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ORIGINAL RESEARCH

Epidemiological Trends of Kidney Cancer Along with Attributable Risk Factors in China from 1990 to 2019 and Its Projections Until 2030: An Analysis of the Global Burden of Disease Study 2019

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Background: Understanding the past and future burden of kidney cancer in China over years provides essential references for optimizing the prevention and management strategies.

Methods: The data on incidence, mortality, disability-adjusted life-years (DALYs) and age-standardized rates of kidney cancer in China, 1990–2019, were collected from the database of Global Burden of Disease Study 2019. The estimated annual percentage change (EAPC) was calculated to depict the trends of kidney cancer burden, and Bayesian age-period-cohort analysis was used to predict the incidence and mortality in the next decade.

Results: Over the past 30 years, the number of new kidney cancer cases sharply increased from 11.07 thousand to 59.83 thousand, and the age-standardized incidence rate (ASIR) tripled from 1.16/100,000 to 3.21/100,000. The mortality and DALYs also presented an increasing pattern. Smoking and high body mass index were mainly risk factors for kidney cancer. We predicted that by 2030, the incident cases and deaths of kidney cancer would increase to 126.8 thousand and 41.8 thousand, respectively.

Conclusion: In the past 30 years, the kidney cancer burden gradually increased in China, and it will continue to rise in the next decade, which reveals more targeted intervention measures are necessary.

Keywords: kidney neoplasms, China, projection, risk factors, trends

Background

Cancer was one of the leading causes of death worldwide.[1] High incidence rates and mortality lead to the large use of social medical resources. Kidney cancer is the 14th most common malignancy worldwide,[2,3] and about 20% of the renal tumors still have metastases at the time of diagnosis.[4] The incidence of kidney cancer varies widely geographically, and it was relatively higher in Europe and North America.[5] Multiple factors influence the occurrence and progression of kidney cancer, including age,[6] gender,[7] inherited genetic factors (such as Birt–Hogg–Dube syndrome[8] and hereditary leiomyomatosis and renal cell carcinoma[9]), lifestyle (such as smoking,[10] excess body weight[11] and hypertension[12]) and so on. The incidence rate of kidney cancer in China was about 4.99/100 000 and the mortality-to-incidence ratio was 0.37.[13] The huge population base of China led to 25600 deaths due to kidney cancer in 2014.[13] Therefore, understanding the kidney cancer burden and its developing status has great significance for cancer control and public health improvement.

The Global Burden of Diseases (GBD) provides epidemiological and some socioeconomic data on cancers.[14] Currently, some studies have described the epidemiological characteristics of renal cancer in some countries,[15–17] but

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the latest epidemiological study of kidney cancer in China used the kidney cancer cohort between 1992 and 2016.[18] Based on the latest GBD (2019) research data, this study comprehensively describes the disease burden and risk factors of kidney cancer in China from 1990 to 2019, and predicts the development trend of incidence rate and mortality of kidney cancer in China.

Methods

Data Source

We employed the suite of estimation methods for the burden of disease used in GBD 2019 to assess the state of population health in China, from 1990 to 2019. Previous researches had elaborated the data collection and analysis methods in full detail.[19,20] The epidemiological information on kidney cancer was collected from the Global Health Data Exchange (GHDx, http://ghdx.healthdata.org/gbd-results-tool), including age-sex-specific incidence, mortality and disability-adjusted life-years (DALYs) rates. We used the following criteria ("China" as the location, "kidney cancer", "incidence", "death" and "DALYs") to retrieve data from the online database. Meanwhile, we analyzed the regional DALYs and age-standardized DALY rate (ASDR) of each province of kidney cancer in China through the data in 2017 to further express the sub-national disease burden difference of kidney cancer in China.[21] The 34 provincial administrative units were divided into four groups (low-middle, middle, high-middle, and high) according to the socio-demographic index (SDI). SDI is a combined average of the incomes per capita, average educational attainment, and fertility rates of all regions included in the GBD study.

Risk Factor Analysis

Eighty-seven risk factors were identified in the GBD 2019 study, including the following four categories: environmental and occupational, behavioral, metabolic, and dietary risks.[22,23] The proportion of DALYs attributable to risk factors by sex and year was evaluated by the comparative risk assessment (CRA) framework.[22] Usually, the framework consists of six steps: (1) identifying strong risk–outcome pairs, (2) estimating relative risks, (3) assessing exposure levels and distribution, (4) determining the theoretical minimum exposure level, (5) calculating the population attributable proportion, and (6) assessing attributable proportion for combined risk factors by considering the mediating effect.

Statistical Analyses

The descriptive analysis of the incidence rate, mortality and DALYs of kidney cancer was conducted by 5-year-old age group, gender, and year. These indicators plot temporal trends from 1990 to 2019. Age was grouped by 5-year period, ranging from under 5 to over 95, a total of 20 specific age groups. Referring to the previous research, we chose the GBD world population age standard to calculate the age-standard rate for the incidence, mortality, and DALYs of kidney cancer.[24,25] The time trends of age-standardized incidence rate (ASIR), age-standardized mortality rate (ASMR), and ASDR were calculated by estimated annual percentage change (EAPC). The EAPC is summative and was widely used to measure the secular trend over a given interval. The EAPC was calculated as $100 \times (\exp(\beta) - 1)$, and its 95% confidence interval (CI) was also obtained from the linear regression model.[26–28] BAPC (Bayesian age-period cohort) and INLA (integrated nested Laplace approximation) packages in R were used for analyzation of the Bayesian age-period-cohort model. We calculated the absolute number of events that would occur if rates had remained stable (baseline reference), with a 2% decrease per year (optimistic reference) or an increase per year (pessimistic reference), to facilitate comparison with predictions. A $P < 0.05$ was recognized as statistically significant.[29]

Results

Current Kidney Cancer Burden in China

In 2019, there were 59.83 thousand (95% UI: 49.51, 71.24) incident cases of kidney cancer for the total Chinese population, and the ASIR was 3.21 per 100,000 (95% UI: 2.7, 3.79) (Table 1). Kidney cancer contributed to 23.95

Table 1 The Number of Incident Cases and the Age-standardized Incidence Rates of Kidney Cancer in China in 1990 and 2019 and the Estimated Annual Percentage Changes from 1990 to 2019

Characteristics	1990		2019		1990–2019
	Incident Cases No.×10^3 (95% UI)	ASIR per 100,000 No. (95% UI)	Incident Cases No.×10^3 (95% UI)	ASIR per 100,000 No. (95% UI)	EAPC in ASIR No. (95% CI)
Overall	11.07 (9.79, 12.59)	1.16 (1.02, 1.31)	59.83 (49.51, 71.24)	3.21 (2.7, 3.79)	4.46 (3.95, 4.98)
Sex					
Male	6.16 (5.06, 7.48)	1.32 (1.09, 1.6)	42.55 (33.14, 53.17)	4.63 (3.67, 5.73)	5.46 (4.88, 6.04)
Female	4.92 (4.24, 5.68)	1.02 (0.88, 1.17)	17.27 (13.84, 21.3)	1.92 (1.58, 2.32)	2.80 (2.38, 3.23)
Age[a]					
Under 5	1.86 (1.52, 2.22)	1.61 (1.32, 1.93)	1.55 (1.26, 1.86)	1.90 (1.54, 2.28)	1.27 (0.80, 1.74)
5–9	0.36 (0.30, 0.42)	0.34 (0.29, 0.40)	0.45 (0.38, 0.53)	0.62 (0.53, 0.73)	2.73 (2.30, 3.16)
10–14	0.15 (0.13, 0.17)	0.14 (0.12, 0.17)	0.23 (0.2, 0.26)	0.32 (0.28, 0.37)	3.74 (3.25, 4.24)
15–19	0.21 (0.18, 0.25)	0.17 (0.14, 0.20)	0.29 (0.24, 0.35)	0.38 (0.32, 0.46)	3.92 (3.26, 4.59)
20–24	0.26 (0.21, 0.31)	0.19 (0.16, 0.23)	0.57 (0.47, 0.69)	0.69 (0.57, 0.85)	5.70 (4.97, 6.43)
25–29	0.27 (0.23, 0.32)	0.25 (0.2, 0.29)	1.07 (0.9, 1.28)	0.97 (0.81, 1.16)	6.32 (5.69, 6.96)
30–34	0.32 (0.27, 0.38)	0.36 (0.3, 0.43)	2.03 (1.68, 2.42)	1.57 (1.30, 1.88)	6.48 (5.86, 7.10)
35–39	0.57 (0.47, 0.67)	0.62 (0.52, 0.73)	2.62 (2.14, 3.18)	2.60 (2.12, 3.15)	6.00 (5.39, 6.62)
40–44	0.62 (0.52, 0.74)	0.92 (0.77, 1.10)	3.86 (3.09, 4.8)	3.80 (3.04, 4.72)	6.01 (5.40, 6.63)
45–49	0.62 (0.51, 0.74)	1.19 (0.99, 1.43)	5.07 (3.98, 6.33)	4.18 (3.28, 5.22)	5.76 (5.12, 6.41)
50–54	0.85 (0.71, 1.02)	1.78 (1.49, 2.14)	6.87 (5.45, 8.59)	5.49 (4.36, 6.86)	5.03 (4.44, 5.62)
55–59	1.09 (0.92, 1.32)	2.52 (2.11, 3.04)	6.65 (5.29, 8.32)	7.02 (5.58, 8.78)	4.51 (3.97, 5.05)
60–64	1.08 (0.91, 1.27)	3.04 (2.58, 3.59)	6.41 (5.28, 7.73)	8.16 (6.73, 9.84)	4.16 (3.72, 4.61)
65–69	0.98 (0.84, 1.13)	3.58 (3.08, 4.11)	6.87 (5.68, 8.22)	9.76 (8.08, 11.67)	4.04 (3.61, 4.46)
70–74	0.82 (0.71, 0.94)	4.34 (3.77, 4.96)	5.93 (4.93, 7.05)	12.38 (10.31, 14.73)	4.19 (3.59, 4.79)
75–79	0.57 (0.50, 0.65)	5.03 (4.37, 5.73)	4.57 (3.82, 5.42)	15.31 (12.81, 18.16)	4.98 (4.36, 5.60)
80–84	0.3 (0.26, 0.34)	5.37 (4.63, 6.09)	2.99 (2.51, 3.5)	15.71 (13.16, 18.35)	4.92 (4.29, 5.56)
85–89	0.12 (0.1, 0.14)	6.44 (5.4, 7.37)	1.51 (1.28, 1.74)	17.72 (15.08, 20.44)	4.56 (4.09, 5.03)
90–94	0.02 (0.02, 0.02)	5.08 (4.17, 5.9)	0.27 (0.22, 0.32)	12.01 (9.81, 14.1)	3.60 (3.26, 3.93)
95+	0.002 (0.002, 0.003)	3.58 (2.93, 4.17)	0.03 (0.02, 0.04)	7.35 (5.51, 9.09)	3.11 (2.74, 3.47)

