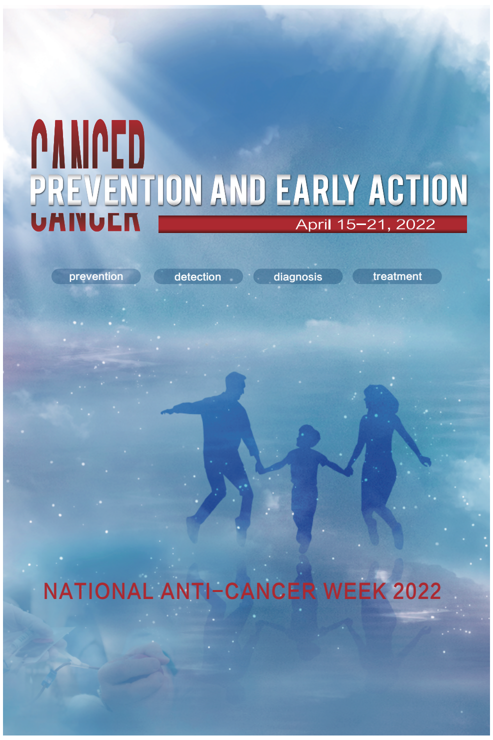
ISSN 2096-7071
CN 10-1629/R1

CHINA CDC WEEKLY

Vol. 4 No. 15 Apr. 15, 2022

CCDC weekly

中国疾病预防控制中心周报



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This week's issue was organized by Guest Editor Jing Wu.

Foreword

Cancer Prevention and Early Action

Jing Wu

April 15–21, 2022 is the 28th "National Anti-Cancer Week" and the theme is "Cancer prevention and early action" (*1*). The *China Statistical Yearbook 2021* (*2*) published by the National Bureau of Statistics indicated cancer was the first leading cause of death for urban residents in China, and the third leading cause of mortality for rural residents. The urban and rural cancer mortality rates in China were 161.4/100,000 and 161.9/100,000 in 2020.

Cancer prevention and early action are key to reducing the disease burden of cancer and represented by support from the Chinese government for four major projects. First, the Rural Cancer Early Diagnosis and Treatment Project was launched in 2005, covering 31 provincial-level administrative divisions (PLADs) and 252 project sites. The second was the Huai River Basin Cancer Early Diagnosis and Early Treatment Project launched in 2007, which was mainly aimed at the early diagnosis and early treatment of esophageal cancer and liver cancer. The third was Early Detection through Screening Project for female breast and cervical cancer in rural areas in 2009. The last project was the Urban Cancer Early Diagnosis and Early Treatment Project launched in 2012, which covered urban residents of more than 60 regions in 26 PLADs. In 2019, China also issued a series of policies and guidelines such as the "Healthy China Initiative: Implementation Plan for Cancer Prevention and Control (2019–2022)" and the "Healthy China Initiative (2019–2030)" to guide China's cancer prevention and control.

China CDC takes advantage of advances in monitoring, multidisciplinary cooperation, local program implementation, and basic prevention, and it can maximize its four-level system (national, provincial, municipal, and county) to strengthen cancer research at the national level and vigorously promote regional practical experience to the whole country in the range (*3*).

The articles in this special issue range from the burden of disease due to cancer in China, cancer mortality and cause eliminated life expectancy in key areas of four provinces, the economic burden of malignant tumors in Yichang City, and colorectal cancer screening in China. We hope to contribute to the in-depth analysis of cancer situation in China from a multi-dimensional perspective, in order to disseminate cancer prevention knowledge, advance basic options for public policy formulation, and promote early interventions at home and abroad.

doi: 10.46234/ccdcw2022.075

Submitted: April 08, 2022; Accepted: April 13, 2022

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Preplanned Studies

Burden of Disease Due to Cancer — China, 2000–2019

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Summary

What is already known about this topic?

Cancer is a major global public health problem and the leading cause of death in China. China has a large population, and therefore has a significant proportion of the global burden of cancer.

What is added by this report?

The age-standardized incidence of cancer has increased in China, while the cancer mortality rate has decreased. Compared with younger age groups, individuals over 70 have a greater burden of cancer. Digestive tract cancer and breast cancer should be targeted for prevention, treatment, and control.

What are the implications for public health practices?

To effectively reduce the burden of cancer, early screening of key populations and age groups should be strengthened, and targeted and precise prevention and control strategies should be adopted.

According to the World Health Organization (WHO), cancer is the second most common cause of death in the world (*1*). China has made considerable efforts to prevent and control cancer, but cancer is still a major national health problem. To understand the current burden of cancer in China, we analyzed the most recent estimates from the Global Burden of Disease Study (GBD 2019). GBD 2019 estimated the burden of disease in China using multiple data sources with unified and internationally comparable methods to comprehensively evaluate cancer mortality and risk factor trends in China. Compared to the standardized incidence of cancer in 2000, the standardized incidence of cancer increased in 2019, the standardized mortality rate decreased, and the number of deaths increased. People older than 70 years of age had the largest burden of cancer in 2019. In particular, breast cancer among females rose in the ranking, ranked by disability-adjusted life years (DALYs), among both sexes in 2019 in China and therefore requires more attention. To reduce the burden of cancer in China, effective cancer prevention and control measures are essential.

Data from 2000 and 2019 GBD studies for comparisons and analyses that included incidence, prevalence, mortality, and burden of cancer were extracted. Standardized rates were based on international populations in 2010 and calculations were based on standardized populations. DALYs refers to the total number of healthy life years lost from the time of illness onset through death, including years of life lost due to premature mortality (years of life lost; YLLs) and years lived with disability (YLDs).

Table 1 shows the incidence, prevalence, and mortality of cancer by gender in China. In 2019, cancer incidence, prevalence, and mortality were 244.75, 973.80, and 140.66 per 100,000 total population — increased by 15.85%, 68.62%, and −18.04%, respectively, compared to those of 2000. The cancer burden among men was significantly higher than among women. The 2019 standardized DALYs, YLLs, and YLDs increased by −24.14%, −25.14%, and 40.77%, respectively, compared to those of 2000.

As shown in Table 2, the burden of cancer was the greatest in people over 70 years of age, with standardized incidence, prevalence, and mortality of 1,545.58 (per 100,000), 4,137.77 (per 100,000), and 1,173.86 (per 100,000), respectively, in 2019. The incidence of cancer in the 15–49 age group increased 36.72% compared to that of 2000.

As shown in Table 3, the leading five cancer categories, as ranked by DALYs rate, were tracheal, bronchial, and lung cancers; stomach cancer; colon and rectal cancers; esophageal cancer; and liver cancer. There were large differences by gender in 2019, and by 2019, the DALYs rate rankings of cancer, regardless of gender, changed greatly compared to those of 2000. However, for both men and women, lung cancer DALYs rate consistently ranked first. The 2019 DALYs rate rankings significantly changed compared to those of 2000, such that the ranking of colon and rectal cancer changed from sixth to third, liver cancer among men changed from third to fifth, and breast cancer among women changed from fourth to second.

TABLE 1. Overall incidence, prevalence, deaths, and burden indicators of all cancers, 2000 and 2019 in China.

Gender	Year	Incidence		Prevalence		Deaths		DALYs		YLLs		YLDs	
		N	P’	N	P’	N	P’	N	P’	N	P’	N	P’
Male													
	2000	1,410,333	259.59	3,199,721	547.30	1,170,487	228.45	33,786,674	5,668.74	33,362,468	5,593.31	424,206	75.43
	2019	2,860,622	309.56	9,723,166	1,030.87	1,746,217	197.23	43,473,268	4,521.80	42,425,745	4,409.62	1,047,523	112.17
	2019 *vs.* 2000 (%)*	102.83	19.25	203.88	88.35	49.19	−13.67	28.67	−20.23	27.17	−21.16	146.94	48.71
Female													
	2000	1,004,000	170.90	3,824,258	620.22	694,220	124.12	20,530,328	3,385.92	20,149,716	3,323.05	380,612	62.87
	2019	1,897,540	191.89	9,056,014	935.05	965,678	95.79	23,867,041	2,402.12	23,055,521	2,319.25	811,520	82.87
	2019 *vs.* 2000 (%)*	89.00	12.28	136.80	50.76	39.10	−22.82	16.25	−29.06	14.42	−30.21	113.21	31.81
Both													
	2000	2,414,332	211.27	7,023,979	577.51	1,864,707	171.62	54,317,002	4,496.44	53,512,183	4,428.32	804,819	68.13
	2019	4,758,162	244.75	18,779,180	973.80	2,711,895	140.66	67,340,309	3,411.12	65,481,266	3,315.22	1,859,042	95.90
	2019 *vs.* 2000 (%)*	97.08	15.85	167.36	68.62	45.43	−18.04	23.98	−24.14	22.37	−25.14	130.99	40.77

Note: N: Number of cases for incidence, prevalence, and deaths; number of person years for disability-adjusted life years (DALYs), years of life lost (YLLs), and years lived with disability (YLDs).
P’: Standardized rate calculated using the 2010 National Census as the standard population, expressed as 1/100,000.
* Percent change (%) was calculated as difference value between 2019 and 2000 divided by quantity in 2000.
Abbreviations: DALYs=disability-adjusted life years; YLLs=years of life lost; YLDs=years lived with disability.

