



Prostate cancer burden and attributable risk factors in East Asia from 1990 to 2021: a systematic analysis

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Abstract

Prostate cancer is a significant health concern in East Asia, where distinctive characteristics of disease presentation and outcomes warrant focused epidemiological investigation. This study evaluated the current status, future trends and risk factors across six East Asian regions. Mortality, incidence, Disability-Adjusted Life-Years (DALYs), and age-standardized rates were estimated using data from the Global Burden of Disease Study 2021. Join point, an age-period-cohort model and decomposition analyses were applied to reflect epidemiological trends. The Autoregressive Integrated Moving Average (ARIMA) model was used to predict the burden of prostate cancer 2022-2050. Taiwan had the highest Age-Standardized Mortality Rate (ASMR: 10.83 [95% uncertainty interval [UI]: 9.48–12.18]), Age-Standardized Incidence Rate (ASIR: 37.68 [95% UI: 32.54–43.34]), and DALY rate (ASDR: 192.07 [95% UI: 170.35–214.13]) in 2021. Mortality increased with age across all regions, while the cohort effect on mortality remained stable. The effects of age, period and cohort on mortality and incidence and the percentage of aging, population and epidemiological changes in the total trend differed across regions. ARIMA projections predicted a “U”-shaped ASMR trends in Japan. The Democratic People's Republic of Korea had the highest DALYs attributable to low in milk and calcium intake, whereas smoking-related ASDR were highest in Taiwan. The prostate cancer burden in East Asia remains substantial, particularly among older populations. Although overall trends appear more favourable than global averages, several regions face concerning future prospects.

Key words: prostate cancer, disease burden, risk factor, East Asia, global burden of disease.

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Introduction

Prostate Cancer (PCa) is one of the most prevalent malignant tumours among males worldwide (Bray *et al.*, 2018). Its presentation and outcomes demonstrate considerable geographical heterogeneity owing to factors such as ethnicity, level of health care and socioeconomic status (Albers *et al.*, 2024). East Asian countries, such as China, Japan, Mongolia, Democratic People's Republic of Korea (North Korea), and Republic of Korea (South Korea), exhibit unique characteristics in the incidence, management and prognosis. First, PCa was initially considered a disease predominantly diagnosed in Western countries; however, the steadily increasing incidence rate indicates that this disease is an emerging health concern of significance in East Asia (Ito, 2014). This could be attributed to the establishment of cancer registration programs and promotion of screening systems based on the Prostate-Specific Antigen (PSA) (Kimura and Egawa, 2018). Second, although the implementation of standardized treatment was somewhat delayed in Asia compared to Europe and North America, investigators in East Asia are constantly exploring treatment models suitable for local populations based on initial evidence derived from Western countries (Ito, 2014). Despite efforts to decrease the age-standardized death rate to 3.5% (per 100,000), it has been claimed that limited access to and availability of treatments remain issues in Asia (Schafer *et al.*, 2025). Finally, significant differences exist with

regard to gene polymorphisms between patients of East Asian and non-East Asian descent who were diagnosed with PCa (Zhu Y *et al.*, 2021). Inherent differences in genes related to testosterone metabolism between East Asian males and white populations would result in a difference in the therapeutic effect of androgen deprivation therapy, whereas the observed mutations in tumour suppressor genes, such as *SPOP*, *PTEN*, *BRCA2*, and *CHD1*, between East Asia and other regions contribute to disparities in tumour progression and prognosis (Zhu Y *et al.*, 2021).

In addition to the abovementioned characteristics of PCa presentation and outcomes, demographic, social and economic statuses also endowed East Asia with distinctive attributes. East Asia is the world's most populous region (Zhu Y *et al.*, 2021). Over the last few decades, this region has witnessed significant economic and scientific growth, which not only extended the lifespan but also has accelerated the aging of its population. Consequently, the incidence of PCa increased among the older men in East Asia (Narita *et al.*, 2022; Yeung & Lee, 2022). Therefore, considering the particularity of East Asia, it is important to assess, monitor, quantify and compare the burden of PCa to provide information for optimizing resource distribution and strategy adjustments.

Based on the epidemiological data of PCa obtained from the Global Burden of Diseases, Injuries and Risk Factors Study (GBD 2021 Risk Factors Collaborators, 2024) we initiated the current study to clarify the current status, regional discrepancy, future tra-

jectories and effects of risk factors on the PCa burden, which is pivotal in facilitating the development of public health policies and strategies aimed at PCa management.

