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Research Article

Temporal Trends and Structural Acceleration in Nutrition- and Cachexia-Associated Mortality Among Pancreatic Cancer Decedents in the United States, 1999–2020: A Nationwide Population-Based Joinpoint Analysis

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Abstract

Objectives: Cancer cachexia contributes substantially to morbidity and mortality in pancreatic cancer (PC), but nationwide mortality data remain limited. We evaluated temporal trends in nutrition- and cachexia-associated mortality among U.S. PC decedents from 1999 to 2020.

Methods: This nationwide study used the CDC WONDER Multiple Cause of Death database. PC deaths were identified by ICD-10 code C25; nutrition- and cachexia-associated mortality was defined by contributing-cause codes R64, E43, E44, and E46. Temporal trends were assessed using joinpoint regression.

Results: Among 810,481 PC deaths, 11,830 (1.46%) had nutrition- or cachexia-related conditions recorded as contributing causes. A significant inflection occurred in 2013. Mortality decreased during 1999–2013 (APC, −0.79%; 95% CI, −1.28 to −0.29; p=0.002) and increased during 2013–2020 (APC, 13.53%; 95% CI, 12.52–14.55; p<0.001). Mortality was higher among males (MRR, 1.10; 95% CI, 1.06–1.14; p<0.001), and 72.6% of deaths occurred in individuals aged ≥65 years. Only 5.0% occurred in hospice facilities.

Conclusion: Documented nutrition- and cachexia-associated mortality increased markedly after 2013, particularly among older adults and males. This death-certificate-based inflection is hypothesis-generating and may partly reflect changes in clinical recognition and coding practices.

Keywords: Cachexia, Mortality, Pancreatic cancer, Temporal trends, United States

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Pancreatic ductal adenocarcinoma (PDAC) remains one of the most lethal malignancies worldwide, characterized by aggressive tumor biology, late-stage presentation, and persistently poor survival outcomes despite advances in systemic therapy.[1] A major and devastating clinical hallmark of this disease is cancer cachexia, a multifactorial syndrome characterized by systemic inflammation, progressive involuntary skeletal muscle loss (with or without adipose tissue depletion), anorexia, and metabolic dysregulation.[2] Clinical studies suggest that up to 80% of patients with advanced pancreatic cancer (PC) experience cachexia during the disease course, contributing substantially to functional decline, impaired tolerance to antineoplastic therapies, reduced quality of life, and shortened survival.[3,4] PC is also projected to become one of the leading causes of cancer-related mortality in many countries due to its increasing incidence, limited opportunities for early detection, and persistently poor long-term survival. Despite therapeutic advances, overall prognosis remains unfavorable, highlighting the importance of understanding factors contributing to morbidity and mortality beyond direct tumor progression.[5,6]

Despite its profound clinical relevance, nationwide epidemiological data regarding nutrition- and cachexia-associated mortality in PC remain limited. Historically, cachexia has been substantially underrecognized within national mortality registries because death certification practices typically prioritize the primary malignancy as the underlying cause of death, while metabolic and nutritional deterioration are frequently omitted from coding.[7] Consequently, existing evidence has largely been derived from small institutional cohorts that are unable to adequately characterize long-term temporal patterns, demographic heterogeneity, and nationwide mortality dynamics.

Over the past two decades, both the clinical recognition of cancer cachexia and the therapeutic landscape of PC have evolved considerably. The international consensus definition proposed by Fearon et al.[2] in 2011 standardized the diagnostic framework for cancer cachexia and likely improved clinical awareness and reporting practices. In parallel, the introduction of modern multi-agent chemotherapy regimens, including FOLFIRINOX in 2011.[8] and nab-paclitaxel plus gemcitabine in 2013[9], significantly altered the natural history of advanced PC by prolonging survival in selected patients. This therapeutic transition raises an important epidemiological question: has the evolving treatment era coincided with a change in documented nutrition- and cachexia-associated mortality?

