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ORIGINAL RESEARCH

Population-Based Incidence, Mortality, And Survival For Gastrointestinal Cancers During 2006–2016 In Wuhan, Central China

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Objective: Incidence and mortality rates of malignant tumors in China are higher than global averages, especially for gastrointestinal (GI) cancers. To advance understanding of the epidemiology of GI cancers and to seek clues for cancer control, this study compared the incidence, mortality, and survival for GI cancers among residents of Wuhan (central China) and Chinese Americans.

Methods: A population-based study of cancer epidemiology was carried out on Wuhan residents and Chinese Americans. Data were collected from the Cancer Registry of Jiang'an District in Wuhan and the Surveillance, Epidemiology, and End Results (SEER) program. Joinpoint regression analyses were used to examine trends in the incidence and mortality of GI cancers in Wuhan. Furthermore, we estimated age-specific rates of incidence and mortality and survival rates of GI cancers in both populations.

Results: Among male GI cancer patients, mortality rates exhibited a significant increasing trend during 2006–2016 in Wuhan, with an annual percentage change (APC) of 7.4% (95% CI 1.7%–13.3%). Among female patients, the incidence of GI cancers showed a declining trend (APC –2.3%, 95% CI –3.4% to –1.3%) during 2006–2013, then escalated with an APC of 6.2% (95% CI 2.3%–10.2%) during 2013–2016. Both male and female patients with esophageal cancer in Wuhan experienced better survival than Chinese Americans. However, survival rates for the other three GI cancers in Wuhan were relatively lower than Chinese Americans.

Conclusion: Escalating trends were observed in incidence among women and mortality among men with GI cancers. In addition, the survival rates of GI cancer patients in Wuhan were lower than Chinese Americans. As such, additional efforts are needed to control GI cancers in Wuhan, central China.

Keywords: mortality, incidence, population-based data, gastrointestinal cancer, China

Introduction

Gastrointestinal (GI) cancers are the most commonly diagnosed cancers and have the highest rate of cancer-related death globally. For example, in 2012, they accounted for nearly 25% of cancers and 31% of all cancer-related deaths.[1] The four most common GI cancers are liver, esophageal, gastric, and colorectal, which are predominantly observed in developing countries.[2] These four cancers are also the leading causes of death in China, where they accounted for approximately 53% of all cancer-related deaths in 2015.[2] An epidemiological study conducted by Xi et al demonstrated that the incidence and mortality of esophageal, stomach, and

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liver cancer showed downward trends, while the incidence of colorectal cancer showed an upward trend in China.[3]

Cancer prevention and control should be based on epidemiological characteristics.[4] Understanding trends in cancer incidence and mortality is critical to developing effective prevention and control strategies. In 2012, >50% of new liver cancer cases and deaths occurred in China, although different trends are observed in various regions.[2,5] For example, an escalating trend in the incidence of liver cancer was observed in China, as well as Zhongshan City.[6,7] However, a decreasing trend was observed in Cixian County.[8] Liver cancer–related mortality also exhibited a downward trend in Nantong City and Hebei Province, although an increase was observed in the general Chinese population.[8,9] In addition, approximately 80% of esophageal cancer–related mortality occurs in less developed regions.[10] In China, decreasing trends in incidence and mortality for esophageal cancer were observed in the cities of Kunshan, Cixian, and Linzhou.[11–13] A decreasing trend in incidence but not mortality for esophageal cancer was observed in Shenyang City.[14]

Furthermore, approximately half of all gastric cancers in the world occur in China.[10] Increasing trends in incidence and mortality for gastric cancer were observed in Zhejiang Province.[15] However, declining trends in incidence and mortality rates were observed in Jiangsu Province.[16] Moreover, China has above-average levels for incidence and mortality for colorectal cancer, which have been on the rise.[10,17] For example, steadily increasing trends have been observed in Beijing, Shanghai, Qidong County, and Linzhou County. Increasing incidence was also observed in Guangzhou, although the mortality rate has fluctuated.[18–20] Among women in Kunshan City, an upward trend in the incidence of colorectal cancer was observed, while mortality showed a downward trend.[21]

Cancer-related outcomes can exhibit broad variations in different regions, even for the same type of cancer.[22] As reported, the incidence and mortality of GI cancers, including esophageal, stomach, and liver cancer, are relatively high in central China.[3] These differences are largely dependent on early detection and accessibility to qualified medical services. Along with the fast socioeconomic improvement in China, urban areas are more likely to become developed regions. Cancer-control strategies in China could learn from those of developed areas around the world, even with varying geography characteristics in cancer epidemiology.[23] Therefore, comparing cancer epidemiology in China with that in developed countries is helpful to improve the understanding of cancer epidemiology. Additionally, to avoid the interference of racial or genetic factors, we compared GI cancer epidemiology in urban Wuhan residents with Chinese Americans. This might provide further evidence for GI cancer control in urban areas in central China.