Abbreviations: ASIR, age-standardized incidence rate; CI, confidence interval; EAPC, estimated annual percentage change; UI, uncertainty interval; [a], crude incidence rate in each age group.

thousand (95% UI: 19.77, 28.48) deaths, and the ASMR of the total population was 1.27 per 100,000 (95% UI: 1.05, 1.49) (Table 2). Kidney cancer caused 642.8 thousand (95% UI: 533.66, 763.98) DALYs, and the ASDR was 34.28 per 100,000 (95% UI: 28.95, 40.16) (Table 3). The incidence, mortality, DALYs and ASIR were about 2.5 times higher in men than in women (Tables 1–3).

The number of incident cases, deaths and DALYs varies by age group. In 2019, the number of incident cases and DALYs of kidney cancer peaked between 50 and 54 years in males (Table 1 and Figure 1). The number of incident cases and DALYs of females and the number of deaths of both sexes of kidney cancer peaked 65–69 years (Table 1 and Figure 1).

The ASIR, ASMR and ASDR also varied with age, and they peaked at 85–89 years among the total population (Tables 1–3). They presented similar trends among both sexes. Due to the peak incidence of Wilms tumor originating from embryonic cells, the incidence rate and mortality of kidney cancer reached a "sub-peak" under 5 years compared with other age groups under 35 years (Tables 1–3 and Figure 1).

Temporal Trends in Kidney Cancer Incidence, Mortality, and DALYs Rates Over Time

For the total population, the absolute number of new cases and deaths had a significant increase from 1990 to 2019, and so does the DALYs (Tables 1–3). The ASIR increased from 1.16 per 100,000 (95% CI: 1.02, 1.31) in 1990 to 3.21 per 100,000 (95% CI: 2.7, 3.79) in 2019, with an EAPC of 4.46 (95% CI: 3.95, 4.98) (Table 1). ASIR increased more significantly in men than in women during this period (EAPC=5.46, CI: (4.88, 6.04) vs EAPC=2.80, CI: (2.38, 3.23), respectively) (Table 1 and Figure 2C). At most ages, the incidence rates presented upward trends among both females and

Table 2 The Number of Deaths and the Age-standardized Mortality Rates of Kidney Cancer in China in 1990 and 2019 and the Estimated Annual Percentage Changes from 1990 to 2019

Characteristics	1990		2019		1990–2019
	Deaths Cases No.×10³ (95% UI)	ASMR per 100,000 No. (95% UI)	Deaths Cases No.×10³ (95% UI)	ASMR per 100,000 No. (95% UI)	EAPC in ASMR No. (95% CI)
Overall	5.88 (5.14, 6.69)	0.7 (0.61, 0.79)	23.95 (19.77, 28.48)	1.27 (1.05, 1.49)	2.79 (2.33, 3.26)
Sex					
Male	3.33 (2.73, 4.07)	0.85 (0.7, 1.01)	16.88 (13.18, 20.84)	1.96 (1.55, 2.38)	3.82 (3.3, 4.34)
Female	2.55 (2.19, 2.94)	0.59 (0.5, 0.67)	7.07 (5.68, 8.62)	0.72 (0.59, 0.87)	1.17 (0.8, 1.53)
Age[a]					
Under 5	0.57 (0.46, 0.67)	0.49 (0.4, 0.58)	0.22 (0.18, 0.26)	0.26 (0.22, 0.32)	−1.72 (−2.11, −1.33)
5–9	0.1 (0.08, 0.12)	0.1 (0.08, 0.11)	0.06 (0.05, 0.08)	0.09 (0.07, 0.1)	0.11 (−0.25, 0.47)
10–14	0.05 (0.04, 0.05)	0.04 (0.04, 0.05)	0.03 (0.03, 0.04)	0.05 (0.04, 0.06)	1.05 (0.64, 1.46)
15–19	0.05 (0.04, 0.06)	0.04 (0.03, 0.05)	0.04 (0.03, 0.05)	0.05 (0.04, 0.06)	1.48 (0.93, 2.03)
20–24	0.07 (0.06, 0.09)	0.05 (0.04, 0.06)	0.08 (0.06, 0.1)	0.1 (0.08, 0.12)	2.93 (2.34, 3.51)
25–29	0.08 (0.07, 0.1)	0.07 (0.06, 0.09)	0.16 (0.13, 0.19)	0.14 (0.12, 0.17)	3.43 (2.93, 3.94)
30–34	0.1 (0.09, 0.12)	0.12 (0.1, 0.14)	0.31 (0.26, 0.38)	0.24 (0.2, 0.29)	3.53 (3.00, 4.06)
35–39	0.2 (0.16, 0.23)	0.21 (0.18, 0.25)	0.43 (0.35, 0.53)	0.43 (0.35, 0.52)	3.14 (2.58, 3.71)
40–44	0.23 (0.19, 0.28)	0.34 (0.28, 0.41)	0.68 (0.54, 0.84)	0.67 (0.54, 0.83)	3.20 (2.66, 3.75)
45–49	0.28 (0.23, 0.34)	0.54 (0.44, 0.65)	1.22 (0.95, 1.51)	1 (0.79, 1.24)	3.30 (2.75, 3.86)
50–54	0.45 (0.37, 0.54)	0.93 (0.78, 1.12)	2.07 (1.62, 2.59)	1.65 (1.3, 2.07)	2.83 (2.32, 3.33)
55–59	0.65 (0.54, 0.78)	1.49 (1.23, 1.79)	2.41 (1.88, 3)	2.54 (1.98, 3.16)	2.55 (2.07, 3.03)
60–64	0.69 (0.58, 0.82)	1.95 (1.63, 2.32)	2.58 (2.1, 3.17)	3.29 (2.67, 4.03)	2.33 (1.92, 2.74)
65–69	0.7 (0.6, 0.81)	2.56 (2.21, 2.97)	3.19 (2.63, 3.8)	4.53 (3.74, 5.4)	2.37 (1.96, 2.78)
70–74	0.65 (0.56, 0.74)	3.42 (2.95, 3.91)	3.13 (2.62, 3.69)	6.53 (5.48, 7.71)	2.63 (2.06, 3.20)
75–79	0.52 (0.46, 0.59)	4.58 (4, 5.2)	2.94 (2.47, 3.47)	9.86 (8.28, 11.63)	3.59 (3.02, 4.17)
80–84	0.32 (0.27, 0.36)	5.68 (4.87, 6.42)	2.4 (2.01, 2.81)	12.57 (10.55, 14.74)	3.81 (3.21, 4.41)
85–89	0.15 (0.13, 0.18)	8.03 (6.77, 9.13)	1.6 (1.37, 1.85)	18.87 (16.16, 21.74)	3.94 (3.49, 4.38)
90–94	0.03 (0.02, 0.03)	7.37 (6.1, 8.44)	0.35 (0.29, 0.41)	15.55 (12.75, 18.35)	3.15 (2.83, 3.47)
95+	0.004 (0.003, 0.004)	6.21 (4.98, 7.22)	0.05 (0.04, 0.07)	11.98 (9.16, 14.75)	2.8 (2.45, 3.15)

Abbreviations: ASMR, age-standardized mortality rate; CI, confidence interval; EAPC, estimated annual percentage change; UI, uncertainty interval; [a], crude mortality rate in each age group.

males. The number of incident cases increased by 4 to 14 times among the population over 30 years (Table 1 and Figure 2A). The incidence rate per 100,000 population increased by 2–4 times among the ≥10 years old group, especially among males (Table 1 and Figure 2B).