To address this question, we conducted a nationwide analysis using the Centers for Disease Control and Prevention Wide-Ranging Online Data for Epidemiologic Research Multiple Cause of Death database (CDC WONDER MCOD) to evaluate temporal trends in nutrition- and cachexia-associated mortality among PC decedents in the United States (U.S.) between 1999 and 2020. Specifically, we investigated overall, sex-specific, and age-specific mortality trajectories using joinpoint regression analysis to identify potential temporal inflection points. In addition, we explored demographic patterns and end-of-life care characteristics associated with nutrition- and cachexia-related mortality in PC.

Methods

Study Design and Data Source

A retrospective, population-based longitudinal time-series study was conducted using the CDC WONDER MCOD database. This nationwide registry compiles mortality data derived from death certificates filed across all 50 U.S. states and the District of Columbia. The study period extended from January 1, 1999, through December 31, 2020.

Because the CDC WONDER database contains fully de-identified, publicly available, and aggregated mortality data, this study was exempt from institutional review board approval and informed consent requirements in accordance with applicable U.S. federal regulations and institutional policies.

Cohort Identification and Case Definition

The primary study cohort included all decedents with PC recorded as the underlying cause of death, identified using the International Classification of Diseases, Tenth Revision (ICD-10) code C25. For comparative analyses, overall pancreatic cancer mortality counts were separately extracted using ICD-10 code C25 without additional contributing-cause restrictions.

To identify nutrition- and cachexia-associated mortality, multiple-cause-of-death fields were additionally queried for the presence of the following ICD-10 codes as contributing causes of death: R64 (cachexia), E43 (unspecified severe protein-calorie malnutrition), E44 (protein-calorie malnutrition of moderate and mild degree), and E46 (unspecified protein-calorie malnutrition). Decedents meeting both criteria were included in the final analytical cohort.

Variables and Data Extraction

Demographic variables extracted from the database included age at death, sex, race, Hispanic origin, and U.S. Census region. Age at death was categorized into six predefined groups: <45, 45–54, 55–64, 65–74, 75–84, and ≥85 years.

End-of-life care characteristics were evaluated using place-

of-death data, categorized as the decedent's home, inpatient medical facility, nursing home/long-term care facility, hospice facility, or other/unknown. Geographic urbanization status was assessed according to the 2013 National Center for Health Statistics (NCHS) Urban–Rural Classification Scheme.[10]

In accordance with CDC WONDER privacy protection policies, data cells containing fewer than 10 deaths were suppressed and classified as "not stated/suppressed."

Statistical Analysis

Descriptive statistics were used to summarize baseline demographic and clinical characteristics of the study cohort. Crude mortality rates and age-adjusted mortality rates (AAMRs) per 100,000 population were calculated and standardized to the 2000 U.S. standard population to account for demographic aging across the study period.

Comparative mortality risk between sexes was assessed using mortality rate ratios (MRRs) with corresponding 95% confidence intervals (CIs). Differences in categorical distributions between cohorts were evaluated using Pearson's chi-square test.

Temporal mortality trends were evaluated using joinpoint regression analysis based on log-linear Poisson models to identify potential inflection points in mortality trajectories over time. Joinpoint regression is a widely used method for detecting statistically significant changes in temporal trends through permutation-based model selection procedures.[11] In these models, annual death counts were treated as the dependent variable, calendar year as the independent continuous variable, and the natural logarithm of the underlying population as the offset term.

Annual percent changes (APCs) and corresponding 95% CIs were calculated for each temporal segment identified by the joinpoint model. Model selection was guided using goodness-of-fit optimization criteria, and statistically significant inflection points were identified iteratively. To evaluate model robustness and potential overdispersion, sensitivity analyses using negative binomial regression models were additionally performed.

All statistical analyses and data processing procedures were conducted using Python version 3.12 (Python Software Foundation, Wilmington, DE, USA), primarily utilizing the pandas, numpy, scipy, and statsmodels libraries. All statistical tests were two-sided, and a p-value <0.05 was considered statistically significant.

Ethics Statement

This study used publicly available, de-identified, aggregated mortality data obtained from the CDC WONDER MCOD database. Because no identifiable human participant data were accessed, institutional review board approval and informed consent were not required. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Results

Baseline Demographic Characteristics

Between 1999 and 2020, a total of 810,481 deaths with PC as the underlying cause were recorded in the U.S. Among these decedents, 11,830 (1.46%) had concurrent nutrition- and cachexia-related conditions documented as contributing causes of death and were included in the final analytical cohort **(Table 1)**.

