Age-sex-specific burden of urological cancers attributable to risk factors in China and its provinces, 1990–2021, and forecasts with scenarios simulation: a systematic analysis for the Global Burden of Disease Study 2021

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The Lancet Regional Health - Western Pacific 2025;56: 101517

Published Online 18 March 2025

https://doi.org/10.1016/j.lanwpc.2025.101517

Summary

Background As global aging intensifies, urological cancers pose increasing health and economic burdens. In China, home to one-fifth of the world's population, monitoring the distribution and determinants of these cancers and simulating the effects of health interventions are crucial for global and national health.

Methods With Global Burden of Disease (GBD) China database, the present study analyzed age-sex-specific patterns of incidence, prevalence, mortality, disability-adjusted life years (DALYs), years lived with disability (YLDs), and years of life lost (YLLs) in China and its 34 provinces as well as the association between gross domestic product per capita (GDPPC) and these patterns. Importantly, a multi-attentive deep learning pipeline (iTransformer) was pioneered to model the spatiotemporal patterns of urological cancers, risk factors, GDPPC, and population, to provide age-sex-location-specific long-term forecasts of urological cancer burdens, and to investigate the impacts of risk-factor-directed interventions on their future burdens.

Findings From 1990 to 2021, the incidence and prevalence of urological cancers in China has increased, leading to 266,887 new cases (95% confidence interval: 205,304–346,033) and 159,506,067 (12,236,0000–207,447,070) cases in

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2021, driven primarily by males aged 55+ years. In 2021, Taiwan, Beijing, and Zhejiang had the highest age-standardized incidence rate (ASIR) and age-standardized prevalence rates of urological cancer in China, highlighting significant regional disparities in the disease burden. Conversely, the national age-standardized mortality rate (ASMR) has declined from 6.5 (5.1–7.8) per 100,000 population in 1990 to 5.6 (4.4–7.2) in 2021, notably in Jilin [−166.7% (−237 to −64.6)], Tibet [−135.4% (−229.1 to 4.4)], and Heilongjiang [−118.5% (−206.5 to −4.6)]. Specifically, the national ASMR for bladder and testicular cancers reduced by −32.1% (−47.9 to 1.9) and −31.1% (−50.2 to 7.2), respectively, whereas prostate and kidney cancers rose by 7.9% (−18.4 to 43.6) and 9.2% (−12.2 to 36.5). Age-standardized DALYs, YLDs, and YLLs for urological cancers were consistent with ASMR. Males suffered higher burdens of urological cancers than females in all populations, except those aged <5 years. Regionally and provincially, high GDPPC provinces have the highest burden of prostate cancer, while the main burden in other provinces is bladder cancer. The main risk factors for urological cancers in 2021 are smoking [accounting for 55.1% (42.7–67.4)], high body mass index [13.9% (5.3–22.4)], and high fasting glycemic index [5.9% (−0.8 to 13.4)] for both males and females, with smoking remarkably affecting males and high body mass index affecting females. Between 2022 and 2040, the ASIR of urological cancers increased from 10.09 (9.19–10.99) to 14.42 (14.30–14.54), despite their ASMR decreasing. Notably, prostate cancer surpassed bladder cancer as the primary subcategory, with those aged 55+ years showing the highest increase in ASIR, highlighting the aging-related transformation of the urological cancer burden. Following the implementation of targeted interventions, smoking control achieved the greatest reduction in urological cancer burden, mainly affecting male bladder cancer (−45.8% decline). In females, controlling smoking and high fasting plasma glucose reduced by 5.3% and 5.8% ASMR in urological cancers. Finally, the averaged mean-square-Percentage-Error, absolute-Percentage-Error, and root-mean-square Logarithmic-Error of the forecasting model are 0.54 ± 0.22, 1.51 ± 1.26, and 0.15 ± 0.07, respectively, indicating that the model performs well.

Interpretation Urological cancers exhibit an aging trend, with increased incidence rates among the population aged 55+ years, making prostate cancer the most burdensome subcategory. Moreover, urological cancer burden is imbalanced by age, sex, and province. Based on our findings, authorities and policymakers could refine or tailor population-specific health strategies, including promoting smoking cessation, weight reduction, and blood sugar control.

Funding Bill & Melinda Gates Foundation.

Keywords: Global Burden of Disease; Urological cancer; Mortality and disability; Risk factor; Attentive deep learning; Forecasting; Scenarios simulation

Introduction

Urological cancers, including prostate, bladder, kidney, and testicular cancers, represent critical global health challenges. According to the Global Cancer Statistics (GLOBOCAN) 2022,[1] prostate cancer is the second most common cancer and the fifth leading cause of cancer-related deaths among males. Bladder cancer and kidney cancer rank 9th and 14th in incidence and 13th and 16th in mortality worldwide, respectively. Despite the increasing prevalence, there has been a scarcity of comprehensive studies focusing on the epidemiology of urological cancers in China, highlighting a significant knowledge gap in understanding regional disease patterns and determinants. China is experiencing rapid aging, which may lead to a continued increase in the burden of urological cancers.[2] The age-standardized incidence rate of prostate cancer in China in 2019 accounted for 10.8% of the global incidence rate and 11.2% of the global mortality rate, both of which were significantly higher than those in 1990.[3] Therefore, monitoring and forecasting the distribution and determinants of urological cancers in China is of global importance, as one-fifth of the global population lives in China.

The Global Burden of Disease (GBD) study collaborators have previously reported the burden of cancer in various countries. However, epidemics in recent years have exacerbated the burden of disease, including cancer, especially in developing countries, such as China. There is a notable lack of standardized studies on the burden of urological cancers within the Chinese population, which limits the ability to formulate targeted public health strategies. GBD recently updated its burden of disease data for 2021,[4] and analysis of the updated data across multiple dimensions, including age, sex, and geographic location, is necessary to further understand the burden of urological cancers in China.

GBD provides a reliable framework for analyzing the burden of disease and attributable burden of risk factors. China has 34 provincial-level administrative regions with large differences in development and healthcare resources between regions. This study used

Research in context

Evidence before this study

We conducted a systematic review of studies on urological cancer epidemiology in China and its provinces by searching PubMed, Web of Science, and Chinese language databases from their inception to December 2023 (no language restrictions). Search terms included combinations of "urological cancers," "prostate cancer," "bladder cancer," "kidney cancer," "testicular cancer," "GBD," "China," "provinces of China", "epidemiology," "incidence," "mortality," "risk factors," and "forecasting." We included studies that reported incidence, prevalence, or mortality of urological cancers in Chinese populations, with or without stratification by age, sex, or location. Reviews and reports without original data were excluded. Our search revealed fragmented data on the provincial burden of prostate and bladder cancers, with sparse provincial coverage of kidney and testicular cancers. Additionally, most studies lacked comprehensive province-level analyses and robust forecasting methods. Although some research identified aging, smoking, and metabolic disorders as important risk factors, few provided age-sex-location forecasts or assessed how risk-factor modifications might influence future burdens. The quality of the existing evidence varied due to inconsistent study designs, heterogeneous populations, and limited modeling approaches.

Added value of this study

This study is the first to provide a systematic, province-level assessment of four major urological cancers (prostate, bladder, kidney, and testicular) in China and its provinces over a three-decade span (1990–2021) using the Global Burden of Disease (GBD) dataset. By implementing a novel multi-attentive deep learning model (iTransformer), we accurately forecasted age-sex-location-specific burdens through 2040 and simulated the potential benefits of risk-factor-directed interventions. Importantly, we showed how prostate cancer is rapidly becoming the leading cause of urological cancer burden in higher GDP per capita (GDPPC) provinces, while bladder cancer remains the predominant concern elsewhere. Moreover, we quantified the impact of major behavioral and metabolic risk factors—particularly smoking, high fasting plasma glucose, and high body mass index—on current and future urological cancer burdens. These insights broaden the existing knowledge base by integrating advanced forecasting methods, nuanced subcategory analyses, and targeted scenario simulations in diverse economic settings.

Implications of all the available evidence

Our findings highlight the urgent need for comprehensive, region-specific strategies to curb the rising incidence and shifting patterns of urological cancers in China. The accelerated transition toward prostate cancer in older populations and high-GDPPC provinces underscores the importance of implementing or expanding screening programs, improving access to early diagnosis, and developing tailored treatments—especially for individuals aged 55 years and above. Smoking cessation emerged as the most impactful intervention for reducing mortality, particularly in bladder cancer among males, suggesting that tobacco control policies and robust smoking cessation campaigns should be prioritized. Additionally, addressing metabolic risk factors (e.g., obesity and dysglycemia) will be critical, especially in regions experiencing rapid demographic and lifestyle changes. Taken together, these measures can help mitigate the growing health and economic burdens of urological cancers in China and may serve as a blueprint for other rapidly aging and industrializing nations worldwide.

the latest GBD 2021 data to provide a comprehensive analysis of the incidence, prevalence, mortality, disability-adjusted life years (DALYs), years of life lost (YLLs), and years lived with disability (YLDs) of urological cancers at national and regional levels in China between 1990 and 2021, stratified by sex, age, and tumor type (prostate, bladder, kidney, and testicular cancer). We also estimated the attributable burden of urological cancers according to national and provincial risk factors in China between 1990 and 2021. Moreover, we forecast the burden of urological cancers in China and at the provincial level up to 2040 using an advanced deep learning model. We simulated changes in the burden of urological cancers under the two intervention scenarios. Implementing targeted healthcare policies is expected to significantly reduce the incidence and mortality rates of urological cancers in China. Enhanced screening programs, improved access to treatment, and public awareness campaigns are anticipated to mitigate the overall cancer burden. Additionally, policies aimed at addressing risk factors such as smoking cessation, obesity prevention, and environmental controls are likely to contribute to a decline in new cancer cases and improve survival rates. The aim of this study was to provide a comprehensive view of the burden of urological cancers in China as a whole and by region and to inform relevant healthcare policies.

Methods

Overall

The Global Burden of Disease 2021 presented detailed assessments of the effects of 371 diseases and injuries in 204 countries and regions. Key epidemiological metrics, including incidence, prevalence, mortality, disability-adjusted life years, years of life lost, years lived with disability, and attributable risk factors, were systematically calculated for these conditions. The methods used to generate these estimates have been comprehensively documented in previous publications.[4–7]

As an extension of the GBD 2021, this study leveraged the GBD 2021 China database and focused on the burden of urological cancers in China and its 34 provinces. Some of these national and provincial data presented here were publicly available on the Global Health Data Exchange website (https://ghdx.healthdata.org/) and additional data can be requested from Institute for Health Metrics and Evaluation. We measured the incidence, prevalence, mortality, DALYs, and risk factors for these cancers, dissected by age and sex at both national and provincial levels, as detailed in Appendix 1. This study conforms to the guidelines for accurate and transparent health estimate reporting (GATHER).[8]

Moreover, to analyze regional disease burden rankings, we employed Robust Rank Aggregation (RRA), a method that aggregates cause-specific rankings across provinces within larger regions. For example, the Central China rankings for incidence, prevalence, deaths, YLL, YLD, and DALY were derived from the rankings of Henan, Hubei, and Hunan provinces. This method minimizes the influence of outliers or inconsistent trends in individual provinces, ensuring a robust and representative regional ranking. The results from RRA provide a comprehensive understanding of the disease burden at the regional level, highlighting the major contributors to urological cancer burdens across broader geographical areas.

Additionally, changes in disease burden are influenced by multiple factors, often following nonlinear trajectories. To explore the relationship between GDP per capita and urological cancer burden, we used Generalized Additive Model (GAM), which can flexibly model nonlinear associations. By fitting smooth functions to the data, GAM enabled us to capture complex trends and interactions that linear models would overlook. This approach revealed nuanced patterns, such as inflection points or saturation effects, in the relationship between economic development and disease burden, providing more accurate and actionable insights for public health planning.