Materials and Methods

Data resource

We used publicly available data from the GBD 2021 database (<https://vizhub.healthdata.org/gbd-results/>), which provides comprehensive and comparable global health data regarding the causes of death or injury and associated risk factors. It evaluates deaths, Disability-Adjusted Life Years (DALYs), prevalence, incidence, Years of Life Lost (YLLs) and Years of life Lived with Disability (YLDs) through metrics giving number, rate and percent for 288 causes of injuries and death and 88 risk factors in the form of age-sex-location-year, which indicates that the database delineate the burden of diseases for 52 age groups from birth to ≥ 95 years of age. This includes age-standardized data for males, females and both sexes combined; for 204 countries and territories, 50 regions, and 27 ‘super regions’; for every year from 1990 to 2021 (GBD 2021 Diseases and Injuries Collaborators 2024). The definitions of the measures and metrics are summarized in supplementary Table S1a. In the GBD 2021 report, cancers are categorized into various groups according to the 10th revision of the International Classification of Diseases (ICD-10) GBD 2021 Causes of Death Collaborators, 2024. The ICD-10 codes for PCa-related deaths in GBD 2021 include C61-C61.9, D07.5, D29.1 and D40.0. Based on the United Nations M49 geographical classification and the location structure of the GBD database, we included six East Asian locations: China, Japan, Mongolia, North Korea, South Korea and Taiwan. We extracted annual statistics and 95% uncertainty intervals (UIs) for the incidence, mortality, prevalence, and DALYs of PCa and their corresponding age-standardized rates (ASRs) for these countries over the period 1990–2021. The assessment of DALYs attributable to PCa involved summing the YLDs and YLLs (GBD 2021 Causes of Death Collaborators, 2024). We obtained 16 age categories based on five-year intervals, covering ages from 20 to 94 years and ≥ 95 years.

Attributable risk factors

In the GBD 2021 framework, 88 risk factors are broadly classified into four hierarchical levels and three parallel categories: environmental and occupational, behavioural, and metabolic (GBD 2021 Causes of Death Collaborators, 2024). The calculation of burden risk involves six methodological procedures: i) clarifying the risk factors and corresponding health outcomes; ii) collecting exposure data from national and regional reports and evaluating their distribution across various ages, sexes, years, and locations; iii) merging research data to yield risk models based on Bayesian statistical methodologies, so as to obtain the quantitative value of relative risk in comparison with the theoretical minimum risk exposure level; iv) determining Population Attributable Fractions (PAFs) for every risk factor; v) multiplying PAF value to deaths and DALYs for every age, sex, location, and year group to yield attributable burden of death and DALYs; and vi) estimating the age-standardized attributable burden to adjust for age-specific risk factors (GBD 2021 Causes of Death Collaborators, 2024). We focused on the risks at level 3 and identified three of them (smoking, diet low in calcium, and diet low in milk) with a non-zero or non-NA value to death and DALYs of PCa. The definitions

are listed in an additional file (Supplementary materials, Table S1b).

Statistical analysis

Analysis was performed between 1990 and 2021 to evaluate the impact of the burden of PCa. In addition to the number of deaths, incidence and DALYs related to PCa, GBD 2021 also calculated ASRs per 100,000 individuals using the formula:

$$ASR = \frac{\sum_{i=1}^A a_i w_i}{\sum_{i=1}^A w_i} \times 100,000 \quad \text{Eq. 1}$$

where a_i represents the age-specific rate of the i^{th} age group; w_i the counts or weights of people in the corresponding i^{th} age group in the standard population; and A the number of age groups included in the current study (GBD 2021 Causes of Death Collaborators, 2024). Estimates for the PCa burden were extracted from GBD 2021, along with 95% UIs, which represent the 25th and 975th values across all 1,000 samples. Estimated Annual Percentage Changes (EAPCs) along with 95% Confidence Intervals (CIs) were calculated to ascertain the trend in the ASRs of PCa burden based on a linear regression model represented by the equation:

$$y, \alpha + \beta x + \quad \text{Eq. 2}$$

where y represents $\ln(\text{ASRs})$; x the calendar year; ε the error term; and β the trend slope. The EAPC was subsequently calculated as $100 \times [\exp(\beta) - 1]$ (Zhu C *et al.*, 2021).

Joinpoint regression (using the “*nlh.joinpoint*” R package (version 0.1.0.9004) developed by the National Cancer Institute (NCI), USA.), was used to identify turning points and determine the Annual Percentage of Change (APC) for each trend segment of the trend curve. Candidate models, containing 0 to a maximum of 5 joinpoints, were evaluated and the optimal number and locations of the joinpoints determined by the NCI program. The APC and its 95% CI were calculated for each identified segment, while the Average Annual Percent Change (AAPC) was used to summarize the overall rate of change over the entire study period. The APC and AAPC were considered statistically significant if the 95% CI did not exceed 0 and $p < 0.05$.