The mean annual number of cachexia-associated deaths was 537.7. The cohort included 6,092 male decedents (51.5%) and 5,738 female decedents (48.5%). The mortality burden was concentrated among older adults, with 72.6% (n=8,504) of decedents with available age data aged ≥65 years. Comparison of age distributions between the overall PC mortality cohort and the cachexia-associated sub-cohort demonstrated a statistically significant difference (p<0.001) **(Table 2)**.

Joinpoint Time-Series Analysis

During the 22-year study period, cachexia-associated PC mortality demonstrated a significant overall increase, with an APC of 3.63% (95% CI: 3.33–3.93; p<0.001).

Joinpoint regression analysis of age-adjusted mortality rates identified a statistically significant inflection point in 2013 (**Fig. 1**). During the initial temporal segment (1999–2013), mortality rates demonstrated a modest but statistically significant downward trend (APC=−0.79%; 95% CI: −1.28 to −0.29; p=0.002). In contrast, the post-2013 period was characterized by a marked and sustained increase in mortality rates. Between 2013 and 2020, mortality rates increased at an APC of 13.53% (95% CI: 12.52 to 14.55; p<0.001), indicating a marked post-2013 increase in documented nutrition- and cachexia-associated mortality.

Sex-Specific Temporal Trends

Sex-stratified trend analysis demonstrated significant mortality increases in both male and female decedents **(Fig. 2)**. Male decedents exhibited a steeper increase over time, with an APC of 4.35% (95% CI: 3.93–4.78; p<0.001), compared with 2.88% (95% CI: 2.46–3.31; p<0.001) among female decedents **(Table 3)**.

Comparative risk analysis further demonstrated a significantly higher mortality burden among males relative to females (MRR=1.10; 95% CI: 1.06–1.14; p<0.001).

Table 1. Baseline demographic characteristics of pancreatic cancer decedents with nutrition- and cachexia-associated mortality (1999–2020)

Characteristics	Value
Overall Pancreatic Cancer Cohort	
Total Pancreatic Cancer Deaths in the US (1999–2020)	810,481
Study Cohort (Cachexia & Malnutrition)	n=11,830 (1.46%)
Study Period	1999–2020
Mean annual deaths, n	537.7
Sex, n (%)	
Male	6,092 (51.5%)
Female	5,738 (48.5%)
Age at death, years, n (%)	
<45	82 (0.7%)
45–54	864 (7.4%)
55–64	2,256 (19.3%)
65–74	3,335 (28.5%)
75–84	3,386 (28.9%)
≥85	1,783 (15.2%)
Age ≥65 years, n (%)	8,504 (72.6%)
Race, n (%) *	
White	9,590 (81.1%)
Black or African American	1,765 (14.9%)
Asian or Pacific Islander	237 (2.0%)
Other / Not Reported†	238 (2.0%)
Hispanic Origin, n (%) *	
Not Hispanic or Latino	10,926 (92.4%)
Hispanic or Latino	475 (4.0%)
Not Stated / Suppressed†	429 (3.6%)
Census Region, n (%) *	
South	4,414 (37.3%)
West	2,869 (24.3%)
Midwest	2,597 (22.0%)
Northeast	1,521 (12.9%)
Not Stated / Suppressed†	429 (3.6%)

Data were obtained from the Centers for Disease Control and Prevention Wide-Ranging Online Data for Epidemiologic Research (CDC WONDER) Multiple Cause of Death database. Underlying cause of death was defined by ICD-10 code C25 (Pancreatic cancer), with contributing causes R64, E43, E44, and E46 (Cachexia and malnutrition-related conditions). Age-group data were available for 11,706 decedents; therefore, age-specific percentages, including the proportion aged ≥65 years, were calculated using this denominator. *Race, Hispanic origin, and Census Region data were extracted exactly as reported in the CDC WONDER database for the study cohort (N=11,830). †Includes populations not stated or suppressed by CDC WONDER (counts <10) to maintain confidentiality.

