

## Preplanned Studies

## Mortality of Common Gastrointestinal Tract Cancers — Huai River Basin, 2008–2018

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### Summary

#### What is already known on this topic?

Gastrointestinal (GI) tract cancer is a leading cause of death and produces a heavy disease burden. GI tract cancer in the Huai River Basin was reportedly higher than the national level during 2004–2006, while current mortality rates and variations have not been reported recently.

#### What is added by this report?

During 2008 to 2018, significant decreases were observed in the rates of esophageal cancer (from 28.5 to 13.2 per 100,000) and stomach cancer (from 32.1 to 16.5 per 100,000). There was no statistical difference for the mortality rates of colorectal cancer, which actually showed a significant increase among men aged 45 to 54 years and women aged below 55 years. Substantial disparities exist among different sexes, age groups, and geographical regions.

#### What are the implications for public health practice?

These results highlight that the mortality of GI tract cancers in the Huai River Basin in 2018 are similar to national levels and still produce a heavy disease burden. More attention is needed to provide important evidence for evaluating the improvement and remaining gaps in cancer prevention and control strategies in the Huai River Basin.

Gastrointestinal (GI) tract cancers, commonly including esophageal, stomach, and colorectal cancer, have been a leading causes of death causing 2.2 million deaths and 46.5 million years of life lost (YLLs) as estimated in the Global Burden of Diseases Study (GBD) 2017 (1). Stomach, esophageal, and colorectal cancers were ranked as the seventh, eleventh, and fifteenth leading causes of YLLs in both men and women in China (2). Previous reports have noted that the cancer mortality in the Huai River Basin was

higher than the national level during 2004–2006 (3). In this study, mortality data was used for the first time to demonstrate temporal trends, population distributions, and geographical distributions of GI tract cancer in the Huai River Basin from 2008 to 2018 (3). Trends of GI tract cancer mortality were examined by sex, age group, and region of the Huai River Basin. Study results indicated that, from 2008 to 2018, age-standardized mortality rate (ASMR) of esophageal and stomach cancer decreased annually by 6.7% and 5.9%, respectively, for both sexes, and the decrease in ASMR also occurred in some specific demographic and geographic subgroups. However, the ASMR of colorectal cancer did not decrease significantly and actually significantly increased among men aged 45 to 54 years (average annual percent change [AAPC]: 3.3%, 95% CI\*: 0.5%–7.2%) and among women aged below 55 years (AAPC aged 0–44 years group: 2.7%, 95% CI: 1.1%–5.3%; AAPC aged 45–54 years group: 7.5%, 95% CI: 3.4%–11.8%). This study also displayed geographic disparities for GI tract cancers, and the mortality of GI tract cancers in the Huai River Basin in 2018 was similar with national levels through related targeted prevention and control measures over the past 11 years (4). Continuous early diagnosis and treatment of GI tract cancers in the Huai River Basin, improved water quality, and improved healthcare conditions may play roles in decreasing mortality. As the lifestyles and dietary habits of Chinese residents have changed, prevention strategies should be further strengthened to target GI tract cancers, and colorectal cancer should be prioritized.

Mortality data of GI tract cancers were obtained from China CDC's Cause of Death Reporting System (CDRS) from 2008 and 2018. According to the International Classification of Diseases, 10<sup>th</sup> revision (ICD-10), esophageal cancer, stomach cancer, and colorectal cancer were coded as C15, C16, and C18–C21, respectively, for this study.

\* CI=confidence interval.