All the analyses were conducted by using R software (version 4.3.1) and python (version 3.8.12). All data employed in this study were anonymized and aggregated, ensuring the exclusion of any personally identifiable information. As a result, ethics approval and consent for participation were not required.

Forecasting with scenarios simulation

The state-of-the-art deep learning model, Inverted Transformers (iTransformer), was modified to predict the incidence, mortality, DALY, YLD, and YLL rates of urological cancer. The risk factors, population, and GDPPC were standardized and incorporated as covariates during model training. By leveraging historical data and covariates, the iTransformer can forecast future time series of these outcomes, which can be mathematically expressed as:

For multivariate time series of risk factors and outcomes $\mathbf{X} \in \mathbb{R}^{T \times N}$, with temporal length T and number of features N, the iTransformer simultaneously represented all variables as $\mathbf{X}_{t,:}$, and denoted $\mathbf{X}_{:,n}$ as the entire time series for the same variables. The embedding layers were utilized to learn the series representation of $\mathbf{X}_{:,n}$, followed by the independent aggregation of global features for each variable:

$$\mathbf{H} = \{h_1, \ldots, h_N\} \in \mathbb{R}^{N \times D}$$

Where $h_i \in \mathbb{R}^D$ encapsulated all temporal variations of the corresponding variable from the past, referred to as the Variate Token, subsequent layers allowed each Variate Token to interact through a self-attention mechanism. Within each Variate Token, layer normalization standardized measurement units and feature distributions across different variables, while the feed-forward network executed fully connected feature encoding. Ultimately, each Variate Token is translated into the prediction result via the mapping layer. The entire computational procedure is as follows:

$$h_n^0 = \text{Embedding}(\mathbf{X}_{:,n})$$

$$\mathbf{H}^{l+1} = TrmBlock(\mathbf{H}^l)$$

$$\widehat{\mathbf{Y}}_{:,n} = \text{Forcasting}(h_n^L)$$

Both the embedding and mapping layers were realized using a multilayer perceptron. The sequential order of time points is inherently captured by the arrangement of neurons, enabling the model to discern temporal relationships without necessitating additional positional embeddings. Moreover, in the iTransformer framework, the data are fed in strictly chronological order so that each neuron corresponds to a specific time point, allowing the model to learn temporal dependencies naturally. This sequential arrangement, combined with the self-attention mechanism, enables the iTransformer to weigh past observations differently and distill time-dependent patterns. Consequently, explicit positional embeddings become unnecessary since the time-order information is preserved through the structure of the embedding and the processing layers.

For the scenario simulations, interventions were applied to the primary risk factors identified in this study, such as smoking and high fasting plasma glucose levels. It was hypothesized that these targeted interventions would gradually reduce the attributed risk factors to zero over the course of a decade. The trained model was then updated with these modified risk factors to perform simulated forecasting.

The detailed forecasting and scenario simulation methods could be found in Appendix 1 section 3.

Role of the funding source

The funder of the study had no role in the study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Age-sex-specific burdens of urological cancers in China

From 1990 to 2021, the age-standardized incidence rate (ASIR) of urological cancers in China experienced a significant increase of 355.6% (166.5–609.4), rising from 8.7 (6.7–10.3) to 13.1 (10.1–16.9), reflecting the additional burden associated with demographic changes (Table 1, Fig. 1, Supplementary Figs. S1–S5). Specifically, testicular cancer exhibited the most substantial rise in ASIR, escalating by 154.2% (83.3–243.0) and reaching to 0.4 (0.3–0.5) in 2021. Prostate cancer followed with an increase of 106.9% (53.2–173.2) to 4.2 (3.0–5.7), kidney cancer by 85.0% (48.0–132.2) to 3.3 (2.7–4.0), and bladder cancer by 9.6% (−18.0 to 61.0) to 5.1 (4.1–6.6). Consequently, China has reported 105,791 (83,240–136,670) new cases of bladder cancer, 65,799 (53,687–79,742) cases of kidney cancer, 88,601 (63,194–120,965) cases of prostate cancer, and 6696 (5181–86,560) cases of testicular cancer in 2021.

In contrast to the general increase in ASIR, the age-standardized mortality rate (ASMR) showed significant declines across many urological cancers during the study period (Table 2, Fig. 1, Supplementary Figs. S1–S5). The ASMR for bladder cancer decreased remarkably by −32.1% (−47.9 to −1.9) to 2.3 (1.9–2.9) in 2021, and testicular cancer decreased by 31.1% (−50.2 to −7.2) to 0.7 (0.6–0.9). Conversely, prostate cancer experienced a slight increase in ASMR by 7.9% (−18.4 to 43.6), rising to 2.0 (1.5–2.7), while kidney cancer experienced a 9.2% (−12.2 to 36.5) increase, reaching 1.2 (1.0–1.5) at the end of the period. These ASMR alterations led to the number of deaths attributable to bladder, kidney, prostate, and testicular cancers being 37,360 (27,132–49,079), 24,868 (20,361–29,828), 45,126 (35,975–56,331), and 1245 (956–1604), respectively, in 2021. The DALYs, YLDs, and YLLs largely mirrored mortality patterns in China (Fig. 1, Supplementary Figs. S1–S5 and Tables S1–S4).

Ranking the burdens for each cancer revealed that among females, kidney cancer surpassed bladder cancer as the leading incidence rate in 2010–2019, but bladder cancer continued to be the primary mortality rate. In 2010, the incidence rate of bladder cancer among Chinese women [182.0 (160.5–205.6)] was higher than that of kidney cancer [181.7 (162.5–206.2)]. However, by 2019, this trend reversed. The incidence rate of kidney cancer in women had increased to 193.4 (149.0–243.9) per 100,000, while

	Incidence (95% UI)		Incidence rates per 100,000 (95% UI)		Age-standardised incidence rates per 100,000 (95% UI)	
	2021	Percentage change, 1990–2021	2021	Percentage change, 1990–2021	2021	Percentage change, 1990–2021
Urological cancers						
Male	227,144 (168,318–301,970)	338.5% (363–369.8)	31.2 (23.1–41.5)	265.5% (285.9–291.5)	24 (18–31.6)	56.8% (65.4–65.9)
Female	39,743 (29,864–50,996)	150.9% (131.1–162.1)	5.7 (4.3–7.3)	105.8% (89.5–114.9)	3.8 (2.9–4.9)	1.9% (−6.4 to 7.4)
Both	266,887 (205,304–346,033)	294.6% (298.3–330.6)	18.8 (14.4–24.3)	226.3% (229.4–256.1)	13.1 (10.1–16.9)	50.7% (52.2–63.8)
Testicular cancer						
Male	6696 (5181–8656)	264% (162–396.9)	0.9 (0.7–1.2)	203.4% (118.4–314.1)	0.8 (0.6–1)	145.8% (77.9–230.8)
Both	6696 (5181–8656)	264% (162–396.9)	0.5 (0.4–0.6)	201% (116.6–310.8)	0.4 (0.3–0.5)	154.2% (83.3–243)
Kidney cancer						
Male	46,529 (36,119–58,923)	367.6% (248.3–524.5)	6.4 (5–8.1)	289.7% (190.3–420.5)	4.8 (3.8–6)	108.3% (57.7–174.4)
Female	19,271 (14,243–25,064)	206.8% (106.3–337.7)	2.8 (2.1–3.6)	151.6% (69.1–258.9)	1.9 (1.4–2.5)	42.7% (−3.9 to 101.8)
Both	65,799 (53,687–79,742)	305.4% (220.9–412.5)	4.6 (3.8–5.6)	235.2% (165.3–323.7)	3.3 (2.7–4)	85% (48–132.2)
Bladder cancer						
Male	85,319 (63,823–113,426)	224.9% (116.3–441.4)	11.7 (8.8–15.6)	170.8% (80.3–351.2)	9.1 (6.9–11.9)	17.7% (−19.6 to 93.3)
Female	20,472 (15,620–25,932)	114.2% (50.4–210.6)	2.9 (2.2–3.7)	75.7% (23.3–154.7)	1.9 (1.4–2.4)	−21.3% (−44.2 to 11.1)
Both	105,791 (83,241–136,670)	195.4% (117.4–340.5)	7.4 (5.9–9.6)	144.3% (79.8–264.3)	5.1 (4.1–6.6)	9.6% (−18 to 61)
Prostate cancer						
Male	88,601 (63,194–120,965)	544.2% (370.2–762.7)	12.2 (8.7–16.6)	436.9% (291.9–619)	9.3 (6.7–12.6)	87.2% (40.9–146.5)
Both	88,601 (63,194–120,965)	544.2% (370.2–762.7)	6.2 (4.4–8.5)	432.7% (288.8–613.4)	4.2 (3–5.7)	106.9% (53.2–173.2)

UI = uncertainty interval.

Table 1: **Number, rate, and age-standardised rate of incidence for urological cancers in 2021 and percentage changes from 1990 and by sex and subcategories in China.**

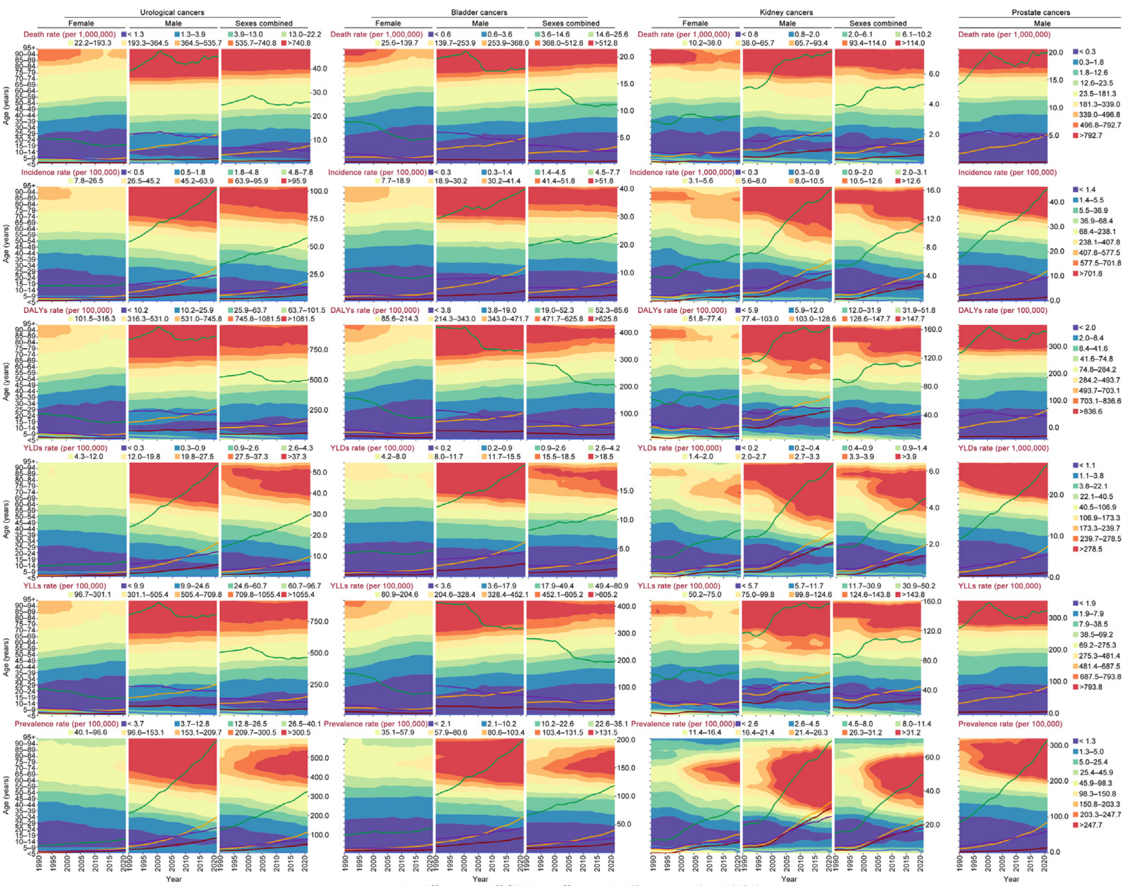

Fig. 1: The age-sex-specific patterns of death, DALY, YLD, YLL, incidence, and prevalence rates of urological cancers and three primary subcategories in China between 1990 and 2021.

the bladder cancer rate of only 184.2 (141.9–228.7). While prostate cancer incidence among males surpassed bladder cancer in 2010–2019, mortality surpassed bladder cancer in 1990–2000. These findings indicate that the burden of prostate cancer has increased in males (Fig. 2A).

