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Divergent trends in the burden of esophageal, gastric, and liver cancers in China

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ABSTRACT

Background: While China's socioeconomic transformation has driven divergent trends in gastrointestinal cancers, comprehensive data on esophageal, gastric, and liver cancer burden remain limited. This study examines the global burden of esophageal, gastric, and liver cancers in 2022 and analyzes the trends of age-standardized incidence and mortality rate (ASRs) in China from 2000 to 2018, thereby providing evidence for the formulation of cancer control strategies.

Methods: The global burden of esophageal, gastric and liver cancers including the estimated number of cases and deaths and the ASRs for incidence and mortality were from GLOBALCAN 2022 dataset. Data from 22 cancer registries in China were employed for the trend analysis of the ASRs for incidence and mortality of these three cancers. The Joinpoint model was used to compute the average annual percentage change (AAPC) of the incidence and mortality of the three cancers from 2000 to 2018.

Results: Globally, esophageal, gastric and liver cancers accounted for 11.8 % of incident cancer cases and 19.1 % of cancer deaths. China bore a disproportionately high burden, representing 43.8 %, 37.0 %, and 42.4 % of global esophageal, gastric, and liver cancer cases respectively, and 42.1 %, 39.4 %, and 41.7 % of corresponding deaths. However, the ASRs for incidence and mortality for all three cancers declined significantly in China (2000–2018), with absolute case numbers decreasing for gastric and esophageal cancers during 2010–2022. Age-specific analysis revealed most pronounced declines in incidence and mortality in populations under 40 years old, with AAPCs of less than –6.0 % for esophageal cancer, around –4.0 % for gastric cancer, and approximately –2.0 % for liver cancer.

Conclusions: China has achieved remarkable progress in controlling esophageal, gastric and liver cancers, yet these malignancies remain major public health challenges. Future efforts should intensify existing prevention measures while expanding screening programs, particularly for aging populations. These findings offer valuable insights for regions undergoing similar epidemiological transitions.

1. Introduction

Cancer remains one of the most formidable global health challenges, accounting for nearly 10 million deaths annually and imposing tremendous socioeconomic burdens on healthcare systems worldwide.[1,2] As one of the world's most populous nation, China exhibits unique epidemiological patterns of cancer burden shaped by its rapid socioeconomic transition, evolving lifestyle factors, and heterogeneous healthcare access.[3,4] The country's unprecedented economic growth over recent decades has spurred significant improvements in medical infrastructure, cancer screening programs, and preventive interventions, driving measurable shifts in the landscape of cancer incidence and mortality.[5,6]

Historically, China's overall cancer burden had risen steadily, primarily due to population aging and the persistent prevalence of traditional risk factors including tobacco use, and excessive alcohol consumption.[7-10] However, emerging evidence reveals intriguing divergences in trends among major gastrointestinal malignancies, particularly esophageal, gastric, and liver cancers.[11,12] These differential patterns likely reflect the complex interplay between China's multifaceted cancer control strategies, ongoing socioeconomic development, and changing exposure patterns across generations, creating a unique natural experiment in cancer epidemiology that warrants comprehensive investigation.

In this context, this study aims to comprehensively analyze the divergent trends in the burden of esophageal, gastric, and liver cancers in

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China. By presenting the global situation in 2022 and in-depth analysis of the trends in China from 2000 to 2018, we aim to inform evidence-based prioritization in China's national cancer control initiatives, such as the "Healthy China 2030" initiative, while offering transferable lessons for other regions undergoing similar epidemiological transitions.

2. Materials and methods

2.1. Data source

The GLOBOCAN 2022 database, accessible via the Global Cancer Observatory (https://gco.iarc.fr/today/home), served as the primary data source for this study.[13] This comprehensive repository provides country-specific estimates of cancer incidence and mortality, stratified by cancer site and sex. We conducted a descriptive secondary analysis of these data to evaluate the burden of esophageal, gastric, and liver cancers globally. Data from 22 cancer registries in China[3] were utilized for the trend analysis of age-standardized rates (ASR) of incidence and mortality from 2000 to 2018. The estimated numbers of cases and deaths of all cancers, esophageal cancer, gastric cancer, and liver cancer in China in 2010,[14] 2011,[15] 2012,[16] 2013,[17] 2014,[18] 2015,[19] 2016,[20] and 2022[21] were compiled from a series of studies reported by China National Cancer Center. To calculate the average annual percentage change (AAPC) from 2000 to 2018, the population numbers and the counts of cancer incidence and deaths for each age group were retrieved from the China Cancer Registry Annual Reports. These reports are authoritative sources that offer detailed and accurate information on cancer-related statistics in China.