In addition, specific data regarding population-based trends are needed to provide targeted medical services at the district level in China, which is the smallest spatial unit for cancer surveillance. In these areas, community-based health services carry out cancer-surveillance measures and are responsible for implementing cancer-control strategies.[24] However, to the best of our knowledge, there are limited data regarding incidence and mortality trends for Jiang'an District in Wuhan, central China. Therefore, the present study aimed to determine trends in the incidence and mortality of GI cancers (liver, esophageal, gastric, and colorectal) in Jiang'an District during 2006–2016, which would be useful for guiding local prevention and control measures. Furthermore, we aimed to enhance the value of those findings by comparing them with Chinese Americans who were included in the Surveillance, Epidemiology, and End Results (SEER) program during 2006–2016.

Methods

Study Area And Data Source

Jiang'an District is one of the seven oldest urban districts in Wuhan, and had a population of approximately 720,000 permanent residents in 2016. It has an area of 70.25 km^2 and is located at a latitude of 30°36′8.05″ and an eastern longitude of 114°18′14.98″. The climate is a subtropical monsoon one, and the area has four distinctive seasons with adequate light and very little change in average annual temperature.

During 2006–2016, cancer incidence and mortality data of Jiang'an District were collected by the Cancer Registration System of China. The population of Jiang'an District is relatively fixed, which enables more accurate cancer surveillance. As with other districts in urban Wuhan, the residents in Jiang'an District have benefited from improvements in medical technology and health-care reform in China. Therefore, we chose Jiang'an District to explore the epidemiological characteristics of GI cancers in Wuhan. Doctors in qualified hospitals for cancer diagnosis and treatment reported newly diagnosed cancer cases in Jiang'an District, and the surveillance-related workers in hospitals or community-health services verified each report. Patients were receiving physician-supervised care at community health–service centers.

Chinese Americans are affected by both Chinese culture and American culture and have lived in a country with highly developed socioeconomic characteristics. GI cancer cases of Chinese Americans from January 1, 2006 to December 31, 2016 were collected from the SEER (www.seer.cancer.gov) program(SEER*Stat Database: Incidence — SEER 9 Regs Research Data, Nov 2018 Sub [1975–2016] <Katrina/Rita Population Adjustment> —- Linked To County Attributes — Total US, 1969–2017 Counties, National Cancer Institute, DCCPS, Surveillance Research Program) released in April 2019, based on the November 2018 submission. We obtained permission to download the database on with SEER ID 15251-Nov2018.

Outcome Measures

We selected four of the most common GI cancers: liver, esophageal, gastric, and colorectal. To conduct a reliable Joinpoint regression analysis, other GI cancers, such as pancreatic, or gallbladder, were excluded for to limit the sample size. Cancers were coded according to the the ICD10 (liver cancer C22, esophageal cancer C15, gastric cancer C16, colorectal cancer C18–C20). To compare the age distributions of patients from Jiang'an District and Chinese Americans (2006–2016), patients were grouped into eighteen 5-year age-groups: <5 years, 5–9 years, 10–14 years, 15–19 years, 20–24 years, 25–29 years, 30–34 years, 35–39 years, 40–44 years, 45–49 years, 50–54 years, 55–59 years, 60–64 years, 65–69 years, 70–74 years, 75–79 years, 80–84 years, and >84 years.