Based on the geographical distribution of the Huai River, its tributaries, and the “Encyclopedia of Rivers and Lakes in China”, 14 districts and counties from 4 provinces (Anhui, Henan, Shandong, and Jiangsu) in the Huai River Basin were divided into 5 categories: the upstream basin (upper stream) including 2 counties; the midstream north basin (midstream-north) including 6 counties or districts; the midstream south basin (midstream-south) including 1 county; the downstream basin (downstream) including 3 counties; and the Yishui River Basin including 2 counties. This report used the Sixth Chinese National Census (2010) as the standard population to calculate the age-standardized mortality rate (ASMR). Joinpoint regression was used to examine the significance of trends and to calculate the AAPC by different sub-regions of the basin, diseases, sex, and age groups during 2008–2018. When AAPC>0, the ASMR showed an upward trend, otherwise it showed a downward trend (5).

A total of 70,691 deaths were reported due to GI tract cancer from 2008 to 2018, with 47,131 males and 23,560 females. The ASMRs per year were higher among men than women by diseases. From 2008 to 2018, the ASMR of esophageal cancer decreased steadily from 28.5 per 100,000 population to 13.2 and for stomach cancer from 32.1 per 100,000 population

to 16.5. For esophageal cancer and stomach cancer, the AAPC decreased  $-6.7%$  (95% CI:  $-7.7%$  to  $-5.8%$ ,  $p<0.001$ ) and  $-5.9%$  (95% CI:  $-7.0%$  to  $-4.9%$ ,  $p<0.001$ ) per year, respectively. Downward trends were significant across both sexes, and the AAPC of ASMR for esophageal and stomach cancers were higher among men compared to women (esophageal cancer: AAPC= $-6.7%$  in men, AAPC= $-7.7%$  in women; stomach cancer: AAPC= $-6.0%$  in men, AAPC= $-6.5%$  in women). However, the ASMR of colorectal cancer showed stability from 2008 to 2018 for both men and women, and there was no statistical difference (Table 1).

The mortality rate of GI tract cancers increased with age in both men and women, and the rate was much higher among those aged 65 years and above. There was an obviously statistical difference for mortality of esophageal and stomach cancer in all age-groups for men and women. For both sexes, the mortality rate of stomach cancer decreased significantly among those aged 55 years and above and decreased to a lesser degree among those aged below 55 years old. The mortality rates of colorectal cancer in different age groups presented different characteristics. The mortality rate increased significantly among men aged 45 to 54 years (AAPC:  $3.3%$ , 95% CI:  $0.5%$ – $7.2%$ ) and women aged below 55 years old (AAPC aged 0–44

TABLE 1. Age-standardized mortality rate (per 100,000) and average annual percent change (%) of gastrointestinal tract cancers in the Huai River Basin by sex, 2008–2018.