Urological cancers manifest a remarkable sex imbalance in incidence, prevalence, mortality, and disability burdens, with males having significantly higher incidence and mortality rates than females. In 2021, there were 227,144 (168,318–301,970) new cases of urological cancers in males, with an ASIR of 24.0 (18.0–31.6), 91,594 (69,263–120,654) deaths, and an ASMR of 11.3 (8.5–14.7). In contrast, females reported 39,743 (29,864–50,996) new cases of urological cancers, with an ASIR of 3.8 (2.9–4.9), 16,995 (12, 841–21, 591) deaths, and an ASMR of 1.6 (1.2–2.0). More specifically, the incidence and mortality rates of urological cancers were similar for males and females in the <5-year age group, and the sex ratio of incidence and mortality decreased with increasing age (Fig. 2B, Supplementary Fig. S6 and Tables S5–S8).

Provincial and economic imbalanced burdens of urological cancers

The burden of urological cancers was distributed heterogeneously across provinces, with higher ASIR and ASMR found in the eastern coastal provinces, such as Guangdong, Shandong, and Zhejiang. From 1990 to 2021, the provinces in China with the highest rise in ASIR for urological cancers were Taiwan 563.3% (416.4–725.9), Fujian 503.5% (172.7–996.8), and Guangdong 480.1% (148.7–971) (Fig. 3A, Supplementary Figs. S7–S12). As for subcategories of urological cancers, the province with the most remarkable increase in ASIR for bladder cancer was Liaoning 48.5% (–2.4 to 128.7) to 9.9 (6.8–13.3), kidney cancer was Taiwan 216.5% (171.3–259.2) to 9.3 (8.3–10.3), prostate cancer was Taiwan 204.7% (157.6–258.1) to 17.1 (14.8–19.7), and testicular cancer was Guangdong 256.6% (108.2–466.5) to 1.1 (0.7–1.5). In contrast, the ASMR was generally decreased in urological cancers across provinces, with Jilin reporting –166.7% (–237 to –64.6), followed by Tibet [–135.4% (–229.1 to 4.4)] and Heilongjiang [–118.5% (–206.5 to –4.6)] (Fig. 3A and B, Fig. 4, Supplementary Figs. S14–S25 and Table S9). The province with the

	Death (95% UI)		Death rates per 100,000 (95% UI)		Age-standardised death rates per 100,000 (95% UI)	
	2021	Percentage change, 1990–2021	2021	Percentage change, 1990–2021	2021	Percentage change, 1990–2021
Urological cancers						
Male	91,594 (69,263–120,654)	171.9% (187.8–187.4)	12.6 (9.5–16.6)	126.6% (139.9–139.5)	11.3 (8.5–14.7)	−9.5% (−4.5 to −6.2)
Female	16,995 (12,841–21,591)	72.4% (59.4–80.5)	2.4 (1.8–3.1)	41.4% (30.7–48)	1.6 (1.2–2)	−39% (−43.8 to −35.6)
Both	108,589 (85,437–139,109)	149.4% (154.4–168.5)	7.6 (6–9.8)	106.2% (110.3–122)	5.6 (4.4–7.2)	−13.6% (−12.4 to −7.8)
Testicular cancer						
Male	1245 (962–1580)	18.8% (−15.4 to 61.5)	0.2 (0.1–0.2)	−1% (−29.5 to 34.6)	0.2 (0.1–0.2)	−31.3% (−49.9 to −8.1)
Both	1245 (962–1580)	18.8% (−15.4 to 61.5)	0.1 (0.1–0.1)	−1.8% (−30 to 33.5)	0.1 (0.1–0.1)	−31.1% (−50.2 to −7.2)
Kidney cancer						
Male	17,635 (13,787–22,254)	206.9% (129.3–309.6)	2.4 (1.9–3.1)	155.8% (91.1–241.4)	1.9 (1.5–2.4)	22.2% (−7.2 to 57.9)
Female	7232 (5387–9315)	118.8% (49.9–212.4)	1 (0.8–1.3)	79.4% (22.9–156.2)	0.7 (0.5–0.9)	−14.7% (−41.2 to 20.2)
Both	24,867 (20,361–29,828)	174.7% (119.3–246.2)	1.7 (1.4–2.1)	127.2% (81.3–186.3)	1.2 (1–1.5)	9.2% (−12.2 to 36.5)
Bladder cancer						
Male	35,350 (26,663–46,454)	118% (48.3–257)	4.9 (3.7–6.4)	81.7% (23.6–197.5)	4.3 (3.3–5.6)	−26.1% (−48.2 to 20.6)
Female	9763 (7454–12,276)	49% (4.9–108.3)	1.4 (1.1–1.8)	22.2% (−14 to 70.8)	0.9 (0.7–1.1)	−49.7% (−64.3 to −31.2)
Both	45,114 (36,263–57,335)	98.2% (50.3–188.6)	3.2 (2.5–4)	63.9% (24.3–138.7)	2.3 (1.9–2.9)	−32.1% (−47.9 to −1.9)
Prostate cancer						
Male	37,363 (27,851–50,366)	249.7% (159.6–360.1)	5.1 (3.8–6.9)	191.5% (116.4–283.5)	4.9 (3.6–6.5)	1.3% (−22.9 to 34.6)
Both	37,363 (27,851–50,366)	249.7% (159.6–360.1)	2.6 (2–3.5)	189.2% (114.7–280.5)	2 (1.5–2.7)	7.9% (−18.4 to 43.6)

UI = uncertainty interval.

Table 2: **Number, rate, and age-standardised rate of incidence for urological cancers in 2021 and percentage changes from 1990 and by sex and subcategories in China.**

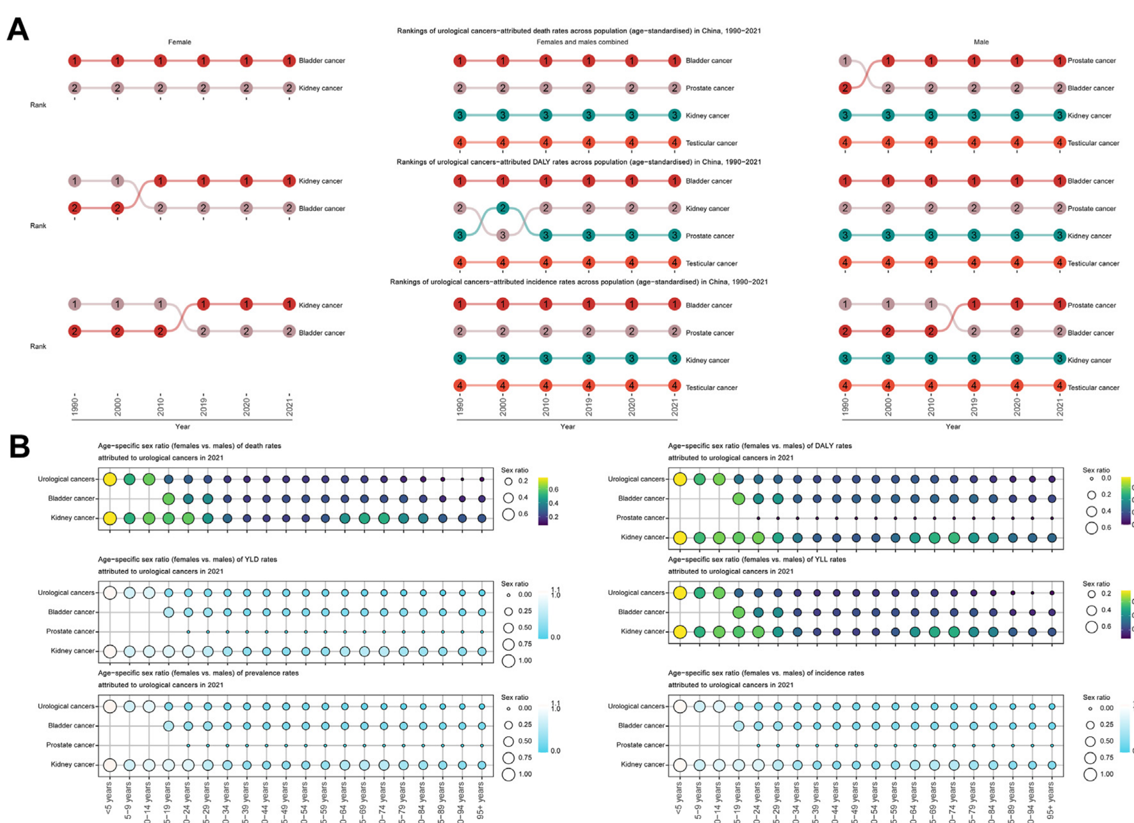

Fig. 2: A) The transformations of ranks in age-standardized mortality, DALY, and incidence rates across urological cancers from 1990 to 2021. B) Age-sex differences in mortality, DALY, YLD, YLL, incidence and prevalence of urological cancer subcategories in China, 2021.

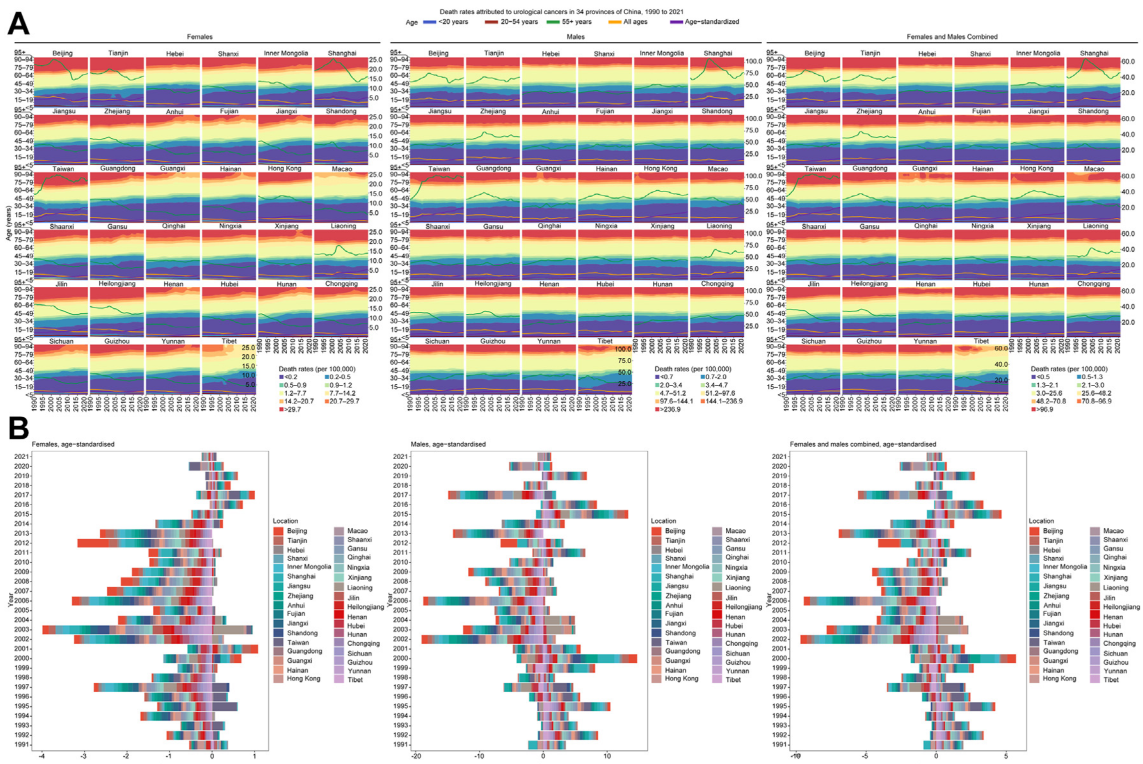

Fig. 3: A) Provincial age-sex-specific trends of mortality rates of urological cancers, 1990–2021. B) The annualized change of death rates across sexes and provinces, 1990–2021.

largest decrease in ASMR for bladder cancer was Tibet −55.5% (−71.2 to −28.3) to 1.6 (1.1–3.1), kidney cancer was Jiangxi −19.7% (−40.9 to 9.1) to 2.5 (1.9–3.3), prostate cancer was Jilin −41.9% (−61.6 to −16.1) to 2.3 (1.4–4.1), and testicular cancer was Hong Kong −61.5% (−73 to −44.7) to 0.5 (0.4–0.7). Despite the emergence of COVID-19, ASIR and ASMR remained stable in 2020 and 2021 for most provinces (except Taiwan and Macau). Taiwan and Macau showed a small decrease in ASIR and ASMR in 2021 compared with 2019 (Fig. 4, Supplementary Figs. S14–S25). The DALY, YLD, and YLD rates in urological cancers largely reflect trends in mortality rates.