Age-standardized incidence and mortality rates in 2006–2016 for Jiang'an District were calculated using the direct method and the World Health Organization's world standard population (2000–2025). Incidence and mortality trends were assessed based on the methods of Kim et al using Joinpoint regression analysis (Joinpoint regression software, version 4.0.4, May 2013; Statistical Methodology and Applications Branch, Surveillance Research Program of the US National Cancer Institute). The model fits the trend of incidence or mortality rates over a period of time by looking for significant turning points ("joinpoints"), and the result usually consists of several continuous lines. Based on the principle of least square regression, the residual sum of squares (RSS) between fitting value and real value is calculated. The joinpoint occurs when the residual sum of squares is smallest. The number of joinpoints (k) is determined by the permutation test. This process should be performed repeatedly until the number of joinpoints is determined.

$$H_0 : k = k_{\min}$$

$$H_1 : k = k_{\max}$$

$$T_{(y)} = \{[\mathrm{RSS}(H_0) - \mathrm{RSS}(H_1)]/(d_1 - d_0)\}/[\mathrm{RSS}(H_1)/(n - d_1)]$$

$$d_0 = 2 + 2k_{\min}$$

$$d_1 = 2 + 2k_{\max}$$

$$\mathrm{RSS}(H_0) = \sum_{i=1}^{n} (y_i - (\mu_i)^{(k_{\min})})^2$$

$$\mathrm{RSS}(H_1) = \sum_{i=1}^{n} (y_i - (\mu_i)^{(k_{\max})})^2$$

$$P = \sum_{a=0}^{N_{p-1}} 1(T_{(y_a)} \geq T_{(y_0)})/N_p$$

This approach fits a series of straight lines to define the best-fit model and identify significant points when real trend change occurs, although we selected a maximum of only one significant point for our analyses.[25] The annual percentage change (APC) and corresponding 95% CI values were estimated to identify the significance of the trend.[26] The annual average ages of incidence and mortality in each population were compared using linear regression. In addition, we calculated survival rates of the two populations. These analyses were performed using SAS software (version 9.4; SAS Institute, Cary, NC, USA), and differences with two-tailed P<0.05 were considered statistically significant.

Results

Age-Specific Incidence And Mortality Rates

There were 8,454 GI cancer cases in Jiang'an District during 2006–2016 (men 1,688 cases of liver cancer, 641 cases of esophageal cancer, 1,492 cases of gastric cancer, and 1,683 cases of colorectal cancer; women 592 cases of liver cancer, 199 cases of esophageal cancer, 757 cases of gastric cancer, and 1,402 cases of colorectal cancer). During 2006–2016, SEER data revealed 12,608 cases involving Chinese Americans (men 1,919 cases of liver cancer, 320 cases of esophageal cancer, 1,249 cases of gastric cancer, and 3,790 cases of colorectal cancer; women 822 cases of liver cancer, 109 cases of esophageal cancer, 963 cases of gastric cancer, and 3,436 cases of colorectal cancer).

Figure 1 shows the age-specific incidence and mortality rates in Jiang'an District. Incidence was low before age 30 years, rapidly increased after age 30 years, and ultimately peaked at age 80–84 years (Figure 1, A and B). The mortality rate was low before age 35 years, rapidly increased after age 35 years, and ultimately peaked at age >84 years (Figure 1, C and D). Age-specific incidence and mortality rates were higher among men than women.

Age-Standardized Incidence And Mortality Rates

Figure 2 shows age-standardized incidence and mortality rates (per 100,000) in Jiang'an District. Table 1 shows the APC for age-specific incidence and mortality rates during 2006–2016 in Jiang'an District. Among women, overall incidence of GI cancers exhibited a decreasing trend

