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Trends and projections of kidney cancer incidence at the global and national levels, 1990–2030: a Bayesian age-period-cohort modeling study

Zhebin Du[1†], Wei Chen[1†], Qier Xia[2†], Oumin Shi[3] and Qi Chen[1*]

Abstract

Background: Identifying the temporal trends of kidney cancer (KC) incidence in both the past and the future at the global and national levels is critical for KC prevention.

Methods: We retrieved annual KC case data between 1990 and 2017 from the Global Burden of Disease (GBD) online database. The average annual percentage change (AAPC) was used to quantify the temporal trends of KC age-standardized incidence rates (ASRs) from 1990 to 2017. Bayesian age-period-cohort models were used to predict KC incidence through 2030.

Results: Worldwide, the number of newly diagnosed KC cases increased from 207.3 thousand in 1990 to 393.0 thousand in 2017. The KC ASR increased from 4.72 per 100,000 to 4.94 per 100,000 during the same period. Between 2018 and 2030, the number of KC cases is projected to increase further to 475.4 thousand (95% highest density interval [HDI] 423.9, 526.9). The KC ASR is predicted to decrease slightly to 4.46 per 100,000 (95% HDI 4.06, 4.86). A total of 90, 2, and 80 countries or territories are projected to experience increases, remain stable, and experience decreases in KC ASR between 2018 and 2030, respectively. In most developed countries, the KC incidence is forecasted to decrease irrespective of past trends. In most developing countries, the KC incidence is predicted to increase persistently through 2030.

Conclusions: KC incidence is predicted to decrease in the next decade, and this predicted decrease is mainly driven by the decreases in developed countries. More attention should be placed on developing countries.

Keywords: Kidney cancer, Incidence, Prediction, Temporal trends, Modeling study

Introduction

Kidney cancer (KC) develops from the renal parenchyma, and approximately 70% of KC cases are clear renal cell carcinomas [1]. According to the latest statistics, there were more than 400 thousand newly diagnosed KC cases and nearly 180 thousand KC-related deaths in 2018 [2]. The KC incidence is highly heterogeneous worldwide, with North America having the highest incidence, followed by Western Europe and Australia [3]. In South America, Africa, and Asia, the KC incidences are relatively low [4, 5]. Within continents, KC incidence rates also differ by country. Across Europe, the incidence ranged more than fourfold: from 4.5 per 100,000 in Albania to approximately 16.8 per 100,000 in the Belarus [6]. Additionally, the temporal trends of KC

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incidence vary worldwide [7]. For example, in the USA, the rate was 8.0/100,000 in males in 1975 and increased steadily to 13.4/100,000 in 2012. In contrast, Austria and Poland have reported significantly decreasing rates since the early 2000s [7].

Many factors, including lifestyle changes, exposure to risk factors, and expanding coverage of tumor detection and reporting, have contributed to the temporal trends of KC incidence. Incidence trends can serve as a good indicator of shifting disease patterns and changing risk factors within a population [8] and are of importance for KC prevention. More importantly, since the marked alterations in risk factors over the last decades [9, 10], KC incidence might be subsequently changed in the near future. Further knowledge of the future trends of KC incidence is therefore critical for understanding and planning in regard to this disease burden and permits the modification of the national health system to respond to future challenges. Previous studies have described KC incidence, but these studies were retrospective in nature and consequently lacked insight into the future KC burden [5, 11–13]. Additionally, the number of cancer cases or deaths is the total number of people within a population who have either been diagnosed with or die from cancer, and this is greatly influenced by the size and age composition of the population. This information is critical to understanding and planning for the disease burden. To address this limitation, we used a Bayesian age-period-cohort (APC) model on KC incidence at the global and nation levels between 1990 and 2017 to project both the future number of cancer cases and incidence through 2030. Our predictions are of importance for the re-allocation of limited medical resources and to update the prevention strategies for KC.

Materials and methods
Study data
We collected annual KC case data between 1990 and 2017 by sex, region (195 countries or territories), age (from under 5 to ≥80 years in 5-year intervals) from the Global Burden of Disease (GBD) online query tool [14]. The general procedures for data collection and processing in the GBD study have been detailed and validated elsewhere [15, 16]. In brief, the annual number of newly diagnosed KC cases was sought from individual cancer registries or aggregated databases of cancer registry data such as "Cancer Incidence in Five Continents (CI5)", EUREG, SEER, or NORDCAN. The ICD-10 codes (C62-C62.92, Z80.43, and Z85.47-Z85.48) and ICD-9 codes (186–186.9, V10.47-V10.48, and V16.43) were used to identify KC cases [15]. The national sociodemographic index (SDI), a composite index measuring average achievement in several basic dimensions of country development, was collected from the GBD database. We also retrieved the corresponding population data for

each country or territory by year (1990–2030), sex, and age (from under 5 to ≥80 years in 5-year intervals) from the United Nations Department of Economics and Social Affairs (DESA) Population Division. Only 185 countries or territories were available at population data.