In 2021, geographical disparities remain remarkable in the burden of urological cancer across provinces (Figs. 5 and 6, Supplementary Figs. S26–S36). In 2021, the provinces of Taiwan, Beijing, and Zhejiang exhibited the highest burden of urological cancer ASIR in China. Specifically, the ASIRs for these provinces were as follows: Taiwan [3651 (3198.1–4123.9)], Beijing [2270.6 (1484.8–3187.1)], and Zhejiang [2227.7 (1370–3244.4)]. These regions also demonstrated a significant prevalence of urological cancer, with age-standardised prevalence rates of 25586.1 (22447.1–29051.5) for Taiwan, 14461.6 (8715.6–21165.8) for Zhejiang, and 13772.9 (8992.8–19529.9) for Beijing. Provinces in north, northeast, and East China documented the highest ASIR of bladder cancer, with Liaoning reporting 9.9 (6.8–13.3), Taiwan 8.9 (7.9–9.8), and Tianjin 8.0 (5.7–11.0), while the lowest was found in Tibet [1.6 (1.1–3.1)], Hong Kong [3.4 (2.4–4.6)], and Gansu [3.4 (2.5–4.7)]. In kidney cancer, the largest ASIR was made Taiwan 8.9 (7.9–9.8), Tianjin 8.0 (5.7–11.0) and Beijing 7.5 (5.2–10.1), while smallest in Macao [1.0 (0.7–1.3)], Yunnan [1.7 (1.3–2.3)], and Sichuan [2.0 (1.5–2.6)]. In prostate cancer, Taiwan demonstrated the highest ASIR of 17.1 (14.8–19.7), followed by Hong Kong [10.0 (4.3–15.6)], and Zhejiang [9.9 (4.6–15.6)], with Tibet [1.0 (0.7–2.0)] reported the lowest. For testicular cancer, the provinces with the highest ASIR were Taiwan 1.2 (1.0–1.4), Guangdong 1.1 (0.7–1.5), and Macao 1.0 (0.7–1.5). In terms of deaths, the provinces with the highest ASMR of bladder cancer in 2021 were Liaoning 3.9 (2.7–5.2), Tianjin 3.8 (2.7–5.1), and Beijing 3.4 (2.3–4.5); and the provinces with the highest ASMR of kidney cancer were Tianjin 3.0 (2.2–3.9), Taiwan 2.8 (2.4–3.1), and Beijing 2.7 (2.0–3.5); the provinces with the highest ASMR of prostate cancer were Taiwan 2.8 (2.4–3.1), Shanghai 2.5 (1.9–3.3), and Zhejiang 1.8 (1.3–2.3); and the provinces with the highest ASMR of testicular cancer were Hainan 0.1 (0.1–0.2), Tibet 0.1 (0.1–0.2), and Xinjiang 0.1 (0.1–0.2) (Fig. 6). Similar patterns were observed for DALY, YLD, and YLL rates.

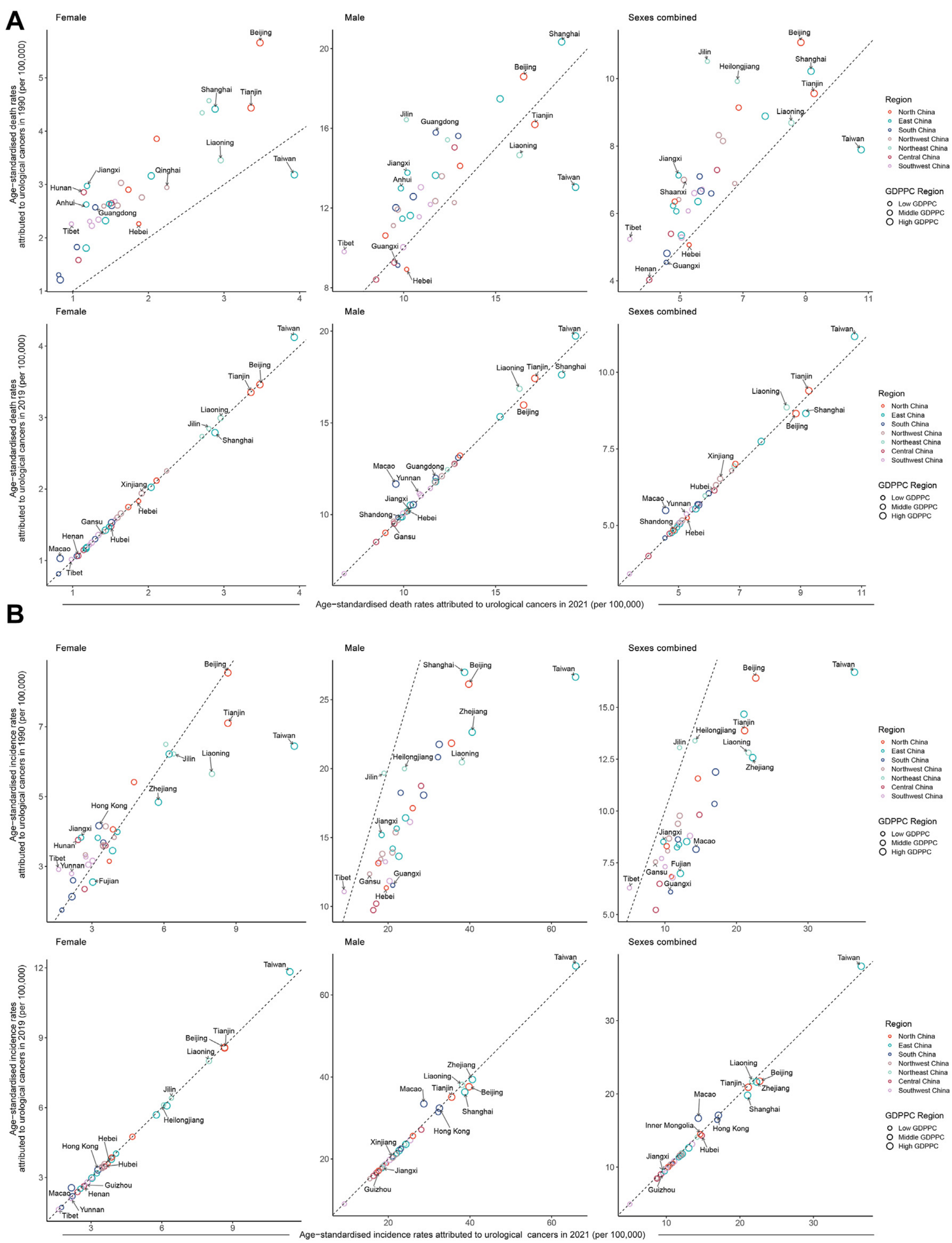

Fig. 4: The ASMR (A) and ASIR (B) alterations between 1990/2019 and 2021 across sexes and provinces.

Sex imbalances were also found in the burden of urological cancer. In 2021, the province exhibiting the highest ASIR for bladder cancer among males was Liaoning [17.3 (11.0–24.3)], while Tibet reported the lowest [2.8 (1.8–5.7)]. For females, Taiwan had the highest ASIR [4.3 (3.8–4.9)], with Tibet again showing

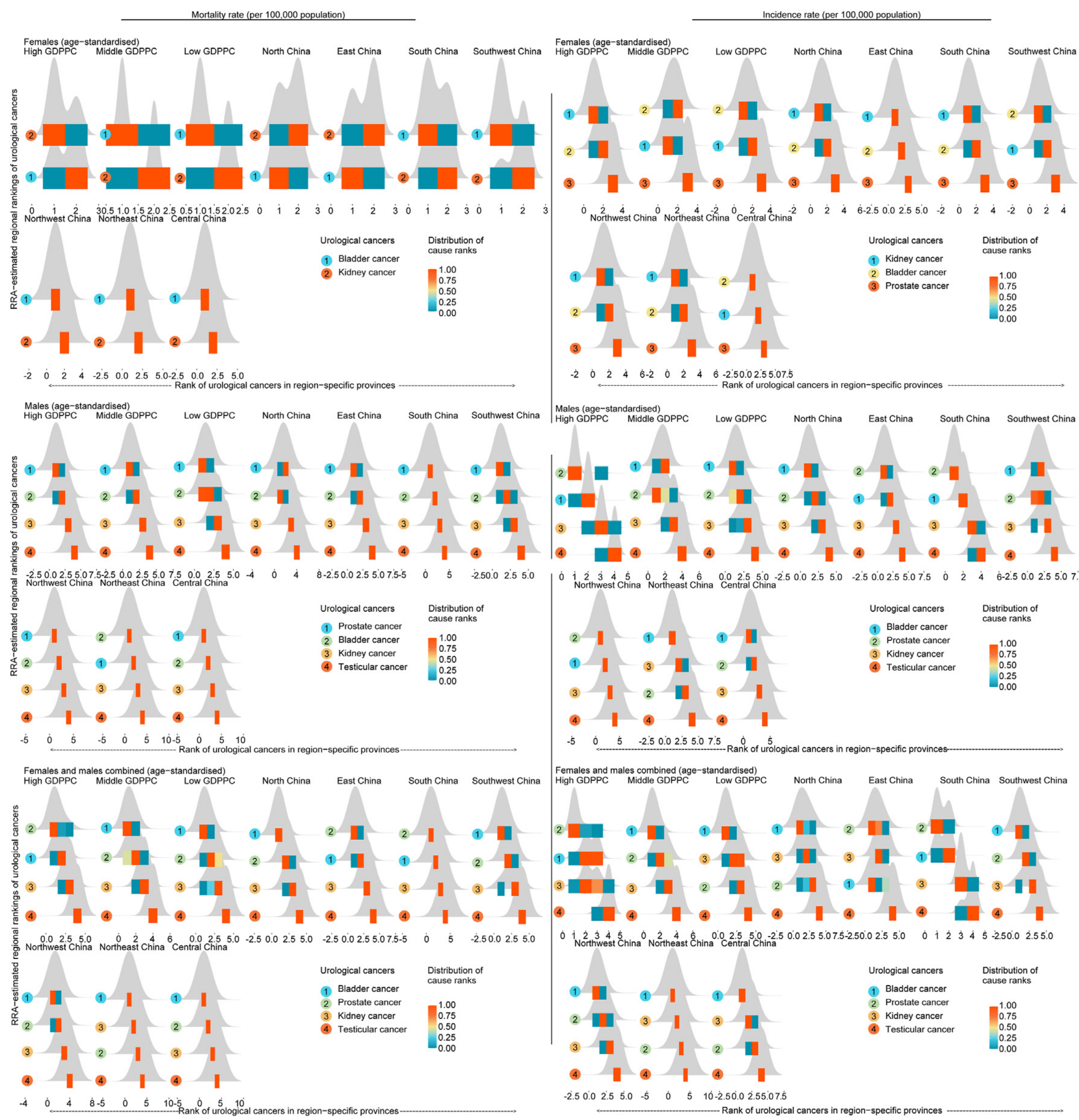

Fig. 5: Regional mortality and incidence classes for urological cancer subclasses and their distribution across region-specific provinces in 2021, as determined by Robust Rank Aggregation (RRA). To represent distribution density, we plotted the empirical cumulative distribution function (ECDF), depicted as the shaded ridge-like areas in the figure. These ridges highlight the inter-provincial distribution of a specific subcategory within a region. To further visualize this distribution, we used color blocks, which map the density of the distribution, as indicated by the legend ("Distribution of cause's rank").