2.2. Statistics

We analyzed the ASRs and absolute counts of new cases and deaths for esophageal, gastric, and liver cancers across six continents and several countries selected. To assess socioeconomic influences, world regions and countries were stratified into quartiles based on the Human Development Index (HDI). Subsequently, we compared ASRs across these HDI categories to identify potential disparities.

For esophageal, gastric, and liver cancers in China, Joinpoint regression was applied to analyze the incidence and mortality trends stratified by age.[22] To assess the magnitude and direction of trends from 2000 to 2018, the AAPC and the corresponding 95 % confidence interval (CI) were calculated every 5 years. The AAPC represents a geometrically weighted average of the annual percentage changes derived from Joinpoint trend analysis, with weights assigned according to the length of each segment during the specified time interval. Joinpoint regression was performed using the Joinpoint Regression Program 5.1.0 (National Cancer Institute, USA).

3. Results

3.1. Global incidence distribution of esophageal, gastric, and liver cancers

Based on the GLOBOCAN 2022 data presented in Table 1, the global burden of esophageal, gastric, and liver cancers exhibited distinct epidemiological patterns. Collectively, there were 2,345,974 new cases (ASR 22.7/100,000), accounting for 11.8 % of all cancer diagnoses worldwide.[13]

Among these three malignancies, gastric cancer was the most prevalent, with 968,784 cases (ASR 9.2/100,000), followed by liver cancer (866,136 cases, ASR 8.6/100,000) and esophageal cancer (511,054 cases, ASR 5.0/100,000). Pronounced gender disparities were observed across all three cancers. Specifically, the ASR in males were 2.9-fold, 2.1-fold, and 2.6-fold higher than those in females for esophageal, gastric, and liver cancers, respectively.

Striking geographical disparities were evident, with Asia bearing 71.7 % of the combined burden. Notably, China alone accounts for a disproportionate 43.8 % of global esophageal cancer cases, 37.0 % of gastric cancer cases, and 42.4 % of liver cancer cases. Mongolia emerged as an extreme outlier with the world's highest incidence rates for both esophageal (ASR 15.7/100,000) and liver cancers (ASR 96.1/100,000). Russia's gastric cancer incidence (ASR 13.7/100,000) was comparable to that of East Asian countries, on par with China.

The analysis also revealed unexpected correlations with the HDI. Very high and high HDI countries exhibited elevated burdens of gastric and liver cancers compared to middle and low HDI countries.

3.2. Global mortality distribution of esophageal, gastric, and liver cancers

The data in Table 2 revealed the global mortality distribution of esophageal, gastric, and liver cancers in 2022, highlighting significant disparities across the world. Collectively, these three types of cancers resulted in 1,864,291 deaths (ASR 17.7/100,000), accounting for 19.1 % of all cancer-related deaths globally.[13]

Among them, liver cancer had the highest mortality, with 758,725 deaths (ASR 7.4/100,000), followed by gastric cancer, which caused 660,175 deaths (ASR 6.1/100,000), and esophageal cancer, responsible for 445,391 deaths (ASR 4.3/100,000). Notably, the gender gap in mortality was more pronounced than that in incidence for all three cancers. Specifically, the male-to-female ratio for esophageal cancer deaths reached approximately 3.0.

Asia emerged as the region most severely affected by the mortality of these cancers, which contributed to 71.0 % of combined mortality of these three cancers. Remarkably, China alone accounted for 42.1 %, 39.4 % and 41.7 % of global esophageal, gastric and liver cancer deaths, respectively. Mongolia stood out as an extreme case, with extremely high mortality rates for all three cancers. In particular, its liver cancer mortality rate (ASR 80.2/100,000) was around 11 times higher than the global average. Russia's gastric cancer mortality (ASR 9.2/100,000) reached the levels seen in East Asian countries and even exceeded those of South Korea and Japan.