TABLE 2. Incidence, prevalence, deaths, and burden indicators of cancer, 2000 and 2019 in China.

Age group (years)	Year	Incidence		Prevalence		Deaths		DALYs		YLLs		YLDs	
		N	P’	N	P’	N	P’	N	P’	N	P’	N	P’
<15													
	2000	105,651	34.28	711,665	230.88	32,244	10.46	2,713,576	880.34	2,656,207	861.73	57,369	18.61
	2019	60,959	27.12	459,596	204.47	11,053	4.92	946,887	421.25	912,783	406.08	34,104	15.17
	2019 *vs.* 2000 (%)*	−42.30	−20.88	−35.42	−11.44	−65.72	−52.99	−65.11	−52.15	−65.64	−52.88	−40.55	−18.48
15–49													
	2000	594,899	79.73	2,481,389	332.56	346,451	46.43	17,176,324	2,302.02	16,933,876	2,269.52	242,448	32.49
	2019	785,629	109.01	4,538,621	629.73	257,870	35.78	12,711,343	1,763.69	12,328,951	1,710.63	382,391	53.06
	2019 *vs.* 2000 (%)*	32.06	36.72	82.91	89.36	−25.57	−22.94	−25.99	−23.39	−27.19	−24.63	57.72	63.28
50–69													
	2000	1,021,067	534.20	2,654,155	1,388.59	800,805	418.96	23,665,394	12,381.16	23,343,021	12,212.50	322,373	168.66
	2019	2,242,887	608.02	9,313,626	2,524.82	1,175,611	318.70	34,719,458	9,412.07	33,820,598	9,168.39	898,860	243.67
	2019vs. 2000 (%)*	119.66	13.82	250.91	81.83	46.80	−23.93	46.71	−23.98	44.89	−24.93	178.83	44.48
70+													
	2000	692,715	1,261.05	1,176,770	2,142.24	685,208	1,247.38	10,761,709	19,591.10	10,579,080	19,258.63	182,629	332.47
	2019	1,668,686	1,545.58	4,467,337	4,137.77	1,267,361	1,173.86	18,962,621	17,563.70	18,418,934	17,060.12	543,687	503.58
	2019 *vs.* 2000 (%)*	140.89	22.56	279.63	93.15	84.96	−5.89	76.20	−10.35	74.11	−11.42	197.70	51.47

Note: N: Number of cases for incidence, prevalence, and deaths; number of person years for disability-adjusted life years (DALYs), years of life lost (YLLs), and years lived with disability (YLDs).

P’: Standardized rate calculated using the 2010 National Census as the standard population, expressed as 1/100,000.

* Percent change (%) was calculated as difference value between 2019 and 2000 divided by the 2000 value.

Abbreviations: DALYs=disability-adjusted life years; YLLs=years of life lost; YLDs=years lived with disability.

TABLE 3. Cancers ranked by DALYs rate among both sexes between 2000 and 2019 in China.

Year	Rank	Cancer site	,Both sexes (1/100,000)	Cancer site	Male	Cancer site	Female
2019							
	1	Tracheal, bronchus, and lung	831.27	Tracheal, bronchus, and lung	1,203.78	Tracheal, bronchus, and lung	492.17
	2	Stomach	481.15	Stomach	718.79	Breast	277.98
	3	Colon and rectal	320.57	Esophageal	458.55	Stomach	260.97
	4	Esophageal	277.50	Colon and rectal	434.50	Colon and rectal	217.28
	5	Liver	264.31	Liver	414.90	Cervical	157.50
	6	Leukemia	163.82	Leukemia	190.81	Leukemia	135.97
	7	Breast	144.15	Pancreatic	176.41	Liver	115.85
	8	Pancreatic	136.57	Brain and central nervous system	143.02	Brain and central nervous system	109.48
	9	Brain and central nervous system	126.24	Prostate	118.94	Esophageal	108.46
	10	Cervical	79.10	Non-Hodgkin lymphoma	95.58	Pancreatic	98.93
2000							
	1	Tracheal, bronchus, and lung	826.23	Tracheal, bronchus, and lung	1173.00	Stomach	519.17
	2	Stomach	796.94	Stomach	1085.18	Tracheal, bronchus, and lung	498.15
	3	Liver	689.47	Liver	1029.41	Liver	339.82
	4	Esophageal	499.63	Esophageal	713.66	Breast	296.44
	5	Leukemia	293.96	Colon and rectum	302.27	Esophageal	289.29
	6	Colon and rectum	258.69	Leukemia	301.19	Leukemia	288.00
	7	Brain and central nervous system	161.76	Brain and central nervous system	175.24	Colon and rectum	220.04
	8	Breast	147.71	Prostate	126.41	Cervical	157.07
	9	Pancreatic	95.80	Pancreatic	115.71	Brain and central nervous system	148.11
	10	Cervical	77.67	Nasopharyngeal	101.15	Pancreatic	76.45

Note: DALY rate: Standardized rate calculated using the 2010 National Census as the standard population, expressed as 1/100,000.
Abbreviation: DALY=disability-adjusted life years.

DISCUSSION

China has a high incidence of cancer. Both incidence and prevalence were on the rise in 2019, while the cancer mortality rate was decreasing. DALYs and YLLs were also decreasing, but YLDs increased. Although mortality rates have declined, the combination of an aging and growing population has resulted in the absolute number of cancer deaths increasing by 45.43% in 2019 compared to that of 2000. In addition, progress in China's medical technology influences the trends. The burden of cancer is greater in men than women, possibly related to men's greater exposure to occupational risk factors, high social pressure, and poorer lifestyles. China has taken a series of effective measures in response to cancer, including promoting tobacco control, pushing for hepatitis B and human papilloma virus (HPV) vaccination to strengthen primary prevention, and developing guidelines for early screening, early diagnosis, and early treatment of cancers.

DALYs rate peaked in the 70-year-old age group, indicating that the elderly are living longer. The 15–49-year age group had the largest increase in cancer incidence, indicating that the burden of cancer is shifting to a younger population. This is consistent with the results of a previous study (*2*), and it shows that it is necessary and important for China to actively conduct cancer screening for early diagnosis and treatment. To effectively reduce the burden of cancer, precise prevention and control of key populations need to be implemented.

The overall DALYs rate rankings of specific cancers only changed slightly from 2000 to 2019, but the DALYs rate rankings among females changed more significantly. Lung cancer rankings did not change from 2000 — lung cancer still ranks first among both men and women. In many countries, lung cancer is the leading cause of cancer death. The high ranking of lung cancer DALYs rate among women may be related to outdoor air pollution and the use of indoor solid fuels for heating and cooking (*3*–*4*).

The DALYs rate ranking of colorectal cancer increased from sixth to third from 2000 to 2019. Colorectal cancer risk is closely related to lifestyle. Increased intake of animal-derived foods, obesity caused by prolonged sitting, and unhealthy habits, such as smoking and drinking, are related to the risk of colorectal cancer (*5*). An important strategy to reduce the burden of colorectal cancer is strengthening primary and secondary prevention.

Breast cancer rose from fourth rank to second rank among women. The change may be due to changes in lifestyle and social culture brought about by economic growth and increases in the proportion of women in the industrial labor force — both of which are associated with breast cancer (*6*). In 2020, breast cancer surpassed lung cancer as the leading cause of cancer globally. WHO recommended that women with an average risk of breast cancer between the ages of 50 and 69 undergo organized, population-based mammography every 2 years in well-resourced countries (*7*).

Liver cancer decreased from third to fifth rank overall, and among women, liver cancer decreased from third to seventh rank. Although the results of this study showed that China's DALYs rate ranking of liver cancer decreased in 2019, the burden of cancer in China will increase further because of population aging. A study showed that limited coverage of health examinations and screenings in China also indicated that the overall 5-year survival rate for liver cancer is low (*8*). Therefore, China should expand adult vaccination to control hepatitis B virus infection and increase hepatitis B virus screening.

This study was subject to several limitations. The study was at the national level and did not include provincial-level data. Economic and medical development varied by region, which might lead to regional differences in the burden of cancer. GBD 2019 data was estimated by model, and some relevant data were unavailable for earlier years. However, by comparing our data with published articles (*9*), the trends of cancer in China were shown to be roughly the same as in previous studies. In the future, in-depth research is needed for different provinces in China. In addition, tumor registries should be expanded by area as much as possible to make the data higher quality and as accurate as possible in China.

With China's aging population, the size of the elderly population will increase, and the burden of cancer will also become greater. In anticipation of this trend, China developed the Healthy China Initiative 2019–2030 (*10*), which includes cancer prevention and treatment as a major special action, requiring the overall 5-year survival rate of cancer to be greater than 46.6% in 2030 and the early diagnosis rate of key cancer types in high-incidence areas to be greater than 55% in 2022, with further increases required in the future (*10*). Early cancer screening with early diagnosis and treatment should be promoted by improving health laws and regulations and improving the medical security system, publicity and education should be carried out appropriately, and residents' attention to cancer prevention and response should be increased so that the overall burden of cancer in China would gradually and steadily decrease.