the lowest [0.6 (0.4–1.3)]. Taiwan recorded the highest ASIR for kidney cancer in both sexes, with 11.7 (10.3–13.2) for males and 7.1 (6.1–8.1) for females; Macao had the lowest ASIR, with 1.7 (1.1–2.4) for males and 0.4 (0.2–0.5) for females. In the same year, Liaoning reported the highest ASMR for bladder cancer among males [7.1 (4.6–9.9)], whereas Tibet had the lowest [2.0 (1.2–4.1)]; for females, Taiwan had the highest ASMR [1.9 (1.6–2.1)] and Tibet the lowest [0.4 (0.3–0.9)]. The highest ASMR for kidney cancer among males was observed in Tianjin [4.5 (3.2–6.2)], with Macao showing the lowest [0.7 (0.5–1.0)]; among females, Taiwan had the highest ASMR [2.0 (1.8–2.3)] and Macao the lowest [0.1 (0.1–0.2)]. The incidence and mortality rates of urological cancers are higher in males than in females in all provinces in the over-25 age group. However, in the younger age groups, the situation varies from province to province. In Taiwan, Beijing, and

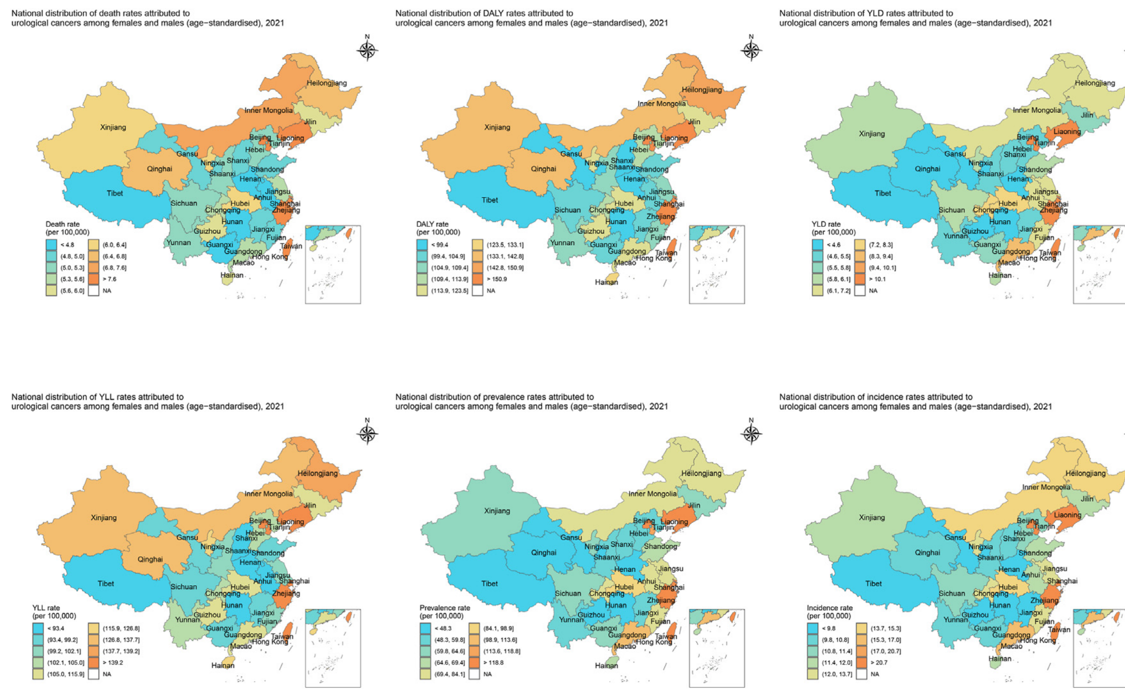

Fig. 6: Provincial distribution of mortality, DALY, YLD, YLL, incidence and prevalence of urological cancers in China in 2021.

Heilongjiang, the incidence rate of urological cancers is higher in females than males in younger age groups. In Macao, the mortality rate of bladder cancer was higher than that of males in the female population aged 15–19 years, while the mortality rate of kidney cancer was higher than that of males in the lower age groups of females in Taiwan, Heilongjiang, and Beijing (Fig. 7A, Supplementary Figs. S39–S44).

The present study analyzed the relationship between urological cancers and provincial GDPPC in China (Fig. 7B, Supplementary Figs. S37 and S38). Overall, the ASIR and ASMR of urological cancers were lower in the low GDPPC regions and extremely high GDPPC regions. In contrast, the ASIR and ASMR of urological cancers in mainland regions other than Hong Kong, Macao, and Taiwan showed an increasing trend with higher GDPPC. For kidney and bladder cancers, regions with low GDPPC, such as Tibet, Qinghai, Yunnan, and other less-developed areas of China, generally exhibit lower incidence and mortality rates. Conversely, regions with higher GDPPC, such as Beijing, Shanghai, Tianjin, and Taiwan, reported the highest incidence and mortality rates. Notably, Hong Kong and Macao, which possessed the highest GDPPC in China, exhibited lower incidence and mortality rates of kidney and bladder cancers. For prostate and testicular cancers, the incidence rate showed an increasing trend with increasing GDPPC levels. Less developed regions, such as Tibet, Qinghai, and Guizhou, displayed lower incidence rates, whereas developed regions in the east, including Shanghai, Taiwan, Zhejiang, and Guangdong, exhibited higher incidence rates. Hong Kong and Macao have also reported elevated morbidity rates. In terms of mortality rates, regions with the highest GDPPC had lower mortality rates, potentially because of more advanced medical care in these areas.

Risk factors for deaths from urological cancers

In 2021, approximately 62.8% (33.6–91.3) of ASMR in urological cancer could be ascribed to risk factors, with smoking, high body mass index, and high fasting glycemic index identified as the leading contributors, accounting for 55.1% (42.7–67.4), 13.9% (5.3–22.4), 5.9% (−0.8 to 13.4) of attributable ASMR, respectively in both sexes (Fig. 8A, Supplementary Fig. S45). Smoking remarkably affected males, responsible for 67.4% (53.1–81.0) of ASMR, while 38.4% (19.8–56.5) of female ASMR was attributed to a high body mass index.

Among urological cancer subcategories, smoking was the leading risk factor for prostate and bladder cancer, accounting for 37.1% (32.3–42.2), 4.9% (2.2–7.5) sexes-combined ASMR, respectively, with smoking also explaining 13.2% (8.2–17.7) ASMR in kidney cancer. A high body mass index was identified as the most important contributor to ASMR in kidney cancer [13.9% (5.3–22.4)]. Interestingly, diets low in milk and diets low in calcium exhibited protective effects on prostate cancers, reducing ASMR by −7.1% (−19.7 to 5.5) and −1.4% (−2.9 to 0.2), respectively. In females, high body mass index surpassed smoking as the leading risk factor of

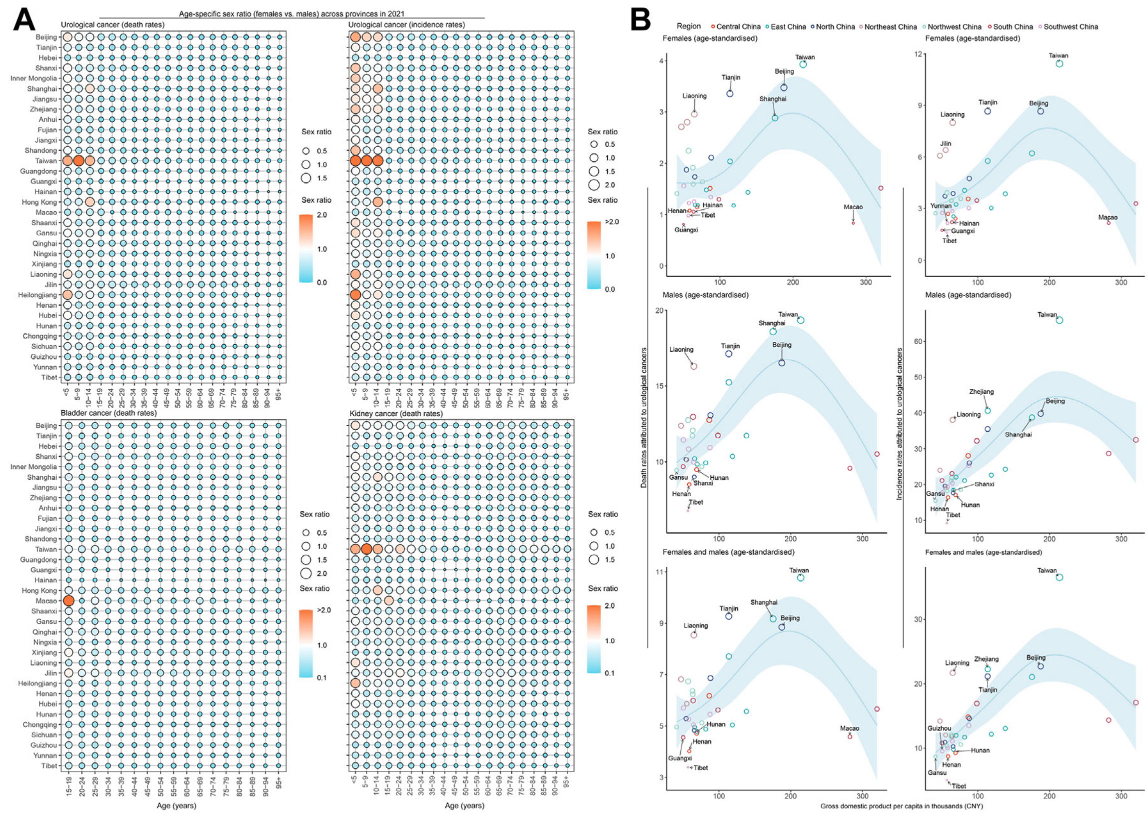

Fig. 7: A) The sex differences in burdens of urological cancers and subcategories across age and provinces. B) Age-standardized associations between GDPPC and mortality and incidence rates in 2021 as detected by the generalized additive model based on cubic curves.

ASMR in kidney cancer [15.9% (6.1–25.7)], and was also the significant contributor of bladder cancer [5.7% (−0.7 to 13)]. Smoking remained the primary risk factor for bladder cancer in female, accounting for 7.8% (5.7–10.1) of ASMR. The risk factor patterns of males mirrored the both-sex trends, with persistent smoking as a leading risk factor for kidney, bladder, and prostate cancer, responsible for 44.9% (39.4–50.2), 17.9% (11.6–23.7), and 4.6% (2.1–7.1) ASMR, respectively. Risk factors did not show significant differences according to age.

At the provincial level, smoking was an important risk factor for bladder cancer in males aged 55 years or older in the provinces of Yunnan [57.2% (51.8–62.0)], Gansu [53.4% (48.0–58.7)], Guizhou [53.2% (47.5–58.1)], and Chongqing [52.7% (47.2–58.1)]. It also made the most impactful contribution to the mortality rate of prostate cancer in Yunnan [7.3% (3.3–11.1)], Gansu [6.2% (2.8–9.6)], Chongqing [6.1% (2.9–9.6)], and Guangdong [5.7% (2.6–9.0)]. Moreover, a high body mass index is a primary risk factor for prostate cancer in the provinces of Tianjin [18.9% (7.3–31.4)], Taiwan [16.6% (6.4–26.9)], Shanghai [16.9% (6.3–27.9)], and Beijing [19.8% (7.7–32.5)] (Fig. 8B, Supplementary Figs. S46–S50).