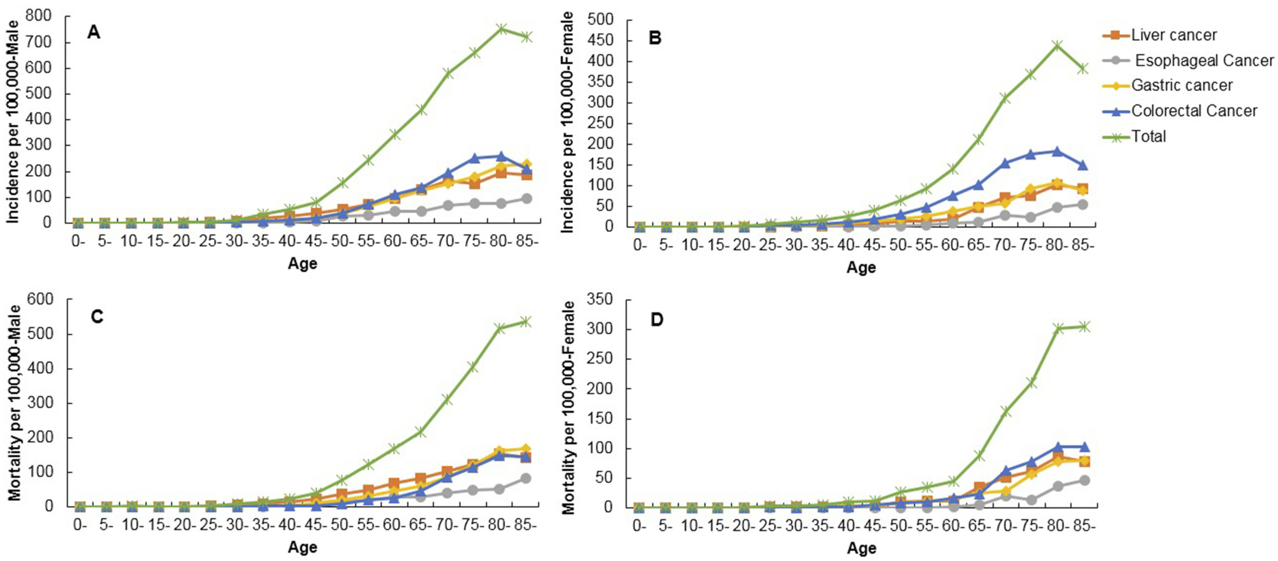

Figure 1 Age-specific incidence and mortality for GI cancers in Wuhan from 2006 to 2016. Age-specific incidence of male (**A**) and female (**B**) GI cancers; age-specific mortality for male (**C**) and female (**D**) GI cancers.

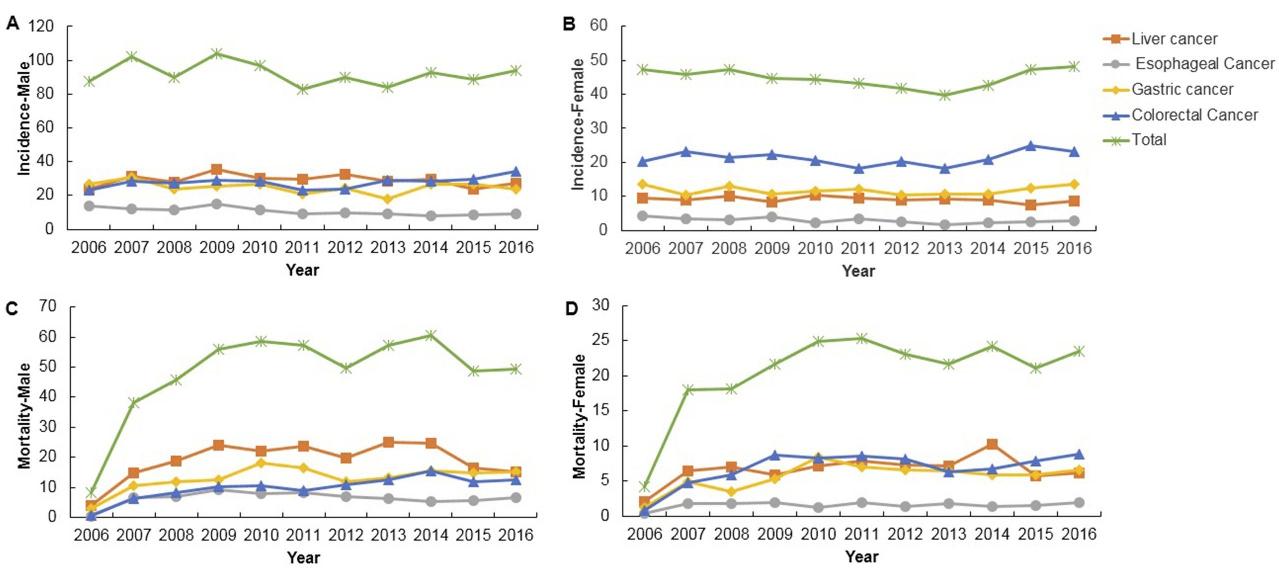

Figure 2 Age-standardized incidence and mortality rates for GI cancers in Wuhan from 2006 to 2016. Age-standardized incidence of male (**A**) and female (**B**) GI cancers; age-standardized mortality for male (**C**) and female (**D**) GI cancers.