Consistent with the incidence patterns, very high and high HDI countries had elevated mortality for gastric cancer and liver cancer, mainly due to the situation in East Asian nations. The mortality-to-incidence ratios varied greatly depending on the cancer type and region. Globally, liver cancer had the highest fatality rate, reaching 87.6 %, which was especially prominent in high-burden regions such as Mongolia and China.

3.3. Temporal trends of esophageal, gastric, and liver cancers in China (2000–2018)

Between 2000 and 2018, China experienced divergent trends in cancer epidemiology (Fig. 1 and Supplementary Table 1). While the overall incidence of all cancers showed a steady rise, the three major gastrointestinal cancers-esophageal, gastric, and liver cancers-exhibited significant declines in both genders. Among males, esophageal cancer exhibited the most substantial reduction. The ASR dropped from 21.7 to 11.0 per 100,000, representing a 49.3 % decline. This was followed by gastric cancer with a 40.6 % decrease and liver cancer with a 34.2 % decrease. Among females, esophageal cancer also exhibited the most pronounced decline in ASR, reaching 64.5 %. Subsequently, gastric cancer showed a 38.6 % decrease, and liver cancer had a 37.4 % decrease.

In terms of mortality, from 2000 to 2018, the mortality rates for all cancers decreased in both males (a 22.9 % decline) and females (a 21.7 % decline) (Fig. 1 and Supplementary Table 1). However, these declines were less pronounced compared to those of esophageal, gastric, and liver cancers. Among females, the mortality of esophageal and gastric cancers decreased by >50 %, specifically 69.5 % and 54.5 % respectively, while liver cancer mortality decreased by 45.2 %. Among males, the mortality of esophageal, gastric, and liver cancers decreased by >40 %, at 49.2 %, 48.9 %, and 42.2 % respectively.

Table 1
Estimated incidence of esophageal, gastric, and liver cancers in 2022.

	Esophageal cancer		Gastric cancer		Liver cancer		All 3 cancers	
Population	Number	ASR (1/100,000)	Number	ASR (1/100,000)	Number	ASR (1/100,000)	Number	ASR (1/100,000)
World								
Total	511,054	5.0	968,784	9.2	866,136	8.6	2,345,974	22.7
Male	365,225	7.6	627,458	12.8	600,676	12.7	1,593,359	33.0
Female	145,829	2.6	341,326	6.0	265,460	4.8	752,615	13.4
Countries								
China	224,012	8.3	358,672	13.7	367,657	15.0	950,341	37.1
Japan	19,926	4.8	126,724	27.6	41,388	9.2	188,038	41.6
United States of America	18,747	2.8	25,554	4.1	43,492	6.8	87,793	13.7
Russian Federation	9345	3.5	38,883	13.7	11,748	4.3	59,976	21.4
Brazil	10,985	3.8	23,021	7.6	13,599	4.5	47,605	15.8
South Korea	2437	2.2	29,267	27.0	14,791	13.7	46,495	42.8
Germany	7310	3.5	14,088	6.4	9959	4.5	31,357	14.5
France	4942	3.6	7673	4.9	12,172	7.8	24,787	16.2
United Kingdom	9601	5.9	6034	3.6	8223	4.8	23,858	14.4
Australia	1755	3.2	2837	5.3	3333	7.2	7925	15.7
South Africa	3312	6.4	1919	3.6	2650	4.9	7881	14.8
Mongolia	401	15.7	1000	35.5	2668	96.1	4069	147.3
Continents								
Asia	382,892	6.2	691,791	11.0	607,361	10.0	1,682,044	27.3
Europe	53,513	3.3	135,610	7.9	88,871	5.1	277,994	16.3
Latin America and the Caribbean	20,366	2.4	74,379	8.5	42,769	5.0	137,514	15.8
Africa	29,965	3.6	33,352	4.0	73,844	8.5	137,161	16.2
Northern America	21,888	2.9	29,675	4.1	48,485	6.7	100,048	13.7
Oceania	2430	3.3	3977	5.5	4806	7.5	11,213	16.3
HDI								
Very high HDI country	107,524	3.1	350,769	9.7	239,368	7.0	697,661	19.8
High HDI country	261,867	6.1	479,344	11.4	495,705	12.3	1,236,916	29.8
Medium HDI country	112,931	5.3	112,658	5.3	91,923	4.3	317,512	14.9
Low HDI country	28,588	4.3	25,717	3.9	38,839	5.5	93,144	13.6

Abbreviations: ASR, age-standardized incidence and mortality rate; HDI, human development index.