Statistical analysis
Model selection
Several models, including the Joinpoint model, age-period-cohort (APC) model, Nordpred model, and Bayesian APC model, have been previously used to predict cancer incidence based on population data [17–20]. We first conducted a model selection in terms of model prediction performance. KC case data from the USA, France, Brazil, Indonesia, and Vietnam, in which the KC incidence ranged from 2.5 per 100,000 to 13.0 per 100,000, were retrieved. These case data were then split into two intervals (1990–2012 and 2013–2017). We used the data between 1990 and 2012 to train the five prediction models (i.e., APC, Bayesian APC, Nordpred, nature-spline, and Joinpoint). KC incidence data between 2013 and 2017 were predicted and compared with the observational values in the same period. The prediction error rate was applied to assess the model performance. The error rate was calculated as $(\hat{y}-y)/y$, where $\hat{y}$ and y denote the prediction values and the observational values, respectively. The results of model selection are shown in S-Figure 1. Because of the relatively lower error rate of the Bayesian APC model, we used it to predict the KC cases and incidence rates through 2030.

The rationalities of the Bayesian APC model have been previously described [21]. Briefly, since the expectation that effects adjacent in time might be similar, the second-order random walk (RW2) model with inverse-gamma prior distribution was used for age, period and cohort effects. RW2 assumes an independent mean-zero normal distribution of the second differences of all time effects. This is a natural target for smoothing since the second differences in APC models are identifiable. Consider the age effects, for which the RW2 prior is identified as follows:

$$f(a|\kappa_a) \propto \kappa_a^{\frac{I-2}{2}} \exp\left(-\frac{\kappa_a}{2}\sum_{i=3}^{I}(a_i-2a_{i-1}+a_{i-2})^2\right)$$

$$= \kappa_a^{\frac{I-2}{2}} \exp\left(-\frac{1}{2}a^T Q a\right)$$

$$Q = \kappa_a \begin{bmatrix} 1 & 2 & 1 & & & \\ -2 & 5 & -4 & 1 & & \\ 1 & -4 & 6 & -4 & 1 & \\ O & O & O & O & O \\ & 1 & -4 & 6 & -4 & 1 \\ & & 1 & -4 & 5 & -2 \\ & & & 1 & -2 & 1 \end{bmatrix}$$

where i denotes the age index that ranges from 1 to $I =$ 17 in this study, because we projected the cancer incidence of people aged 0 to 84, and age was divided into 17 groups. Moreover, κ_α^{-1} denotes the variance parameter. Note that Q is rank deficient. To complete the RW2 model specification, we use the usual conjugate hyperprior for precision, $\kappa_\alpha \sim Gamma(\alpha, \lambda)$. This leads to the full conditional $\kappa_\alpha|\alpha \sim Gamma(\alpha + 0.5\ rank(Q),$ $\lambda + 0.5\alpha'Q\alpha)$, which may be directly simulated [20]. In this study, we used the parameter values $\alpha = 0.5, 1$, and 1 and $\lambda = 0.0005, 0.00005$, and 0.00005 for age, period, and cohort effects, respectively. The World-2000 population was used to standardize the KC incidence rates. To ensure the smoothness of predictions, countries or territories that experienced a striking fluctuation in KC case numbers within a small time interval were excluded. A total of 172 countries or territories were finally included.

Quantifying the KC incidence trends

The average annual percentage change (AAPC) was used to quantify the temporal trends of KC age-standardized incidence rates (ASRs) in 1990–2017 and 2018–2030, which indicate the past trends and future trends, respectively. A regression line was fitted to the natural logarithm of the rates, i.e., $y = \alpha + \beta x + \varepsilon$, where $y =$ ln (ASR) and $x =$ calendar year, and the AAPC was calculated as $100 \times (exp(\beta)\text{-}1)$ [22]. To overcome over dispersion, the AAPC of 2018–2030 was calculated with the inverse of the standardized error (i.e., $1/se$) of the estimated incidence rate as the weights in the regression models [20].

Sensitivity analysis

Because the KC case data in the GBD database were estimates from surveillance data instead of the surveillance data itself [23], we conducted a sensitivity analysis to verify the robustness of the prediction results derived from our models. Herein, we collected the KC case data from the Cancer Incidence in Five Continents *plus* (*CI5p*) database. Bayesian APC model was used to predict the KC cases and incidence rates based on the surveillance data from *CI5p* database [24]. Cancer surveillance data that covering more population and having a longer time span were preferable. Finally, data from Australia (from 1993 to 2012 and covering 7 cancer registries), Spain (from 1993 to 2010 and covering9 cancer registries), France (from 1998 to 2010 and covering 9 cancer registries), Italy (from 1998 to 2010 and covering 8 cancer registries), and the USA (from 1990 to 2012 and covering 9 cancer registries) were used. All statistical analyses were conducted in the R program (R core team, V3.5.1). A *P* value less than 0.05 was deemed statistically significant.