Acknowledgements: The GBD 2019 team and the National Center for Chronic and Noncommunicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention.

Conflicts of interest: No conflicts of interest.

Funding: Supported by National Key Research and Development Program "Research on key technologies for monitoring and controlling major malignant tumor risk factors based on big data, guided by precise prevention and control" (2016YFC1302600).

doi: 10.46234/ccdcw2022.036

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Submitted: June 29, 2021; Accepted: October 26, 2021

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Preplanned Studies

Economic Burden of Malignant Tumors — Yichang City, Hubei Province, China, 2019

Xiaojuan Long[1,&]; Fangfang Lu[2,&]; Xianglong Xiang[1]; Jiajuan Yang[2]; Chengzhong Xu[2]; Pei Zhang[2]; Shicheng Yu[1]; Qiqi Wang[1,#]; Chi Hu[2,#]

Summary

What is already known about this topic?

Malignant tumors are common chronic non-communicable disease and have caused serious health hazards to residents and heavy economic burden of disease to the society.

What is added by this report?

This is the first report on the economic burden of multiple types of malignant tumors in Yichang City. In 2019, the direct medical burden of lung cancer in Yichang was the highest, reaching 561.67 million CNY, and the indirect economic burden of lung cancer in Yichang was higher than that of other malignant tumors, costing 326.49 million CNY.

What are the implications for public health practice?

The results can provide evidence for the formulation of local cancer prevention and control strategies and public health decision-making.

Economic burden of disease is the economic loss of patients, families, and society caused by morbidity, disability, and premature death, as well as the consumption of health resources from disease prevention and treatment (*1–2*). Domestic and foreign studies show that the morbidity and mortality of malignant tumors have increased year by year (*3*), which brings heavy economic burden to the world. For example, economic burden of malignant tumors in Spain was 39.61 million CNY in 2015 (*4*), and economic burden of malignant tumors of a region in Southwest China was 18.86 billion CNY in 2016 (*5*). In this study, data from the cause of death surveillance, tumor registration, and big data platform of health management in Yichang City were used to calculate the direct medical burden of 14 types of malignant tumors and to estimate indirect economic burden by human capital method. The results showed that direct medical burdens of lung cancer, liver cancer, and colorectal carcinoma in 2019 were higher than those of other malignant tumors, being 561.67 million CNY, 386.08 million CNY, and 177.49 million CNY, respectively; indirect economic burdens of lung cancer, liver cancer, and esophageal cancer were also higher, being 326.49 million CNY, 188.17 million CNY, and 66.03 million CNY, respectively. Therefore, the economic burden of lung cancer, liver cancer, colorectal carcinoma, and esophageal cancer was significant, and these cancers should be the focus of disease prevention and control in Yichang City.

In this study, cancer mortality was derived from the cause of death surveillance that covers all 9 counties and 5 districts in Yichang. Cancer incidence was obtained from the tumor registration that includes 5 districts and 2 counties. Outpatient and inpatient diagnostic data and expense data of malignant tumors were gained from the big data platform of health management that contains medical information from all hospitals in 5 districts and 2 counties in Yichang. Yichang's population data and per-capita GDP (per-capita Gross Domestic Product) from the statistical yearbook were employed to estimate direct medical burden and indirect economic burden of 14 types of malignant tumors for the year of 2019 in Yichang.

The 2019 outpatient and inpatient diagnostic databases from the big data platform of health management were linked with the expense database by unique personal identification number to get annual average medical cost of a patient for the year 2019. Items of medical cost include western medicine fee, Chinese herbal medicine fee, Chinese patent medicine fee, radiation fee, laboratory fee, examination fee, radiography fee, operation fee, blood transfusion fee, oxygen delivery fee, diagnosis fee, treatment fee, bed companion fee, nursing fee, hospitalization fee, bed fee, registration fee, material fee, and others. The following formula was applied to calculate direct medical burden for a cancer.

$$\text{Direct medical burden} = \text{Annual average medical cost per patient} \times \text{prevalence rate} \times \text{population size} \quad (1)$$

This study analyzed the median, smaller fourth quartile, and higher fourth quantile of the direct medical burden of 14 malignant tumors. The 2019 values of prevalence rate and number of populations in Yichang were taken for the above calculation. The calculation of prevalence rate of a cancer was illustrated in the calculation of years lived with disability (YLDs).

A human capital method was employed to estimate indirect economic burden of a malignant tumor for the year of 2019 in Yichang. The disability-adjusted life years (DALYs) and productivity weight were combined to estimate indirect economic burden. The formula is shown below.

$$\text{Indirect economic burden} = \text{per-capita GDP} \times \text{DALYs} \times \text{productivity weight} \quad (2)$$

Through consulting relevant literature on economic burden research, several assumptions were made. The contribution of different age groups to production was different, so the productivity weight was different by age group and their values were set at 0.15, 0.75, 0.80, and 0.1 for 0–14, 15–44, 45–59, and 60 years old and above, respectively, and the productivity weight of the overall population was 0.5 (*6–8*). The per-capita GDP of Yichang was 11,410.52 CNY for all age groups. The four age groups were applied for the above calculation and were then summed to obtain indirect economic burden of a cancer. The DALYs for the four age groups were estimated as follows.

After adjusting for missing report rate and garbage codes, the mortality rate of malignant tumors by age group for the year 2019 in Yichang was estimated. The years of life lost (YLLs) caused by early death of a malignant tumor were further calculated.

$$\text{YLLs} = D \times L \quad (3)$$

D was the number of deaths by age group, L was the life loss value by age group from the standard life expectancy table of the GBD 2013.

The YLDs caused by cancer disability were estimated by the following formula.

$$\text{YLDs} = P \times DW \quad (4)$$

P was the prevalence by age group; DW was the disability weight that reflected the severity of disability caused by disease, and its value was between 0 and 1, in which 0 represents complete health and 1 represents death (*9*). Hereby, the value of disability weight for all 14 types of cancers was 0.451 as estimated from the GBD 2013. A five-year period was utilized for calculating the cancer prevalence of 2019, therefore the above number of prevalence was accumulated from 2015 to 2019.

The incidence data of malignant tumor surveillance in Yichang from 2015 to 2018 were obtained, but the incidence data of malignant tumors in 2019 were lacking. Therefore, this study needed to estimate the incidence of malignant tumors in 2019 first, and then the incidence data and prevalence rate of malignant tumors in 2019, and further estimate the YLDs of malignant tumors.

The specific estimation process was as follows. First, a linear model was established based on the incidence of cancer in counties and cancer types in tumor registration regions from 2015 to 2018 to estimate the incidence of malignant tumors in 2019. Second, the number of deaths of patients with new malignant tumors in 2019 was estimated based on the proportion of deaths and incidence of cancer types and counties in tumor registration regions from 2015 to 2018, combined with the incidence of malignant tumors in 2019. Then, according to the number of cancer incidence and death from 2015 to 2019, the number and prevalence of malignant tumors in 2019 were calculated. Finally, the YLDs of malignant tumors in Yichang in 2019 were estimated according to the above formula.

The DALYs of malignant tumors were estimated using the following formula.

$$\text{DALYs} = \text{YLLs} + \text{YLDs} \quad (5)$$

In short, the above estimation was applied to each type of cancer. YLDs were estimated as the product of an estimate of prevalence and a disability weight for the cancer; YLLs were expressed as the product of mortality estimates and years of life lost due to premature death; and DALYs were calculated as the sum of YLLs and YLDs. All statistical analyses were performed using SAS (version 9.4, SAS Institute Inc., Cary, USA).

The results showed that the top five malignant tumors of medical cost per patient for the year 2019 in Yichang were pancreatic cancer, cerebral cancer, liver cancer, esophageal cancer, and lung cancer, which were 15,670 CNY, 12,136 CNY, 11,744 CNY, 11,474 CNY, and 10,144 CNY, respectively. The results were shown in Table 1.

From Table 2, the direct medical burdens of lung cancer, liver cancer, colorectal carcinoma, esophageal cancer, and breast cancer were ranked top five for direct medical burden, which were 561.67 million CNY, 386.08 million CNY, 177.49 million CNY, 151.80 million CNY, and 1,113.45 million CNY, respectively.

TABLE 1. Medical cost per patient by types of malignant tumors in Yichang City, Hubei Province, 2019.

Type of malignant tumors	Number of patients	Medical cost per patient (1 CNY)		
		Median	Q_1	Q_3
Pancreatic cancer	242	15,670	3,043	41,299
Cerebral cancer	229	12,136	1,470	50,196
Liver cancer	1,700	11,744	3,139	27,286
Esophageal cancer	940	11,474	2,380	38,946
Lung cancer	4,863	10,144	2,094	30,468
Lymphoma	1,388	8,667	1,379	32,043
Prostate cancer	827	8,073	1,987	21,566
Colorectal carcinoma	2,201	7,855	1,525	38,651
Gastric cancer	555	6,857	664	7,820
Leukemia	1,023	6,512	846	31,078
Cervical cancer	1,466	4,895	1,035	27,000
Bladder cancer	708	3,694	725	16,202
Breast cancer	3,379	3,344	956	17,950
Corpus cancer	675	2,348	810	17,337

Note: Q_1, known as the "Smaller fourth Quartile", is equal to the 25% of all values in the sample, from smallest to largest. Q_3, known as the "higher fourth quantile", is equal to the 75% of all values in the sample, from smallest to largest.

