancer mortality has improved at the population level over time. Our study sought to measure trends in pancreatic cancer mortality from 1999 to 2020 and investigate potential disparities across different demographics. We present this article in accordance with the STROBE reporting checklist (available at https://jgo.amegroups.com/article/view/10.21037/jgo-24-213/rc).

Methods

Data source

Death certificate data from the Centers for Disease Control and Prevention's Wide-Ranging Online Data for Epidemiologic Research (CDC WONDER) U.S. was analyzed from 1999 to 2020 to determine the longitudinal trends of pancreatic cancer mortality among the U.S. population aged ≥35 years. CDC WONDER is a publicly available online database that contains public health data, including mortality data, since the year 1999. It is more nationally representative compared to other existing database as it captures data based on death certificates of the U.S. residents and is inclusive of all races. Institutional review approval is not required as the population data is de-identified. Patients with pancreatic cancer mortality were identified using the International Statistical Classification of Diseases and Related Health Problems-10th Revision (ICD-10 codes C25.0–C25.9 being listed as the underlying cause of death). Those aged below 35 years old were excluded due to low case numbers. The datasets generated during and/or analyzed during the current study are available in the CDC WONDER, https://wonder.cdc.gov/. Further information is available from the corresponding author upon request. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Statistical analysis

Age-adjusted mortality rates (AAMRs) per 100,000 individuals were calculated by standardizing the year 2000 U.S. population. We organized the data into line graphs to show the overall AAMR trends of the individuals with pancreatic cancer over the study period. We then grouped the data based on different demographic characteristics including sex, race, age, US census region, urbanization level. The Joinpoint regression program (version 4.9.1.0; National Cancer Institute) was employed to analyze trends in AAMR across various subgroups. This approach assesses the significance of changes in AAMR over time through log-linear regression models that account for temporal variations. The annual percent change (APC) in AAMR, along with its 95% confidence interval (CI), was determined using the Monte Carlo permutation test at identified segments connecting Joinpoints. Subsequently, the average annual percent change (AAPC), representing the weighted averages of the APCs, was calculated with corresponding 95% CIs. Statistical significance was considered at $P \leq 0.05$ using a two-tailed *t*-test for all analyses.

Highlight box

Key findings

- The age-adjusted mortality rates (AAMRs) of pancreatic cancer increased from 20.74 per 100,000 individuals in 1999 to 21.60 per 100,000 individuals in 2020.
- The highest AAMR was observed in non-Hispanic Black males (30.11 per 100,000 individuals), and the lowest, in non-Hispanic White females (18.51 per 100,000 individuals).
- Patients aged 75–84 years had the highest AAMR (6.87 per 100,000 individuals) compared to the younger patients.
- The highest AAMR was observed in the Northeast region (22.07 per 100,000 individuals) and rural regions (21.29 per 100,000 individuals).

What is known and what is new?

- Pancreatic cancer is known to be a cancer with low survival rate.
- Our study reports that pancreatic cancer mortality that has not improved in the last twenty years and disparities persisted through the study period.

What is the implication, and what should change now?

- Our findings emphasize the dire need for increased funding and patient advocacy to support efforts in advancing systemic therapy and improving patients' access to multidisciplinary cancer care.

Results

From 1999 to 2020, pancreatic cancer attributed to 809,197

Table 1 Demographic characteristics of pancreatic cancer decedents in the United States, 1999–2020