Age-period-cohort analysis was performed separately for each location to evaluate the independent temporal patterns associated with age, calendar period, and birth cohort. Age and calendar year were grouped into 5-year intervals, and birth cohort was calculated as calendar year minus age. A log-linear age-period-cohort model was specified as follows:

$$D_{ap} \sim \text{Poisson}(N_{ap} r_{ap}) \quad \text{Eq. 3}$$

$$\log(r_{ap}) = \mu + \alpha_a + \beta_p + \gamma_c, \quad c = p - a$$

where D_{ap} represents the number of incident cases in age group a and period p ; N_{ap} the corresponding population; r_{ap} the incidence rate; and α_a , β_p , and γ_c the age, period and cohort effects, respectively. The age effect reflects changes in incidence across age groups, while period and cohort effects were expressed as rate ratios relative to the reference period and reference cohort, respectively. A rate ratio > 1 indicates a higher incidence rate than the reference group, whereas a value < 1 indicates a lower rate.

The age-period-cohort model serves as a highly effective and significant instrument in the fields of epidemiological and public health research, depending on its ability to decompose the disease burden into three interrelated dimensions of time effects (age, period and birth cohort). APC analysis requires age interval alignment with the period interval. Hence, the age and year data downloaded from GBD 2021 were both segmented with 5-year periods as done by (Huang *et al.*, 2024).

The Das Gupta Decomposition analysis was used to disentangle the overall changes in PCa incidence, mortality and DALYs into the share of changes contributed by population aging, population growth and epidemiological changes. This method enabled us to quantify the effect of factors on the total change and interpret the underlying causes of fluctuations in the disease burden from 1990 to 2021 (Han *et al.*, 2024). To forecast future mortality and incidence of PCa in East Asia, the Autoregressive Integrated Moving