TABLE 2. The direct medical burden of malignant tumors in Yichang City, Hubei Province, 2019.

Type of malignant tumors	Direct medical burden (10,000 CNY)
Lung cancer	56,166.73
Liver cancer	38,608.42
Colorectal carcinoma	17,749.18
Esophageal cancer	15,179.58
Breast cancer	11,344.66
Cervical cancer	10,142.83
Lymphoma	8,287.72
Prostate cancer	6,772.66
Gastric cancer	6,607.42
Leukemia	6,181.25
Bladder cancer	4,742.55
Pancreatic cancer	4,634.35
Cerebral cancer	3,437.72
Corpus cancer	1,762.43

Table 3 showed that the indirect economic burdens of lung cancer, liver cancer, esophageal cancer, colorectal carcinoma, and gastric cancer in Yichang were higher than those of other malignant tumors, which were 326.49 million CNY, 188.17 million CNY, 66.03 million CNY, 57.30 million CNY, and 39.86 million CNY, respectively. The indirect economic burden of malignant tumors varied greatly by age group, of those, the indirect economic burden of 45–59 years old group was among the highest, 15–44 years old group was the second.

DISCUSSION

The direct medical burden of lung cancer, liver cancer, colorectal carcinoma, esophageal cancer, and breast cancer in Yichang was higher among all malignant tumors in 2019, and the indirect economic burdens of lung cancer, liver cancer, esophageal cancer, colorectal carcinoma, and gastric cancer were among the top five. It can be seen that lung cancer, liver cancer, colorectal carcinoma, esophageal cancer, breast cancer, and gastric cancer had a great impact on residents' health and the economy in Yichang. The results of burden of malignant tumors in Yichang from 2005 to 2015 from a study and those of other cities also suggest that lung cancer, liver cancer, colorectal carcinoma, and other malignant tumors have caused a serious disease burden on Yichang (*10*). Therefore, the prevention and control of these cancers is not only the difficulty of the prevention and control of malignant tumors in Yichang, but also the focus of upcoming prevention and control work.

The indirect economic burden of malignant tumors for the year 2019 in Yichang varied greatly by age groups. The indirect economic burden of 45–59 years

TABLE 3. The indirect economic burden of malignant tumors by age group in Yichang City, Hubei Province, 2019.

Type of malignant tumors	Indirect economic burden (10,000 CNY)				
	Total	Age group (years)			
		0–14	15–44	45–59	60 and above
Lung cancer	32,648.90	9,794.67	48,973.34	52,238.23	6,529.78
Liver cancer	18,816.81	5,645.04	28,225.22	30,106.90	3,763.36
Esophageal cancer	6,602.55	1,980.76	9,903.82	10,564.07	1,320.51
Colorectal carcinoma	5,730.22	1,719.07	8,595.33	9,168.36	1,146.04
Gastric cancer	3,986.32	1,195.90	5,979.48	6,378.11	797.26
Cervical cancer	3,372.08	1,011.62	5,058.12	5,395.32	674.42
Pancreatic cancer	3,368.99	1,010.70	5,053.48	5,390.38	673.80
Breast cancer	2,966.14	889.84	4,449.21	4,745.82	593.23
Cerebral cancer	2,925.18	877.56	4,387.78	4,680.30	585.04
Leukemia	2,534.64	760.39	3,801.96	4,055.43	506.93
Bladder cancer	1,777.94	533.38	2,666.91	2,844.71	355.59
Lymphoma	1,655.38	496.61	2,483.06	2,648.60	331.08
Prostate cancer	1,202.95	360.89	1,804.43	1,924.73	240.59
Corpus cancer	728.69	218.61	1,093.03	1,165.90	145.74

old group was higher than that of 0–14 years old, 15–44 years old, 60 years old and above, and the indirect economic burden of 15–44 years old group was the next highest. The indirect economic burden caused by malignant tumor patients in 45 to 59 years old and 15 to 44 years old in Yichang was relatively heavy, and the prevention and treatment of malignant tumors should pay more attention to these two groups.

This study was subject to some limitations. First, the economic burden includes direct economic burden, indirect economic burden, and intangible economic burden; the direct economic burden contains direct medical cost burden and direct non-medical burden. Neither the direct non-medical burden nor the intangible economic burden was included in this study, so the economic burden may be underestimated. Second, the number of years of malignant tumor incidence data available for collection in Yichang was short, so the estimated prevalence of malignant tumors may be low, which may further lead to a low estimated economic burden.

In conclusion, malignant tumors such as lung cancer, liver cancer, colorectal cancer, esophageal cancer, breast cancer, and gastric cancer not only cause great harm to the health of local residents, but also cause a huge economic burden and a great impact on societal and economic development in Yichang. Local health authority should place priority to these cancers when formulating cancer prevention and control strategies and allocate resources for chronic disease prevention and control. In addition, the indirect economic burden caused by the 45–59 age group was relatively high. Relevant departments in Yichang should pay more attention to economic burden caused by a certain malignant tumor in this age group. The focus of cancer prevention and control should be targeting this age group of people. Therefore, Yichang can reduce the economic burden of malignant tumors by early detection, early diagnosis, early treatment, screening of key cancer species, and health education.

Conflicts of interest: No conflicts of interest.

Acknowledgements: The office of Epidemiology, China Burden of Disease Study Collaboration Center, and Chinese Center for Disease Control and Prevention.

Funding: Supported by National Key Research and Development Program “Applied Study on the Data-driven Prevention and Control Strategies of the Major Chronic Diseases” (2018YFC1315305).

doi: 10.46234/ccdcw2022.037

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Submitted: August 21, 2021; Accepted: November 03, 2021

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Vital Surveillances

Cancer Mortality and Cause Eliminated Life Expectancy in Key Areas of Four Provinces — China, 2008–2018

Baohua Wang[1]; Qiutong Wang[1]; Ning Wang[1]; Jinlei Qi[1]; Jing Wu[1,#]

ABSTRACT

Introduction: Cancer is a major health problem in China. Integrated interventions have been implemented in key areas of Anhui, Henan, Jiangsu, and Shandong provinces with historically higher than average cancer mortality. Assessing the cancer mortality trend and its impact on life expectancy (LE) could help evaluate the effectiveness of interventions in these regions.

Methods: Based on the National Cause-of-Death Surveillance, we analyzed the standardized mortality rate (SMR) of cancer, cause eliminated life expectancy (CELE), potential gains in life expectancy (PGLEs), and rate of life lost in key areas of 4 provinces from 2008 to 2018. Joinpoint program was used to compute the average annual percentage change (AAPC) of cancer mortality. Arriaga's decomposition method was used to estimate the contribution of cancer to LE in each age group.

Results: From 2008 to 2018, cancer SMR decreased in the study region (AAPC=−3.09%, *P*<0.001), which increased LE. The positive effect was the greatest in the 75–79 age group (0.120 years, 2.90%), and the negative effect was the greatest in the 50–54 age group (−0.094 years, −2.20%). Compared to 2008, cancer CELE increased by 3.95 years, PGLEs increased by 0.32 years, and rate of life lost increased by 0.21% in 2018.

Conclusions: Cancer SMR decreased in key areas of 4 provinces from 2008 to 2018. This change had a positive effect on the increase of LE. However, the rate of life lost due to cancer increased. Integrated interventions should continue to further reduce the cancer burden.

INTRODUCTION

Cancer has become a major threat to public health in China (*1*). GLOBOCAN 2020 showed that there were approximately 4.6 million new cancer cases and 3.0 million cancer deaths in China in 2020, accounting for 23.7% of the total new cancer cases and 30.2% of cancer deaths worldwide, although China only makes up 18.6% of the global population (*2*). The burden of cancer continues to increase as population aging accelerates and exposure to cancer-related risk factors increases (*3*).

Previous reports have noted that the cancer mortality in areas along the Huai River in Anhui, Henan, Jiangsu, and Shandong provinces was higher than the national level during 2004–2006 (*4*–*5*). An integrated cancer prevention and control program has been implemented to reduce cancer risk in the region since 2007. The program selected 14 representative rural counties and districts along the Huai River as key areas for cancer intervention including cancer screening, environmental improvement, and health education, etc. It has also gradually improved the integrated health and environment surveillance system that tracks deaths, birth and birth defects, drinking water quality, etc. (*1*,*6*).

Evaluating cancer mortality trends and analyzing the impact of cancer on life expectancy (LE) can help better understand the burden of disease caused by cancer and provide a basis for assessing the effectiveness of cancer intervention program (*7*). Therefore, based on the National Cause-of-Death Surveillance data, this study analyzed the trends of cancer mortality and the impact of cancer death on LE in key areas along the Huai River of the 4 provinces from 2008 to 2018.