Results

KC case numbers and incidence, 1990–2017

Worldwide, the number of newly diagnosed KC cases increased from 207.3 thousand in 1990 to 393.0 thousand in 2017, and the KC ASR increased from 4.72 per 100,000 to 4.94 per 100,000 during the same period (AAPC = 0.14, 95% confidence interval [CI] 0.08, 0.20) (Table 1; Figs. 1 and 2). The case numbers increased in both sexes (Table 1; Fig. 1). The ASR increased significantly among males (AAPC = 0.38, 95% CI, 0.30, 0.46). In contrast, a significant decrease in ASR was detected among females (AAPC = – 0.26, 95% CI -0.30, – 0.23). The KC case numbers increased in all age groups, with the exception of people aged 0–19 years (Table 1; Fig. 3). The most pronounced increase was found in older people (≥ 65 years), among whom the case number increased by more than 100 thousand between 1990 and 2017. At the national level, the highest KC ASR was found in Uruguay (16.15 per 100,000), followed by Slovakia, Iceland, and the Czech Republic in 2017 (Fig. 4a). During the study period, a total of 134, 8, and 30 countries or territories experienced increases, remained stable, and experienced decreases in KC ASR, respectively (Fig. 4c; S-Table 1). The greatest increase was detected in Armenia (AAPC = 6.24, 95% CI 5.12, 7.36), followed by Bulgaria and Belarus (Fig. 4c; S-Table 1). The most pronounced decrease was found in Sri Lanka (AAPC = – 2.71, 95% CI -3.85, – 1.56), followed by Trinidad and Tobago and Qatar (Fig. 4c; S-Table 1).

KC case numbers and incidence, 2018–2030

Between 2018 and 2030, the KC case number will further increase to 475.4 thousand (95% highest density interval [HDI] 423.9, 526.9) (Table 1; Fig. 1). The KC ASR will decrease slightly to 4.46 per 100,000 (95% HDI 4.06, 4.86) during the same period (AAPC = – 0.97, 95% CI -0.99, – 0.95) (Table 1; Fig. 2). A decreasing trend is expected for both sexes, although the case numbers will still increase (Table 1; Fig. 2). The case numbers are predicted to decrease for people aged 0–19 years and 20–39 years between 2018 and 2030. However, a persistent increase is expected for people aged 40–64 years and ≥ 65 years (Table 1; Fig. 3). S-Tables 2 and 3 show the predicted KC case numbers and ASRs at the national level. Briefly, the case numbers will increase in all 172 countries or territories from 2018 to 2030. The temporal trends of KC ASR varied from country to country. In 2030, the highest KC ASR will be found in Uruguay (17.71 per 100,000), followed by the USA and Iceland (Fig. 4b; S-Table 3). A total of 90, 2, and 80 countries or territories will experience increases, remain stable, and experience decreases in KC ASR between 2018 and 2030 (Fig. 4d; S-Table 1). The greatest increase is expected in the United Arab Emirates (AAPC = 3.68, 95% 3.63, 3.73),

Table 1 The case numbers and incidence rates of kidney cancer between 1990 and 2030 at the global level

	1990		2017		2030		AAPC (95% CI) of ASR	
	No. of cases (× 1000)	ASR (/100,000)	No. of cases (×1000)	ASR (/100,000)	No. of cases (×1000) (95% HDI)	ASR (/100,000) (95% HDI)	1990–2017	2018–2030
Overall	207.3	4.72	393.0	4.94	475.4 (423.9, 526.9)	4.46 (4.06, 4.86)	0.14 (0.08, 0.20)*	−0.97 (−0.99, −0.95) *
Sex								
Male	114.6	5.65	240.8	6.38	298.1 (270.7, 325.6)	5.81 (5.29, 6.32)	0.38 (0.30, 0.46)*	−0.82 (−0.84, − 0.80)*
Female	92.7	3.96	152.3	3.68	187.4 (171.3, 203.4)	3.39 (3.11, 3.67)	−0.26 (− 0.30, − 0.23)*	−0.73 (− 0.75, − 0.72)*
Age years[a]								
0–19	27.0	–	24.4	–	18.4 (15.5, 21.4)	–	–	–
20–39	17.0	–	23.3	–	21.7 (19.7, 23.7)	–	–	–
40–64	90.3	–	171.5	–	189.6 (172.5, 206.7)	–	–	–
65+	73.0	–	173.8	–	248.8 (226.4, 271.3)	–	–	–

ASR Age-standardized incidence rate, AAPC Average annual percentage change, CI Confidence interval, HDI Highest density interval
[a], for each age group, only the number of cancer cases is shown because the ASR was not available when the age was grouped
*, P < 0.001

followed by Burkina Faso and Ghana. The most pronounced decrease is expected in Ukraine (AAPC = − 6.62, 95% CI -6.65, − 6.58), followed by Croatia and Slovakia (Fig. 4d; S-Table 1).

Correlations between past trends and future trends of KC incidence

Between 1990 and 2030, 18 and 72 countries or territories experienced a continuous decrease and increase in KC ASR, respectively. Ten countries or territories experienced a decrease in the past but will experience an unfavorable increase in the future. For example, we found that the decreasing trend of KC ASR will be reversed in the USA after 2017. In contrast, a total of 61 countries or territories will experience a significant decrease in KC ASR in the future despite the past increases in these regions. Figure 5 displays the correlations between past trends and future trends of KC ASR. No significant association was found when taking all countries into consideration as a whole ($\rho = 0.044$, $P = 0.566$). However, a significant negative association was detected for countries with a high SDI ($\rho = − 0.320$, $P = 0.009$), which means that most developed countries will undergo a favorable decrease in KC ASR between 2018 and 2030. In contrast, for countries with low SDI, a significant positive association was found ($\rho = 0.665$, $P = 0.005$), which means that past trends will remain in the future in most countries.