Variable	N (%)	AAMR per 100,000 (95% CI)	AAPC (95% CI)
Overall	809,197 (100.00)	21.26 (21.22–21.31)	0.23 (0.17–0.28)
Sex			
Male	408,292 (50.46)	24.43 (24.35–24.50)	0.24 (0.17–0.23)
Female	400,905 (49.54)	18.60 (18.54–18.66)	0.18 (0.11–0.24)
Race			
Non-Hispanic White	638,815 (78.94)	21.35 (21.30–21.40)	0.39 (0.33–0.45)
Non-Hispanic Black	95,519 (11.80)	26.92 (26.74–27.09)	–0.21 (–0.29 to –0.13)
Asian or Pacific Islander	21,632 (2.67)	14.85 (14.65–15.05)	–0.02 (–0.23 to 0.18)
American Indian	3,383 (0.42)	15.83 (15.26–16.39)	0.65 (–0.02 to 1.32)
Hispanic	48,363 (5.98)	16.63 (16.48–16.78)	0.19 (0.02–0.36)
Age, years			
35–44	10,938 (1.35)	0.37 (0.37–0.37)	–0.90 (–1.22 to –0.57)
45–54	57,896 (7.15)	1.65 (1.63–1.67)	–0.19 (–0.34 to –0.03)
55–64	153,862 (19.01)	3.43 (3.41–3.45)	0.40 (0.28–0.52)
65–74	228,115 (28.19)	5.77 (5.75–5.79)	0.19 (0.08–0.31)
75–84	233,603 (28.87)	6.87 (6.85–6.89)	0.37 (0.26–0.48)
85+	124,783 (15.42)	3.17 (3.15–3.19)	0.17 (–0.03 to 0.38)
US census region			
Northeast	163,253 (20.17)	22.07 (21.96–22.17)	0.11 (0.02–0.20)
Midwest	186,985 (23.11)	21.95 (21.85–22.05)	0.52 (0.44–0.59)
South	294,100 (36.34)	21.08 (21.01–21.16)	0.24 (0.17–0.30)
West	164,859 (20.37)	20.16 (20.07–20.26)	0.08 (–0.03 to 0.19)
2013 urbanization			
Urban	667,520 (82.49)	21.25 (21.20–21.30)	0.15 (0.09–0.21)
Rural	141,677 (17.51)	21.29 (21.18–21.40)	0.63 (0.53–0.72)

AAMR, age-adjusted mortality rate; AAPC, average annual percent change; CI, confidence interval.

deaths. The demographic characteristics of patients who met the inclusion criteria are shown in *Table 1*. The overall AAMR of pancreatic cancer is 21.26 (95% CI, 21.22–21.31) which increased significantly from 20.74 (95% CI, 20.50–20.97) per 100,000 individuals in 1999 to 21.60 (95% CI, 21.40–21.80) per 100,000 individuals in 2020, with AAPC of +0.23 (95% CI, 0.17–0.28). When stratified by race and sex, the highest AAMR was observed among non-Hispanic Black males [30.11 (95% CI, 29.82–30.41) per 100,000 individuals], followed by non-Hispanic White males [24.83 (95% CI, 24.74–24.91) per 100,000 individuals], non-Hispanic Black females [24.40 (95% CI, 24.19–24.62) per 100,000 individuals], and non-Hispanic White females [18.51 (95% CI, 18.44–18.58) per 100,000 individuals] (*Figure 1A*).

More than 90% of the deaths from pancreatic cancer occur among patients aged 55 years and older. Increasing trends of AAMR across the years were recorded among patients aged 55 years and older. The highest AAMR [6.87 (95% CI, 6.85–6.89) per 100,000 individuals] was reported in patients aged 75–84 years, whereas the lowest AAMR [0.37 (95% CI, 0.37–0.37) per 100,000 individuals] was