Table 2
Estimated mortality of esophageal, gastric, and liver cancers in 2022.

	Esophageal cancer		Gastric cancer		Liver cancer		All 3 cancers	
Population	Number	ASR (1/100,000)	Number	ASR (1/100,000)	Number	ASR (1/100,000)	Number	ASR (1/100,000)
World								
Total	445,391	4.3	660,175	6.1	758,725	7.4	1,864,291	17.7
Male	318,433	6.5	427,575	8.6	521,826	10.9	1,267,834	26.0
Female	126,958	2.2	232,600	3.9	236,899	4.1	596,457	10.3
Countries								
China	187,467	6.7	260,372	9.4	316,544	12.6	764,383	28.7
Japan	12,161	2.6	43,807	7.2	26,420	4.3	82,388	14.1
United States of America	16,469	2.4	10,976	1.6	30,931	4.4	58,376	8.4
Russian Federation	8359	3.1	27,306	9.2	11,377	4.0	47,042	16.3
Brazil	10,393	3.5	18,138	5.9	13,041	4.3	41,572	13.7
South Korea	6399	2.9	8729	3.6	8712	3.5	23,840	10.0
Germany	1521	1.2	8517	6.5	12,595	10.7	22,633	18.4
France	8595	4.9	4232	2.3	7326	4.0	20,153	11.2
United Kingdom	4304	2.6	4963	2.9	10,478	5.9	19,745	11.4
Australia	3025	6.0	1622	3.1	2401	4.5	7048	13.6
South Africa	1526	2.6	1335	2.3	2591	4.8	5452	9.7
Mongolia	363	14.4	854	31.5	2164	80.2	3381	126.1
Continents								
Asia	329,803	5.3	462,606	7.2	530,928	8.7	1,323,337	21.2
Europe	47,212	2.8	95,431	5.2	79,091	4.2	221,734	12.2
Latin America and the Caribbean	28,276	3.5	28,730	3.5	70,315	8.2	127,321	15.2
Africa	18,895	2.2	57,895	6.5	39,351	4.5	116,141	13.2
Northern America	19,116	2.4	13,367	1.7	35,075	4.4	67,558	8.5
Oceania	2089	2.7	2146	2.8	3965	5.7	8200	11.2
HDI								
Very high HDI country	88,639	2.5	183,126	4.7	196,390	5.4	468,155	12.6
High HDI country	222,730	5.1	355,361	8.1	438,036	10.7	1,016,127	23.8
Medium HDI country	106,923	5.0	98,721	4.7	86,943	4.1	292,587	13.8
Low HDI country	26,967	4.1	22,728	3.5	37,075	5.3	86,770	12.8

Abbreviations: ASR, age-standardized incidence and mortality rate; HDI, human development index.