Table 1 Annual Percentage Change (APC) In Incidence And Mortality Of GI Cancers In Wuhan In 2006–2016

Site	Male				Female			
	Trend 1		Trend 2		Trend 1		Trend 2	
	Years	APC, % (95% CI)	Years	APC, % (95% CI)	Years	APC (%)	Years	APC (%)
Incidence								
Liver cancer	2006–2016	−0.9 (−3.5 to 1.7)			2006–2016	−1.2 (−3.0 to 0.6)		
Esophageal cancer	2006–2016	−5.0 (−7.5 to −2.4)*			2006–2016	−5.2 (−9.2 to −1.0)*		
Gastric cancer	2006–2016	−1.2 (−4.0 to 1.8)			2006–2016	0.0 (−2.4 to 2.5)		
Colorectal cancer	2006–2016	2.1 (−0 to 4.3)			2006–2013	−2.1 (−5.9 to 1.8)	2013–2016	8.7 (−4.2 to 23.4)
Total	2006–2016	−0.6 (−2.1 to 1.0)			2006–2013	−2.3 (−3.4 to −1.3)*	2013–2016	6.2 (2.3–10.2)*
Mortality								
Liver cancer	2006–2009	48.2 (−16.7 to 163.5)	2009-2016	−5.1 (−13.5, 4.1)	2006–2016	3.1 (−3.3 to 10.0)		
Esophageal cancer	2006–2016	−2.4 (−8.4 to 4.1)			2006–2016	1.2 (−5.1 to 7.9)		
Gastric cancer	2006–2016	3.8 (−2.3 to 10.2)			2006–2010	30.1 (−6.8 to 81.6)	2010–2016	−3.8 (−13.4 to 6.9)
Colorectal cancer	2006–2016	7.5 (1.5 to 13.9)*			2006–2016	3.8 (−3.0 to 11.0)		
Total	2006–2016	7.4 (1.7 to 13.3)*			2006–2016	3.5 (−2.1 to 9.5)		

Note: *P<0.05.

during 2006–2016, with an APC of –2.3% (95% CI –3.4% to –1.3%), although it subsequently increased during 2013–2016, with an APC of 6.2% (95% CI 2.3%–10.2%). Among men, the overall mortality rate exhibited an increasing trend, with an APC of 7.4% (95% CI 1.7%–13.3%) during 2006–2016. For cancer-specific trends, the incidence of esophageal cancer decreased during 2006–2016 among both men (APC –5.0%, 95% CI –7.5% to –2.4%) and women (APC –5.2%, 95% CI –9.2% to –1.0%). Furthermore, colorectal cancer-related mortality exhibited an increasing trend (APC 7.5%, 95% CI 1.5%–13.9%) among men.

Average Age For Incidence And Mortality

Figures 3 and 4 show the average ages for GI cancer incidence and mortality in Jiang'an District residents and Chinese Americans (2006–2016). Table 2 shows the average age for the entire study period and trends in average age by year. In total, during 2006–2016, average ages for GI cancer incidence and mortality increased each year among men and women in Jiang'an District (*P*<0.001). However, no significant change was observed in average age of GI cancer incidence among Chinese Americans (*P*>0.05), and the average age of GI cancer mortality among female Chinese Americans actually decreased (*P*=0.0001).

For specific GI cancers in Jiang'an District, increasing trends were observed in average age of incidence for male patients with liver, gastric, and colorectal cancers, as well as female patients with liver and colorectal cancers (*P*<0.01). In addition, average age of mortality in Jiang'an District exhibited increasing trends for both men and women with liver and colorectal cancers (*P*<0.05). For Chinese Americans, the average age of mortality for male patients with liver cancer showed an escalating trend (P=0.0007) and colorectal cancer a declining trend (*P*<0.0001). Additionally, the average age of mortality for female patients with colorectal cancer showed a downward trend (*P*<0.001).