Forecasting the burden of urological cancers from 2022 to 2040

The present study used a modified iTransformer model for the long-term prediction of the incidence, prevalence, mortality, DALY, YLD, and YLL rates in China and its provinces, with attributable risk factors, population, and GDPPC as covariates. The covariates were normalized and embedded to facilitate independent fitting of each measure. After hyper-parameter adjustment, the model achieved practicable performance, with average MSPE, MSAE, and RMSLE of 0.54 ± 0.22, 1.51 ± 1.26, and 0.15 ± 0.07, respectively, in comparisons of actual burdens with forecasts (Fig. 9, Supplementary Figs. S51–S56).

Between 2022 and 2040, the ASIR of urological cancers mirrored the historical increase patterns if no intervention was applied, with the sex-combined rates increasing by 10.09% (9.19–10.99) to 14.42 (14.30–14.54) in 2040 (Fig. 9, Supplementary Figs. S51–S56). During the forecasting period, prostate cancer surpassed bladder cancer as the leading subcategory with the highest ASIR in both sexes, reaching to 4.8 (4.8–4.9) in 2040, whereas the ASIR of bladder cancer rose by 5.50% (4.52–5.01) to 5.40 (5.38–5.42). The population aged 55 years and over suffered higher incidence rate of urological cancers

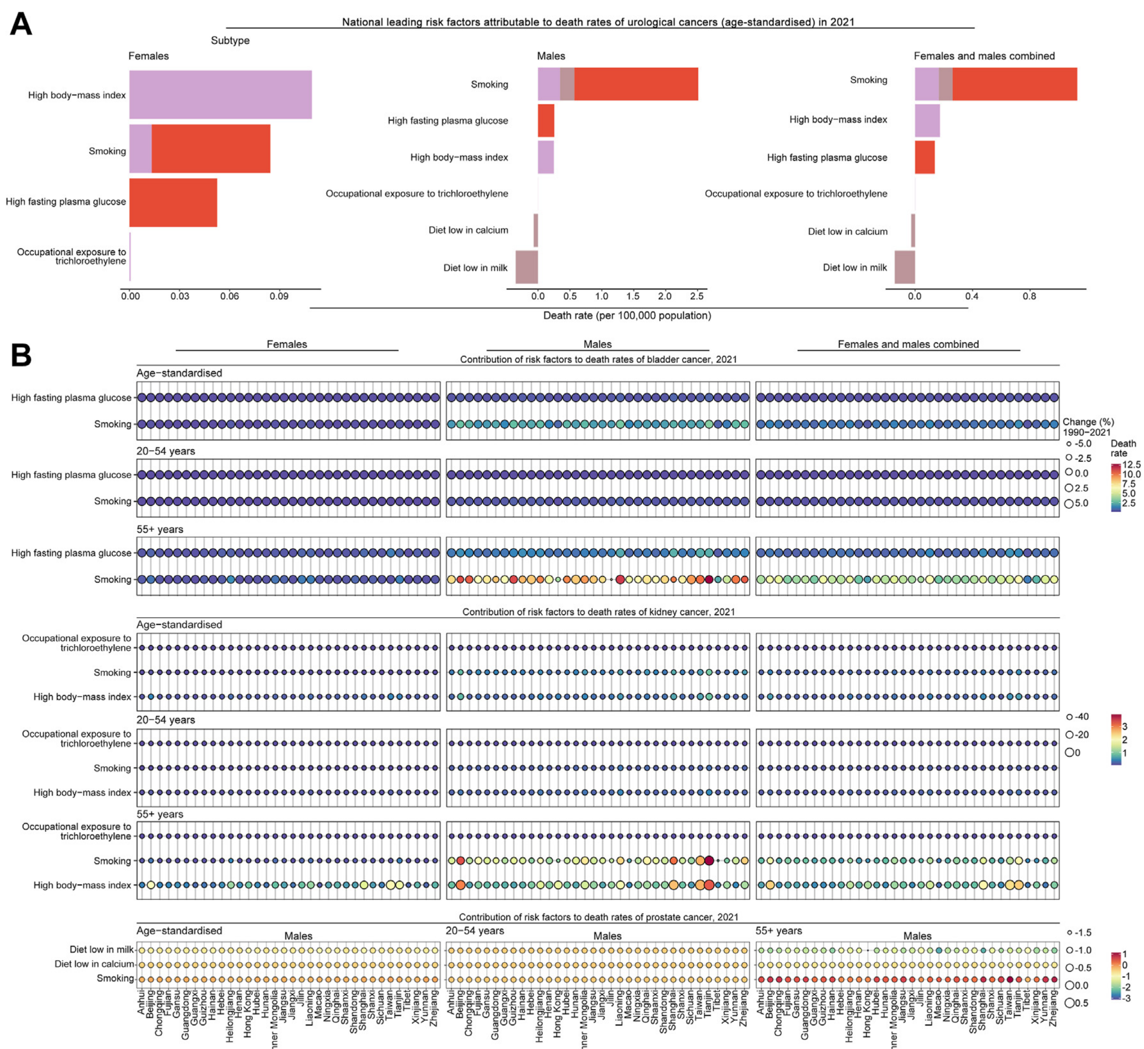

Fig. 8: A) The national leading risk factors attributable to death rate of urological cancers (age-standardized) for male, female, and sexes-combined in 2021. B) The death rates (2021) and change (1990–2021) in bladder, kidney, and prostate cancer attributable to leading risk factors.

[64.7 (64.0–65.3)] than others in 2040, with prostate cancer ranking as the primary urological cancer that significantly affects males >55 years [25.7 (25.3–26.0)]. The incidence rate of urological cancers among Chinese individuals aged 20–54 is relatively low [7.9 (7.8–8.1)]. Kidney cancer is the predominant contributor to this rate, accounting for 3.5 (3.4–3.5) per 100,000. Provincially in 2040, the highest ASIR for prostate cancer is reported in Taiwan by 18.5 (18.3–18.6), for bladder cancer in Liaoning by 10.2 (10.2–10.2), for kidney cancer in Taiwan by 10.4 (10.3–10.4), and for testicular cancer in Taiwan by 1.6 (1.6–1.7). The largest decreases in ASMR for bladder cancer are expected in Tianjin [3.60 (3.56–3.63)], Liaoning [3.59 (3.57–3.61)] and Taiwan [3.1 (3.0–3.1)]. The burden of urological cancers in males was persistently higher than females, primarily driven by the increased burden of prostate cancer (Supplementary Figs. S57–S70).

In China, the ASMR for urological cancers will continue to decline over the next 20 years, despite forecasts that the ASIR for urological cancers will rise (Fig. 9, Supplementary Figs. S51–S56). By 2040, the ASMR for bladder cancer will decrease to 2.19 (2.18–2.20) and for kidney cancer to 1.23 (1.22–1.24). Prostate cancer is forecasted to decrease in male ASMR to 4.61 (4.53–4.70). The overall trend was similar in males and females with kidney and bladder cancers.

At provincial level, most of the bladder cancer ASMRs were predicted to decline, while alterations in ASMRs in Shandong, Taiwan and Hebei remain stable, with their ASMRs of 2.16 (2.14–2.18), 3.06 (3.02–3.10)

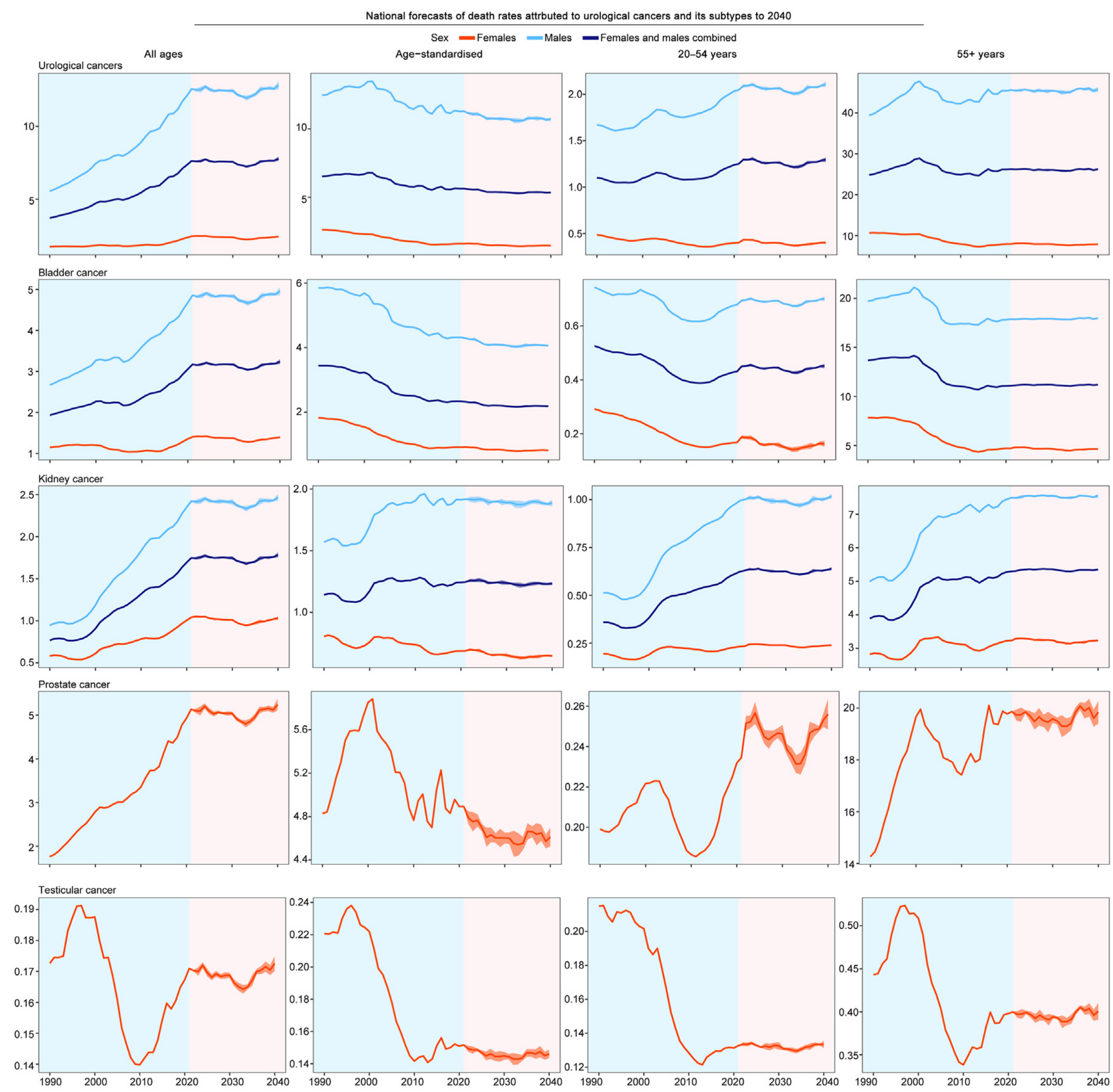

Fig. 9: The forecasted age-sex-specific mortality rates of urological cancers and subtypes from 1990 to 2040.

and 2.88 (2.85–2.92) by 2040. The provinces with the highest forecasted ASMR for bladder cancer by 2040 were Liaoning and Tianjin with 3.59 (3.57–3.61) and 3.60 (3.56–3.63). ASMR for kidney cancer was similar to that for bladder cancer, which also showed a decreasing trend, but the ASMR for kidney cancer in Chongqing, Guizhou, Hainan, and Ningxia was forecasted to plateau or slightly increase, reaching to 0.88 (0.87–0.89), 1.05 (1.04–1.06), 1.22 (1.21–1.23) and 1.27 (1.26–1.28) by 2040. The provinces with the highest ASMR for kidney cancer by 2040 were Tianjin and Taiwan at 3.00 (2.96–3.04) and 2.73 (2.70–2.75). ASMR for prostate cancer exhibited a decreasing trend in most provinces, whereas the trend for ASMR in Taiwan remained stable, with Taiwan [10.68 (10.62–10.74)] and Shanghai [8.52 (8.33–8.71) possessed the highest ASMR by 2040 (Supplementary Figs. S57–S70).