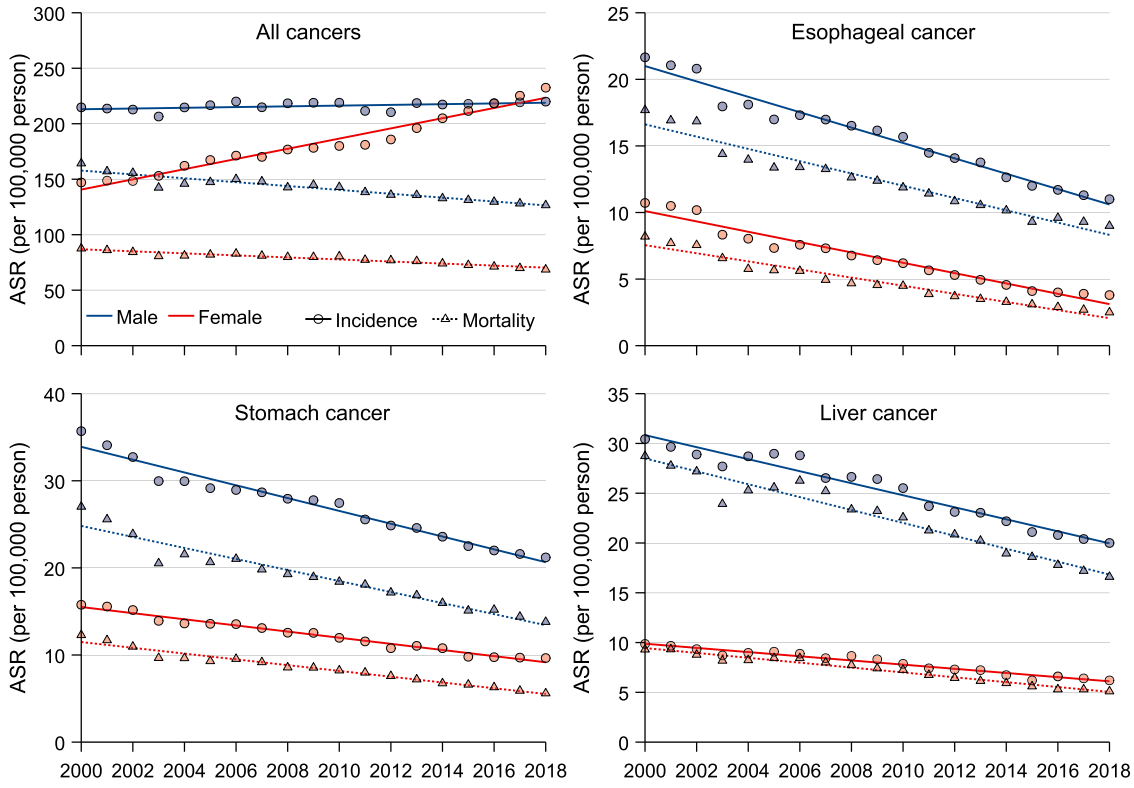

Fig. 1. Trends in age-standardized incidence and mortality rates of all cancers, esophageal cancer, gastric cancer, and liver cancer in China from 2000 to 2018. ASR, age-standardized incidence and mortality rate.

3.4. Trends in estimated case numbers of esophageal, gastric, and liver cancers in China (2010–2022)

The analysis of absolute estimated case numbers revealed distinct patterns for gastrointestinal cancers compared to overall cancer trends in China from 2010 to 2022 (Fig. 2 and Supplementary Table 2). While both total cancer incidence cases and mortality cases demonstrated a steady increase, the three major gastrointestinal cancers showed varied trajectories.

Esophageal cancer exhibited the most favorable trend, representing a 22.1 % reduction in incidence and 10.1 % reduction in mortality. Gastric cancer cases also declined, albeit more moderately and consistently. The incidence and mortality of gastric cancer decreased by 11.3 % and 9.5 %, respectively.

In contrast to the trends in ASR, liver cancer displayed a gradual increase in both the absolute numbers of incidence and mortality over the study period. The estimated number of liver cancer cases rose from 358,840 in 2010 to 367,700 in 2022, and the estimated number of liver cancer deaths increased from 312,432 in 2010 to 316,500 in 2022. This upward trend persisted despite the declining ASR, suggesting demographic factors, particularly population growth and aging, may have contributed to the growing absolute burden of liver cancer.

3.5. Age-specific trends in cancer burden of esophageal, gastric and liver cancers (2000–2018)

The age-stratified analysis revealed significant heterogeneity in temporal patterns across cancer types and age cohorts (Fig. 3). For all cancers combined, there was a concerning rise in incidence rates among populations below 55 years, in contrast to modest but consistent mortality declines across all age groups.

Gastric cancer exhibited the most substantial and widespread improvements, with the ASR for both incidence and mortality showing declines across nearly all age groups. The most dramatic reductions occurred in populations under 40 years (AAPC: around –4.0 % for both incidence and mortality), and these improvements gradually diminished in older cohorts. Esophageal cancer also displayed similarly favorable trends, with significant reductions in both incidence and mortality for all age groups except those above 70 years. The declines were most pronounced in younger populations, reaching an AAPC of less than –6.0 % in the under 40 group. Liver cancer presented a distinct epidemiological profile, with more modest but consistent improvements across populations under 80 years. While the AAPC showed less age variation than other gastrointestinal malignancies, the under 40 cohort still demonstrated accelerated declines (maintaining relatively stable AAPC values of around -2.0 %), likely reflecting the population-level impact of universal Hepatitis B virus (HBV) vaccination programs initiated in the 1990s.