Survival Outcomes

Table 3 shows survival rates for GI cancers in Jiang'an District residents and Chinese Americans during 2006–2011. In total, 1-year to 5-year survival rates in Jiang'an District were lower than those among Chinese Americans. However, for specific GI cancers, both men and women with esophageal cancer had better survival outcomes in Jiang'an District compared to their Chinese

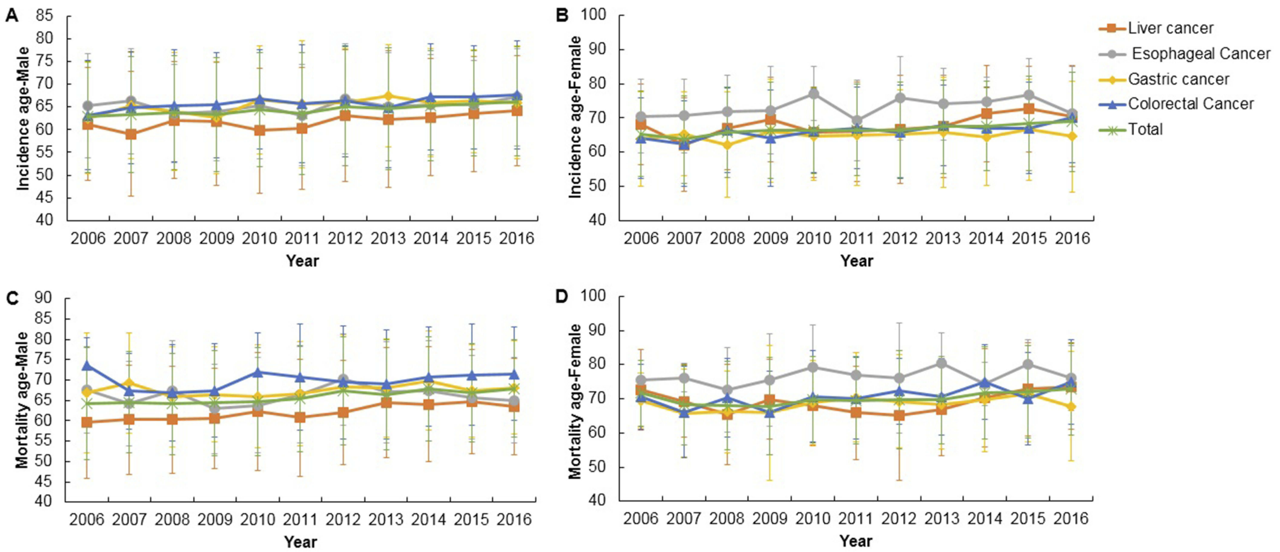

Figure 3 Average age of GI cancer incidence and mortality in Wuhan from 2006 to 2016. Average age of incidence for GI cancers in males (**A**) and females (**B**); average age of mortality for GI cancers in males (**C**) and females (**D**).

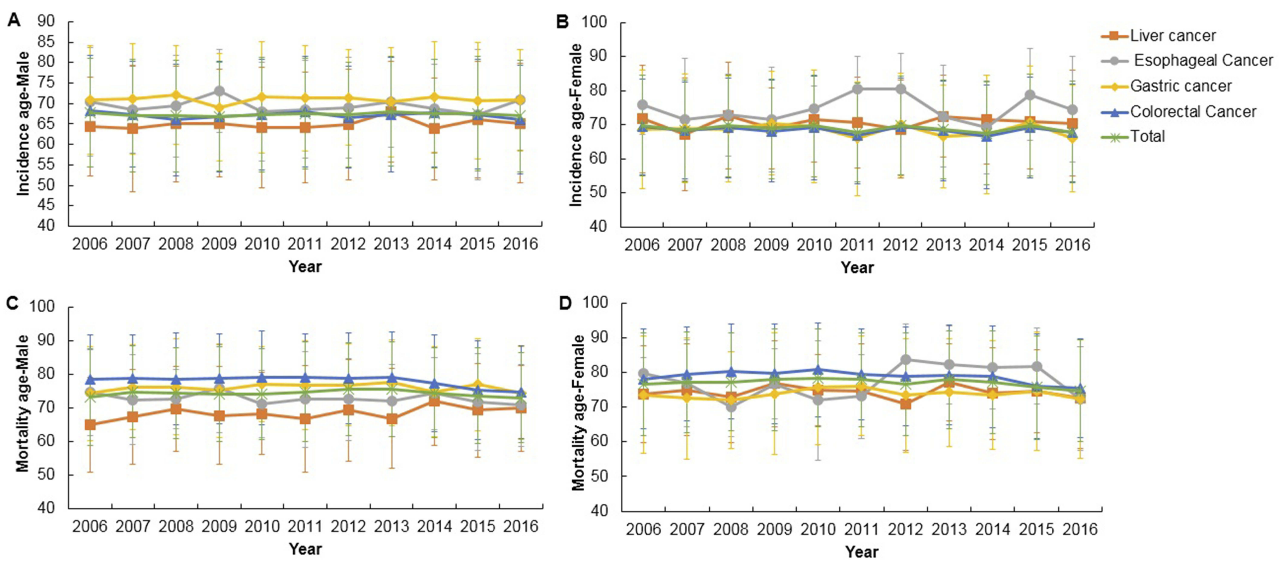

Figure 4 Average age for GI cancer incidence and mortality in Chinese Americans from 2006 to 2016. Average age for incidence of GI cancers in males (**A**) and females (**B**); average age for mortality of GI cancers in males (**C**) and females (**D**).