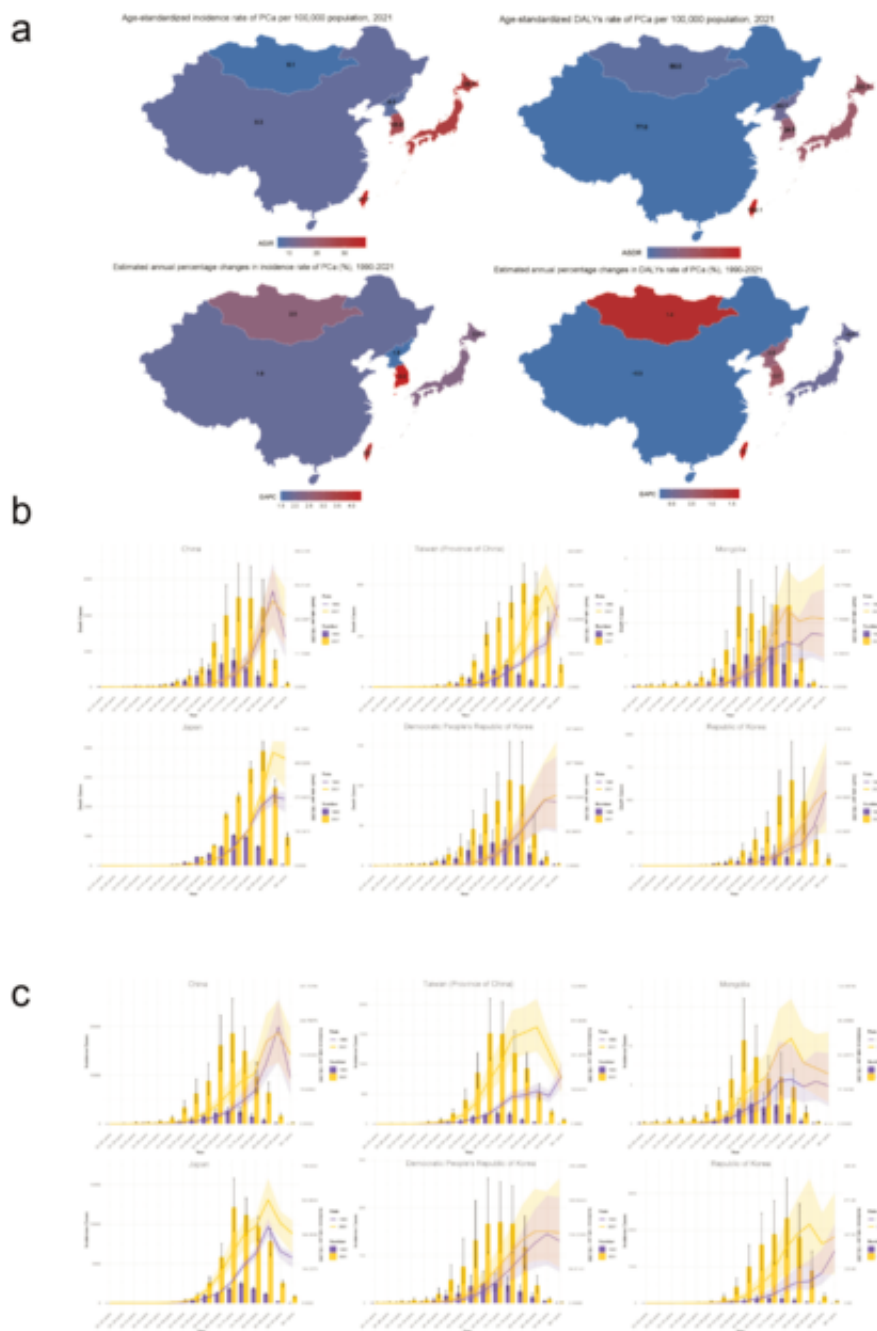


Figure 1. Map of PCa ASIR, ASDR and corresponding EAPC in East Asia (a). The dual-axis charts of PCa mortality (b) and incidence (c) number and rate across different age groups. PCa, prostate cancer; ASIR, age-standardized incidence rate; ASDR, age-standardized disability-adjusted life-year rate; EAPC, estimated annual percentage change.

Average (ARIMA) model was utilized to predict trends from 2022 to 2050. ARIMA has three fundamental parameters (p, d, q) representing the Autoregressive (AR) model, Moving Average (MA) model and differencing order, respectively. The Akaike Information Criterion (AIC) was applied to determine the optimal order parameters. The predictive capability of the ARIMA model depends on the linear combination of the AR component and the errors generated by the MA component (Li *et al.*, 2023). Data analysis and plotting were accomplished through the R software (version 4.5.1) with R packages “GlobalBurdenR,” which integrates functions from several R packages—including “dplyr,” “ggplot2,” “ggrepel,” “tidyverse” and “purrr”—and provides specialized tools for manipulating, analyzing, and visualizing data from the GBD database. The maps generated by R were used to visualize the geographical distribution and temporal changes in the burden of PCa across the six locations.

Results

Descriptive analysis of PCa burden

Tables 1, 2, and 3 provides an overview of the number and ASRs of mortality, incidence, and DALYs worldwide and in East Asian countries. In 2021, the largest number of deaths, incidence cases and DALYs were recorded in mainland China, whereas the lowest numbers were observed in Mongolia. Notably, the global ASIR was on a downward trend from 1990 to 2021; however, all six East Asian locations experienced upward changes. To facilitate

a more intuitive comparison of the burden of PCa in East Asia, regional maps of the ASIR, ASDR, and EAPC are shown in Figure 1a. A dual-axis chart of mortality numbers and rates across different age groups is presented in Figure 1b. The mortality rate of PCa increased significantly from the age of 75 years to 94 years in all six East Asian regions. However, China, Taiwan and Japan exhibited distinct differences in the obvious decline in the mortality rate among patients with PCa aged ≥ 95 years (Figure 1c).

Time trends of PCa incidence, mortality and DALYs

The joinpoint regression model was used to analyze the temporal trends of the PCa burden. Figure 2 shows the APC and AAPC of PCa incidence, death, and DALYs worldwide and across the six East Asian regions. Contrary to the decline in the ASIR of PCa worldwide, all East Asian regions exhibited an overall rising trend from 1990 to 2021.

Age-period-cohort effect on PCa mortality and incidence rate

Figure 3 illustrates the results of the age-period-cohort effects obtained from the age-period-cohort analysis, involving both global data and data specific to the East Asian regions. The mortality rate increased rapidly with advancing age in the six East Asian regions, which was generally consistent with the global pattern (Figure 3a). China, Japan and South Korea experienced an initial escalating death risk attributed to the period effect before declining continuously. The situation in Mongolia and Taiwan was unfavor-

Table 1. Mortality and Age-Standardized Mortality Rate (ASMR) for prostate cancer 1990 and 2021, with the temporal trend for the period 1990–2019.

Time Metric per country	1990 Mortality ^a	1990 ASMR ^b	2021 Mortality ^a	2021 ASMR ^b	1990–2021 EAPC of ASMR (95% CI)
Global	2119.72 [1942.22–2243.28]	16.35 [15.02–17.28]	4324.63 [3818.73–4636.45]	12.63 [11.16–13.55]	-1.05 [-1.14 to -0.05]
China	106.83 [80.15–139.18]	4.83 [3.65–6.49]	373.63 [278.51–503.66]	4.89 [3.58–6.53]	-0.34 [-0.57 to -0.11]
Taiwan	3.59 [3.29–3.93]	6.18 [5.61–6.8]	20.92 [18.31–23.51]	10.83 [9.48–12.18]	1.64 [1.27–2.01]
Japan	43.88 [41.32–45.79]	7.2 [6.7–7.54]	159.92 [138.77–171.1]	7.69 [6.77–8.18]	-0.13 [-0.43–0.17]
Mongolia	<i>0.11 [0.08–0.2]</i>	<i>3 [1.96–5.28]</i>	<i>0.31 [0.22–0.41]</i>	4.39 [3.14–5.89]	1.36 [1.28–1.44]
North Korea	1.76 [1.16–2.34]	4.97 [3.42–6.77]	5 [3.44–6.6]	5.36 [3.73–7.06]	0.42 [0.31–0.53]
South Korea	82.84 [62.76–137.51]	97.06 [72.36–161.06]	470.68 [288.12–612.82]	124.04 [75.33–159.89]	0.72 [0.38–1.05]