4. Discussion

Our analysis of 2022 GLOBOCAN data reveals that esophageal, gastric, and liver cancers remain major global health burdens with striking geographical disparities. Asia, particularly China, shoulders the heaviest disease burden of these malignancies. Despite comprising about 20 % of the world's population, China bore a disproportionately high burden, representing 43.8 %, 37.0 %, and 42.4 % of global esophageal, gastric, and liver cancer cases respectively, and 42.1 %, 39.4 %, and 41.7 % of corresponding deaths. This substantial overrepresentation underscores the urgent need for sustained and targeted interventions. Encouragingly, our findings reveal consistent downward trends in both incidence and mortality rates for all three cancers between 2000 and 2018. Notably, for gastric and esophageal cancers, these improvements extend to reductions in absolute case numbers, reflecting the efficacy of China's expanding cancer prevention and control measures.

The most marked improvements have been observed in esophageal cancer, particularly among individuals under 40 years of age, where the AAPC reached –6 %. This substantial decline can be attributed

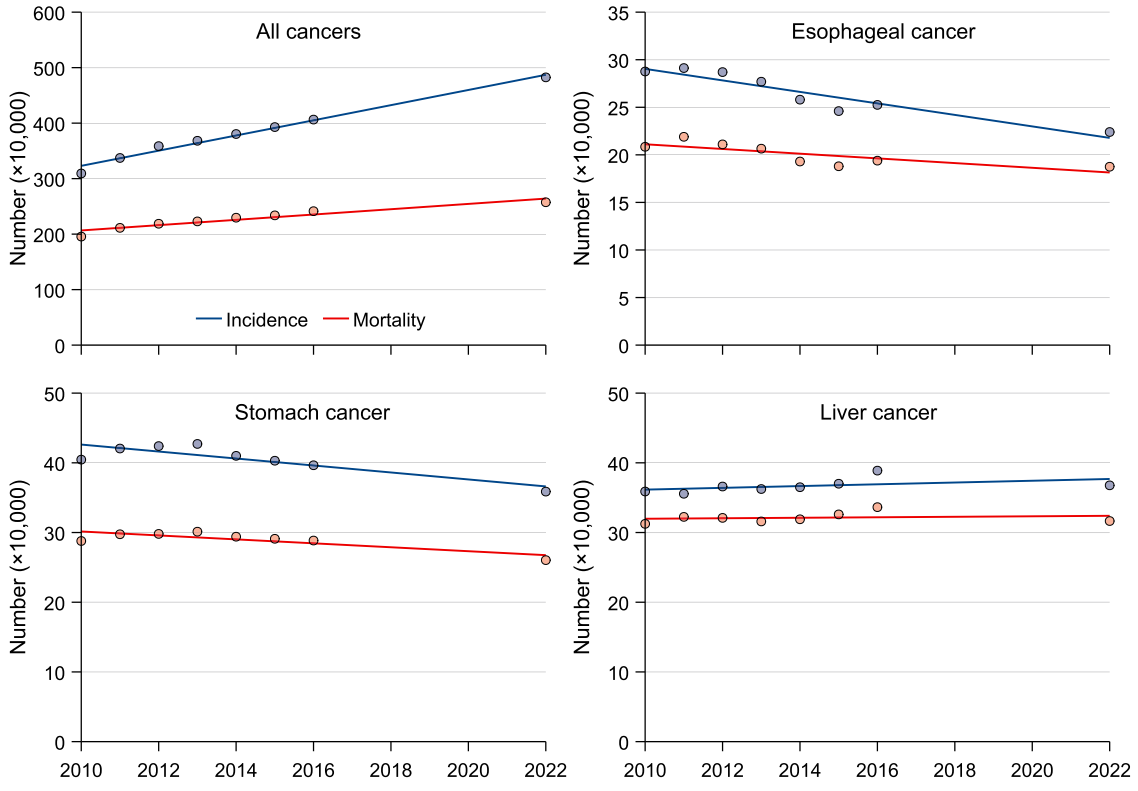

Fig. 2. Trends in the number of cases and deaths of all cancers, esophageal cancer, gastric cancer, and liver cancer in China from 2010 to 2022.