American counterparts. However, survival rates for liver, gastric, and colorectal cancers were relatively lower in Jiang'an District compared to Chinese Americans.

Discussion

The present study examined incidence, mortality, and survival rates for GI cancers in Jiang'an District (Wuhan, central China). Increasing trends were observed in mortality from GI cancer among men and in incidence among women. Interestingly, incidence and mortality rates for liver, gastric, and colorectal cancers in Jiang'an District were similar to the national averages.[27–29] However, incidence and mortality rates in Jiang'an District for esophageal cancer were lower than those in China.[30] Unequal trends were observed among men and women in Jiang'an District, although the incidence of esophageal cancer decreased significantly among both men and women during 2006–2016. Nevertheless, the mortality trend of colorectal cancer among men exhibited an APC of 7.5%. Moreover, compared to Chinese Americans, survival outcomes in Jiang'an

District were relatively poorer during 2006–2011. Therefore, additional efforts are needed to control GI cancers in Central China.

There are some limitations of this study. First, it was based on cancer surveillance. As such, missing or false reports might undermine its precision. Second, this paper considered only trends in incidence and mortality rates and survival of GI cancers, and excluded specific risk factors, such as environmental factors, infectious factors, and lifestyle. Third, representation was limited to one district in urban Wuhan. Therefore, generalization of the results may be limited. Fourth, we failed to take into account the different regions in which Chinese Americans may live, which might undermine the comparison results.

Despite the limitations, this study points to the increasing trend of GI cancer incidence in 2006–2016. In addition, there were decreasing trends in the incidence of esophageal cancer among both men and women during 2006–2016. This finding agrees with previous findings of a decreasing trend in incidence of esophageal cancer in China.[30,31] These trends may be related to public-health efforts to avoid unhealthy dietary habits in populations, especially high-temperature food, which has been proved to be a risk factor for esophageal cancer.[32,33] Nevertheless, it remains concerning that colorectal cancer mortality significantly increased among men in Jiang'an District (APC 7.5%) and was much higher than the national level (APC 4.1%).[34] Further studies are needed to determine the risk factors contributing to this increasing trend in mortality, as no significant trend was observed in the incidence of colorectal cancer among men.

Compared to Chinese Americans, the average ages of incidence and mortality in GI cancers were lower in Jiang'an District and kept increasing during the study period. This increase may be related to the aging population of both Wuhan residents and Chinese Americans. Moreover, the increased consumption of spicy and salty foods could have led to the younger age for GI cancer incidence in urban Wuhan.[35,36] In contrast, Chinese Americans may have received public-health education to avoid risk factors earlier than mainland China, which may have delayed the onset age of GI cancers.[37,38] In addition, the coverage of cancer screening and access to qualified medical services in the US might be better, which also might explain in part the older age for GI cancer mortality than Jiang'an District.[38,39]

Interestingly, survival rates in Jiang'an District and among Chinese Americans were higher than among the

Table 2 Trends In Average Age For GI Cancers In Wuhan And Chinese Americans From 2006 To 2016