UI, uncertainty interval; CI, confidence interval; EAPC, estimated annual percentage changes; ASMR, age-standardized mortality rate; ^acases * 100 (95% UI); ^bper 100,000 (95% UI). Bold indicates the highest value in each column; italics indicates the lowest value in each column.

Table 2. Incidence and Age-Standardized Incidence Rate (ASIR) for prostate cancer 1990 and 2021, with the temporal trend for the period 1990–2019.

Time Metric per country	1990 Incidence ^a	1990 ASMR ^b	2021 Incidence ^a	2021 ASIR ^b	1990–2021 EAPC of ASIR (95% CI)
Global	5064.05 [4808.51–5246.97]	32.64 [30.86–33.86]	13243.83 [12173.21–14002.22]	34.05 [31.27–36]	-0.06 [-0.21–0.08]
China	137.54 [101.54–177.72]	4.99 [3.75–6.51]	886.01 [631.94–1209.65]	9.34 [6.68–12.57]	1.83 [1.71–1.96]
Taiwan	8.12 [7.4–8.95]	11.19 [10.16–12.35]	74.63 [64.26–85.63]	37.68 [32.54–43.34]	3.73 [3.12–4.34]
Japan	101.15 [94.53–107.16]	15.41 [14.29–16.3]	541.37 [471.58–599.59]	29.75 [26.1–32.9]	2.28 [1.73–2.83]
Mongolia	<i>0.13 [0.08–0.22]</i>	<i>3.14 [2.05–5.47]</i>	<i>0.5 [0.36–0.67]</i>	6.05 [4.37–8.2]	2.49 [2.34–2.64]
North Korea	2.48 [1.62–3.33]	5.8 [3.93–7.83]	9.6 [6.65–12.52]	8.52 [6.04–11.13]	1.49 [1.37–1.61]
South Korea	6.04 [4.48–10.05]	7.58 [5.55–12.78]	103.87 [62.95–138.48]	25.78 [15.49–34.2]	4.35 [3.74–4.96]

UI, uncertainty interval; CI, confidence interval; EAPC, estimated annual percentage changes; ASIR, age-standardized incidence rate; ^acases * 100 (95% UI); ^bper 100,000 (95% UI).

able, with the period risk ratio increasing with each passing year (Figure 3b). Regarding the cohort effect, death risks remained relatively stable with little fluctuation in East Asia, whereas the global risk dropped from the 1915 cohort to the 2000 cohort (Figure 3c). Figure 3d shows that the age effect on the PCa incidence rate

across the Taiwan Province of China, Japan, North Korea and South Korea exhibited similar patterns, with a sudden decline after 85 years of age. Compared with that in other regions, the incidence rate in China did not rebound at a specific point but continued to rise. The period-specific incidence rate ratio in Japan displayed