Scenarios simulation towards future mortality and disability burden

Smoking and high fasting plasma glucose levels were identified as the leading risk factors for urological cancers, notably prostate cancer. Based on these challenges, we simulated two scenarios on the future impact of controlling smoking and high fasting plasma glucose levels on the burden of urological cancers.

Smoking control achieved the greatest reduction in mortality from urological cancers (Fig. 10, Supplementary Figs. S71–S76). By 2040, bladder cancer ASMR will be reduced by −37.9% for both sexes, −45.8% for males,

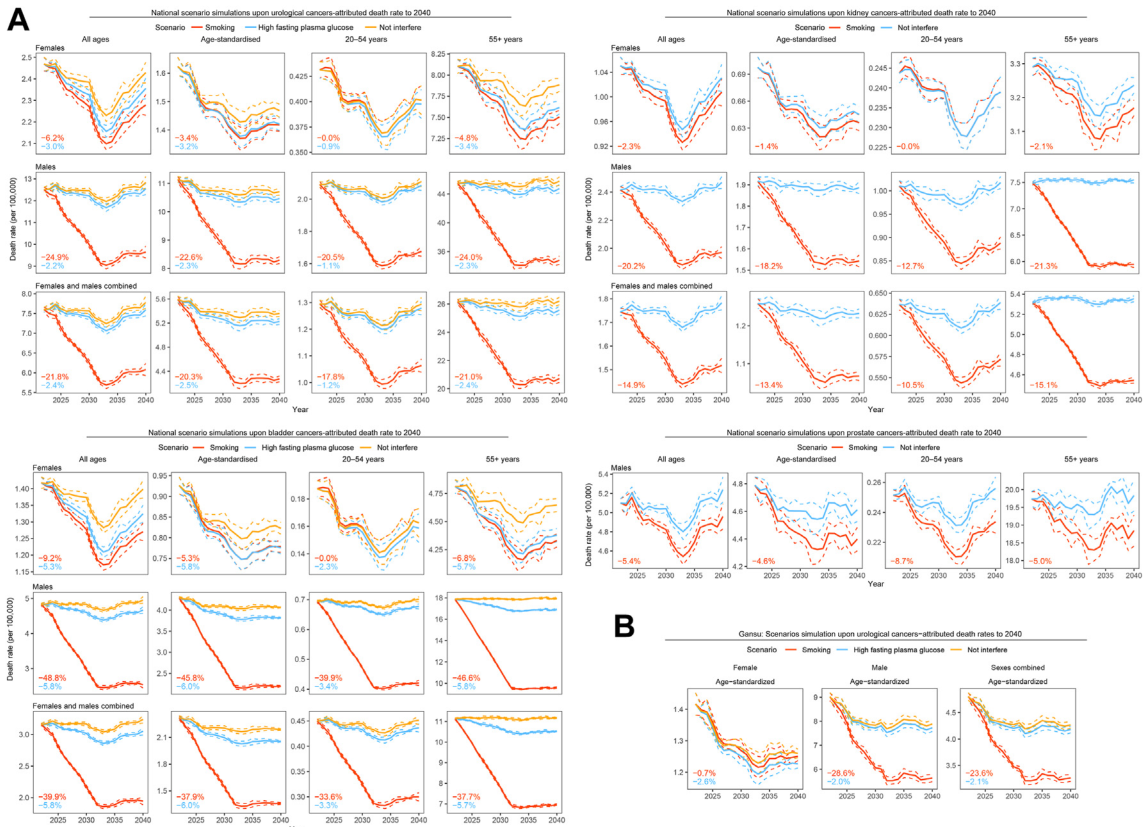

Fig. 10: A) The national scenario simulations upon mortality rates of urological cancers, as well as kidney cancer, bladder cancer, and prostate cancer between 2022 and 2040. B) The scenario simulations upon urological cancers in Gansu, which displayed the highest reduction of mortality under smoking control.

and –5.3% for females compared to 2021. Kidney cancer ASMR will be reduced by –13.4% for both sexes, –18.2% for males, and –3.4% for females. Prostate cancer has a –4.6% lower ASMR among males. However, these benefits in both sexes were mainly driven by males, who reported a much higher reduction in ASMR across urological cancers than in females. A similar sex imbalance was forecasted in the DALY, YLD, and YLL rates of urological cancers, with males reporting age-standardized rates of –20%, –18.6%, and –20.3% by 2040 national, and females of –2.3%, –4.6%, and –22.2%, respectively.

Geographically, the ASMRs of urological cancers under smoking control generally decreased across provinces; however, geographical heterogeneity was observed. Gansu was forecasted to benefit the most from the intervention, with an ASMR reduction of –28.6% during the period (Fig. 10B), while Hong Kong only had a decline of –6.7%. As for urological cancer subcategories, the largest reduction in ASMR was predicted in bladder cancer in Guangdong at –45.2%, and the smallest ASMR of bladder cancer was documented in Tibet at –18.3% by 2040. Furthermore, the ASMR of kidney cancer was remarkably reduced in Hunan (–16.8%), while Hong Kong (–6.0%) reported a marginal decrease under smoking control. Yunnan exhibited a considerable decline in prostate cancer ASMR by –6.8%, with Tibet displaying the smallest at –1.6%.

Control of high fasting plasma glucose levels reduces bladder cancer mortality. By 2040, bladder cancer ASMR was reduced by –6.0% in both sexes, –6.0% in males, and –5.8% in females. There is little difference in the effectiveness of blood glucose control in reducing the burden of urological cancers in males and females. Geographically, the reduction in bladder cancer ASMR was greater in Shanghai and Taiwan, at –8.5% and –7.9% for both sexes, –9.0% and –7.7% for males, –7.1% and –8.7% for females. The provinces with smaller decreases in ASMR for bladder cancer were Hubei and Macao, with –4.5% and –4.4% for both sexes, –4.2% and –4.2% for females, –4.4% and –4.6% for males.

Discussion

Main findings

This study revealed the progress and continuing challenges in the prevention and control of urological cancers in China by analyzing the burden of urological cancers in China and its 34 provincial administrative units from 1990 to 2021. By systematically analyzing the national and provincial distributions of incidence, mortality, and disability burden, we present the following key findings. (1) Overall, the burden of urological cancers in China have continued to increase from 1990 to 2021, with a significant increase in ASIR but a small decline in ASMR. (2) The incidence and mortality rates of urological cancers are higher in older age groups above 55 years, and the incidence and mortality rates of urological cancers are higher in males than in females. (3) The main risk factors for urological cancers are smoking, high fasting plasma glucose, and high body mass index. (4) The burden of urological cancers in different regions of China showed geographic differences, with higher incidence and mortality rates in the eastern, southern, and higher GDPPC regions. Prostate cancer burden was ranked as the first subcategory in the high GDPPC provinces, while others suffered remarkable burdens of bladder cancer. (5) Bladder, kidney, and prostate cancers will show a small increase in ASIR and a decrease in ASMR by 2040. (6) Reductions in urological cancer incidence and mortality can be achieved by controlling smoking and fasting blood glucose, with smoking control being the most effective leverage.

The excessive burdens of urological cancers attributable to aging

Over the past 30 years, China has experienced rapid economic growth and significant transformation, leading to enhanced material and spiritual conditions and a notable increase in life expectancy. Currently, China is transitioning into an aging society.[2] However, aging is the most critical risk factor for various cancers, including urological cancers, with incidence rates increasing with age, peaking at 85 years.[9] Aging is characterized by four hallmarks: genomic instability, epigenetic alterations, chronic inflammation, and dysbiosis.[10] These hallmarks closely resemble the four determinants of tumors: genomic instability, non-mutational epigenetic reprogramming, inflammation, and a polymorphic microbiome.[9] Our findings suggest that from 1990 to 2021, the ASIR of urological cancers in China rose by 355.6%, with the most significant impact observed in individuals aged 55 years and above, underscoring the additional cancer burden in the aging population. In contrast to the historical increases in ASIR, the ASMR for urological cancers in China has slightly declined, reflecting extensive efforts to improve healthcare services, including the National Basic Public Health Service Program,[11] and better health insurance coverage.[12]

Among the four urological cancers, the highest incidence and mortality rates in 2021 were observed for prostate cancer followed by bladder, kidney, and testicular cancers. Specifically, in the male population, prostate cancer exhibited the highest incidence rate of 1216.9 (867.9–1661.4) per 100,000 individuals and a mortality rate of 513.2 (382.5–691.7). Bladder cancer followed with an incidence rate of 1171.8 (876.6–1557.8) and a mortality rate of 485.5 (366.2–638.0). Kidney cancer had an incidence rate of 639.0 (496.1–809.3) and a mortality rate of 242.2 (189.4–305.6), while testicular cancer presented the lowest incidence and mortality rates, recorded at 92.0 (71.2–118.9) and 17.1 (13.2–21.7), respectively. With an aging population, the burden of prostate cancer in China is expected to continue to increase. Globally, prostate cancer remains a significant health burden, and it is the fourth most commonly diagnosed cancer.[1] The rising incidence of prostate cancer in China aligns with global patterns observed in recent years, as detailed in the GLOBOCAN 2022 report. This concurrence underscores the influence of shared risk factors, such as an aging population, lifestyle changes, and enhanced diagnostic capabilities, which are driving the increase in prostate cancer cases both within China and internationally. The early detection of localized prostate cancer plays a crucial role in reducing mortality rates.[13] However, the 5-year survival rate for prostate cancer patients in China lags behind that of patients in developed countries. To address this issue, China has implemented measures to screen for prostate cancer, targeting individuals aged 40 years and above, particularly those with BRCA2 pathogenic mutations.[14] Despite these advancements, our findings highlight the potential benefits of early screening, it is essential to focus these strategies on urological cancers where screening is currently recommended, personalize targeted treatments to address aging-induced distinct cancer heterogeneity, prolong the survival of the elderly, and restrict the excessive burden of urological cancers.

Sex-imbalance in burdens of urological cancers

The burden of urological cancers is significantly sex-imbalanced, with males experiencing much higher incidence and mortality rates for bladder and kidney cancers than females. In bladder cancer, for example, sex-related heterogeneity in hepatic pathways is responsible for the varying degradation of carcinogens, leading to differential exposure of the urothelium to these harmful substances.[15] Tobacco, a known carcinogen for bladder cancer, has a more pronounced effect on males because of the restriction of the enzyme uridine 5′-diphosphoglucuronosyltransferase by androgen receptors, impairing the hepatic detoxification of aromatic amines found in tobacco.[16] Additionally, the activity of sex steroid hormone pathways plays a critical role in the development of bladder cancer.[15]

Notably, prostate cancer has the highest incidence and mortality rates among urological cancers in Chinese males, mirroring the global trends.[17] The prostate is an androgen-dependent organ present only in males, and most prostate cancers retain this androgen dependence, at least in the early stages.[18] Overexpression and mutation of androgen receptors, dysregulation of 3β-hydroxysteroid dehydrogenase, and adrenal-derived 11-oxyandrogens, in conjunction with aging, exacerbate the burden of prostate cancer in males.

Females had the highest incidence of kidney cancer among urological cancers, while bladder cancer had the highest mortality rate, although both rates were significantly lower than those in males. Estrogen stimulation and activation of estrogen receptor β (ERβ) inhibit the proliferation of kidney cancer cells and induce apoptosis; however, this effect is lost when ERβ is downregulated.[19]

These findings highlight the urgency to develop personalized treatment strategies to address the heterogeneous cancer physiology driven by distinct sex steroid hormones to control urological cancers, especially prostate and bladder cancers in males and kidney cancer in females.