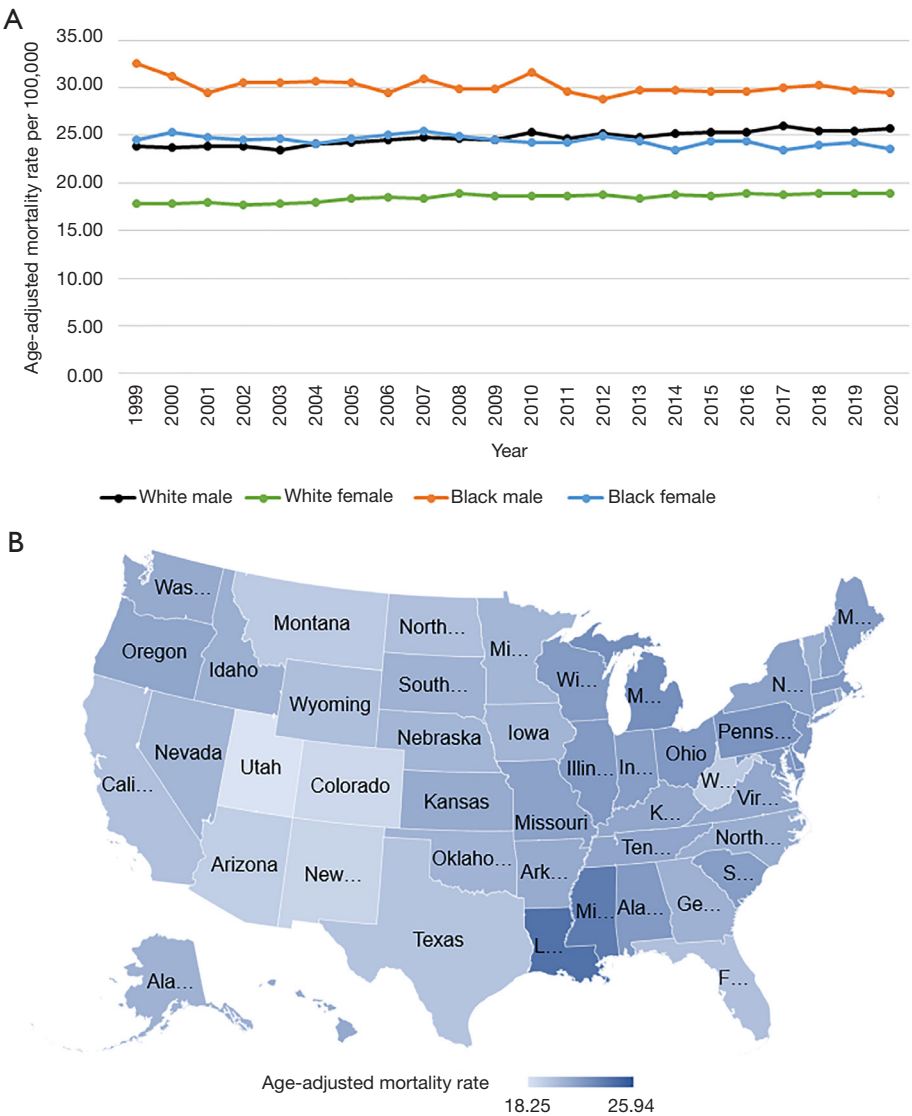

Figure 1 Age-adjusted mortality rates of pancreatic cancer. (A) Trends in age-adjusted mortality rates of pancreatic cancer stratified by race and sex; (B) age-adjusted mortality rates of pancreatic cancer stratified by state. Produced with permission from Americas Hepato-Pancreato-Biliary Association.

reported in patients aged 35–44 years. By U.S. census region, the Northeast region had the highest AAMR from pancreatic cancer [22.07 (95% CI, 21.96–22.17) per 100,000 individuals], followed by the Midwest region [21.95 (95% CI, 21.85–22.05) per 100,000 individuals], the South region [21.08 (95% CI, 21.01–21.16) per 100,000 individuals], and the West region [20.16 (95% CI, 20.07–20.26) per 100,000 individuals] (*Figure 1B*). The rural population had a higher AAMR than the urban population [21.29 (95% CI, 21.18–21.40) *vs.* 21.25 (95% CI, 21.20–21.30) per 100,000 individuals] with a higher AAPC as well [+0.63 (95% CI, 0.53–0.72) *vs.* +0.15 (95% CI, 0.09–0.21)].