METHODS

Based on cancer prevalence level, geographical features, and routine environmental monitoring sites, 14 counties (districts) were selected as the key areas of the cancer prevention and control program in the 4 provinces to reduce the cancer burden in the region along the Huai River: Lingbi County, Mengcheng County, Shou County, Yingdong District, and Yongqiao District in Anhui Province; Fugou County, Luoshan County, Shenqiu County, and Xiping County in Henan Province; Jinhu County, Sheyang

County, and Xuyi County in Jiangsu Province; and Juye County and Wenshang county in Shandong Province. Data on cancer death in the 14 counties (districts) — all rural areas — and national rural areas between 2008 and 2018 were obtained from the National Cause-of-Death Surveillance. ICD-10 codes (C00-C97) were used to confirm cancer deaths.

CDCs at all levels were responsible for the quality control of the National Cause-of-Death Surveillance. Village doctors or community doctors routinely collected and reported death and population information. The data were regularly checked with public security and civil affairs departments. Under-reporting surveys were conducted annually or every three years to adjust the estimation of cancer mortality (*7*). The standardized mortality rate (SMR) was calculated based on the population structure of the sixth national census.

LE in this study referred to the LE of the 0-year group in the abbreviated LE table. Cause eliminated life expectancy (CELE) referred to the LE after eliminating deaths caused by a certain disease and was calculated by compiling an abbreviated LE table of causes of cancer deaths (*8*). Potential gains in life expectancy (PGLEs) referred to the years of increased LE in a population after removing a specific cause of death, which was calculated by subtracting LE from CELE (*9*). The rate of life lost referred to the proportion of PGLEs in LE (*10*). The Arriaga decomposition method was used to estimate the contribution of the change in age-specific mortality to the change in LE (*11*).

SAS(version 9.4; SAS Institute Inc., Cary, USA) was used for statistical analysis and Microsoft Office Excel (version 2019; Microsoft, USA) was used for data visualization. Joinpoint Regression Program (version 4.9.0.0; Information Management Services, Inc, Calverton, MD, USA) was used to calculate the average annual percentage change (AAPC) of cancer mortality at $P < 0.05$ (two-sided).

RESULTS

From 2008 to 2018, the total population in key areas of 4 provinces decreased from 12,452,653 to 11,732,726. During the study period, there were 909,916 total deaths in these key areas, of which 206,179 (22.66%) were due to cancer. The SMR of cancer decreased (AAPC=–3.09%, *P*<0.001). The trends of SMR for different gender groups were similar to the overall trend, and cancer SMR for men was consistently higher than that for women. From 2008 to 2018, national average SMR of cancer in Chinese rural areas also showed a decreasing trend (AAPC=–2.53%, *P*<0.001). SMR in study areas was higher than the national average level of rural areas by 16.68/100,000 in 2008, but the difference decreased to 1.19/100,000 in 2018 (Table 1 and Figure 1).

Among the 4 provincial key areas from 2008 to 2018, there was little change in cancer mortality in people aged under 40 years old and a marked decrease in cancer mortality of those aged 40 years or older,

TABLE 1. Cancer mortality in key areas of 4 provinces and in national rural areas in China, 2008–2018.

Year	Death	Crude mortality rate (/100,000)	Under-reporting adjusted mortality rate (/100,000)	SMR in study area (/100,000)	SMR in national rural areas (/100,000)
2008	19,441	156.12	171.63	198.30	181.62
2009	19,032	150.07	164.02	187.21	174.11
2010	19,646	155.80	170.22	193.18	172.49
2011	19,880	174.07	187.89	189.14	160.51
2012	19,222	167.40	180.52	164.75	161.82
2013	19,131	166.88	179.69	165.29	159.78
2014	19,446	169.25	183.19	164.60	160.58
2015	20,027	173.55	184.86	163.49	150.12
2016	20,387	174.50	186.03	155.10	142.47
2017	20,180	172.34	183.43	153.38	142.70
2018	19,687	167.80	178.40	140.99	139.80
AAPC (%)	0.40	1.15	0.81	−3.09	−2.53
P	0.058	0.010	0.037	<0.001	<0.001

Abbreviations: SMR=standardized mortality rate; AAPC=average annual percentage change.

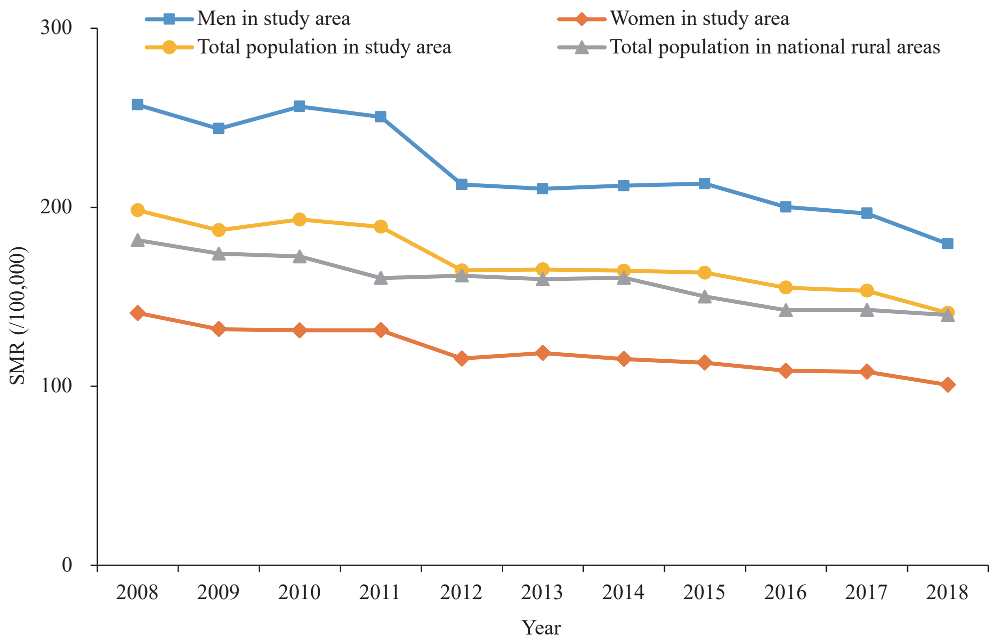

FIGURE 1. Trends of cancer SMR in key areas of 4 provinces and in national rural areas in China, 2008 to 2018.
Abbreviation: SMR=standardized mortality rate.

TABLE 2. Cancer mortality for different age groups in key areas of 4 provinces in China, 2008 and 2018.

Age group (years)	Cancer mortality (/100,000)		Change (/100,000)
	2008	2018	
0	5.07	5.44	0.37
1−4	5.06	3.21	−1.85
5−9	3.76	4.58	0.82
10−14	3.03	6.11	3.08
15−19	5.34	3.58	−1.76
20−24	5.73	4.25	−1.48
25−29	10.97	13.32	2.34
30−34	18.04	18.69	0.65
35−39	31.72	25.32	−6.40
40−44	64.99	34.95	−30.04
45−49	123.61	85.07	−38.54
50−54	192.87	264.52	71.65
55−59	297.78	200.37	−97.40
60−64	537.19	401.48	−135.71
65−69	805.56	614.98	−190.58
70−74	1,141.87	878.25	−263.61
75−79	1,539.41	1,035.42	−504.00
80−84	2,028.91	1,196.76	−832.15
85−	3,771.44	1,410.41	−2,361.02

except for the 50–54 age group, in which cancer mortality increased 71.65/100,000 (Table 2).

Overall, changes in cancer mortality contributed positively to the increase in LE in the key areas of 4 provinces between 2008 and 2018. The higher positive contribution was in the age group 55 years or older, the greatest contribution was in the age group of 75 to 79 years old (0.12 years, 2.90%), and the greatest negative contribution was in the age group of 50 to 54 years old (−0.09 years, −2.20%). Compared to men, the change in cancer mortality in women contributed less to the increase in LE (Figure 2).

LE in the key areas of 4 provinces increased by 4.27 years from 2008 (74.07 years) to 2018 (78.34 years), with an increase of 3.94 years for men and 4.54 years for women. Cancer CELE increased by 4.59 years, PGLEs increased by 0.32 years and the rate of life lost increased by 0.21%. Between 2008 and 2018, LE and cancer CELE were consistently higher for women than for men, and PGLEs and rate of life lost rates were consistently lower for women than for men (Table 3).