Year	Esophageal cancer						Stomach cancer						Colorectal cancer					
	Both		Male		Female		Both		Male		Female		Both		Male		Female	
	CMR	ASMR	CMR	ASMR	CMR	ASMR	CMR	ASMR	CMR	ASMR	CMR	ASMR	CMR	ASMR	CMR	ASMR	CMR	ASMR
2008	24.3	28.5	31.0	40.5	17.3	18.4	27.4	32.1	36.0	46.6	18.3	19.6	5.9	6.8	6.5	8.4	5.2	5.6
2009	21.0	24.3	27.1	35.2	14.5	15.2	25.6	29.6	33.3	42.6	17.5	18.5	5.8	6.8	6.5	8.6	5.0	5.3
2010	21.5	24.8	29.1	37.1	13.6	14.4	26.1	29.9	34.9	43.9	16.8	17.8	6.2	7.2	7.2	9.3	5.2	5.6
2011	23.8	23.4	31.7	34.3	15.8	14.1	28.6	28.3	39.1	42.3	18.1	16.5	7.5	7.5	8.5	9.4	6.4	5.9
2012	21.8	19.4	29.6	27.8	14.0	11.5	25.6	23.0	35.5	33.5	15.5	13.2	7.1	6.5	7.8	7.5	6.5	5.5
2013	20.9	18.9	27.3	25.9	14.5	12.3	25.2	22.8	34.2	32.4	16.2	13.6	7.4	6.7	8.1	7.8	6.7	5.7
2014	20.8	18.1	29.1	26.6	12.5	10.1	25.4	22.4	34.7	32.1	16.1	13.3	7.9	7.1	9.0	8.5	6.8	5.8
2015	20.8	17.8	27.9	25.2	13.9	11.2	25.2	21.8	34.9	31.7	15.6	12.7	9.0	7.9	10.4	9.6	7.6	6.3
2016	20.7	16.2	28.0	23.4	13.4	9.6	24.7	20.0	33.8	28.5	15.6	12.0	8.3	6.8	9.9	8.4	6.8	5.3
2017	19.4	15.1	27.4	22.7	11.4	8.0	24.2	19.5	33.8	28.6	14.5	11.1	9.4	7.7	10.8	9.3	7.9	6.1
2018	18.1	13.2	24.5	19.2	11.5	7.6	21.8	16.5	29.8	23.9	13.6	9.4	8.9	6.8	10.4	8.5	7.4	5.3
AAPC	-6.7 <sup>*</sup>		-6.7 <sup>*</sup>		-7.7 <sup>*</sup>		-5.9 <sup>*</sup>		-6.0 <sup>*</sup>		-6.5 <sup>*</sup>		0.5		0.2		0.4	
(95% CI)	- (-7.7 to -5.8)		- (-7.8 to -5.5)		- (-9.1 to -6.3)		- (-7.0 to -4.9)		- (-7.2 to -4.8)		- (-7.6 to -5.5)		- (-0.9 to 1.9)		- (-1.5 to 1.9)		- (-0.8 to 1.7)	

Abbreviations: CI=confidence interval, CMR=Crude Mortality Rate, ASMR=age-standardized mortality rate, AAPC=average annual percent change.

<sup>\*</sup> $p<0.05$ .

years group: 2.7%, 95% CI: 1.1%–5.3%; AAPC aged 45–54 years group: 7.5%, 95% CI: 3.4%–11.8%). There were no significant differences in mortality rate between men and women aged 55 years old and above (Table 2).

Overall, the ASMRs by spatial distribution of the Huai River Basin were presented in Table 3. The downstream basin had the highest ASMR of GI tract cancers for men and women from 2008 to 2018, among which, the mortalities of 2 cancers decreased significantly (esophageal cancer: from 47.2 to 21.3 per 100,000; AAPC=–6.3%, 95% CI: –7.7% to –5.0%; stomach cancer: from 40.7 to 21.7 AAPC=–5.9%, 95% CI: –6.6% to –5.2%), and mortality of colorectal cancer did not decrease significantly (from 8.6 to 9.3 AAPC=1.2%, 95% CI: –0.5% to 3.1%), followed by the Yishui River Basin and midstream-south basin. The ASMR of colorectal cancer increased significantly among women in the Yishui River Basin (AAPC=4.2%, 95% CI: 0.1% to 8.3%).

## DISCUSSION

Long-term real-time surveillance for cancer incidence and mortality can not only indicate clues to influence factors but also provide important evidence for evaluating the effectiveness of cancer prevention and treatment. GI tract cancers are important causes of death worldwide, and the total number of deaths has been increasing globally (1). According to the Global Cancer Statistics Report 2018, there were approximately 400,000 esophageal cancer deaths worldwide in 2014, among which 37.0% of them occurred in China (6). Stomach cancer was the first leading cause of cancer death in 1970–1990 (3) and was still one of the main public health problems over the following several decades (4). This is the first study to demonstrate temporal trends of GI tract cancer mortality during a recent 11 year period in the Huai River Basin, which is a key area. In the findings, the ASMR of esophageal and stomach cancer declined rapidly from 2008 to 2018. By contrast, the ASMR of colorectal cancer showed stability during the study period, and even a substantial upward trend could be found among people aged 55 and below of colorectal cancer, especially for women living in the Yishui River

TABLE 2. Mortality rate (per 100,000) and average annual percent change (%) of gastrointestinal tract cancers in the Huai River Basin, by sex and age group, 2008 and 2018.