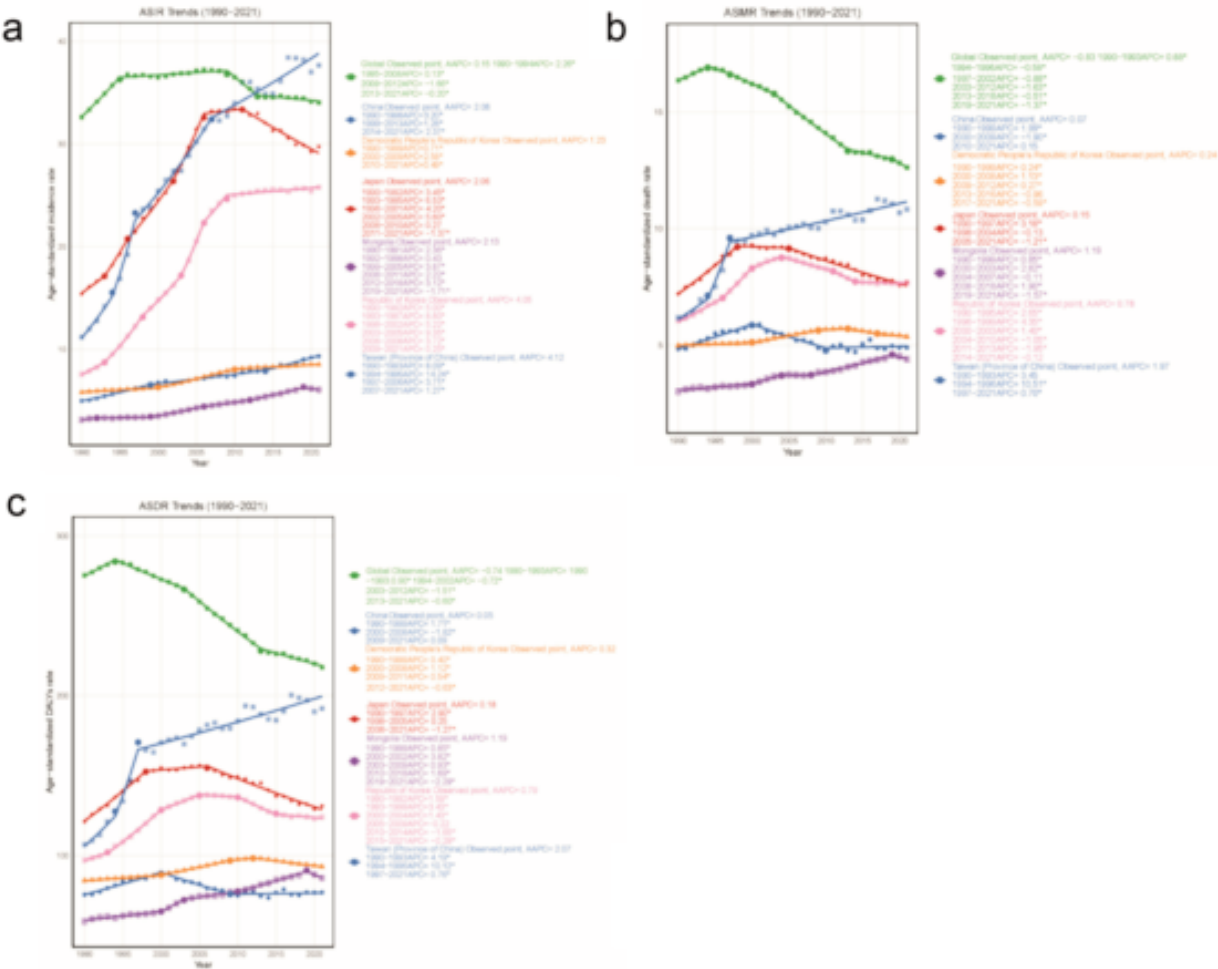


Figure 2. Joinpoint regression of PCa ASIR (a), ASMR (b), and ASDR (c) in East Asia from 1990 to 2021. PCa, prostate cancer; ASIR, age-standardized incidence rate; ASMR, age-standardized mortality rate; ASDR, age-standardized disability-adjusted life-year rate

Table 3. Disability-Adjusted Life-Years (DALYs) and Age-Standardized DALY Rates (ASDR) for prostate cancer 1990 and 2021, with the temporal trend for the period 1990-2019.

Time		1990		2021		1990–2021
Metric per country	DALY ^a	ASDR ^b	DALY ^a	ASDR ^b	EAPC of ASDR (95% CI)	
Global	2119.72 [1942.22–2243.28]	16.35 [15.02–17.28]	4324.63 [3818.73–4636.45]	12.63 [11.16–13.55]	-1.05 [-1.14 to -0.95]	
China	106.83 [80.15–139.18]	4.83 [3.65–6.49]	373.63 [278.51–503.66]	4.89 [3.58–6.53]	-0.34 [-0.57 to -0.11]	
Taiwan	3.59 [3.29–3.93]	6.18 [5.61–6.8]	20.92 [18.31–23.51]	10.83 [9.48–12.18]	1.64 [1.27–2.01]	
Japan	43.88 [41.32–45.79]	7.2 [6.7–7.54]	159.92 [138.77–171.1]	7.69 [6.77–8.18]	-0.13 [-0.43–0.17]	
Mongolia	0.11 [0.08–0.2]	3 [1.96–5.28]	0.31 [0.22–0.41]	4.39 [3.14–5.89]	1.36 [1.28–1.44]	
North Korea	1.76 [1.16–2.34]	4.97 [3.42–6.77]	5 [3.44–6.6]	5.36 [3.73–7.06]	0.42 [0.31–0.53]	
South Korea	3.92 [2.91–6.52]	6.05 [4.5–10.25]	26.02 [15.24–34.07]	7.68 [4.43–9.97]	0.57 [0.21–0.94]	

UI, uncertainty interval; CI, confidence interval; EAPC, estimated annual percentage changes; DALYs, disability-adjusted life-years; ASDR, age-standardized DALY rates; ^acases *100 (95% UI); ^bper 100,000 (95% UI).

trends similar to the global trend and ratios in North Korea. However, the situation in China, Taiwan, Mongolia, and South Korea was not optimistic. A progressive increase in the incidence risk in these regions was noted over the years (Figure 3e). As for the birth cohort effect on incidence risk (Figure 3f), North Korea and South Korea both remained stable throughout the study period, while a discernibly improved risk was observed in China, Taiwan and Japan for the population born in 2000.