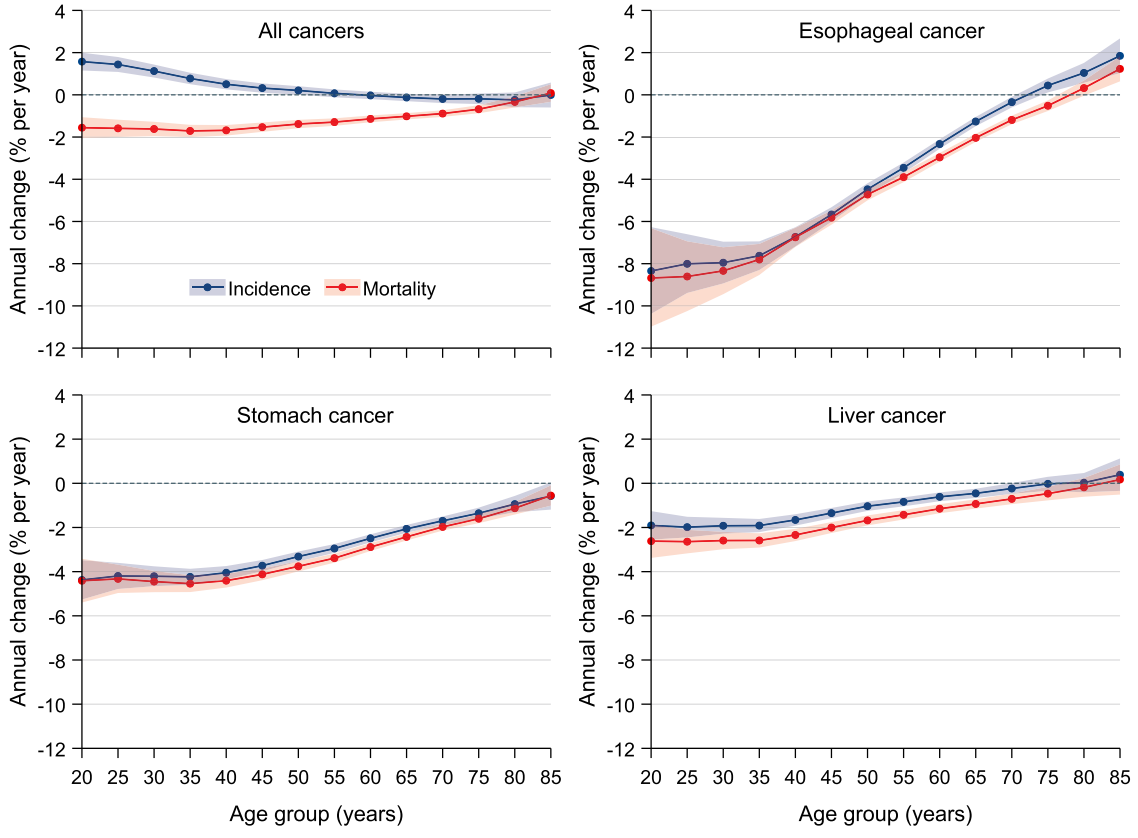

Fig. 3. Age-specific average annual percent change in all cancers, esophageal cancer, gastric cancer, and liver cancer in China from 2000 to 2018.

to two major factors. First, China's rapid economic development has transformed dietary patterns, which plays a crucial role given that most esophageal cancers in China are squamous cell carcinomas strongly associated with behavioral factors.[23] Historically, high consumption of preserved/pickled foods containing carcinogenic N-nitroso compounds, along with habits of consuming extremely hot beverages and alcohol, contributed significantly to disease burden.[24,25] However, economic growth has brought urbanization, widespread refrigeration, and greater access to fresh produce, leading to decreased reliance on traditional salt-preserved vegetables and fermented foods that were once dietary staples in rural areas. These changes have likely driven the observed incidence declines, particularly among generations born after the 1980s who experienced this nutritional transition during their formative years.

Second, the implementation of nationwide endoscopic screening programs has been instrumental in driving down esophageal cancer incidence and mortality rates. Since 2005, China has established three major national cancer screening initiatives, all of which include systematic endoscopic screening for esophageal cancer.[5,26] Robust evidence, including our team's recent multicenter randomized controlled trial, confirms that this organized screening approach in high-risk areas significantly reduces both incidence and mortality of esophageal cancer.[27-29]

However, while incidence and mortality rates have declined more sharply in younger age groups, the elderly population remains a critical target for esophageal cancer prevention and control. China's current screening guidelines recommend screening for individuals aged 45–74 years.[30] Yet, our study reveals a persistent increase in esophageal cancer incidence among those aged 75 and older. This suggests a need to optimize screening strategies by increasing the ending ages of screening, though such adjustments must be carefully evaluated for cost-effectiveness and health economic impact.