The ASMR increased from 0.7 per 100,000 (95% CI: 0.61, 0.79) to 1.27 per 100,000 (95% CI: 1.05, 1.49) from 1990 to 2019, with an EAPC of 2.79 (95% CI: 2.3, 3.26) (Table 2). In this period, it observed an increasing trend of ASDR and the EAPC was 2.28 (95% CI: 1.83, 2.73) (Table 3). It also observed overall upward trends in ASMR and ASDR in age groups ≥10 years among both sexes (Figure S1), with about 2 times increasing among both sexes ≥30 years old (Table 2, Table 3, Figure S1).

Province-Level Burden of Kidney Cancer in China

In addition, we summarized the ASDRs and their changes for 33 provinces. In 2017, the age-standardized DALY rates were highest in Taiwan, Tianjin, Liaoning, Shanghai, and Beijing, which showed two- to three-fold differences compared with the lowest rates in Macau SAR, Hainan, Guangdong, Chongqing and Yunnan (Figure 3A). The ASDR in northern and eastern China is generally higher than that in southern and western China. The ASDR is related to the local SDI (Figure 3B). Comparing the changes in the ASDR of kidney cancer between 1990 and 2017, it had increased in most provinces except Macau SAR (Figure 3, Figure S2). Among them, the ASDR in Taiwan, Liaoning, and Tianjin increased quickly and the ASDR in Tibet, Guizhou, Qinghai, and Ningxia increased slowly.

Table 3 The Number of DALYs and the Age-standardized DALYs Rates of Kidney Cancer in China in 1990 and 2019 and the Estimated Annual Percentage Changes from 1990 to 2019

Characteristics	1990		2019		1990–2019
	DALYs No.×10^3 (95% UI)	Age-Standardized DALYs Rate per 100,000 No. (95% UI)	DALYs No.×10^3 (95% UI)	Age-Standardized DALYs Rate per 100,000 No. (95% UI)	EAPC in Age-Standardized DALYs Rates No. (95% CI)
Overall	215.76 (190.36, 243.56)	21.59 (19.04, 24.4)	642.8 (533.66, 763.98)	34.28 (28.95, 40.16)	2.28 (1.83, 2.73)
Sex					
Male	121.56 (100.81, 146.97)	24.44 (20.39, 29.5)	462.87 (363.08, 571.56)	49.65 (39.57, 60.57)	3.33 (2.82, 3.85)
Female	94.21 (81.14, 107.59)	19.04 (16.49, 21.63)	179.93 (147.91, 216.68)	20.07 (16.75, 23.75)	0.55 (0.19, 0.9)
Age[a]					
Under 5	50.18 (40.99, 59.23)	43.49 (35.52, 51.33)	19.47 (15.95, 23.36)	23.89 (19.57, 28.66)	−1.63 (−2.02, −1.24)
5–9	8.35 (7.00, 9.73)	7.97 (6.68, 9.29)	5.45 (4.65, 6.51)	7.51 (6.40, 8.96)	0.19 (−0.17, 0.56)
10–14	3.53 (3.01, 4.11)	3.43 (2.93, 4.00)	2.73 (2.36, 3.19)	3.87 (3.34, 4.52)	1.14 (0.73, 1.55)
15–19	3.89 (3.19, 4.59)	3.06 (2.51, 3.62)	2.91 (2.41, 3.50)	3.87 (3.21, 4.66)	1.58 (1.03, 2.13)
20–24	4.83 (3.93, 5.83)	3.65 (2.97, 4.41)	5.60 (4.55, 6.77)	6.84 (5.55, 8.27)	3.04 (2.45, 3.63)
25–29	5.03 (4.17, 6.03)	4.56 (3.78, 5.47)	10.22 (8.56, 12.09)	9.23 (7.73, 10.92)	3.56 (3.05, 4.07)
30–34	6.03 (5.01, 7.09)	6.81 (5.67, 8.01)	18.81 (15.69, 22.69)	14.57 (12.15, 17.58)	3.65 (3.12, 4.19)
35–39	10.33 (8.59, 12.21)	11.29 (9.39, 13.35)	23.6 (19.27, 28.69)	23.39 (19.1, 28.44)	3.27 (2.71, 3.83)
40–44	10.93 (9.13, 13.18)	16.25 (13.58, 19.6)	33.92 (27.16, 41.32)	33.37 (26.72, 40.65)	3.33 (2.78, 3.87)
45–49	11.91 (9.80, 14.37)	23.03 (18.94, 27.79)	53.45 (42.05, 65.79)	44.04 (34.65, 54.21)	3.41 (2.85, 3.97)
50–54	16.92 (14.07, 20.15)	35.39 (29.42, 42.16)	80.04 (63.03, 99.36)	63.98 (50.39, 79.42)	2.91 (2.41, 3.42)
55–59	21.38 (17.79, 25.72)	49.20 (40.93, 59.18)	81.08 (64.54, 100.05)	85.50 (68.06, 105.50)	2.62 (2.13, 3.10)
60–64	19.65 (16.39, 23.33)	55.49 (46.28, 65.87)	74.70 (60.92, 91.15)	95.09 (77.56, 116.03)	2.40 (1.98, 2.81)
65–69	16.69 (14.36, 19.32)	60.98 (52.49, 70.60)	77.06 (64.05, 91.61)	109.49 (91, 130.16)	2.43 (2.02, 2.84)
70–74	12.59 (10.90, 14.34)	66.76 (57.78, 76.04)	61.90 (52.08, 72.46)	129.35 (108.83, 151.42)	2.69 (2.12, 3.26)
75–79	8.08 (7.05, 9.15)	70.83 (61.82, 80.23)	45.92 (38.79, 54.14)	153.84 (129.98, 181.41)	3.63 (3.06, 4.2)
80–84	3.81 (3.27, 4.31)	67.62 (58.02, 76.47)	28.60 (24.09, 33.49)	149.99 (126.32, 175.62)	3.82 (3.22, 4.42)
85–89	1.40 (1.18, 1.60)	73.24 (61.70, 83.30)	14.58 (12.52, 16.79)	171.41 (147.25, 197.43)	3.92 (3.48, 4.37)
90–94	0.20 (0.16, 0.22)	52.50 (43.36, 60.07)	2.47 (2.04, 2.91)	110.07 (90.75, 129.67)	3.14 (2.82, 3.46)
95+	0.02 (0.02, 0.02)	34.24 (27.55, 39.83)	0.29 (0.22, 0.35)	64.11 (49.18, 78.73)	2.69 (2.33, 3.04)

Abbreviations: CI, confidence interval; DALYs, disability-adjusted life-years; EAPC, estimated annual percentage change; UI, uncertainty interval; [a], crude DALYs rate in each age group.

Risk Factors for Kidney Cancer

In all age-specific groups, smoking among males, high body mass index among females, and high body mass index among males were the first three contributions to DALYs. The proportions of DALYs attributed to smoking, high body mass index, and occupational exposure to trichloroethylene differed between genders. The most significant contribution to DALYs for males was smoking, accounting for more than 19.5% from 1990 to 2019. The contribution of smoking to kidney cancer DALYs was about 10 times higher for males than that for females. However, a high body mass index more significantly contributed to DALYs among females than that of males. Occupational exposure to trichloroethylene accounted for the lowest proportion of DALYs in both sexes (Figure 4A). Age-specific groups analysis indicated that smoking had a great impact on the elderly male groups and occupational exposure to trichloroethylene had a great impact on middle-aged groups. The influence of high body mass index did not show a significant difference between age-specific groups (Figure 4B). Increased trends of DALYs attributable to smoking and high body mass index were observed in the elderly population and males (Figure S3). Therefore, smoking was the most significant contributor, and the high body mass index was the most increasing risk factor.