Age-Specific Temporal Trends

Age-specific mortality trajectories demonstrated substantial heterogeneity across age groups (Figure 3). Mortality rates among younger and middle-aged populations (45–54 and 55–64 years) remained relatively stable throughout the study period. In contrast, the post-2013 increase was predominantly observed among older age groups, particularly individuals aged 65–74, 75–84, and ≥85 years, all of whom demonstrated progressively increasing mortality trajectories beginning after 2013.

The proportion of nutrition- and cachexia-associated mortality among overall pancreatic cancer deaths was lowest in individuals aged <45 years (0.67%) and highest in the 45–54-year age group (1.49%). Thereafter, the proportion remained relatively stable across older age groups, ranging from 1.43% to 1.47% **(Table 2)**.

End-of-Life and Geographic Characteristics

Analysis of place-of-death data demonstrated that 43.6% (n=4,678) of cachexia-associated deaths occurred at the decedent's home, whereas 36.3% (n=3,890) occurred in inpatient medical facilities. Only 5.0% (n=537) of decedents died in designated hospice facilities **(Table 4)**.

Geographically, the majority of cachexia-associated deaths occurred in metropolitan regions (81.3%; n=8,717), while non-metropolitan areas accounted for 18.7% (n=2,004) of deaths.

Discussion

This nationwide study involving 11,830 decedents over a 22-year period provides a comprehensive epidemiological evaluation of nutrition- and cachexia-associated mortality in PC. The principal findings were threefold: first, mortality trajectories showed a statistically significant inflection followed by a marked increase beginning in 2013; second, the increasing mortality burden was predominantly observed among older adults and male decedents; and third, only 5.0% of deaths occurred in designated hospice facilities.

The identification of a statistically significant inflection point in 2013 represents one of the notable findings of this study. Prior epidemiological investigations in PC have primarily relied on conventional linear trend analyses, which may fail to detect temporal transitions within longitudinal mortality trajectories.[12] By applying joinpoint regression to nationwide mortality data, our analysis identified a marked change in the trajectory of documented nutrition- and cachexia-associated mortality beginning after 2013. This temporal shift coincided with major developments in both cachexia recognition and PC therapeutics, including publication of the international cachexia consensus definition

Table 2. Age-group distribution: Overall pancreatic cancer mortality vs. nutrition- and cachexia-associated mortality (1999–2020)

Age Group	Overall Pancreatic Cancer Deaths (n=810,481)	Nutrition- and cachexia-associated mortality (n=11,706*)	Proportion with Nutrition- and cachexia (%)
<45 years	12,222 (1.5%)	82 (0.7%)	0.67%
45–54 years	57,896 (7.1%)	864 (7.4%)	1.49%
55–64 years	153,862 (19.0%)	2,256 (19.3%)	1.47%
65–74 years	228,115 (28.1%)	3,335 (28.5%)	1.46%
75–84 years	233,603 (28.8%)	3,386 (28.9%)	1.45%
≥85 years	124,783 (15.4%)	1,783 (15.2%)	1.43%

Exact age was not stated or suppressed for a small number of decedents in the CDC WONDER database, resulting in a slightly lower sub-total (11,706) compared to the overall cachexia cohort (11,830). Proportion with Cachexia indicates the percentage of total pancreatic cancer deaths within each specific age group that involved nutrition and cachexia-related conditions. *Chi-square test comparing the age distribution between the overall pancreatic cancer cohort and the cachexia-associated cohort indicated a statistically significant difference ($p < 0.001$).

in 2011[2] and the introduction of modern multi-agent chemotherapy regimens such as FOLFIRINOX and nab-paclitaxel-based therapies.[8,9] However, temporal concurrence alone does not establish a causal relationship.

Several factors may have contributed to the observed post-2013 increase. Greater clinical awareness following publication of consensus criteria, together with evolving death-certificate documentation and coding practices, may have increased the likelihood that cachexia or malnutrition was recorded as a contributing cause of death. Changes in systemic therapy and survival duration may also plausibly increase the period during which patients are exposed to progressive metabolic and nutritional deterioration; however, CDC WONDER does not contain treatment histories or longitudinal clinical data needed to test this mechanism. Accordingly, the association between the 2013 inflection and changes in treatment or cachexia recognition should be considered hypothesis-generating rather than causal.