The results of the sensitivity analysis are shown in S-Figure 2. Generally, the predictions based on the GBD data and CI5plus data were comparable in all five countries. The predicted trends of KC ASR based on GBD data were similar to these based on CI5plus data, although the ASR values differed to some extent. These disparities were mainly ascribed to the differences in population coverage rate between these two databases.

Discussion

Kidney cancer (KC) is a malignancy whose incidence varies widely worldwide. Although KC incidence is relatively low compared to bladder and prostate cancer incidence rates, KC is of particular relevance in certain regions, such as Europe and North America, because of locally high incidence rates and significantly increasing rates in most countries in recent decades [5, 13, 15]. In the current study, we used GBD data to both describe the temporal trends of KC incidence over the last three decades and predicted its future trends in the next decade at the global and national levels. Globally, the number of KC cases is expected to increase consistently from 1990 through 2030, whereas the KC ASR is expected to decrease after 2017. The future decreasing trend was consistent in both sexes and in approximately half of all countries or territories. Of note, more than half of countries or territories, particularly developing regions, are expected to experience a significant increase in KC ASR between 2018 and 2030. These unfavorable trends might constitute a major obstacle for KC management and prevention in the near future.

The established risk factors, both environmental and genetic, for KC have been widely investigated and well documented [4, 25]. The impact of smoking on KC risk is modest, with an approximate 30% increased risk in current smokers and a 15% increased risk in former smokers compared with the risk among never smokers [26]. In developed countries, it is estimated that 6 and 24% of kidney cancer deaths are a result of tobacco smoking among females and males, respectively [13]. Fortunately, these proportions were shown to have decreased in the