Predictions of Kidney Cancer Incidence and Death Rates in China

Based on the kidney cancer data from the GBD database from 1990 to 2019 in China, the disease burden in the next 10 years was further predicted. Our projection indicated that the rates of incidence, mortality, and the number of new cases and deaths would continue to increase in both sexes in the next decade. It is predicted that the ASIR will increase significantly in the next 10 years, especially for males (EAPC = 4.25 for males; EAPC = 2.60 for females) (Figure 5A and

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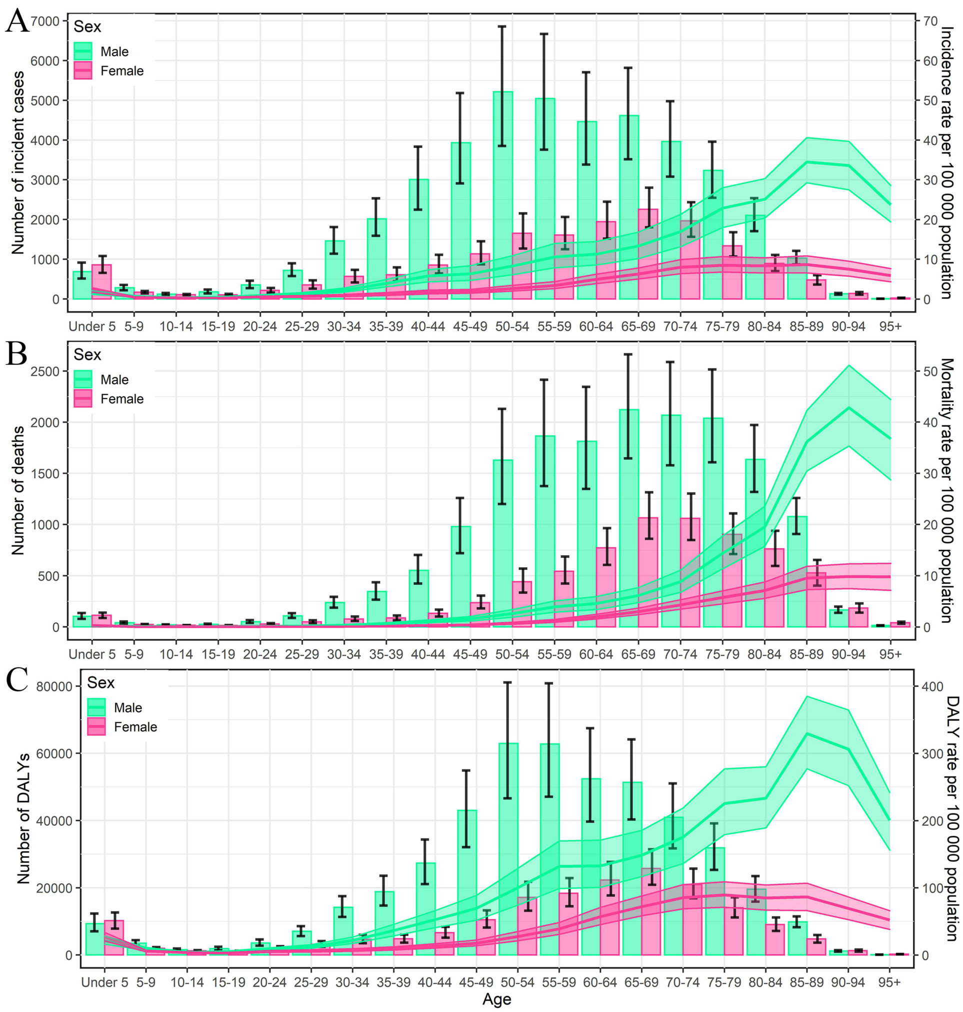

Figure 1 Disease burden of kidney cancer in 2019 in China. Numbers and rates of incidence (**A**), mortality (**B**), and DALYs (**C**) of kidney cancer by age and sex in 2019 in China. Shading represents the upper and lower limits of the 95% uncertainty intervals (95% UIs). DALYs, disability-adjusted life-years.

C). In contrast, the growth rate for ASMR somewhat slowed for both sexes over the next decade (EAPC = 2.14 for males; EAPC = 1.20 for females) (Figure 5B and D). In 2030, the predicted ASIR and ASMR of kidney cancer would increase to 7.53 per 100,000 and 2.46 per 100,000 in men, and 2.54 per 100,000 and 0.82 per 100,000 in women, respectively. In addition, although it is expected that the number of new cases and deaths of kidney cancer in China were expected to continue to increase in the next decade (126.8 thousand incident cases and 41.8 thousand deaths by 2030), the number of increased cases will be mainly male, and only slightly female (Figure 5E and F).

Discussion

Using the latest GBD 2019 data, this study reported the disease burden of renal cancer in China, and analyzed the risk factors and the time trend of incidence rate, mortality and DALYs rate of renal cancer in China. In 2019, there were about 5.983 million new cases of kidney cancer and 2.395 million deaths in China. The ASIR was 3.21 per 100,000 and the ASMR was 1.27 per 100,000. Our study indicated that the ASIR of renal cancer in males was higher than that in females, and the difference will continue into the next decade. Smoking was the most important risk factor for male renal cancer, while the high body mass index was the important risk factor for both sexes.

The ASDR of kidney cancer varied across provinces in China. The inter-provincial differences burden of kidney cancer may be partly because of the different distribution of risk factors.[30] Smoking is relatively more prevalent in southern provinces, such as Yunnan, Hunan, and Guizhou, compared with others.[31] However, the kidney cancer burden

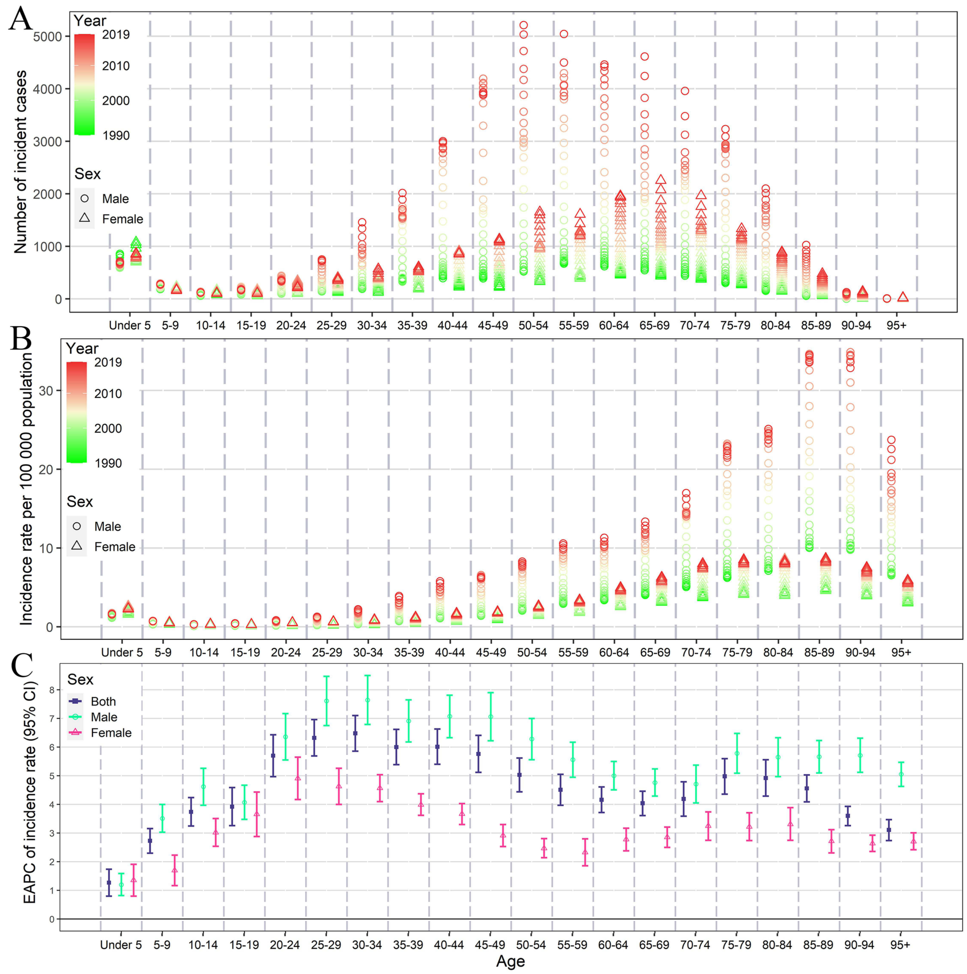

Figure 2 Temporal trends in kidney cancer burden from 1990 to 2019 in China. The number of incident cases (**A**), incidence rate (**B**) of kidney cancer by age and sex, from 1990 to 2019 in China; EAPC of incidence rate (**C**) of kidney cancer by age and sex in 2019 in China. EAPC, estimated annual percentage change.

distribution is significantly different from that of smoking. High body mass index was another risk factor for renal cancer. The body mass index of people in northern China is generally higher than that in other regions of China,[32] which is consistent with the distribution of ASDR of kidney cancer. In addition, this study indicated that the distribution of the kidney cancer burden was related to the level of regional economic development. Previous studies showed that the body mass index was positively correlated with economic income,[33] which might be the reason.