Our findings regarding age- and sex-specific disparities further expand upon existing physiological and clinical observations. Previous studies have suggested that aging-related sarcopenia and baseline differences in skeletal muscle composition may contribute to increased susceptibility to cancer-associated catabolic decline.[2,13-15] In our analysis, the post-2013 increase in mortality was driven predominantly by patients aged ≥65 years, whereas younger age groups demonstrated relatively stable mortality trajectories. Similarly, male decedents experienced

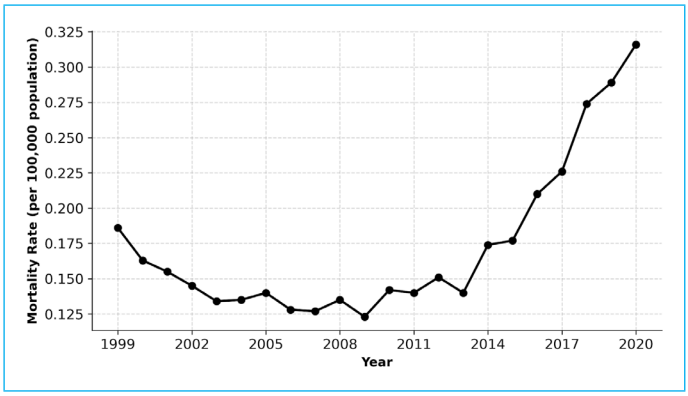

Figure 1. Overall temporal trends in nutrition- and cachexia-associated mortality among pancreatic cancer decedents in the United States, 1999–2020

AAMR: Age-adjusted mortality rate; PC: Pancreatic cancer.

AAMRs (per 100,000 population) for nutrition- and cachexia-associated mortality among PC decedents in the United States between 1999 and 2020. Rates were standardized to the 2000 U.S. standard population. Joinpoint regression identified a significant inflection point in 2013, after which mortality rates increased substantially.

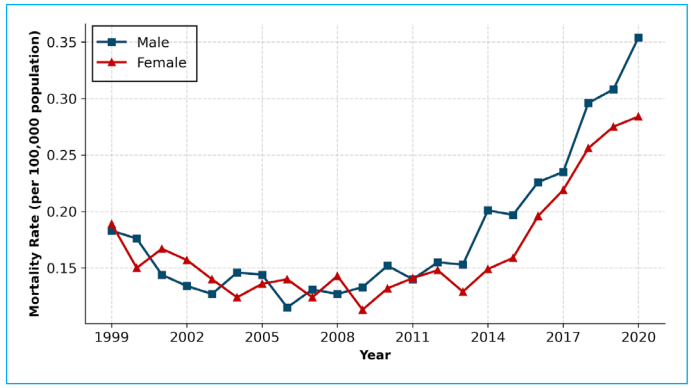

Figure 2. Sex-Specific Temporal Trends in Nutrition- and Cachexia-Associated Mortality Among Pancreatic Cancer Decedents in the United States, 1999–2020

AAMR: Age-adjusted mortality rate; PC: Pancreatic cancer

Age-adjusted mortality rates (per 100,000 population) for nutrition- and cachexia-associated mortality among male and female pancreatic cancer decedents in the United States between 1999 and 2020. Rates were standardized to the 2000 U.S. standard population. Mortality rates increased in both sexes during the study period, with a steeper increase observed among males, particularly after 2013.

Table 3. Sex-specific temporal trends in nutrition- and cachexia-associated mortality among pancreatic cancer decedents (1999–2020)