Decomposition analysis of PCa mortality and incidence from 1990 to 2021

After completing the analysis of the long-term trends in mortality and incidence from the aspects of age, period and birth cohort, we quantitatively decomposed the overall changes in mortality and incidence into three contributing factors. The detailed percentages of each component of the PCa burden across East Asia are shown in Supplementary materials, Table S2. China had the highest PCa incidence among the six East Asian regions over the three decades, with epidemiological changes recognized as the primary contributor followed by population growth (Figure 4a). North Korea was the only location where a negative effect of aging was observed, China accounted for the majority of PCa deaths in East Asia with epidemiological changes being the main contributors (Figure 4b). Interestingly, aging effect largely decreased death by PCa in North Korea.

Prediction of PCa mortality and incidence

The ARIMA model quantified changes in PCa mortality and incidence rates over the following three decades. Figure 5a shows that the ASMR trends in Taiwan, Mongolia, North Korea and South Korea were smooth and stable. However, the ARIMA model projected that the ASMR in Japan would initially increase and then gradually decline. The ASIR trends from 2022 to 2050 are shown in Figure 5b. The ASIR is expected to increase in Taiwan in 2050, while the incidence rates in Mongolia and North Korea are expected to decline in the next 30 years.

PCa-related ASDR attributable to risk factors

The burden of DALYs attributable to the three identified risk factors (smoking, diet low in milk and diets low in calcium) was analyzed and classified by region. The detailed values of the risk factors attributed to the ASDR number/rate in 1990 and 2021 and the changes in the ASDR during the study period are provided in the Supplementary materials, Table S3. It should be noted that the values of the ASDR caused by diets low in milk were negative, which meant that dietary deficiency caused a loss of health in the population, and the more negative the value, the greater the disease burden caused by this deficiency. By contrast, the ASDR values and rates attributable to smoking were positive, indicating that the PCa burden related to smoking was caused by excessive exposure rather than deficiency (GBD 2019 Risk Factors Collaborators, 2020). China ranked the first in the absolute number of DALYs attributable to risk factors, with a diet low in milk and the highest percentage of smoking-caused ASDR occurred in Taiwan. Mongolia stands out when comparing the PCa burden of DALYs in 2021 with 1990 (Figure 6), with an obvious increase in the ASDR attributable to smoking. The most significant increase in the ASDR caused by diets low in milk and calcium was observed in North Korea.

Discussion

The comprehensive analysis of the PCa burden in six East

Asian regions from 1990 to 2021 carried out in this study predicts future burden trends for the coming 25 years. From the overall per-