Gastric cancer exhibited similarly favorable trends, with incidence and mortality declining across all age groups, particularly among younger individuals (AAPC up to –4 %). The elevated incidence of gastric cancer in China has been primarily attributed to high *Helicobacter pylori* (*H. pylori*) infection rates and the widespread consumption of traditionally salted and smoked foods.[31] As sanitary conditions improve and antibiotic use becomes widespread, the incidence of *H. pylori* infection is gradually declining, probably leading to a decrease in gastric cancer rates.[32] In addition, the occurrence and development of gastric cancer are associated with unhealthy lifestyles.[33] With a growing awareness of health, dietary habits are gradually improving, characterized by increased intake of fresh vegetables and fruits, and reduced salt in processed foods, consequently lowering the risk of gastric cancer. Endoscopic screening may also contribute to these declines. Similar to esophageal cancer, China's national cancer screening programs also include gastric cancer screening, and studies have confirmed that a single upper gastrointestinal endoscopy can reduce both incidence and mortality of gastric cancer.[28,29]

Nevertheless, the slower decline in older age groups suggests that early-life exposures continue to influence cancer risk in later years. Notably, recent data indicate that *H. pylori* infection remains prevalent in China, with an overall infection rate of 40.66 % and an even higher rate of 43.45 % among adults.[34] Strong evidence confirms that *H. pylori* eradication can significantly reduce gastric cancer incidence and mortality, underscoring the importance of implementing nationwide *H. pylori* screening and treatment programs.[35]

Liver cancer presents a more complex epidemiological profile. While incidence and mortality rates have shown modest declines, the absolute number of cases has actually slightly increased, reflecting demographic growth and population aging. The most significant improvements have occurred in younger age groups, attributable largely to the successful implementation of universal HBV vaccination programs in 1990s.[36-38] However, older cohorts have shown stagnant trends, likely due to persistent HBV/ Hepatitis C virus (HCV) infections, ongoing aflatoxin exposure in some regions, and alcohol-related liver disease.

Unlike esophageal and gastric cancers, the impact of screening on liver cancer mortality remains uncertain. Although liver cancer screening, primarily based on alpha-fetoprotein (AFP) testing and ultrasound, has been incorporated into the three national programs, current evidence regarding its effectiveness in reducing mortality is inconclusive. While our recent study suggest that AFP-ultrasound combined surveillance may improve survival rates, the relatively low sensitivity of AFP for early-stage liver cancer detection raises questions about its population-level impact.[39] This uncertainty underscores the urgent need to identify more sensitive and specific biomarkers for liver cancer early detection, as well as to develop improved screening strategies.

In addition, while significant progress has been made in controlling esophageal, gastric, and liver cancers among populations under 40, mortality reductions have been less pronounced in aging populations, particularly those aged 70+. This attenuated effect likely reflects the cumulative impact of prolonged exposure to risk factors during earlier life stages, which underscores the critical need to expand targeted screening programs for elderly populations.

5. Conclusions

China has made remarkable progress in controlling esophageal, gastric, and liver cancers, as evidenced by significant declines in incidence and mortality rates. These improvements, particularly among younger populations, reflect the success of nationwide interventions, including economic development-driven dietary improvements, endoscopic screening programs for upper gastrointestinal cancers, and universal HBV vaccination for liver cancer prevention. However, these malignancies remain major public health challenges, with China still bearing a disproportionate share of the global burden.

Moving forward, cancer control strategies should adopt a dual approach: intensifying primary prevention measures (*e.g., H. pylori* treatment, dietary modifications, and alcohol/tobacco control) and optimizing secondary prevention by expanding targeted screening programs, particularly for aging populations where risk factor accumulation has led to persistently high disease burden. Special attention should be given to revising age cutoffs for screening eligibility and developing more sensitive early detection methods for liver cancer. These findings not only inform China's ongoing "Healthy China 2030" initiative but also provide a valuable framework for other regions undergoing similar epidemiological transitions.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Author contributions

C.W. designed the study. X.C. conducted the data quality control. X.Y., W.J. and W.Y. analyzed the data. C.W. supervised the whole study. X.Y. drafted the original manuscript. C.W. and X.C. revised the manuscript. All authors reviewed the manuscript drafts and approved the final manuscript.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jncc.2025.05.001.

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