CONCLUSIONS

The study presented a decreasing trend of cancer mortality and a positive effect of this change on LE in the key areas of the four provinces between 2008 and 2018, based on the long-term and high-quality surveillance data of cancer mortality. The results indicated that the integrated cancer intervention program was effective in reducing cancer mortality in

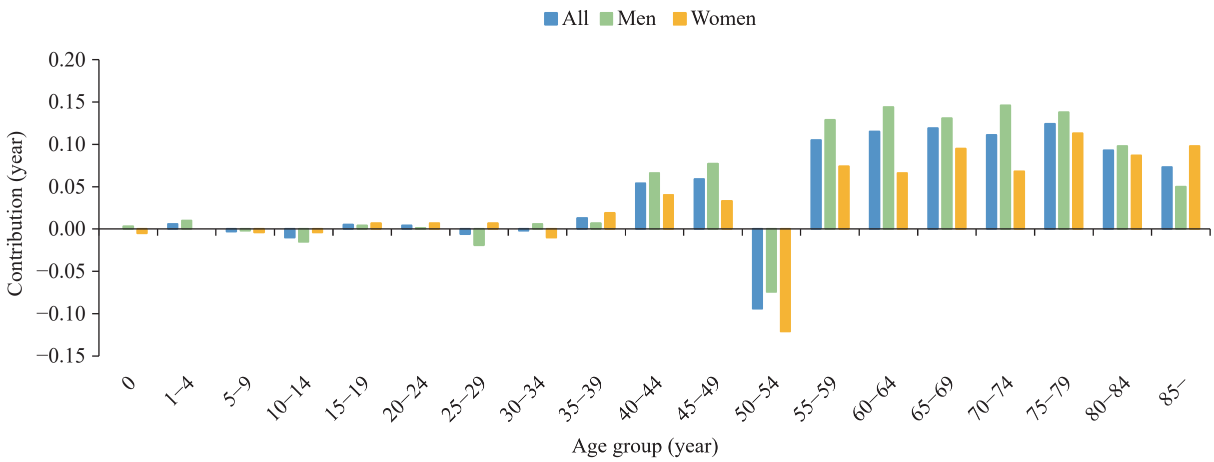

FIGURE 2. Contribution of changes in cancer mortality to LE by sex and age group, key areas of 4 provinces in China, between 2008 and 2018.
Abbreviation: LE=life expectancy.

TABLE 3. LE, cancer CELE, PGLEs and rate of life lost in key areas of 4 provinces in China, 2008 to 2018.

Year	LE (years)			CELE (years)			PGLEs (years)			Rate of life lost (%)		
	All	Men	Women	All	Men	Women	All	Men	Women	All	Men	Women
2008	74.07	71.68	76.79	76.82	74.85	78.90	2.75	3.17	2.11	3.71	4.42	2.75
2009	74.83	72.47	77.52	77.47	75.52	79.54	2.64	3.05	2.02	3.53	4.21	2.61
2010	74.33	71.73	77.35	77.00	74.83	79.34	2.67	3.10	1.99	3.59	4.32	2.57
2011	74.49	71.61	77.71	77.33	74.86	79.90	2.84	3.25	2.19	3.81	4.54	2.82
2012	75.85	73.00	79.09	78.80	76.32	81.43	2.95	3.32	2.34	3.89	4.55	2.96
2013	76.15	73.58	79.01	79.16	76.99	81.41	3.01	3.41	2.40	3.95	4.63	3.04
2014	76.60	73.87	79.68	79.70	77.40	82.12	3.10	3.53	2.44	4.05	4.78	3.06
2015	76.91	74.15	79.97	80.06	77.76	82.42	3.15	3.61	2.45	4.10	4.87	3.06
2016	77.67	74.95	80.67	80.90	78.67	83.18	3.23	3.72	2.51	4.16	4.96	3.11
2017	77.85	75.16	80.85	81.06	78.83	83.36	3.21	3.67	2.51	4.12	4.88	3.10
2018	78.34	75.62	81.33	81.41	79.12	83.77	3.07	3.50	2.44	3.92	4.63	3.00

Abbreviations: LE=life expectancy; CELE=cause eliminated life expectancy; PGLE=potential gains in life expectancy.

this region. However, the increase in the rate of life lost illustrated the increased contribution of cancer to LE during the study period, highlighting the necessity of the constant and strengthened cancer prevention and program and cancer surveillance in this region.

To extend healthy LE and improve health equity, the Chinese government has initiated Healthy China 2030 — a national strategy which aims to mobilize governments and relevant departments at all levels to actively create a healthy ecological and social environment, encouraging individuals to adopt a healthy lifestyle. Cancer prevention is a critical component of this national strategy. Our results found that the cancer mortality in key areas of four provinces was still higher than the national average level in rural areas, although the cancer mortality in key areas decreased more strikingly. Sustained efforts on intensive environmental improvement, healthy lifestyles promotion, cancer screening, and cancer early diagnosis and treatment are still needed in the region to continue the downward trend in cancer death and realize the goal of Healthy China 2030 (*1*).

The analysis of the contribution of cancer mortality by age group to LE found that the decline in cancer mortality in the age of 55 years or older played a greater positive role in the increase in LE of the study population. The greatest contribution was seen in the age group of 75 to 79 years old, the group with the highest cancer incidence (*12*), suggesting that the effects of interventions were more pronounced in those with a high prevalence of cancer. In contrast, the change in cancer mortality in the age group of 50 to 54 years old played a negative role in LE. Considering the statistical principles, the increased cancer mortality in the age group of 50 to 54 years old could partially explain the increase in the rate of life lost due to cancer in this age group. The same result has been observed in the contribution of cancer mortality to LE in the overall rural areas of China, according to the National Cause-of-Death Surveillance Dataset. Although further exploration is needed for its specific reason, this finding implies that greater attention should be paid to the cancer prevention and control in this age group.

This study found that cancer CELE increased in key areas of the 4 provinces from 2008 to 2018, while PGLEs and the rate of life lost increased, suggesting an increase in the proportion of life lost due to cancer among all causes of death. This could be due to population aging increasing the burden of cancer (*12*) or this may be associated with a more rapid decline in the disease burden of other chronic diseases and infectious diseases (*13*). These results indicated that the burden of cancer in the study region could not be overlooked. Constant efforts in cancer prevention and control are needed to reduce the rate of life lost from cancer in the context of an aging population.

There were some limitations in this study. First, although we have adjusted the under-reporting of mortality in the data analysis, we could not fully rule out the under-reporting of mortality that might have led to the overestimation of LE. Second, this study provided a comprehensive analysis of the overall disease burden of cancer without the estimates for cancer of different types. Further studies on the estimation of disease burden and risk factors of different cancer types in sub-counties (districts) are needed to provide a reference for policy formulation tailored for different cancer types and risk factors.

In summary, cancer SMR in key areas of 4 provinces in China gradually decreased from 2008 to 2018 and the changes in cancer mortality made a positive contribution to the increase of LE, indicating the success of the comprehensive cancer prevention and control program in the region. However, the increase in the rate of life lost due to cancer call for sustained cancer control effort to further reduce the burden of cancer. Local governments need to further strengthen environmental improvement, enhance health education on cancer prevention, and carry out cancer early diagnosis and treatment programs, particularly for the population aged 50 to 54 years old. Continuous surveillance is needed to assess the long-term effects of these interventions.

Conflicts of interest: No conflicts of interest reported.

Acknowledgements: All staff from local CDCs involved in the Cause-of-Death Surveillance in the study areas.

Funding: Supported by The National Key Research and Development Program of China (2016YFC 1302603, 2016YFC1302600).

doi: 10.46234/ccdcw2022.076

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Submitted: January 23, 2022; Accepted: March 11, 2022

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Perspectives

Colorectal Cancer Screening in China: Status, Challenges, and Prospects — China, 2022

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ABSTRACT

Colorectal cancer (CRC) ranks third among the most commonly diagnosed cancers in China. Despite proof that screening can decrease CRC incidence and mortality, there are still gaps remaining between CRC screening objectives and reality in China. In this review, we provided an overview of the status of CRC screening in China. First, we summarized the current CRC screening programs and strategies in China. Second, we reviewed the authoritative CRC screening and early detection guidelines in China to orient future evidence-based guideline development. Finally, we identified current challenges and further provided some suggestions to improve the implementation of CRC screening programs. To maximize the effectiveness of CRC screening, further research on risk prediction models including polygenic risk scores and prior screening outcomes, novel biomarkers and artificial intelligence, and personalized screening strategies are recommended. Both cohort study and microsimulation techniques are recommended for long-term evaluations of the effectiveness of CRC screening strategies.

INTRODUCTION

According to the recently released data from GLOBOCAN (https://gco.iarc.fr/), an estimated 555,477 newly diagnosed colorectal cancer (CRC) and 286,162 CRC-related deaths occurred in China in 2020 (*1*). With population aging, socioeconomic development, and lifestyle changes, the disease burden of CRC in China has been increasing in the past decades, especially in urban and eastern regions. Numerous practices and studies have demonstrated that the early detection and early treatment of CRC and its precancerous lesions through screening were effective in reducing mortality and incidence for CRC (*2*–*4*). In this article, we first reviewed the current status of CRC screening programs conducted in China; we also summarized the major achievements and challenges regarding the CRC screening practices conducted in China; we further reviewed the current research advances in the aspect of CRC screening and possible further direction. We anticipated that this review could provide evidence to guide future CRC screening programs in China.

CRC SCREENING PROGRAM IN CHINA

Organized cancer screening programs targeting highly prevalent types of cancer (including esophagus, stomach, liver, colorectum, breast, cervix, and nasopharynx) have been conducted in China for over 20 years. To date, there are four organized cancer screening programs in China, which are public health service programs supported by the central government (detailed information is shown in Table 1). Through these programs, over 2,000,000 high-risk individuals have been screened by the end of 2016, and 55,000 were diagnosed with cancer, with an early diagnosis rate of 80% (*5*).