Sites/Age group (years)	2008			2018			AAPC (95% CI)		
	Both	Male	Female	Both	Male	Female	Both	Male	Female
<b>Esophageal cancer</b>									
<45	0.3	0.4	0.2	0.1	0.1	0.1	–9.7*(–16.4 to –2.5)	–8.2(–17.5 to 2.3)	–11.8*(–18.7 to –4.4)
45–54	12.1	18.4	5.5	4.3	7.2	1.6	–8.5*(–11.1 to –5.8)	–7.1*(–9.8 to –4.2)	–12.1*(–16.8 to –7.1)
55–64	50.6	71.0	29.6	24.1	37.7	10.1	–7.6*(–9.7 to –5.4)	–6.5*(–8.8 to –4.2)	–10.5*(–13.0 to –8.0)
65–74	157.4	214.8	100.0	79.2	113.3	43.7	–5.4*(–6.8 to –4.0)	–5.1*(–6.5 to –3.7)	–6.4*(–9.0 to –3.7)
≥75	352.7	495.2	250.0	164.7	229.2	113.6	–6.6*(–8.5 to –4.7)	–7.0*(–8.5 to –5.5)	–6.7*(–8.2 to –5.2)
<b>Stomach cancer</b>									
<45	1.1	1.2	1.0	0.6	0.7	0.5	–3.7(–9.0 to 2.0)	–3.3(–7.3 to 0.8)	–6.2(–12.3 to 0.3)
45–54	16.9	25.3	8.3	11.5	16.3	7.0	–3.8*(–6.5 to –1.0)	–3.5*(–5.9 to –1.1)	–3.7(–8.2 to 0.9)
55–64	56.5	82.5	29.8	31.1	46.5	15.4	–6.5*(–8.9 to –4.1)	–6.0*(–7.8 to –4.1)	–6.7*(–9.2 to –4.2)
65–74	171.2	246.1	96.3	94.2	137.0	49.8	–4.8*(–6.0 to –3.6)	–4.7*(–6.0 to –3.3)	–5.7*(–7.2 to –4.1)
≥75	375.7	537.4	259.2	173.2	248.8	113.3	–7.0*(–8.5 to –5.6)	–7.0*(–8.7 to –5.4)	–7.6*(–9.1 to –6.1)
<b>Colorectal cancer</b>									
<45	0.9	0.7	1.0	0.5	0.8	0.3	0.0(–3.9 to 4.0)	2.6(–4.1 to 6.5)	2.7*(1.1 to 5.3)
45–54	4.3	6.0	2.5	6.6	7.2	6.1	4.9*(1.7 to 8.3)	3.3*(0.5 to 7.2)	7.5*(3.4 to 11.8)
55–64	13.3	15.7	10.8	13.6	17.2	10.0	0.2(–2.3 to 2.7)	0.5(–2.1 to 3.3)	–0.4(–3.3 to 2.7)
65–74	30.7	36.2	25.2	31.1	35.7	26.4	1.5(–0.9 to 3.9)	2.1(–1.0 to 5.4)	0.5(–2.3 to 3.3)
≥75	70.4	89.8	56.5	70.6	92.4	53.2	–0.6(–2.3 to 1.1)	–1.2(–3.3 to 0.9)	–0.1(–2.3 to 2.1)

Abbreviations: CI=confidence interval, AAPC=average annual percent change.

\* $p < 0.05$ .

TABLE 3. Mortality rate (per 100,000), age-standardized mortality rate (per 100,000), and average annual percent change (%) of gastrointestinal tract cancers in the Huai River Basin, by sex and basins, 2008 and 2018.