Consistent with previous studies, we found the incidence of renal cancer in men is significantly higher than that in women,[6] and so do the ASIR, ASMR and DALYs. It also showed that the cancer burden gap between males and females was and will be increasing from 1990 to 2030. Smoking is an important risk factor for renal cell carcinoma. The significantly higher prevalence of smoking among males (57.4%) compared with females (2.6%) may help explain the huge incidence gap.[34] Researches showed that hormone level contributes to the occurrence and development of kidney cancer. Overexpression of androgen receptor (AR) promoted the occurrence, invasion and migration of kidney cancer.[35] Lee et al found histone demethylase 1 affects kidney cancer progression by regulating androgen receptor activity.[36] In addition, studies found expression of estrogen receptor β (ERβ) increases with tumor stage and grade and ERβ increases ccRCC stem cell phenotype, and estrogens can reduce RCC tumor growth and invasion significantly in mouse models.[37,38] This suggested that gender might be an independent risk factor for kidney cancer.[39]

Smoking is one of the most important risk factors for kidney cancer, especially for men. The risk of kidney cancer among male ever smokers was higher compared to female ones.[40] Liu et al found that the risk of renal cancer increased nonlinearly with the increase in smoking intensity, and the risk increased sharply under relatively low smoking

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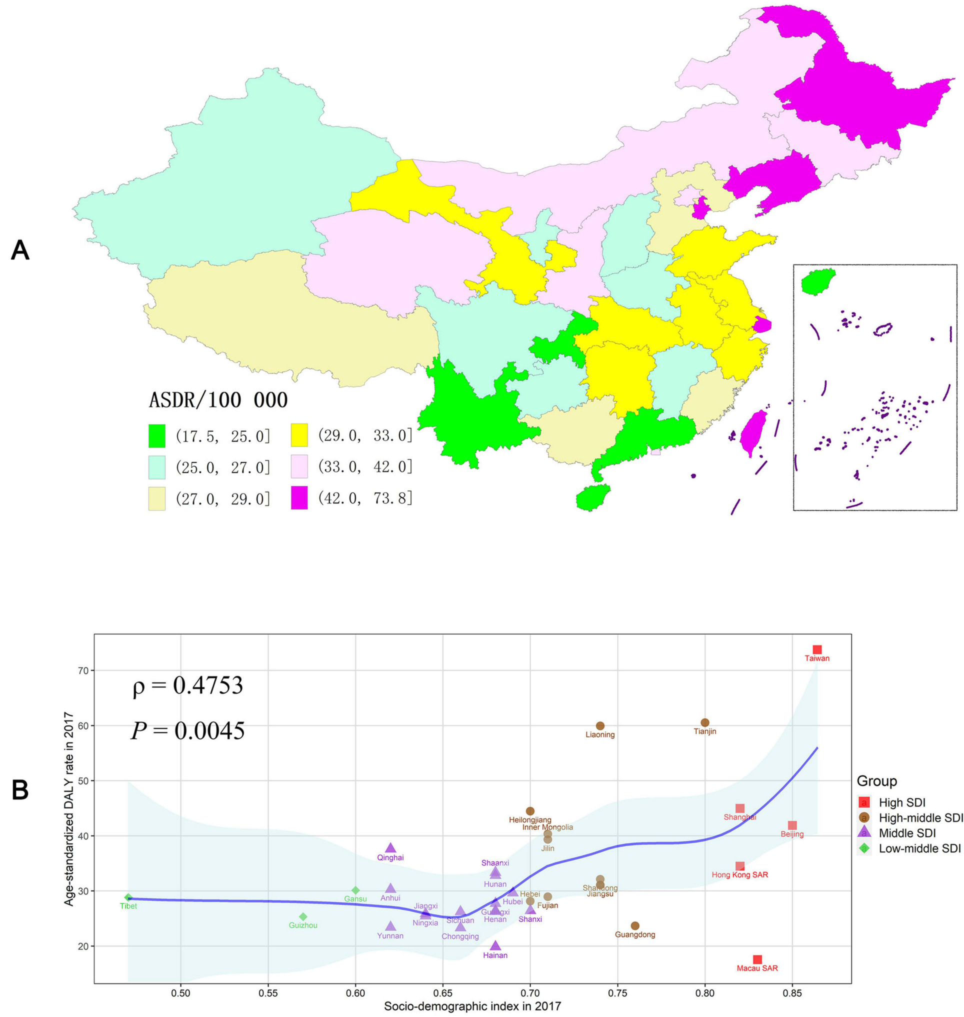

Figure 3 The province-level burden of kidney cancer in 2017 in China. Age-standardized DALY rate per 100,000 population by the province of China in 2017 (**A**) and age-standardized DALY rates for kidney cancer and SDI by province, for 2017 (**B**). DALY, disability-adjusted life-years, ASDR, age-standardized DALY rate, SDI, social-demographic index.

intensity.[41] Previous studies have shown that the susceptibility of renal cell carcinoma caused by smoking is related to a gene mutation on chromosome 3p, and it has been found von Hippel Lindau gene on chromosome 3p is one of the earliest and most common mutation sites in renal cell carcinoma.[42,43] In addition, oxygen free radicals generation and oxidative DNA damage may promote the pathogenesis of smoking-related renal cancer.[44,45] Long-term exposure to nicotine and other chemical substances increases protein kinase B expression and angiogenesis, which is conducive to the proliferation of cancer cells and the progression of kidney cancer.[46]

High body index mass was another risk factor of kidney cancer, especially for females. The tissue hypoxia, increasing adipose stromal cells, changing of immune microenvironment, and the increase of fatty acids caused by obesity may contribute to the development of kidney cancer.[47] However, Obesity not only increases the risk of RCC development but also decreases the risk of recurrence and increases overall survival [48–51], which is called the "obesity paradox". Albiges et al reported that high body mass index is related to better overall survival and progression-free survival.[52] The cause of this phenomenon is still unclear, so further studies are needed to explore its potential mechanism.

The persistent upsurge in the incidence of kidney cancer in China can be partially attributed to the recent advancements in diagnostic modalities that have facilitated a greater rate of early detection[53] and stage T1 tumors accounted for the majority.[54] In Europe, similarly, the proportion of patients diagnosed with early-stage RCC has experienced an upward trend over the past few decades, owing to the influence of stage migration.[55] Besides, it is similar to the