last decade, which was mainly ascribed to the "smoke-free" campaign in these countries [27, 28]. In contrast, overweight or obesity, another established risk factor for KC, has increased strikingly over the past
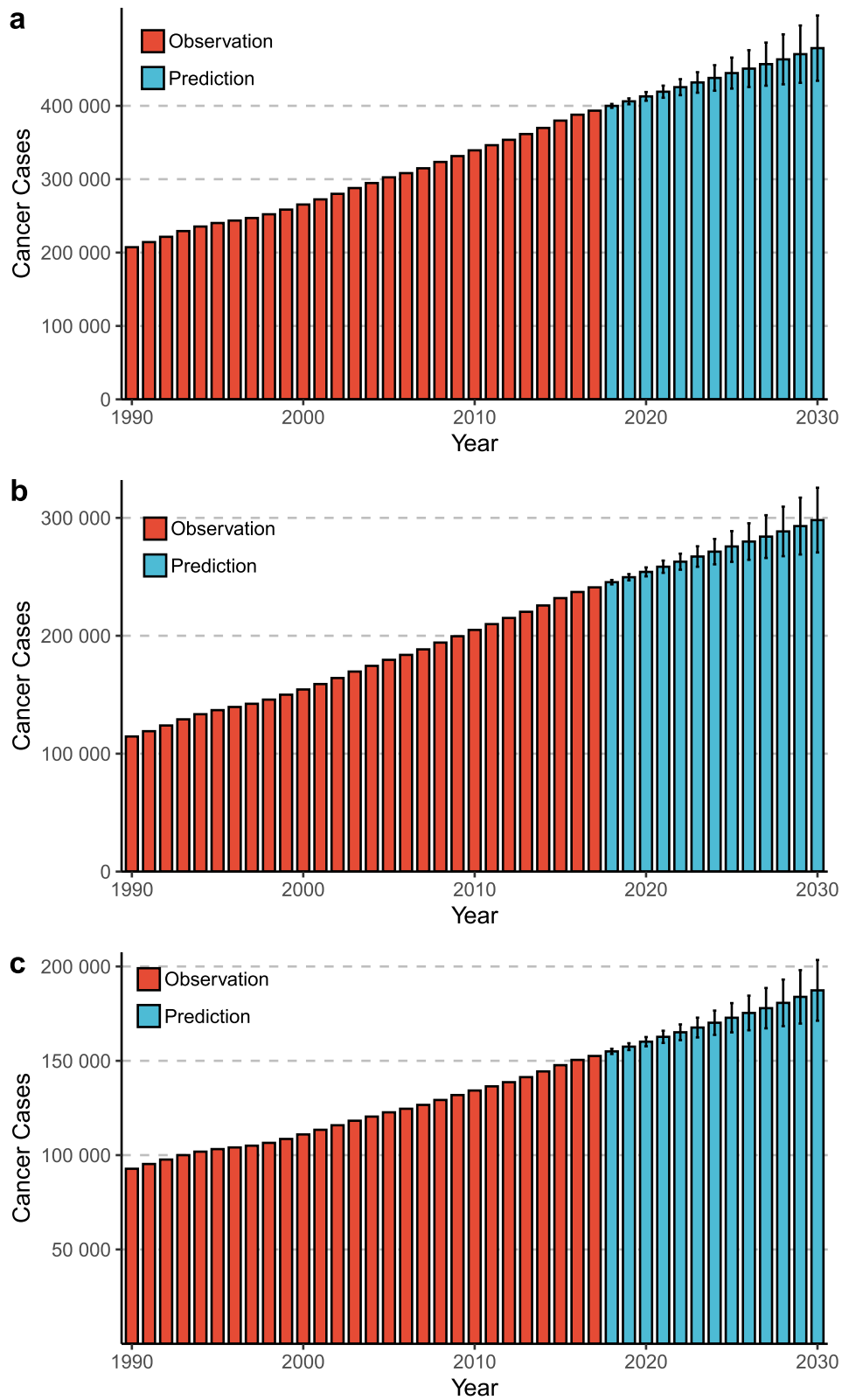
Fig. 1 The increasing trends in the numbers of kidney cancer cases between 1990 and 2030 at the global level by sex (**a**, both sexes; **b**, male; **c**, female). The error bar denotes the 95% highest density interval (HDI) of the prediction values
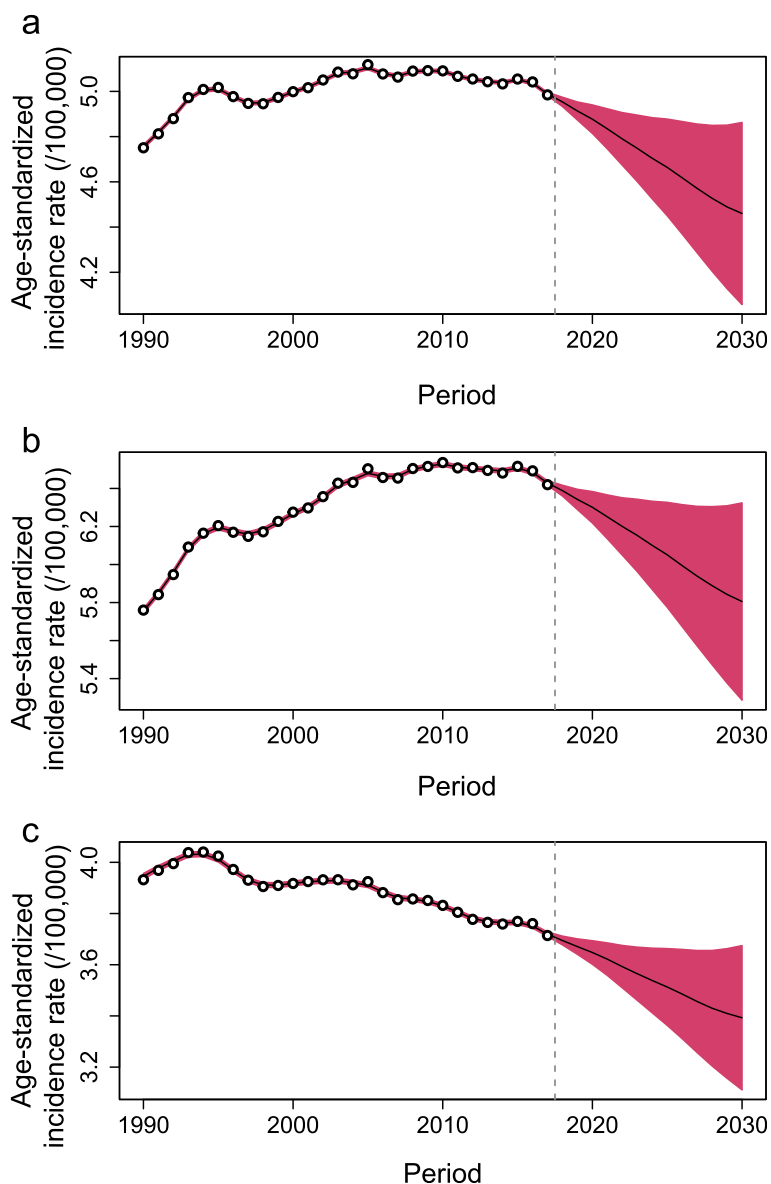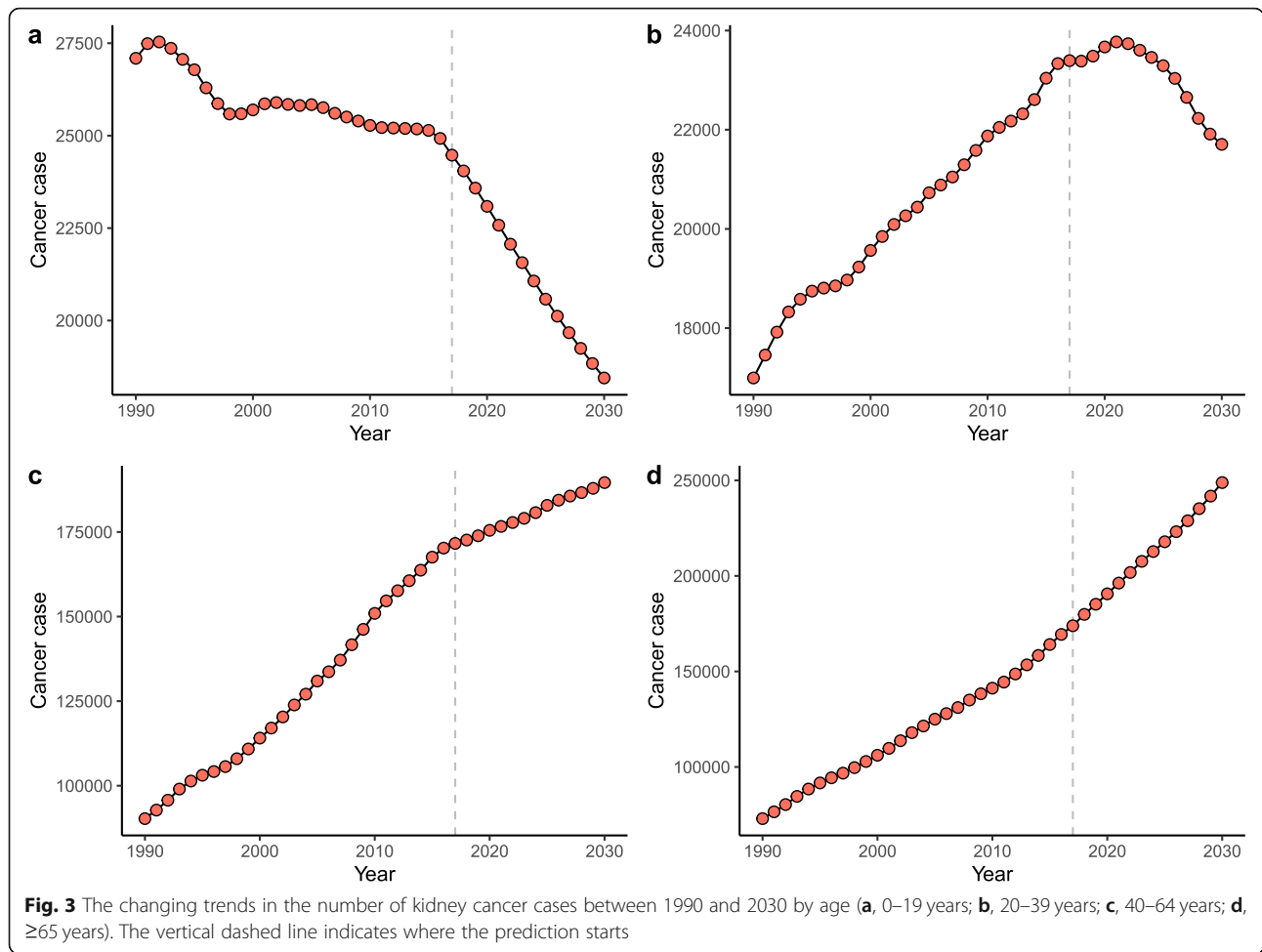
Fig. 2 The temporal trends of age-standardized incidence rates (ASRs, per 100,000) of kidney cancer between 1990 and 2030 at the global level in both sexes (**a**), males (**b**), and females (**c**). The open dots represent the observational values from GBD dataset, and the brick red shadow denotes the 95% highest density interval of prediction values. The predictive mean value is shown as a black solid line. The vertical dashed line indicates where the prediction starts