Discussion

This study provides important insights into the trends of pancreatic cancer mortality. Our study demonstrates a slowly but constantly increasing trend of pancreatic cancer mortality by 0.23% per year from 1999 to 2020. While the clinical significance of such an increase can be debated,

the lack of improvement in the setting of advances made in treatment therapeutics is disappointing. Progress has been made in pancreatic cancer treatment over the years, with gemcitabine surpassing single-agent 5-fluorouracil as the systemic treatment of choice in 2000 (5), and the PRODIGE 4 trial demonstrated superior survival in patients with metastatic pancreatic cancer treated with FOLFIRINOX versus gemcitabine in 2011 (3). However, there is an incongruency between therapeutic advances and non-improvement in cancer-specific mortality rates. This may be explained by multiple factors. First, the aging population (6) and increasing prevalence of obesity (7) may contribute to the increasing mortality trend. Obesity is associated with higher incidences of pancreatic cancer and disease-specific mortality as well (8,9). Additionally, patients with obesity are more likely to present with advanced pancreatic cancer (10), and this is hypothesized to be due to chronic inflammation and the higher postoperative complications among patients with obesity after pancreatoduodenectomy (11). Additionally, access to care may represent a significant barrier to improvement in pancreatic cancer mortality. More than 70% of patients with stage I pancreatic cancer do not undergo surgical resection, the only treatment modality that offers an opportunity at cure, with patients on Medicaid being less likely to be offered surgery and more likely to refuse surgery (12). The aforementioned advances may only benefit a small, select group of patients who are treated at tertiary referral cancer centers and are inadequate in moving the needle in efforts to improve pancreatic cancer mortality (13). Finally, intraductal papillary mucinous neoplasms (IPMN) are precursor lesions to pancreatic cancer and were thought to be an opportunity to intervene before cancer progression. Disappointingly, the rise in resection for incidentally discovered IPMN pancreatic cystic lesions has not moved the needle in pancreatic cancer mortality (14).

Our study shows higher AAMR among male and black individuals, similar to previous studies (15,16). This disparity may be explained by the higher burden of modifiable risk factors such as tobacco smoking, alcohol intake, diabetes mellitus, and obesity among these two populations (17,18). Additionally, it was found that black individuals with clinical stage I pancreatic cancer are less likely to be offered surgery (12). They are also associated with worse postoperative outcomes, including higher rates of sepsis and postoperative bleeding (19). Our study also shows that the rural population has a higher AAMR compared to the urban population, which is consistent with a study done by Brooks and colleagues (20). This can be explained by the lack of access to primary medical care in rural areas, which may potentially result in late-stage detection of pancreatic cancer (21) and pancreatectomy among the rural population (20).

A previous SEER study examining pancreatic cancer-related mortality rates over the last 4 decades similarly demonstrated an increase in mortality rates over time albeit not finding any racial disparities in mortality rates (15). However, it is important to note that SEER covers 16 participating states that account for approximately 48% of US cancer incidences. Additionally, validation study has demonstrated that SEER only captures 42% of White patients and up to 70% of Asian patients, making the dataset less appropriate for disparities-based analyses (22). Our study utilizes CDC WONDER that captures mortality across all races in the US and is better reflective of real-world trends. While our study corroborates the findings of rising pancreatic cancer-associated mortality rates over time, it uncovered important racial disparities that were previously not reported. A single state analysis capturing patients of all races had similarly reported racial disparities in pancreatic cancer mortality (16); our study went beyond that and demonstrated that this disparity unfortunately extends nationally as well.

There are some limitations in our study. First, we are unable to determine treatment rates that might explain the observed pancreatic cancer mortality rates. We are also unable to account for important confounders of mortality, such as comorbidity burden and performance status. In addition, this study relies heavily on accuracy in coding due to the nature of the CDC WONDER database which captures data based on death certificates. However, the CDC WONDER is one of the only datasets that will allow a complete capture of cancer-specific deaths across the country, providing an accurate assessment of progress (or lack thereof) made throughout the years.

Conclusions

Despite the aforementioned limitations, our study provides critical information on contemporary, temporal trends of pancreatic cancer mortality that have not improved in the last two decades despite improved chemotherapeutics and treatment sequencing. These sobering findings emphasize the dire need for increased funding and patient advocacy to support efforts in advancing systemic therapy and improving patients' access to multidisciplinary cancer care.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jgo.amegroups.com/article/view/10.21037/jgo-24-213/rc

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jgo.amegroups.com/article/view/10.21037/jgo-24-213/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

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