Basin/Sites	2008						2018						AAPC (95% CI) for ASMR		
	Both		Male		Female		Both		Male		Female		Both	Male	Female
	CDR	ASMR	CDR	ASMR	CDR	ASMR	CDR	ASMR	CDR	ASMR	CDR	ASMR			
<b>Upper stream</b>															
Esophageal cancer	20.1	21.3	26.9	32.1	12.9	12.3	15.9	11.3	21.4	17.1	10.1	6.1	-6.4* (-7.8 to -5.0)	-6.1* (-7.6 to -4.6)	-7.1* (-8.9 to -5.3)
Stomach cancer	32.7	34.0	46.2	52.6	18.4	18.0	26.0	19.3	37.7	30.2	14.0	9.3	-5.3* (-6.7 to -4.0)	-5.3* (-7.4 to -3.1)	-6.0* (-8.1 to -3.9)
Colorectal cancer	8.2	8.5	9.4	10.4	6.9	6.6	10.8	8.1	12.2	9.7	9.4	6.5	1.0 (-1.6 to 3.8)	1.0 (-2.3 to 4.3)	0.8 (-2.6 to 4.3)
<b>Midstream-north</b>															
Esophageal cancer	15.9	19.7	19.2	26.9	12.4	13.7	11.9	9.4	16.0	13.5	7.7	5.5	-7.3* (-8.4 to -6.1)	-7.1* (-9 to -5.3)	-8.4* (-10.2 to -6.6)
Stomach cancer	20.4	25.4	25.2	35.4	15.2	17.0	16.6	13.8	21.6	19.2	11.6	8.6	-5.7* (-7.2 to -4.1)	-5.8* (-7.5 to -4.1)	-6.1* (-7.6 to -4.5)
Colorectal cancer	4.8	5.9	5.4	7.5	4.1	4.6	6.8	5.6	8.3	7.4	5.2	4.0	-0.1 (-2.1 to 1.8)	-0.6 (-2.7 to 1.6)	0.1 (-2.5 to 2.7)
<b>Midstream-south</b>															
Esophageal cancer	26.5	29.3	39.5	44.2	12.6	13.9	15.5	11.0	24.1	16.7	6.1	4.5	-9.5* (-10.9 to -8.1)	-9.7* (-11.3 to -8.1)	-10.5* (-13.5 to -7.3)
Stomach cancer	31.7	35.8	46.4	54.6	15.8	17.5	27.0	19.2	38.0	26.7	14.9	10.8	-6.4* (-8.0 to -4.7)	-7.0* (-8.9 to -5.0)	-6.0* (-7.6 to -4.4)
Colorectal cancer	5.3	5.7	5.9	6.4	4.7	4.9	9.1	7.0	11.2	8.7	6.7	5.2	-0.8 (-4.3 to 2.8)	0.8 (-3.1 to 4.8)	-2.9 (-6.1 to 0.3)
<b>Downstream</b>															
Esophageal cancer	42.9	47.2	54.5	67.6	30.9	30.9	33.9	21.3	43.3	29.9	24.5	13.8	-6.3* (-7.7 to -5.0)	-6.4* (-7.9 to -4.8)	-7.0* (-8.9 to -5.0)
Stomach cancer	38.5	40.7	52.6	62.1	24.0	23.4	33.3	21.7	47.2	32.7	19.6	11.9	-5.9* (-6.6 to -5.2)	-6.1* (-6.9 to -5.3)	-6.2* (-8.1 to -4.3)
Colorectal cancer	8.1	8.6	8.2	10.5	7.9	7.6	13.9	9.3	16.3	11.7	11.5	7.4	1.2 (-0.5 to 3.1)	1.4 (-0.5 to 3.4)	0.2 (-2.4 to -2.8)
<b>Yishui River Basin</b>															
Esophageal cancer	35.3	42.4	44.9	60.3	25.5	27.4	26.3	18.9	37.4	29.1	14.9	9.5	-5.7* (-7.4 to -3.9)	-5.4* (-7.2 to -3.6)	-7.1* (-9.9 to -4.3)
Stomach cancer	33.0	40.1	41.2	55.2	24.6	27.0	20.9	15.8	29.0	23.6	12.6	8.4	-7.4* (-11.9 to -2.6)	-5.9* (-10.3 to -1.4)	-8.6* (-11.5 to -5.6)
Colorectal cancer	6.1	7.3	6.9	8.8	5.3	5.8	9.6	7.1	9.6	7.7	9.6	6.6	1.7 (-0.3 to 3.8)	-0.4 (-2.5 to 1.8)	4.2* (0.1 to 8.3)