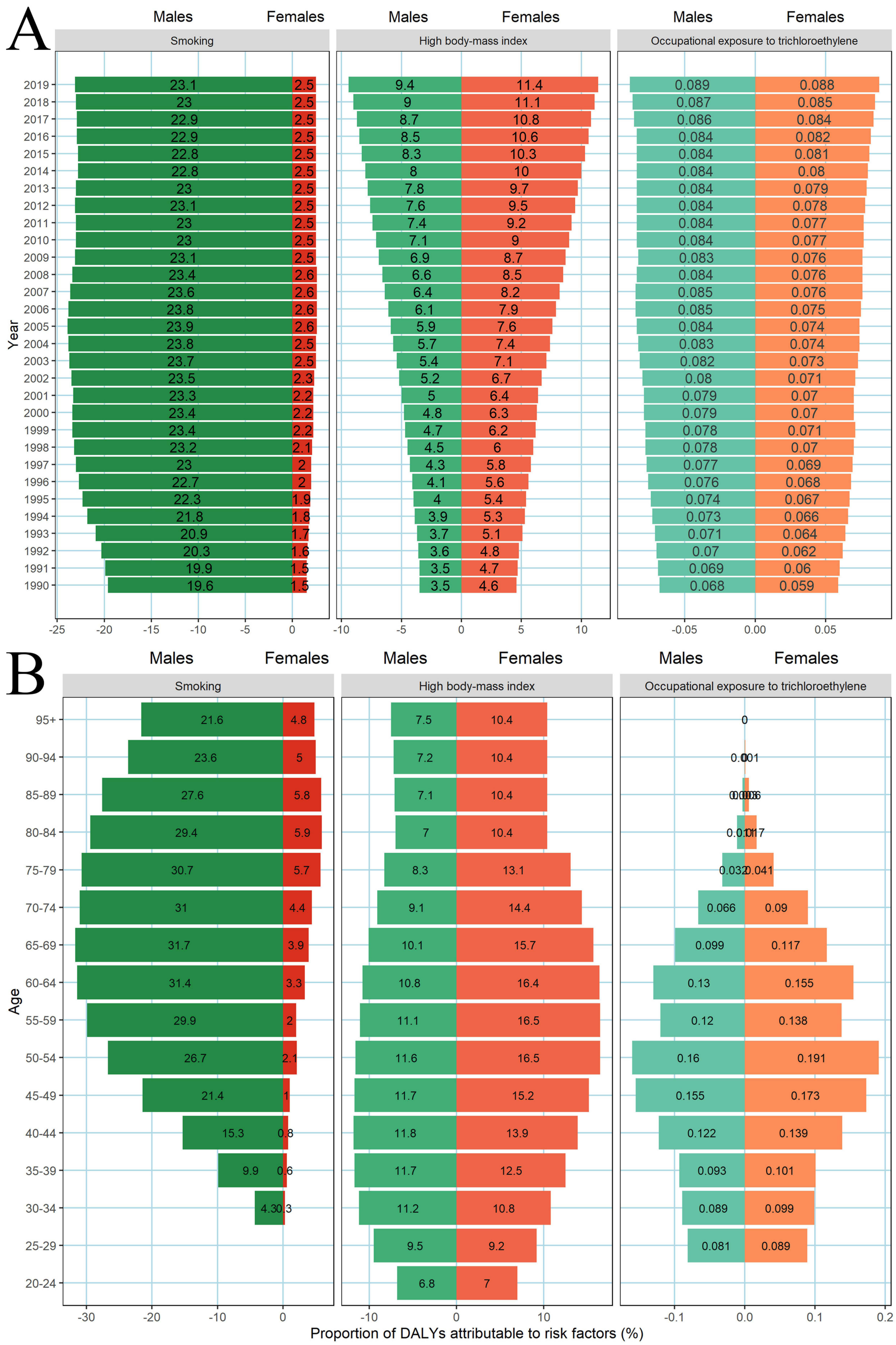

Figure 4 Risk factor analysis for kidney cancer in China. Proportions of DALYs of kidney cancer attributable to risk factors by sex from 1990 to 2019 in China (**A**); and proportions of DALYs attributable to risk factors by age and sex in 2019 in China (**B**). DALYs, disability-adjusted life-years.

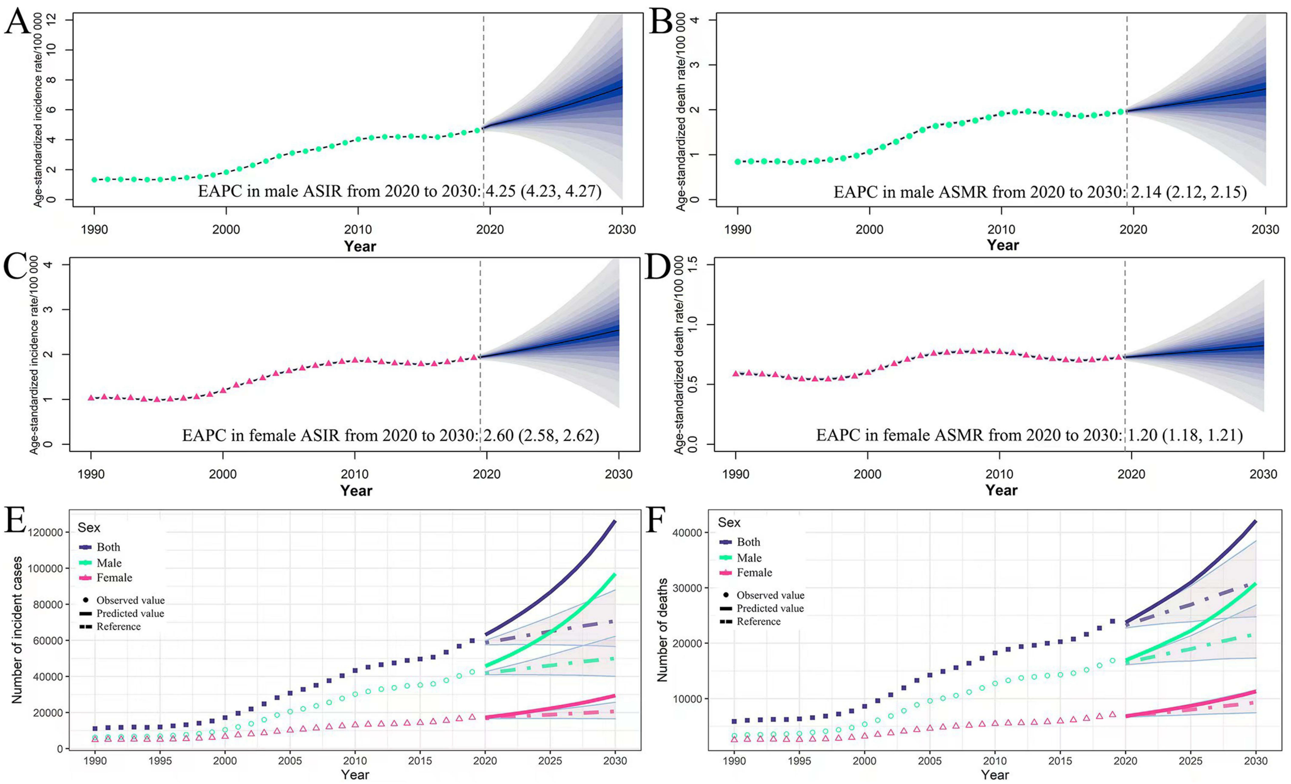

Figure 5 Predictions of kidney cancer incidence and death rates in China until 2030. Temporal trends and projected age-standardized incidence rate and age-standardized death rate by sex, from 1990 to 2030 in China (**A** and **B** for male, **C** and **D** for female); Trends in observed (dashed lines) and projected (solid lines) kidney cancer in the number of incidence cases (**E**) and deaths (**F**) from 1990 to 2030. Shading represents a 2% decreasing and increasing interval based on the 2019 rate.

epidemiological trend of kidney cancer in China that the incidence, mortality, ASIR and ASMR increased in most European Union (EU) 15+ countries and World Health Organization (WHO) regions from 1990 to 2019.[56] Chinmay et al also reported the mortality-to-incidence ratio (MIR) decreased in all EU countries and WHO regions. Although MIR was not evaluated in this article, we predicted the growth rate for ASMR somewhat slowed for both sexes over the next decade, which may bring a slowdown in MIR.

The incidence of kidney cancer is still rising in China. As the trend of the elderly population increases in China,[57] the incidence of kidney cancer will further increase and bring considerable pressure on the public health system in China. To reduce the incidence of kidney cancer, the top priority in China is to control the body mass index and smoking rates of the population.[58] The government should fully promote the smoke-free policy and actively publicize the harm of tobacco. With the development of the economy and the improvement of income level, the body mass index of Chinese people is on the rise. The government should widely advocate a healthy diet and promote nationwide fitness. At the same time, the application of a screening program, which integrates abdominal ultrasound scans and the analysis of urinary biomarkers, may be beneficial in enabling the early detection of kidney cancer and facilitating the administration of minimally invasive surgical therapies.[59] It is similar to most health problems, that promoting early prevention and screening programs is the most important and economic measure for renal cancer prevention.

This study still has some limitations. Firstly, the data provided by GBD 2019 comes from different sources, and the quality of the original data may affect the results of this study. Although various mathematical models were used in this study to correct the data, the effects cannot be ignored. Secondly, the study did not involve the impact of other risk factors such as genetic factors on the burden of renal cancer. Thirdly, this study mainly involved renal cell carcinoma. Other histological classifications, such as ccRCC and pRCC, although their oncological characteristics and prognosis are different, due to their low incidence, did not make the separate analysis.

Conclusions

In conclusion, the total burden of kidney cancer increased gradually over the latest 30 years, and it would still increase in the next decade, especially for males, in China. Smoking and high body mass index are the most important risk factors for renal cell carcinoma, and the influence of high body mass index is increasing year by year. We should formulate detailed and targeted prevention and control strategies, such as health education publicity and high-risk population screening, to reduce the socioeconomic pressure brought by kidney cancer.