Year	Total Deaths (AAMR*)	Male Deaths (AAMR*)	Female Deaths (AAMR*)
1999	521 (0.2)	251 (0.2)	270 (0.2)
2000	460 (0.2)	244 (0.2)	216 (0.1)
2001	443 (0.2)	201 (0.2)	242 (0.1)
2002	419 (0.1)	189 (0.2)	230 (0.1)
2003	389 (0.1)	182 (0.1)	207 (0.1)
2004	396 (0.1)	211 (0.2)	185 (0.1)
2005	414 (0.1)	210 (0.2)	204 (0.1)
2006	381 (0.1)	170 (0.1)	211 (0.1)
2007	384 (0.1)	195 (0.1)	189 (0.1)
2008	411 (0.1)	191 (0.1)	220 (0.1)
2009	377 (0.1)	202 (0.1)	175 (0.1)
2010	439 (0.1)	233 (0.2)	206 (0.1)
2011	437 (0.1)	216 (0.1)	221 (0.1)
2012	475 (0.1)	241 (0.2)	234 (0.1)
2013	444 (0.1)	239 (0.1)	205 (0.1)
2014	555 (0.2)	316 (0.2)	239 (0.1)
2015	570 (0.1)	312 (0.2)	258 (0.1)
2016	679 (0.2)	360 (0.2)	319 (0.2)
2017	736 (0.2)	377 (0.2)	359 (0.2)
2018	898 (0.2)	477 (0.3)	421 (0.2)
2019	953 (0.2)	499 (0.3)	454 (0.2)
2020	1,049 (0.3)	576 (0.3)	473 (0.2)

*AAMR: Age-Adjusted Mortality Rate per 100,000 standard population. Note: Rates are based on the 2000 U.S. standard population. Data were extracted from the CDC WONDER Multiple Cause of Death database. *Trend analysis via Poisson regression revealed a significant increase over the study period (Overall APC = 3.63%, p <0.001).

steeper increases in mortality rates compared with female decedents. Collectively, these findings suggest that elderly and male populations may represent particularly vulnerable demographic groups in the evolving epidemiology of cachexia-associated PC mortality.

The present study also provides important insights into end-of-life care patterns. Despite contemporary recommendations advocating early integration of palliative and hospice care for advanced gastrointestinal malignancies[16], only 5.0% of cachexia-associated deaths occurred in designated hospice facilities, whereas more than one-third occurred in inpatient medical settings. Importantly, place-of-death categories do not capture hospice enrollment or hospice services delivered outside dedicated facilities, including at home; therefore, the 5.0% figure should not be interpreted as the overall rate of hospice utilization. Nevertheless, the observed distribution underscores the need for more granular evaluation of supportive and palliative care delivery in patients with terminal nutritional and metabolic decline. Our findings complement prior studies emphasizing the importance of supportive and palliative care interventions in advanced cancer populations.[17]

This study has several notable strengths. The nationwide design, extended 22-year observation period, and utilization of comprehensive CDC WONDER mortality data allowed evaluation of large-scale temporal trends while minimizing regional selection bias. In addition, application of joinpoint regression modeling enabled objective identification of changes in mortality trajectories that may not be apparent using conventional linear analyses. Several limitations should also be acknowledged. First, the study relied on death-certificate coding, which is inherently susceptible to underreporting and coding variability. Importantly, the study endpoint does not represent clinically confirmed cancer cachexia according to consensus diagnostic criteria. Rather, it represents nutrition- and cachexia-related conditions documented as contributing causes of death using ICD-10 codes R64, E43, E44, and E46, encompassing both cachexia and protein-calorie

Table 4. End-of-Life Care and Geographic Urbanization Characteristics (1999–2020)

Characteristics	Nutrition- and cachexia-associated mortality (n=10,721*)	Proportion (%)
Place of Death		
Decedent's home	4,678	43.6%
Medical Facility (Inpatient)	3,890	36.3%
Nursing home / Long-term care	1,472	13.7%
Hospice facility	537	5.0%
Other / Unknown	144	1.3%
2013 Urban-Rural Classification		
Metropolitan (Urban)	8,717	81.3%
Large Central Metro	*2,971*	*27.7%*
Medium Metro	*2,574*	*24.0%*
Large Fringe Metro	*2,182*	*20.4%*
Small Metro	*990*	*9.2%*
Non-Metropolitan (Rural)	2,004	18.7%
Micropolitan	*1,207*	*11.3%*
NonCore	*797*	*7.4%*

Data reflects available records. The sub-total differs slightly from the overall cohort (n=11,830) due to CDC WONDER suppression rules for counts <10 or missing "Place of Death" status in certain early years.