four decades [29, 30]. Moreover, the global adult per-capita alcohol consumption increased from 5.9 L to 6.5 L and is forecasted to reach 7.6 L by 2030 [31]. These alarming increases might drive an unexpected increase in KC incidence rates worldwide. For example, the KC incidence experienced an unfavorable reversal in the USA after 2017, despite the prior decrease. Additionally, the KC incidence trend was also predicted to be increasing in both the UK and Germany, whereas the incidence trend in the surrounding countries was decreasing. We speculated that this increase might be attributed to the

following reasons: 1) the dramatic increases in overweight and obesity and alcohol use [32, 33]; 2) immigrants from Africa and Asia might contribute to some extent [34]; and 3) the increase among blacks, especially in the USA, might surpass the decrease among whites [7]. The underlying causes need further investigation, and the unexpected increase indicates that KC remains a hard-to-ignore health concern in those highly developed countries.
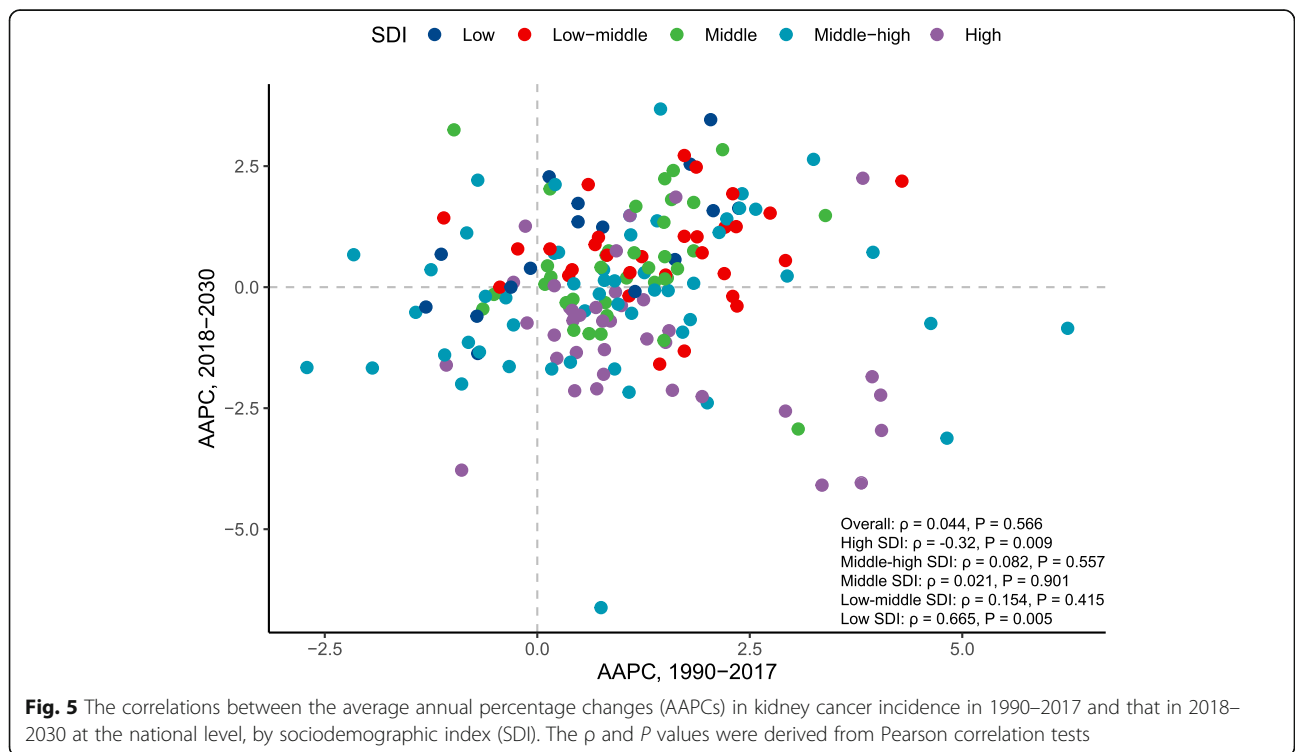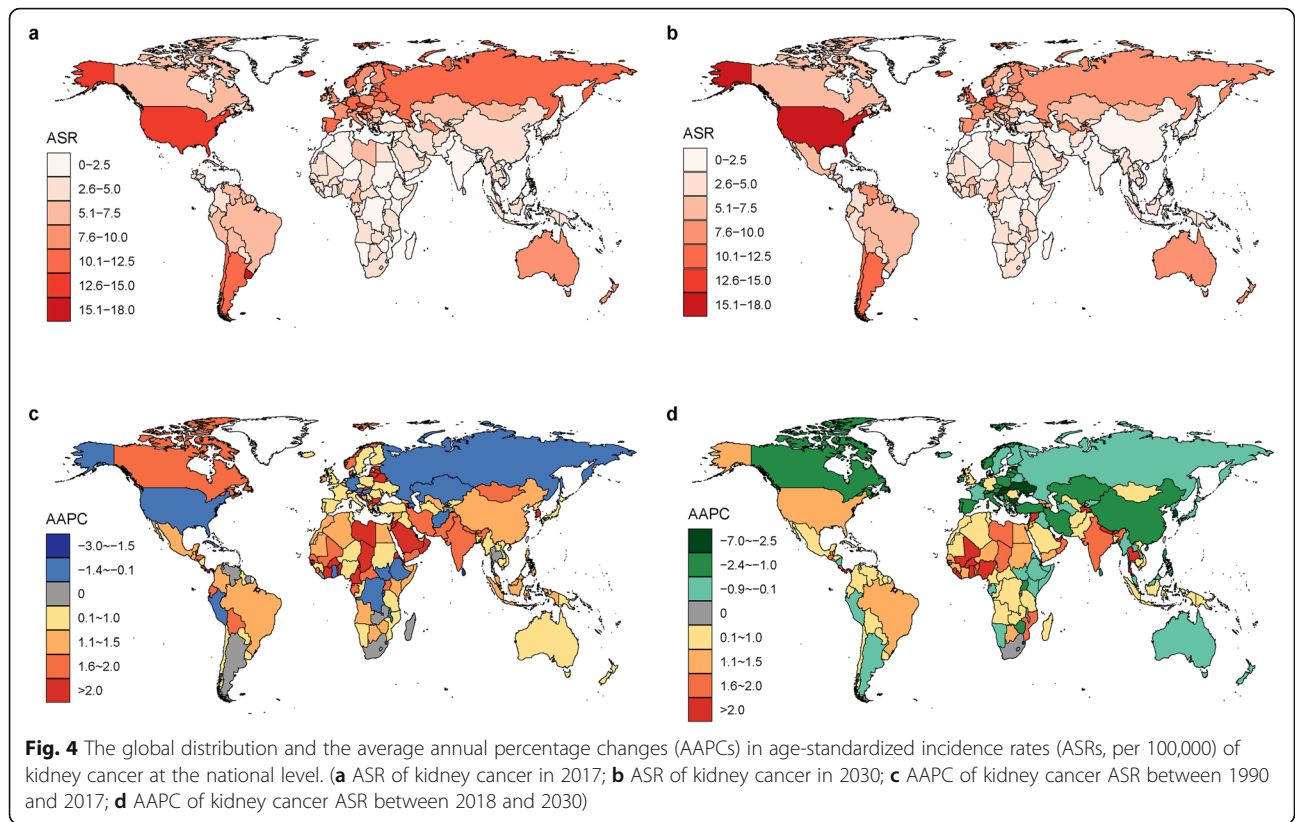
For most countries in Europe and Australia, we observed a favorable decrease in KC incidence after 2017,