Abbreviations

DALYs, disability-adjusted life-years; EAPC, estimated annual percentage change; ASIR, age-standardized incidence rate; RCC, renal cell carcinoma; ccRCC, clear cell RCC; pRCC, papillary RCC; GBD, Global Burden of Diseases; GHDx, Global Health Data Exchange; ASDR, age-standardized DALY rate; SDI, socio-demographic index; CRA, comparative risk assessment; ASIR, age-standardized incidence rate; ASMR, age-standardized mortality rate; CI, confidence interval; BAPC, Bayesian age-period cohort; INLA, integrated nested Laplace approximation; AR, androgen receptor; STAT5, signal transducer and activator of transcription 5; BARE trial, Blockade of Androgens in Renal cell carcinoma using Enzalutamide; EU, European Union; WHO, World Health Organization; MIR, mortality-to-incidence ratio.

Data Sharing Statement

The GBD 2019 study is a publicly available database (http://ghdx.healthdata.org/gbd-2019), and we fully complied with the GBD data usage requirements.

Ethics Approval and Consent to Participate

The GBD 2019 study is a publicly available database, and all data were anonymous. Our study protocol was approved by the Institutional Review Boards of Qilu Hospital of Shandong University with approval number KYLL-202011(KS)-239.

Consent for Publication

Not applicable due to no individual information.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

All authors declare that they have no competing interests.

References

1. World Health Organization. Global health estimates 2020: deaths by cause, age, sex, by country and by region, 2000–2019; 2020. Available from: http://who.int/data/gho/data/themes/mortality-and-global-health-estimates/ghe-leading-causes-of-death. Accessed March 16, 2023.
2. Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2021;71:209–249. PMBI: 33538338. doi:10.3322/caac.21660
3. Moch H, Cubilla AL, Humphrey PA, et al. The 2016 WHO classification of tumours of the urinary system and male genital organs-part a: renal, penile, and testicular tumours. *Eur Urol*. 2016;70:93–105. PMBI: 26935559. doi:10.1016/j.eururo.2016.02.029
4. Cochetti G, Cari L, Nocentini G, et al. Detection of urinary miRNAs for diagnosis of clear cell renal cell carcinoma. *Sci Rep*. 2020;10(1):21290. PMBI: 33277569. doi:10.1038/s41598-020-77774-9
5. Bukavina L, Bensalah K, Bray F, et al. Epidemiology of renal cell carcinoma: 2022 update. *Eur Urol*. 2022. PMBI: 36100483. doi:10.1016/j.eururo.2022.08.019
6. Znaor A, Lortet-Tieulent J, Laversanne M, et al. International variations and trends in renal cell carcinoma incidence and mortality. *Eur Urol*. 2015;67:519–530. PMBI: 25449206. doi:10.1016/j.eururo.2014.10.002
7. Scelo G, Li P, Chanudet E, et al. Variability of sex disparities in cancer incidence over 30 years: the striking case of kidney cancer. *Eur Urol Focus*. 2018;4:586–590. PMBI: 28753845. doi:10.1016/j.euf.2017.01.006
8. Zbar B, Alvord WG, Glenn G, et al. Risk of renal and colonic neoplasms and spontaneous pneumothorax in the Birt-Hogg-Dubé syndrome. *Cancer Epidemiol Biomarkers Prev*. 2002;11:393–400. PMBI: 11927500.
9. Grubb RL, Franks ME, Toro J, et al. Hereditary leiomyomatosis and renal cell cancer: a syndrome associated with an aggressive form of inherited renal cancer. *J Urol*. 2007;177:2074–9;discussion 2079–80. PMBI: 17509289. doi:10.1016/j.juro.2007.01.155
10. Roger VL, Go AS, Lloyd-Jones DM, et al. Heart disease and stroke statistics--2011 update: a report from the American Heart Association. *Circulation*. 2011;123:e18–18e209. PMBI: 21160056. doi:10.1161/CIR.0b013e3182009701
11. Bhaskaran K, Douglas I, Forbes H, et al. Body-mass index and risk of 22 specific cancers: a population-based cohort study of 5·24 million UK adults. *Lancet*. 2014;384:755–765. PMBI: 25129328. doi:10.1016/S0140-6736(14)60892-8
12. Kaelin WG Jr. The VHL tumor suppressor gene: insights into oxygen sensing and cancer. *Trans Am Clin Climatol Assoc*. 2017;128:298–307. PMBI: 28790514.
13. Liu SZ, Guo LW, Cao XQ, et al. 2014年肾癌发病与死亡分析[Estimation on the incidence and mortality of kidney cancer in China, in 2014中国]. *Zhonghua Liu Xing Bing Xue Za Zhi*. 2018;39:1346–1350. PMBI: 30453435. PMBI: 30453435. doi:10.3760/cma.j.issn.0254-6450.2018.10.011
14. Vos T, Lim SS, Abbafati C, et al. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet*. 2020;396:1204–1222. PMBI: 33069326. doi:10.1016/S0140-6736(20)30925-9
15. Pinheiro PS, Medina HN, Callahan KE, et al. Kidney cancer mortality disparities among Hispanics in the US. *Cancer Epidemiol*. 2021;72:101938. PMBI: 33862414. doi:10.1016/j.canep.2021.101938
16. Azawi NH, Joergensen SM, Jensen NV, et al. Trends in kidney cancer among the elderly in Denmark, 1980–2012. *Acta Oncol*. 2016;55(Suppl 1):79–84. PMBI: 26784139. doi:10.3109/0284186X.2015.1115121
17. Assouad E, El Hage S, Safi S, et al. Kidney cancer trends and risk factors in Lebanon: a 12-year epidemiological study. *Cancer Causes Control*. 2022;33:303–312. PMBI: 34839395. doi:10.1007/s10552-021-01525-y
18. Wang YZ, Hu Y. 1992-2016年中国肾癌死亡趋势的年龄-时期-队列分析[Age-period-cohort analysis on kidney cancer mortality trend in China, 1992–2016]. *Zhonghua Liu Xing Bing Xue Za Zhi*. 2021;42:508–512. PMBI: 34814421. PMBI: 34814421. doi:10.3760/cma.j.cn112338-20200224-00156
19. Zhang T, Chen H, Yin X, et al. Changing trends of disease burden of gastric cancer in China from 1990 to 2019 and its predictions: findings from Global Burden of Disease Study. *Chin J Cancer Res*. 2021;33:11–26. PMBI: 33707924. doi:10.21147/j.issn.1000-9604.2021.01.02
20. Wang H, Abbas KM, Abbasifard M, et al. Global age-sex-specific fertility, mortality, healthy life expectancy (HALE), and population estimates in 204 countries and territories, 1950–2019: a comprehensive demographic analysis for the Global Burden of Disease Study 2019. *Lancet*. 2020;396:1160–1203. PMBI: 33069325. doi:10.1016/S0140-6736(20)30977-6
21. Zhou M, Wang H, Zeng X, et al. Mortality, morbidity, and risk factors in China and its provinces, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet*. 2019;394:1145–1158. PMBI: 31248666. doi:10.1016/S0140-6736(19)30427-1
22. Murray CJ, Aravkin AY, Zheng P, et al. Global burden of 87 risk factors in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet*. 2020;396:1223–1249. PMBI: 33069327. doi:10.1016/S0140-6736(20)30752-2
23. Wiseman M. The second World Cancer Research Fund/American Institute for Cancer Research expert report. Food, nutrition, physical activity, and the prevention of cancer: a global perspective. *Proc Nutr Soc*. 2008;67:253–256. PMBI: 18452640. doi:10.1017/S002966510800712X
24. Chen J, Chen H, Zhang T, et al. Burden of pancreatic cancer along with attributable risk factors in China from 1990 to 2019, and projections until 2030. *Pancreatology*. 2022;22:608–618. PMBI: 35513974. doi:10.1016/j.pan.2022.04.011
25. Fang Y, Li Z, Chen H, et al. Burden of lung cancer along with attributable risk factors in China from 1990 to 2019, and projections until 2030. *J Cancer Res Clin Oncol*. 2022;2022:1. doi:10.1007/s00432-022-04217-5
26. Gao S, Yang WS, Bray F, et al. Declining rates of hepatocellular carcinoma in urban Shanghai: incidence trends in 1976–2005. *Eur J Epidemiol*. 2012;27:39–46. PMBI: 22160277. doi:10.1007/s10654-011-9636-8
27. Wang H, Zhao S, Wang S, et al. Global magnitude of encephalitis burden and its evolving pattern over the past 30 years. *J Infect*. 2022;84(6):777–787. PMBI: 35452715. doi:10.1016/j.jinf.2022.04.026
28. Zhang T, Yin X, Chen H, et al. Global magnitude and temporal trends of idiopathic developmental intellectual disability attributable to lead exposure from 1990 to 2019: results from Global Burden of Disease Study. *Sci Total Environ*. 2022;834:155366. PMBI: 35460796. doi:10.1016/j.scitotenv.2022.155366
29. Zhang L, Cao F, Zhang G, et al. Trends in and predictions of colorectal cancer incidence and mortality in china from 1990 to 2025. *Front Oncol*. 2019;9:98. PMBI: 30847304. doi:10.3389/fonc.2019.00098
30. Zhou M, Wang H, Zhu J, et al. Cause-specific mortality for 240 causes in China during 1990-2013: a systematic subnational analysis for the Global Burden of Disease Study 2013. *Lancet*. 2016;387:251–272. PMBI: 26510778. doi:10.1016/S0140-6736(15)00551-6