In China, population-based organized CRC screening was first conducted in the 1970s in high-incidence regions of CRC (Jiashan and Haining cities, Zhejiang Province) (*6*). Given the satisfactory screening effectiveness observed in these regions, along with the increasing disease burden of CRC, CRC screening programs have been conducted in many regions. Initiatives included the Cancer Screening Program in Rural Areas [initiated in 2005, covering 234 counties in 31 provincial-level administrative divisions (PLADs) in 2016] and Cancer Screening Program in Urban Areas (initiated in 2012, covered 42 cities in 20 PLADs in 2021) (*7*–*8*). In addition, opportunistic CRC screening during outpatient visits in hospitals and clinics has also been introduced (*9*). In population-based organized screening, the screening costs are typically compensated by the program. However, for the opportunistic CRC screening, the costs are typically paid by the patients or the health

TABLE 1. Description of four major cancer screening programs in China.

Year of initiation	Program	Targeted cancer type	Targeted population	Coverage (year)
2005	Cancer screening program in rural areas	Esophagus, stomach, liver, colorectum, cervix*, nasopharynx, and lung	High-risk population selected by questionnaire-based risk assessment	234 counties in 31 provincial-level administrative divisions (2016)
2007	Cancer screening program in Huaihe River areas	Esophagus, stomach, and liver	High-risk population selected by questionnaire-based risk assessment	32 counties in 4 provinces (2019)
2009	Cervical cancer and breast cancer screening program for women in rural areas	Cervix and breast	Women aged 35 to 64 years	1,448 counties for cervical cancer and 953 counties for breast cancer (2016)
2012	Cancer screening program in urban areas	Esophagus, stomach, liver, colorectum, lung, and breast	High-risk population selected by questionnaire-based risk assessment or prescreening tests among individuals aged 40 to 74 years	42 cities in 20 provincial-level administrative divisions (2021)

* Terminate in 2009.

insurance. Currently, there are no nationwide CRC screening programs that cover all suitable populations in China, but local cancer screening programs supported by the local government have been implemented in many cities.

CRC SCREENING STRATEGIES IN CHINA

In China, due to the large population and limited healthcare resources, a two-step screening strategy was adopted in most CRC screening programs; i.e., using a non-invasive or minimally invasive approach to select high-risk individuals and those who should undertake colonoscopy (the gold standard for CRC screening) examinations in the following step. Regarding the preselection of the target population, a combination of a questionnaire-based risk assessment tool and fecal occult blood test was typically used. To date, several CRC risk prediction tools have been established, and a detailed description of widely used and recommended CRC risk prediction models in China was listed in Table 2 (*10*–*14*). Earlier risk prediction models usually included risk factors of symptoms and were typically used in an opportunistic screening setting or early diagnosis (*13*). For the risk prediction in asymptomatic population, some models for population-based screening were developed. The Asia-Pacific Colorectal Screening (APCS) score was a commonly used model in Asia-Pacific area which showed medium discriminatory power in identifying high-risk populations with the area under the receiver operating characteristics curve (AUC) of 0.64 (*10*). To further improve the predictive efficiency of APCS, some studies have added scoring items and changed scoring principles. However, the 2 typical developed models only had nearly the same AUC as APCS [0.62 (*12*) and 0.65 (*14*), respectively].

Based on the risk prediction models, researchers also explored novel risk-stratified strategies rather than age-stratified strategies by offering different screening techniques to individuals at different risk strata (*15*). For instance, Asia-Pacific Working Group on Colorectal Cancer has performed a multicenter prospective study to test the use of APCS scoring system combined with fecal immunochemical test (FIT) in CRC screening which showed a reduced colonoscopy workload (*16*). Our team has also conducted a randomized controlled trial (RCT) to comparatively evaluate the effectiveness of colonoscopy, FIT, and a novel risk-adapted screening approach for CRC screening in China (*17*). The baseline results of this trial demonstrated that the proposed risk-adapted screening approach (high-risk populations for colonoscopy and low-risk populations for FIT) had higher participation rates and yielded superior detection rates for advanced colorectal neoplasm than FIT-based screening strategy.

CURRENT CRC SCREENING GUIDELINE AND CONSENSUS IN CHINA

To standardize the screening process and improve the screening yield, a series of guidelines and consensus on CRC screening have been released by authoritative scientific societies (Table 3) (*18*–*24*). The majority of guidelines in China recommended average-risk individuals screening between 50 and 75 years of age using colonoscopy, flexible sigmoidoscopy, or fecal occult blood test (mainly FIT). Colon capsule

TABLE 2. Summary of widely used CRC risk prediction tools in China.

Reference	Year	Outcome	Scoring items / scoring principles	Discriminatory power
Yeoh et al. (2011) (*10*)	2004	ACN	Age, years (<50: 0; 50–69: 2; ≥70: 3) Gender (male: 1; female: 0) Family history of CRC in a first-degree relative (no: 0; yes: 1) History of smoking (never-smoker: 0; current or past smoker: 1)	0.66 (0.62–0.70) in derivation set; 0.64 (0.60–0.68) in validation set
Cai et al. (2012) (*11*)	2006–2008	ACN	Age, years (40–49: 0; 50–59: 1; 60–69: 2; >69: 3) Sex (male: 2; female: 0) Smoking (0–20 pack-years: 0; >20 pack-years: 2) DM (no: 0; yes: 1) Green vegetables (occasional: 1; regular: 0) Pickled food (occasional: 0; regular: 2) Fried food (occasional: 0; regular: 1) White meat (occasional: 2; regular: 0)	Sensitivity: 82.8% in derivation set; 80.3% in validation set; Specificity: 50.8% in derivation set; 51.2% in validation set; AUC: 0.74 (0.70–0.78) in derivation set; 0.74 (0.70–0.78) in validation set
Wong et al. (2014) (*12*)	2008–2012	CN	Age, years (50–55: 0; 56–70: 1) Sex (male: 2; female: 0) Family history of CRC in a first-degree relative (no: 0; yes: 1) History of smoking (no-smoker: 0; current or past smoker: 1) BMI (<25 kg/m^2: 0; ≥25 kg/m^2: 1) DM (no: 0; yes: 1)	0.62 (0.61–0.63) in derivation set; 0.62 (0.61–0.63) in validation set
Ye et al. (2017) (*13*)	2007–2014	CRC	Age is defined as ≥ 40 years and ≤ 74 years and have one or more of the following items: 1) history of intestinal polyps; 2) history of cancer; 3) family history of CRC in first-degree relatives; 4) 2 or more of the following items: (a) chronic diarrhea; (b) chronic constipation; (c) stressful life events that caused psychiatric trauma in the last two decades (e.g., divorce, death of relatives); (d) mucous and bloody stool; (e) history of appendicitis or appendectomy; (f) history of chronic cholecystitis or cholecystectomy	Sensitivity: 24.51% (19.61%–30.16%) Specificity: 89.78% (89.59%–89.97%)
Sung et al. (2018) (*14*)	2008–2012	ACN	Age, years (50–54: 0; 55–64: 1; 65–70: 2) Sex (male: 2; female: 0) Family history of CRC in a first-degree relative (no: 0; yes: 1) History of smoking (never-smoker: 0; current or past smoker: 1) BMI (<23 kg/m^2: 0; ≥23 kg/m^2: 1)	0.65 (0.61–0.69) in validation set

Abbreviations: ACN=advanced colorectal neoplasm; AUC=area under the curve; BMI=body mass index; CN=colorectal neoplasia; CRC=colorectal cancer; DM=diabetes mellitus; iFOBT=immunochemical fecal occult blood test.

endoscopy, Computed Tomography Colonography (CTC), and multi-target DNA, et al. were also recommended in some guidelines or consensus. For the next steps, it was essential to promote the application of the guidelines to clinicians who were involved in CRC screening and to update the recommendation regularly based on the accumulating newly high-rank evidence of CRC screening (*25*).

CHALLENGES OF CRC SCREENING IN CHINA

Although CRC screening programs have reached certain social benefits, to further optimize the screening effectiveness and reduce the disease burden in the future, there are still many challenges that need to be addressed. We summarized some major challenges of CRC screening in China from the perspectives of screening the target population, clinicians, and service providers.

Screening the Target Population

The current guidelines typically recommended having CRC screening in the average-risk population above a certain age (mostly 50 years old). However, such a whole population strategy may not be suitable for China given the large population and restrained healthcare resources. Therefore, the establishment of precise risk-prediction models and precise identification of high-risk populations who may benefit most from screening is a major task for researchers. Previous studies have proposed a series of risk prediction models based on the sociodemographic and lifestyle factors, but only yielded modest predictive efficacy (*26*). Recent studies have revealed that genetic

TABLE 3. Summary of current China colorectal cancer screening guidelines.