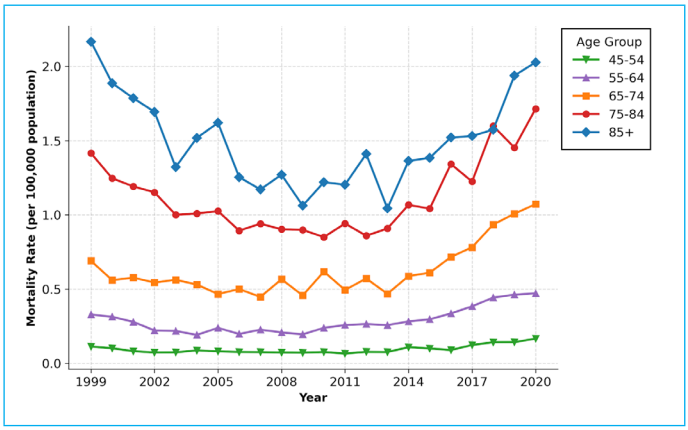

Figure 3. Age-specific temporal trends in nutrition- and cachexia-associated mortality among pancreatic cancer decedents in the United States, 1999–2020

AAMR, age-adjusted mortality rate; PC, pancreatic cancer.

Age-adjusted mortality rates (per 100,000 population) for nutrition- and cachexia-associated mortality among pancreatic cancer decedents stratified by age group in the United States between 1999 and 2020. Rates were standardized to the 2000 U.S. standard population. Mortality rates remained relatively stable among younger and middle-aged adults (45–54 and 55–64 years), whereas a marked increase after 2013 was observed among older age groups, particularly those aged 65–74, 75–84, and ≥85 years. The <45-year age group is not displayed because of the small number of annual deaths and instability of age-specific mortality estimates.

malnutrition. The recorded proportion of 1.46% is therefore substantially lower than clinical estimates indicating that cachexia may occur in up to 80% of patients with advanced PC.[3,4] This discrepancy likely reflects both the difference between clinical diagnosis and death-certificate coding and underdocumentation of nutritional or metabolic conditions when the malignancy dominates cause-of-death reporting. Thus, the 1.46% value should be interpreted as a death-certificate documentation proportion rather than as the clinical prevalence of cancer cachexia. Temporal increases may also reflect improved clinical recognition, diagnostic awareness, and coding over time, particularly following publication of standardized diagnostic criteria, rather than a true increase in disease burden alone. Nevertheless, the observed temporal patterns may remain informative epidemiological signals, although their underlying causes cannot be resolved from these data. Second, the CDC WONDER database lacks granular clinical variables, including tumor stage, treatment regimens, performance status, nutritional interventions, and longitudinal body composition measurements. Finally, the observational and ecological nature of the study precludes causal interpretation of the observed temporal associations.

Conclusion

In the U.S., documented nutrition- and cachexia-associated mortality among PC decedents showed a significant temporal inflection followed by a marked increase after 2013, with

the greatest increases observed among older adults and male decedents. Because the endpoint was based on contributing conditions recorded on death certificates rather than clinically adjudicated cachexia, these findings should be interpreted as trends in documented nutrition- and cachexia-related mortality. The post-2013 pattern may reflect multiple factors, including changes in clinical recognition and coding practices, and any relationship with evolving cancer treatment remains hypothesis-generating. These findings support continued attention to nutritional assessment, supportive oncology, and palliative care in patients with PC at risk of progressive metabolic deterioration.

Disclosure

Ethics Committee Approval: Not applicable. Because this study used publicly available, de-identified, aggregated mortality data from the CDC WONDER Multiple Cause of Death database, Institutional Review Board approval was not required.

Informed Consent: Not applicable. Individual informed consent was waived because no identifiable patient information was available.

Conflict of Interest: None.

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Author Contributions: Concept – GCU, HŞ, ÖBÇÖ, OS; Design – GCU, KB, HŞ, ÖBÇÖ, OS; Supervision – HŞ, ÖBÇÖ, OS; Materials – GCU, KB, EY; Data Collection and/or Processing – GCU, KB, EY; Analysis and/or Interpretation – GCU, KB, HŞ, ÖBÇÖ, OS; Literature Review – GCU, KB, EY; Writing – GCU; Critical Review – HŞ, ÖBÇÖ, OS.

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