Abbreviations: CI=confidence interval, CDR=crude death rate, ASMR=age-standardized mortality rate.  
\*p<0.05.

Basin. A higher mortality rate and ASMR among men than women were observed in all given years by cancer site, and cancer mortality increased with age.

Some evidence showed that the mortality of GI tract cancers in the Huai River Basin was higher than the national level during 2004–2006. The mortality in certain counties for esophageal cancer was 2.8 times higher than national levels and for stomach cancer 1.6 times higher (3). By contrast, the reduction of mortality declined to national levels in 2018 (4), which could presumably be due to a series of prevention strategies implemented by the government. Rapidly reduced ASMRs from esophageal and stomach cancers can be observed, which is consistent with previous findings from the Chinese Burden of Disease 2017 study (2). With economic growth and population aging, the increased number of cancer deaths was closely related to changing patterns of dietary habits and lifestyles. Previous studies showed healthy lifestyle changes among the general public have associations with reduced deaths, such as smoking cessation, low-sodium diet, restricted drinking and processed meat intake, sufficient consumption of vegetables and fruits, and so forth (7–8). Among high-risk individuals, earlier detection, diagnosis, and treatment were introduced for specific cancer sites, such as *Helicobacter pylori* infection screening, which may improve the effectiveness of disease management and prolong the survival time of patients and reduce mortality.

Previous studies showed increasing trends of colorectal cancer death (9). In this study, the ASMR of colorectal cancer did not differ significantly, while mortality increased and the ASMR trended upward among young people during the study period. The diet-structure and other personal risk behaviors, such as lack of physical activity, high-fat, and low-fiber diet intake have become increasingly common and could increase colorectal cancer mortality (7). Colorectal cancer statistics (2020) reported that colorectal cancer death rates increased by 1.3% annually in those aged younger than 50 years from 2008 to 2017 in the United States, which is similar to results found in this study (9). The rapid growth of obesity among young people could contribute to increasing colorectal cancer death, and lifestyle differences may be the main reason contributing to the mortality differences between men and women. For example, many studies showed that unhealthy lifestyle habits such as drinking, smoking, and insufficient vegetable and fruit intake for men (7). Exploring reasons contributing to stable periods is difficult, and the observation period needs to be

extended to determine trends in the long-term mortality in the future.

Unsafe sanitation was the main environmental risk factor of GI tract cancers, including drinking untreated water, using non-sanitary toilets, discharging wastewater freely, and increasing usage of pesticides (10). Environmental governance of water supplies and transitions to a greener economy might play a crucial role in effectively reducing cancer mortality. Nevertheless, a higher ASMR in the downstream basin and Yishui River Basin could be speculated as partially related to inferior sanitation conditions compared to upstream areas, which reminded stakeholders of promoting geo-specific measures to ameliorate the situation.

This study was subject to some limitations. First, the geographical distribution of the Huai River made the midstream-south basin classification include just one county, and the results could be affected by the quality of the reporting area. Second, cause-of-death diagnosis ascertainment bias was inevitable, which required redistribution algorithms for undetermined codes.

In summary, GI tract cancer deaths over the 11 years in the Huai River Basin showed significant improvements. The ASMR of GI tract cancer decreased or remained stable primarily due to enhancements in health awareness, environmental governance, and improvements in access to prevention, diagnosis, and treatment. Therefore, tailored strategies should be developed for target population.

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