	Incidence — male			Incidence — female			Mortality — male			Mortality — female		
	Age	t	P	Age	t	P	Age	t	P	Age	t	P
Wuhan												
Liver cancer	61.9 (13.6)	0.09	0.0004	68.0 (13.8)	0.13	0.0011	61.9 (13.6)	0.12	<0.0001	68.1 (13.6)	0.10	0.0349
Esophagealcancer	65.3 (11.2)	0.04	0.2571	72.8 (11.3)	0.10	0.1628	65.3 (11.1)	0.04	0.3782	72.8 (11.3)	0.09	0.3640
Gastric cancer	65.4 (12.2)	0.08	0.0018	64.9 (14.5)	0.03	0.3733	65.4 (12.3)	0.05	0.1782	64.9 (14.5)	0.07	0.1379
Colorectal cancer	66.1 (12.1)	0.08	0.0006	66.4 (12.8)	0.14	<0.0001	66.1 (12.3)	0.09	0.0220	66.4 (12.9)	0.17	0.0001
Total	64.5 (12.6)	0.08	<0.0001	66.8 (13.5)	0.10	<0.0001	64.5 (12.7)	0.10	<0.0001	66.8 (13.5)	0.11	<0.0001
Chinese Americans												
Liver cancer	65.0 (13.7)	0.03	0.1450	70.5 (14.1)	0.03	0.4457	68.5 (14.0)	0.08	0.0007	74.2 (13.0)	−0.02	0.5922
Esophageal cancer	69.3 (12.3)	−0.02	0.7834	74.8 (12.9)	0.04	0.6565	72.7 (12.1)	−0.06	0.2703	76.9 (12.7)	0.01	0.8890
Gastric cancer	71.0 (13.0)	−0.003	0.9039	68.5 (16.0)	−0.04	0.2544	75.8 (13.3)	−0.01	0.7083	73.7 (16.3)	−0.004	0.9111
Colorectal cancer	67.2 (13.4)	−0.01	0.5301	68.4 (14.6)	−0.02	0.1471	76.5 (13.4)	−0.11	<0.0001	78.0 (14.3)	−0.10	<0.0001
Total	67.4 (13.5)	0.005	0.6574	68.9 (14.8)	−0.02	0.1963	74.2 (13.9)	−0.02	0.1399	76.6 (14.6)	−0.06	0.0001

Table 3 Survival rates for GI cancers in Wuhan and Chinese Americans from 2006 to 2011

	Male (%)					Female (%)				
	1-year	2-year	3-year	4-year	5-year	1-year	2-year	3-year	4-year	5-year
Wuhan										
Liver cancer	49.48	37.14	33.91	31.60	30.80	41.83	32.03	29.08	26.80	24.84
Esophageal cancer	57.94	42.62	38.72	37.33	36.49	63.48	52.17	46.96	46.09	45.22
Gastric cancer	64.87	53.03	48.95	46.58	45.13	66.41	55.47	50.00	46.61	44.01
Colorectal cancer	82.01	74.07	68.24	64.27	61.54	79.45	70.77	65.85	62.52	61.22
Total	64.15	52.83	48.53	45.85	44.31	67.18	57.49	52.81	49.87	48.13
Chinese Americans										
Liver cancer	61.22	51.71	45.29	40.02	37.02	59.37	48.55	41.42	38.52	36.68
Esophageal cancer	56.72	40.30	33.58	29.10	27.61	65.91	43.18	43.18	40.91	40.91
Gastric cancer	67.81	57.73	50.72	48.02	46.58	65.87	53.94	49.16	46.78	45.35
Colorectal cancer	89.47	83.55	78.82	75.62	72.96	87.58	81.99	77.55	74.01	71.01
Total	76.40	68.33	62.65	58.89	56.38	79.31	71.57	66.75	63.52	61.00

general population of Americans and 17 Chinese registries (2003–2005).[40,41] This is likely related to the fact that Jiang'an District has ten first-level hospitals providing first-level medical care in Wuhan, Central China. Moreover, in line with another study conducted in China, 1-year to 5-year survival rates for esophageal cancer were higher in Jiang'an District compared to Chinese Americans.[42] Nevertheless, survival rates of the other three GI cancers were lower in Jiang'an District, which indicates that medical services or access to GI cancer care still requires improvement in Wuhan. In the US, colorectal cancer–screening services started from 2001, and screening-adherence rates have been increasing since then.[43] Earlier diagnosis of GI cancers could contribute to better survival outcomes in Chinese Americans.

Conclusion

Upward trends were observed in mortality among men and incidence among women with GI cancers in Wuhan. Therefore, targeted strategies in cancer control should be reinforced. In addition, this study also demonstrated that GI cancer patients in Jiang'an District experienced poorer survival compared with Chinese Americans. It is suggested that accessibility and quality of cancer medical services be improved. Further studies are recommended to identify risk factors for GI cancer trends in both populations.

Ethics Approval And Informed Consent

This study used population-based surveillance data without any individual patient identifiers.

Author Contributions

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data, took part in drafting the article or revising it critically for important intellectual content, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

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