Provincial and economical heterogeneity of urological cancer burdens

Consistent with national historical trends, the ASIR of urological cancers has been rising across all provinces, particularly in the population aged 55 years and above, while the ASMR has plateaued. However, the burden of urological cancer varies significantly among provinces with different GDPPC.

In high GDPPC settings, such as East and South China, including Beijing, Shanghai, Guangdong, and Taiwan, the burden of urological cancers is higher, with prostate cancer being the most prevalent. These areas face an additional burden related to aging as they have higher levels of population aging and longer life expectancies.[20] Furthermore, some high-income settings are potentially plagued by air pollution, particularly PM2.5, a well-known carcinogen that induces chronic inflammation and immune responses.[21] Additionally, these locations have high population densities and significant lifestyle pressures, with psychological stress contributing to the incidence and progression of urological cancers.[22] The booming food delivery industry in these economically developed provinces also poses a risk, as the use of plastic utensils has been linked to chronic inflammation and gut microbiome disruption due to nanoplastic particles, which can induce various cancers.[23]

Conversely, in regions with low to medium GDPPC levels, particularly outside East and South China, bladder cancer has the highest incidence and mortality rates among urological cancers. This is likely due to the lower degree of population aging, which shifts the cancer burden from prostate to bladder cancer. Additionally, the industrial structure in these regions differed significantly from that of the high GDPPC areas. In high GDPPC regions, the predominant industries often require prolonged desk work, with individuals sitting for eight or more hours per day facing a 22% increased risk of prostate cancer.[24] In contrast, there were fewer sedentary workers in the low-to-medium GDPPC provinces.

Our findings suggest that authorities and policymakers can tailor or optimize health strategies based on location-specific urological cancer burden. For instance, prioritizing prostate cancer control in high GDPPC regions, such as East and South China, while focusing on bladder cancer in other areas, can effectively reduce the additional health losses associated with urological cancers by addressing the specific burden patterns of each region.

Attributable risk factors of urological cancers in 2021

Nationally and provincially, smoking remains the leading risk factor for all urological cancers, primarily affecting prostate and bladder cancers, with Beijing, Tianjin, Chongqing, and Liaoning being remarkably affected. While most previous epidemiological studies found no association between smoking and overall prostate cancer risk,[25] recent research indicates a significant link between smoking and fatal prostate cancer, with smokers bearing a relative risk of 1.42 (95% CI 1.20–1.68) compared to nonsmokers.[26] This association may be attributed to the presence of carcinogenic compounds in tobacco smoke, such as polycyclic aromatic hydrocarbons and nitrosamines, which can induce genetic mutations and promote tumor aggressiveness in prostate cells. This pattern aligns with our findings in China, where 4.6% of prostate cancer-related deaths are attributable to smoking. Genetically, smokers exhibit higher frequencies of gene mutations and tumor mutation burdens than nonsmokers, with notable mutations in genes such as PREX2, PTEN, AGO2, and KMT2C, contributing to increased prostate cancer mortality.[27] Additionally, approximately half of the global bladder cancer cases are attributable to smoking globally.[28] Smoking is a major risk factor for bladder cancer due to the presence of carcinogenic compounds in tobacco smoke that are metabolized and concentrated in the bladder, leading to urothelial cell damage, DNA alterations, and subsequent carcinogenesis. A cohort study involving over 400,000 individuals with a 30-year follow-up demonstrated that smokers have approximately three times the risk of developing bladder cancer compared to nonsmokers.[28] This trend is consistent with data from China, where 45% of bladder cancer-related deaths can be attributed to smoking. These findings underscore the critical need for targeted smoking cessation programs and public health initiatives to reduce the burden of smoking-related urological cancers in China and worldwide. Specifically, implementing region-specific smoking cessation strategies in high-risk provinces requires tailored public education, enhanced access to cessation services, stringent policy enforcement, community engagement, specialized training for healthcare providers, effective monitoring, incentive programs, and integration with broader health initiatives. For example, Australia's national tobacco control program, which includes comprehensive public education campaigns, strict advertising regulations, and robust support for cessation services, has successfully reduced smoking rates and could serve as a model for similar initiatives in China. Additionally, adopting Finland's approach of combining high taxation on tobacco products with extensive public support systems can further enhance the effectiveness of smoking cessation efforts in targeted regions. These comprehensive measures are essential to effectively reduce smoking prevalence and the associated burden of urological cancers in targeted regions.

Low milk and calcium intake has been identified as a protective factor against prostate cancer. Studies indicate that high calcium intake is a risk factor for prostate cancer, and the consumption of milk and yogurt is associated with increased risks of both kidney and prostate cancers, potentially due to elevated levels of insulin-like growth factor.[29,30] High fasting blood glucose is a major risk factor for bladder cancer, particularly in Chinese females aged 55 years. Our findings align with a global meta-analysis of six cohorts, which demonstrated that for every 1 mmol/l increase in blood glucose levels, the relative risk of bladder cancer increases by 1.45 (95% CI 1.05–2.01) in females and 1.17 (95% CI 1.00–1.37) in males.[31] Pathologically, bladder cancer relies on a high glycolytic flux to sustain uncontrolled growth and proliferation.[32] Glycogen metabolism pathways also play crucial roles in bladder cancer progression. The glucose transporter GLUT-1 is selectively expressed in malignant urothelial tissues, including both non-muscle-invasive and muscle-invasive bladder cancers, but is not expressed in normal urothelial tissue or benign bladder papillomas.[32] These findings highlight the importance of dietary and metabolic factors in the etiology of urological cancers and suggest targeted preventive strategies. Reducing high calcium intake and controlling blood glucose levels, especially in high-risk populations, could be effective measures for lowering the incidence of prostate and bladder cancer.

Scenario forecasts of age-sex-location-specific burdens of urological cancers

This study employed advanced deep learning methods to predict the incidence of urological cancer in China and its provinces by 2040. If no interventions are made, the ASIR of urological cancers in China will continue to rise over the next two decades, whereas the ASMR for bladder, prostate, and testicular cancers is projected to decline, with the ASMR remaining stable. This trend is consistent with previously observed historical patterns. Among the four urological cancers, prostate cancer remains the most significant challenge in China, followed by bladder cancer. By 2040, Tianjin, Taiwan, and Liaoning are expected to have the highest male bladder cancer ASMR, while Taiwan, Shanghai, and Zhejiang will have the highest prostate cancer incidence. The burden of urological cancers will remain high in economically developed regions, highlighting the triple health challenges posed by an aging population, sustained economic growth, and industrial transformation. We recommend more effective measures in these regions, such as promoting early screening and controlling the risk factors.

Smoking is the primary risk factor for urological cancer in China and its provinces. As the world's largest producer and consumer of tobacco, China's smoking rates significantly impact urological cancer mortality, especially among males. Our simulations indicate that implementing stringent smoking control policies could significantly reduce the mortality rates of urological cancers, particularly bladder cancer, underscoring the effectiveness of smoking cessation in mitigating the bladder cancer burden. The mortality rates of prostate and kidney cancers have also shown a notable decline. However, regions such as Tibet, Xinjiang, Hong Kong, Macau, and Taiwan showed relatively smaller reductions. This could be attributed to the strict smoking controls in economically developed areas, such as Hong Kong, Macau, and Taiwan, and the initially low incidence and mortality rates in less developed areas, such as Tibet and Xinjiang, which may result in less pronounced effects from smoking cessation. The direct pathophysiological link between tobacco and urological cancers has been well-documented.[33] Tobacco smoke contains aromatic amines such as β-naphthylamine and polycyclic aromatic hydrocarbons, known carcinogens for bladder cancer, which are excreted by the kidneys and exert carcinogenic effects throughout the urinary system. Research has shown that smoking cessation improves bladder cancer treatment outcomes and that smoking status can predict recurrence-free survival in patients with non-muscle-invasive bladder cancer. Collectively, targeted health strategies, including smoking cessation programs and early cancer screening, are crucial in high-risk regions to effectively reduce urological cancer burden in China.

Diabetes is a significant health challenge in China.[34] Effective control of fasting blood glucose levels has been shown to reduce bladder cancer mortality, although not as significantly as tobacco control. The data indicated that Shanghai and Taiwan experienced greater reductions in bladder cancer mortality following interventions aimed at managing fasting glucose levels. This finding suggests that addressing unhealthy lifestyles in economically developed areas can help alleviate the burden of bladder cancer. Therefore, it is imperative for the government to prioritize the promotion of blood glucose testing for early diabetes detection and advocate for healthier lifestyle changes. Such measures could play a crucial role in reducing the incidence and mortality of bladder cancer, which is associated with elevated blood glucose levels. These strategies can also address metabolic abnormalities and reduce chronic inflammation. Additionally, they can decrease exposure to environmental and lifestyle-related risk factors, thereby lowering both the incidence and mortality rates.

Limitations of the study

This study had some limitations. First, our data did not contain information on the pathology of patients with urological cancers, such as stage, grading, and distal metastasis, which may affect the estimation of risk factors. Without pathological details, it is challenging to accurately assess the association between specific risk factors and cancer progression or severity, potentially leading to biased or incomplete identification of significant predictors. In addition, the risk factors only considered the influence of lifestyle and did not include information on educational background, cultural practices, and other socioeconomic factors. The data in this study were only accurate to the first level of administrative units in China and lacked information on sub-provincial administrative areas. Furthermore, the rise in epidemiological figures may be attributed to better and more complete reporting of cases over time due to enhancements in the reporting structure. Additionally, differences in cancer reporting mechanisms across various geographical regions and provinces may hinder direct comparisons, making it difficult to ensure consistency and reliability of the data.

Conclusions

In conclusion, the incidence of and deaths from urological cancers in China will continue to rise or plateau from 1990 to 2021, highlighting a severe and escalating public health crisis. Different provinces have their own epidemiological contexts, and government departments should tailor comprehensive strategies and interventions including strict tobacco control policies, weight control policies, and balanced diets. In addition, implementing effective regulatory and accountability systems, promoting healthy lifestyles among the public, and implementing universal early cancer screening programs will help reduce the burden of urological cancers. Given the urgent need to address this growing health threat, immediate and sustained efforts are essential to mitigate the impact of urological cancers on the population. Future research should focus on the impact of environmental factors, such as air pollution, on urological cancer incidence. Additionally, longitudinal studies are needed to evaluate the effectiveness of smoking cessation programs and other interventions on reducing urological cancer mortality over time. Moreover, we did not perform comprehensive multiple logistic regression analyses to account for confounding variables, which may limit the causal inferences drawn from the identified risk factors.

Contributors

Participated in study conception design: Mingyang Xue, Wenyi Jin, Weiheng Guo, Queran Lin, Yundong Zhou, and Pengpeng Ye. Data analysis: Mingyang Xue, Wenyi Jin, Yundong Zhou, Liming Pan, Pengpeng Ye, Queran Lin, Yanfang Ye, You Zeng, and Zhifei Che. Wrote or contributed to the writing of the manuscript: Mingyang Xue, Weiheng Guo, Wenyi Jin, Liang Zhang, João Conde, Pengpeng Ye, and Queran Lin. Obtained the funding: Pengpeng Ye and Queran Lin. Pengpeng Ye, Queran Lin, and Wenyi Jin verified the data, Pengpeng Ye had access to raw data, and João Conde, Pengpeng Ye, Queran Lin, and Wenyi Jin had final responsibility for the decision to submit for publication. Senior author: Pengpeng Ye. All authors contributed to the article and approved the submitted version.

Data sharing statement

Some of these data presented here are publicly available on the Global Health Data Exchange website and additional data can be requested from Institute for Health Metrics and Evaluation.

Editor note

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Declaration of interests

All authors declare no competing interests.

Acknowledgements

We appreciate Prof. Ye Tian for his valuable suggestions to this work. We also extend our gratitude to the National Supercomputer Center in Guangzhou for providing invaluable support during the data analysis process for this study.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lanwpc.2025.101517.

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