31. Astell-Burt T, Zhang M, Feng X, et al. Geographical inequality in tobacco control in China: multilevel evidence from 98 058 participants. *Nicotine Tob Res*. 2018;20:755–765. PMBI: 28520988. doi:10.1093/ntr/ntx100
32. Tang D, Bu T, Feng Q, et al. Differences in overweight and obesity between the North and South of China. *Am J Health Behav*. 2020;44:780–793. PMBI: 33081876. doi:10.5993/AJHB.44.6.4
33. Xu F, Yin XM, Zhang M, et al. Family average income and body mass index above the healthy weight range among urban and rural residents in regional Mainland China. *Public Health Nutr*. 2005;8:47–51. PMBI: 15705245. doi:10.1079/phn2005653
34. Yang GH, Ma JM, Liu N, et al. 中国人群2002年吸烟和被动吸烟的现状调查[Smoking and passive smoking in Chinese, 2002]. *Zhonghua Liu Xing Bing Xue Za Zhi*. 2005;26:77–83. PMBI: 15921604. PMBI: 15921604.
35. He D, Li L, Zhu G, et al. ASC-J9 suppresses renal cell carcinoma progression by targeting an androgen receptor-dependent HIF2α/VEGF signaling pathway. *Cancer Res*. 2014;74:4420–4430. PMBI: 24924778. doi:10.1158/0008-5472.CAN-13-2681
36. Lee KH, Kim BC, Jeong SH, et al. Histone demethylase LSD1 regulates kidney cancer progression by modulating androgen receptor activity. *Int J Mol Sci*. 2020;21(17):6089. PMBI: 32847068. doi:10.3390/ijms21176089
37. Wang Y, Yang Z, Gu J, et al. Estrogen receptor beta increases clear cell renal cell carcinoma stem cell phenotype via altering the circPHACTR4/miR-34b-5p/c-Myc signaling. *FASEB J*. 2022;36(2):e22163. PMBI: 35061326. doi:10.1096/fj.202101645R
38. Song W, He D, Chen Y, et al. Targeting newly identified ERβ/TGF-β1/SMAD3 signals with the FDA-approved anti-estrogen Faslodex or an ERβ selective antagonist in renal cell carcinoma. *Mol Oncol*. 2018;12(12):2055–2071. PMBI: 30171816. doi:10.1002/1878-0261.12377
39. Peired AJ, Campi R, Angelotti ML, et al. Sex and gender differences in kidney cancer: clinical and experimental evidence. *Cancers*. 2021;13:1. PMBI: 34572815. doi:10.3390/cancers13184588
40. Hunt JD, van der Hel OL, McMillan GP, et al. Renal cell carcinoma in relation to cigarette smoking: meta-analysis of 24 studies. *Int J Cancer*. 2005;114:101–108. PMBI: 15523697. doi:10.1002/ijc.20618
41. Liu X, Peveri G, Bosetti C, et al. Dose-response relationships between cigarette smoking and kidney cancer: a systematic review and meta-analysis. *Crit Rev Oncol Hematol*. 2019;142:86–93. PMBI: 31387065. doi:10.1016/j.critrevonc.2019.07.019
42. Koul H, Huh JS, Rove KO, et al. Molecular aspects of renal cell carcinoma: a review. *Am J Cancer Res*. 2011;1:240–254. PMBI: 21969126.
43. Zhu Y, Horikawa Y, Yang H, et al. BPDE induced lymphocytic chromosome 3p deletions may predict renal cell carcinoma risk. *J Urol*. 2008;179:2416–2421. PMBI: 18433782. doi:10.1016/j.juro.2008.01.092
44. Arany I, Reed DK, Grifoni SC, et al. A novel U-STAT3-dependent mechanism mediates the deleterious effects of chronic nicotine exposure on renal injury. *Am J Physiol Renal Physiol*. 2012;302:F722. PMBI: 22169004. doi:10.1152/ajprenal.00338.2011
45. Guo X, Li X, Wang Y, et al. Nicotine induces alteration of H3K27 demethylase UTX in kidney cancer cell. *Hum Exp Toxicol*. 2014;33:264–269. PMBI: 23925944. doi:10.1177/0960327113499043
46. Heeschen C, Jang JJ, Weis M, et al. Nicotine stimulates angiogenesis and promotes tumor growth and atherosclerosis. *Nat Med*. 2001;7:833–839. PMBI: 11433349. doi:10.1038/89961
47. Gluba-Brzózka A, Rysz J, Ławiński J, et al. Renal cell cancer and obesity. *Int J Mol Sci*. 2022;23:1. PMBI: 35328822. doi:10.3390/ijms23063404
48. Choi Y, Park B, Jeong BC, et al. Body mass index and survival in patients with renal cell carcinoma: a clinical-based cohort and meta-analysis. *Int J Cancer*. 2013;132:625–634. PMBI: 22610826. doi:10.1002/ijc.27639
49. Parker AS, Lohse CM, Cheville JC, et al. Greater body mass index is associated with better pathologic features and improved outcome among patients treated surgically for clear cell renal cell carcinoma. *Urology*. 2006;68:741–746. PMBI: 17070345. doi:10.1016/j.urology.2006.05.024
50. Waalkes S, Merseburger AS, Kramer MW, et al. Obesity is associated with improved survival in patients with organ-confined clear-cell kidney cancer. *Cancer Causes Control*. 2010;21:1905–1910. PMBI: 20652393. doi:10.1007/s10552-010-9618-2
51. Hakimi AA, Furberg H, Zabor EC, et al. An epidemiologic and genomic investigation into the obesity paradox in renal cell carcinoma. *J Natl Cancer Inst*. 2013;105:1862–1870. PMBI: 24285872. doi:10.1093/jnci/djt310
52. Albiges L, Hakimi AA, Xie W, et al. Body mass index and metastatic renal cell carcinoma: clinical and biological correlations. *J Clin Oncol*. 2016;34(30):3655–3663. PMBI: 27601543. doi:10.1200/JCO.2016.66.7311
53. Pang C, Guan Y, Li H, et al. Urologic cancer in China. *Jpn J Clin Oncol*. 2016;46(6):497–501. PMBI: 27049022. doi:10.1093/jjco/hyw034
54. Bai T, Wang L, Wang D, et al. Clinicopathological epidemiological characteristics and change tendencies of renal cell carcinoma in Shanxi Province of China from 2005 to 2014. *PLoS One*. 2015;10(12):e0144246. PMBI: 26633179. doi:10.1371/journal.pone.0144246
55. Bianchi L, Schiavina R, Bortolani B, et al. Interpreting nephrometry scores with three-dimensional virtual modelling for better planning of robotic partial nephrectomy and predicting complications. *Urol Oncol*. 2021;39(12):836.e1–836.e9. PMBI: 34535356. doi:10.1016/j.urolonc.2021.07.024
56. Jani C, Abdallah N, Mouchati C, et al. Trends of kidney cancer burden from 1990 to 2019 in European Union 15 + countries and World Health Organization regions. *Sci Rep*. 2022;12(1):22368. PMBI: 36572700. doi:10.1038/s41598-022-25485-8
57. Wu L, Huang Z, Pan Z. The spatiality and driving forces of population ageing in China. *PLoS One*. 2021;16:e0243559. PMBI: 33428682. doi:10.1371/journal.pone.0243559
58. Tahbaz R, Schmid M, Merseburger AS. Prevention of kidney cancer incidence and recurrence: lifestyle, medication and nutrition. *Curr Opin Urol*. 2018;28:62–79. PMBI: 29059103. doi:10.1097/MOU.0000000000000454
59. Cochetti G, Cari L, Maulà V, et al. Validation in an independent cohort of MiR-122, MiR-1271, and MiR-15b as urinary biomarkers for the potential early diagnosis of clear cell renal cell carcinoma. *Cancers*. 2022;14(5):1112. PMBI: 35267420. doi:10.3390/cancers14051112