Guideline	Year	Starting age, years	Stopping age, years	Sex and race	Endorsed screening tests	Preferred screening test
NCC (*20*)	2020	50 (low and medium risk) 40 (high risk)	75	No tailoring	FIT, mtFIT-DNA, colonoscopy, CTC, FS	Colonoscopy
CSO (*24*)	2020	40	74	No tailoring	FIT, mtDNA, colonoscopy	Colonoscopy
NCRCDD (*21*)	2019	50	75	No tailoring	FIT, gFOBT, mtFIT-DNA, colonoscopy, CTC, FS, CCE, mSEPT9 test, M2-PK test	FIT, mtFIT-DNA, colonoscopy
Colon Cancer Society of CACA (*18*)	2018	40	74	No tailoring	FOBT, mtDNA, colonoscopy, CTC, FS, questionnaire assessment, M2-PK test, mSEPT9 test	FIT, mtDNA, colonoscopy, questionnaire assessment
Multi-Collaborative Group of CMA (*19*)	2014	50	74	No tailoring	FIT, colonoscopy, questionnaire assessment, DRE, chromoendoscopy, electronic chromoendoscopy	None
CSDE, Oncology Endoscopy Society of CACA (*22*)	2014	50	75	No tailoring	FIT, gFOBT, mtDNA, colonoscopy, FS, CCE, mSEPT9 test, VC	Three-tier: gFOBT, FIT, colonoscopy
CSGE (*23*)	2011	50	74	No tailoring	FOBT, questionnaire assessment, colonoscopy, FS	Two-tier: questionnaire assessment + FIT, colonoscopy

Abbreviations: CACA=China Anti-Cancer Association; CCE=colon capsule endoscopy; CMA=Chinese Medical Association; CSDE=Chinese Society of Digestive Endoscopology; CSGE=Chinese Society of Gastroenterology; CSO=Chinese Society of Oncology; CTC=computed tomography colonography; DRE=digital rectal examination; FIT=fecal immunochemical test; FS=flexible sigmoidoscopy; gFOBT=guaiac-based fecal occult blood test; mtDNA=multi-target DNA; NCC=National Cancer Center of China; NCRCDD=National Clinical Research Center for Digestive Diseases; VC=visual colonoscopy.

variants, stool- or blood-based biomarkers may help to identify individuals with an elevated risk of CRC (*15*,*27*).

Another important issue is the low participation rate of colonoscopy screening in China. In a multicenter CRC screening program covering 12 PLADs conducted from 2012–2015 (*7*), the overall uptake rate of screening colonoscopy among high-risk populations was only 14.0%. In the most recent CRC screening trial conducted in 6 centers (*17*), the participation rate of screening colonoscopy was 42.5%, which was higher than other studies but was much lower than FIT-based screening in the same studies (94.0%). All the evidences suggested that although colonoscopy was regarded as the gold standard of CRC screening, it was not feasible to be used as the first-line screening modality in a population-based CRC screening program. Implementation of health promotion campaigns to improve the population awareness of screening and using effective non- or minimally invasive approaches to firstly select high-risk populations suitable for subsequent colonoscopy screening may help to improve the overall screening uptake rate.

Clinician

Clinicians played an essential role in CRC screening. First, clinicians could evaluate the patient's risk during their hospital visit. For patients with an elevated risk of CRC, professional advice on choosing appropriate screening techniques could be provided. Though such personal consultation typically occurred in an opportunistic screening setting, the uptake rate of screening may be strongly improved. Second, the clinicians could target patients who might benefit from chemoprevention and other targeted prevention strategies such as lifestyle modification to reduce the future risk of CRC. Third, the effectiveness of screening strongly depend on the quality of examination and diagnosis made by the clinicians. As shown in previous studies, strong heterogeneity of diagnostic performance among endoscopists who performed screening colonoscopy existed in multi-center screening programs (*28*).

To optimize the screening effectiveness, the following aspects need to be addressed in the future: 1) clinicians should be familiar with the well-established risk assessment tool and cancer screening techniques; 2) clinicians should provide tailored CRC screening advice based on the risk assessment results and patients' preference; 3) only experienced clinicians should be involved in the screening, who should also routinely attend training to master the most recent advances regarding diagnosis and treatment; and 4) the quality of screening endoscopy and pathology should be routinely reviewed by an independent scientific panel.

Service Provider

The major challenge from the service provider's perspective is the healthcare legislation on improving the access to CRC screening. The only access to free CRC screening is through organized CRC screening programs initiated by the central and local government, which are limited by their budget. It is therefore urgent to formulate new policies on tackling the scheme of screening payments for eligible individuals to improve the overall attendance rate of CRC screening. In addition, it is also necessary to implement health promotion campaigns to enhance the population's awareness of cancer prevention.

Cost-effectiveness analysis about CRC screening is essential for policymakers and there have been a series of relevant studies being published in China. Wang et al. (*29*) reported a systematic review which included 12 studies of the economic evaluation evidence of CRC screening in mainland China, and this study concluded that CRC screening was generally cost-effective in Chinese population, but the optimal technology and strategy was not conclusive. To maximize the screening yield of CRC screening under limited health expenditure, high-quality health economic evaluations addressing the optimal screening strategy for different populations in China are still needed.

RESEARCH ADVANCES AND PROSPECT

Despite the idea of risk-adapted CRC screening having been introduced nearly 30 years (*30*), no national screening program adopted it so far with the need for reliable risk prediction models. A cost-effectiveness analysis has shown that a discriminatory performance of at least 0.65 is required for risk-adapted screening to be more cost-effective than uniform screening (*31*). To promote the discriminatory power of the model, a combination of traditional risk factors with novel indicators might be a promising direction in the future. The polygenic test can be used to estimate personal polygenic risk score (PRS) based on the absence or presence of specific risk alleles. Jeon et al. (*32*) found that the model combined lifestyle, environmental, and PRS yielded better discrimination than model only included environmental-score with the AUC of 0.63 and 0.59, respectively. Except for the estimation of background risk, an alternative type of potential indicator was the outcomes of prior screening. Several studies have shown that fecal hemoglobin concentrations in previous screening rounds were highly predictive for future detection of advanced neoplasia (*33–34*) and risk prediction models combining this factor were being developed (*35*).

Apart from the risk assessment model, novel screening techniques like biomarkers and artificial intelligence (AI) could also optimize CRC risk-adapted screening. Food and Drug Administration (FDA) in the US has approved several novel screening techniques, for example, multi-target stool DNA test known as Cologuard (*36*), gut microbiota known as Lifekit (*37*), and methylated SEPT9 test known as the Epi proColon (*38*). These new screening techniques available in the US offered new options for developing screening guidelines with a diagnostic efficacy similar to or superior to FIT (*39*).

Coloclear, a multi-target stool DNA test method approved by the National Medical Products Administration for registration of innovative Class III medical devices in 2020, is known as the first certification of the CRC screening method in China. The registration of Coloclear indicated the development and implementation potential of biomarkers in CRC screening in China. Most AI tools in CRC screening aim at increasing detection of small abnormalities to increase screening sensitivity and referred to as computer-aided detection (CADe). In China, Wang et al. (*40–41*) did both nonblinded and blinded RCT to assess the effectiveness of a CADe system that avoided potential operational bias and found a significant increase in the number of diminutive adenomas detected.

Traditional cohort studies and RCTs need long duration and high cost in verifying the long-term cost-effectiveness of a new screening strategy, in addition, screening strategies with a broad variation of test characteristics are too many to evaluate. To avoid these drawbacks, several countries adopt the way of model simulation to evaluate the effect of screening strategies. The microsimulation model, which simulates individual disease histories using stochastic parameters describing transitions between specified health states, could flexibly and quickly conduct estimation. In the US, the results from microsimulation model studies have assisted policymakers in decision-making relative to screening guideline (*3*). Hence, the long-term reality study and microsimulation study will both provide solid evidence for decision-making in CRC screening. To date, the application of microsimulation model in CRC screening in China is sparse.

CONCLUSION

Pilot population-based CRC screening programs have been implemented in most PLADs of China and have served as a good policy informing platform for future CRC screening practices. Authoritative scientific societies have formed a series of CRC screening and early detection guidelines or expert consensus to ensure overall quality and effectiveness. To orient future screening practices and effectively reduce the disease burden, future research addressing the aspects of population risk prediction and stratification, novel effective screening and early detection biomarkers, development of personalized screening strategy, long-term evaluation of the effectiveness of different screening strategies using cohort and microsimulation techniques should be highly recommended.

Conflicts of Interest: No conflicts of interest.

Funding: Supported by the National Natural Science Foundation of China (82173606), the Natural Science Foundation of Beijing Municipality (7202169) and the Beijing Nova Program of Science and Technology (Z191100001119065).

doi: 10.46234/ccdcw2022.077

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Submitted: January 16, 2022; Accepted: March 10, 2022

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Indexed by PubMed Central (PMC), Emerging Sources Citation Index (ESCI), Scopus, and Chinese Scientific and Technical Papers and Citations

The inauguration of *China CDC Weekly* is in part supported by Project for Enhancing International Impact of China STM Journals Category D (PIIJ2-D-04-(2018)) of China Association for Science and Technology (CAST).

CCDC weekly

Vol. 4 No. 15 Apr. 15, 2022

Responsible Authority
National Health Commission of the People's Republic of China

Sponsor
Chinese Center for Disease Control and Prevention

Editing and Publishing
China CDC Weekly Editorial Office
No.155 Changbai Road, Changping District, Beijing, China
Tel: 86-10-63150501, 63150701
Email: weekly@chinacdc.cn

CSSN
ISSN 2096-7071
CN 10-1629/R1