Fig. 3 The changing trends in the number of kidney cancer cases between 1990 and 2030 by age (**a**, 0–19 years; **b**, 20–39 years; **c**, 40–64 years; **d**, ≥65 years). The vertical dashed line indicates where the prediction starts

which might largely drive the global declining trend. The rising incidence of KC over the last decades in Western populations has been attributed to the increased use of imaging techniques, which can result in incidental findings of small renal masses and has been reported to contribute as much as 50% to the overall incidence [7, 35]. The declining trends therefore might be ascribed to not only the reduction in risk factors but also to the plateau of imaging utilization. Although a relatively low incidence rate was observed, a consistent increase was observed in most countries in Latin America, Africa, South Asia, and Southeast Asia from 1990 to 2017. This increase was predicted to remain through 2030. We speculated that this increase might be partly explained by the following causes: 1) the increasing KC detection rates and reporting rates [7]; 2) the growing population, particularly the aging population [20]; 3) shifting trend toward the adoption of Western diets, change in occupational patterns, increased high-risk behaviors (e.g., excessive calorie intake and physical inactivity), and changes in established cancer risk factors (e.g., smoking and obesity) [20, 36]; and 4) the increasing prevalence of

chronic kidney diseases [37, 38]. Given the persistent increase, KC might be one of the main public health concerns in the near future in countries that previously had a lighter disease burden.

Our study has limitations. First, the GBD data were estimates from mathematical models based on surveillance data rather than surveillance data itself. However, the GBD study provides global-scale data and offers us an unprecedented opportunity to explore the global disease burden. Additionally, to ensure the robustness of our predictive results, we conducted sensitivity analyses based on observations from the *CI5plus* database. Whereas only five countries were included to validate the prediction values because of the limited data availability. This incomplete validation might limit the clinical value of our study. Second, the temporal trends of KC incidence in both the past and the future might be partly influenced by the detection and reporting rates, which reflect the quality of cancer registry data for each country. Cancer registry data can be biased in multiple ways. For example, changes between coding systems can lead to artificial differences in disease estimates;

Fig. 4 The global distribution and the average annual percentage changes (AAPCs) in age-standardized incidence rates (ASRs, per 100,000) of kidney cancer at the national level. (**a** ASR of kidney cancer in 2017; **b** ASR of kidney cancer in 2030; **c** AAPC of kidney cancer ASR between 1990 and 2017; **d** AAPC of kidney cancer ASR between 2018 and 2030)

Fig. 5 The correlations between the average annual percentage changes (AAPCs) in kidney cancer incidence in 1990–2017 and that in 2018–2030 at the national level, by sociodemographic index (SDI). The ρ and P values were derived from Pearson correlation tests

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however, this bias has been adjusted by mapping the different coding systems to the GBD causes. Misclassification of metastatic sites as primary cancer can lead to overestimation of cancer sites that are common sites for metastases such as the brain or liver. Third, the dearth of histological information of KC in the GBD database prevented us from pinpointing the KC incidence trends by histological subtype. Despite these limitations, using the most up-to-date data and advanced modeling strategies, our study provides a comprehensive understanding of KC incidence from the past to the future.

Conclusions

In summary, the KC incidence was predicted to decrease in the next decade. However, both the past and the future trends of KC incidence were highly heterogeneous from country to country. In most developed countries, the KC incidence is forecasted to decrease irrespective of past trends. In most developing countries, the KC incidence is expected to increase persistently through 2030. The long-term best practice approach must include the primary prevention of smoking and obesity, alongside careful monitoring of trends using high-quality population-based cancer registries and corresponding national registration sources.

Supplementary information

Supplementary information accompanies this paper at https://doi.org/10.1186/s40364-020-00195-3.

Additional file 1: Figure S1. The prediction error rate of five models based on data from Brazil, France, Indonesia, USA, and Vietnam. **Figure S2.** The predictions of kidney cancer incidence based on GBD data and IARC data (CI5 plus database). (IARC data: Australia, 1993–2012; Spain, 1993–2010; France, 1998–2010; Italy, 1998–2010; USA, 1990–2012). The blue triangles were point estimates of kidney cancer incidence based on CI5p data. The white open dots were point estimates of kidney cancer incidence based on GBD data.

Additional file 2: Table S1. The AAPC of kidney cancer incidence in 1990–2017 and 2018–2030.

Additional file 3: Table S2. The predicting kidney cancer cases at the national level from 2018 to 2030.

Additional file 4: Table S3. The age-standardized incidence rate of kidney cancer at the national level from 1990 to 2030.

Abbreviations
KC: Kidney cancer; AAPC: Average annual percentage change; ASR: Age-standardized incidence rate

Authors' contributions
Study conception and design: CQ and DZ; Data collection: DZ, CW, and XQ; Data analyses: DZ, CW, XQ, and OS; Results interpretations: all authors; Manuscript drafting: DZ, CW, and XQ; Manuscript proofing: CQ and DZ. The authors read and approved the final manuscript.

Availability of data and materials
The datasets supporting the conclusions of this article are included within the article.

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
None.

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