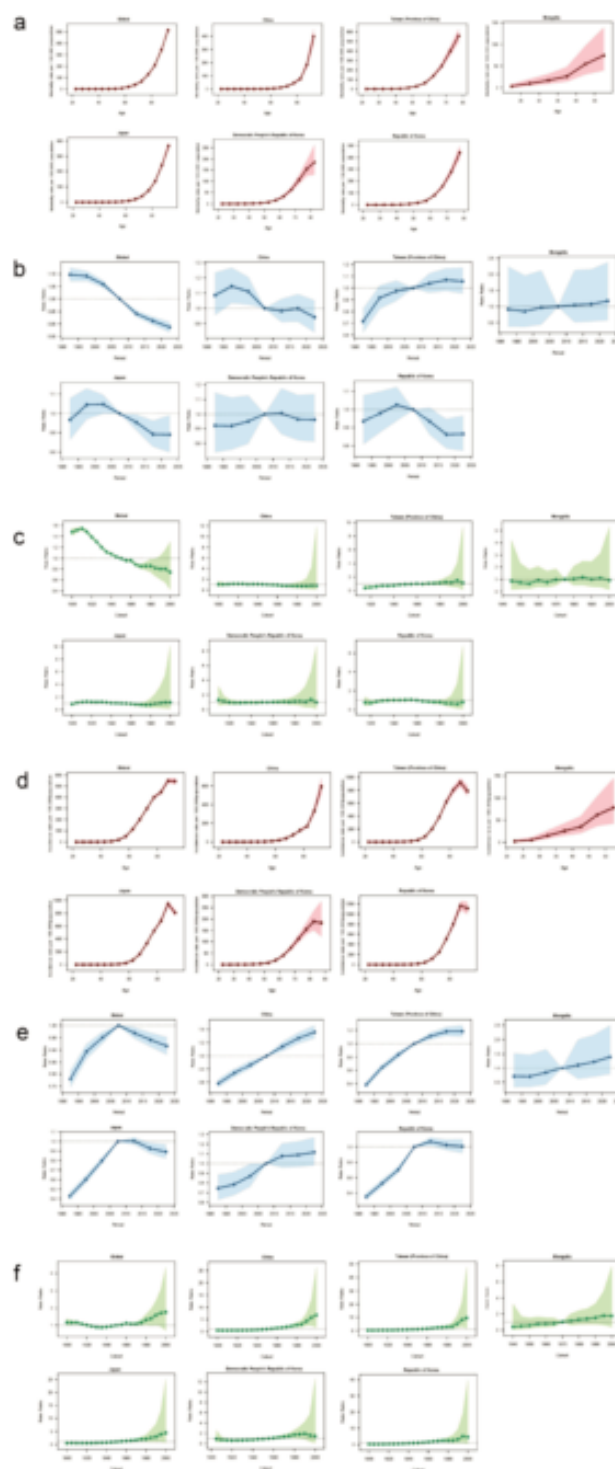


Figure 3. Prostate cancer burden in the world and East Asia from 1990 to 2021. (a) Age-period-cohort model analysis of the PCa; (b) Age-specific changes of mortality rate; (c) period-specific changes of death risk ratio; cohort-specific changes of death risk ratio; (d) age-specific changes of incidence rate; (e) period-specific changes of incidence risk ratio; (f) cohort-specific changes of incidence risk ratio. Shaded areas indicate 95% confidence intervals.

spective in 2021, the ASMR and ASIR of PCa among older people aged ≥ 75 years were relatively high. Age-period-cohort analysis also indicated that mortality and incidence risk increased with age after accounting for the interference of period and birth cohort, confirming that PCa is a typical old-aged disease, with advancing age recognized as one of the definitive risk factors for its incidence and mortality (Cooperberg *et al.*, 2009).

Considering that Western food was introduced into Taiwan in 1990, it could have affected the disease via the metabolic syndrome as claimed by Rhee *et al.* (2016) and Lin *et al.* (2020). As shown in Figure 3e, the risk ratio increased steadily with each passing year in all age groups, which suggests that the incidence risk is influenced by an external factor.

Significant heterogeneity was observed in each analytical method between regions. The ASIR in Taiwan rose rapidly and surpassed the global level by the end of the study period, a finding in line with a previous observational study in this area (Lin *et al.*, 2020) that deduced that the trend of the incidence rate was closely related to the increasing prostate-specific (PSA) screening. As this malignancy does not show obvious physical symptoms in the initial stages, early detection of PCa largely depends on screening (Litwin & Tan, 2017). Along with the development of screening practices and the enhancement of medical accessibility in Taiwan, a large number of previously undetected cases were identified and registered, leading to increasing ASIR values. China, North Korea, and Mongolia mirrored these findings. As related to increased screening practises, these results do not necessarily mean that the «real risk» of PCa among men in these countries is increasing. Indeed, the possible concerns of over-diagnosis and overtreatment arising from the popularity of PSA screening warrant vigilance. The European Association of Urology guidelines claim that

screening is correlated with the identification of localized and indolent PCa rather than advanced cases (Cornford *et al.*, 2024), and the effect of screening on long-term PCa-specific survival remains controversial (Hugosson *et al.*, 2019; Ilic *et al.*, 2018). Therefore, clinicians in these countries should carefully determine the indications for prostate biopsy to minimize the occurrence of related complications.

The ASMR, ASDR in 2021, and the corresponding AAPC from 1990 to 2021 in the Taiwan Province of China ranked the highest in East Asia. A high ASMR serves as a direct indicator of a significantly higher proportion of individuals who succumb to PCa. Additionally, a high ASDR suggests that PCa not only results in a considerable number of fatalities but also inflicts substantial suffering and disability in patients who survive (GBD 2021 Diseases and Injuries Collaborators, 2024). Therefore, standardized treatment, strict follow-up, and meticulous nursing are required in Taiwan to relieve the burden in the future. Additionally, a regional epidemiological study is required in Taiwan. Interestingly, the trends of ASMR and ASDR in Japan and the Republic of Korea were outstanding for their shape of “^” in joint-point regression as seen in Figure 2, suggesting that the rising trend for both parameters were halted around 2005 and experienced a gradual decline in the subsequent years till 2021. This phenomenon can be interpreted based on the results of other studies. An older population-based study indicated that a high socioeconomic status is correlated with a low PCa mortality rate (Chang *et al.*, 2012) and another study revealed that patients with PCa with high education and income tend to pursue curative treatment more actively, have shorter wait times, and have better short-term surgical prognosis (Tomic *et al.*, 2018). Japan and South Korea are the only two fully developed countries in East Asia, and economic fac-

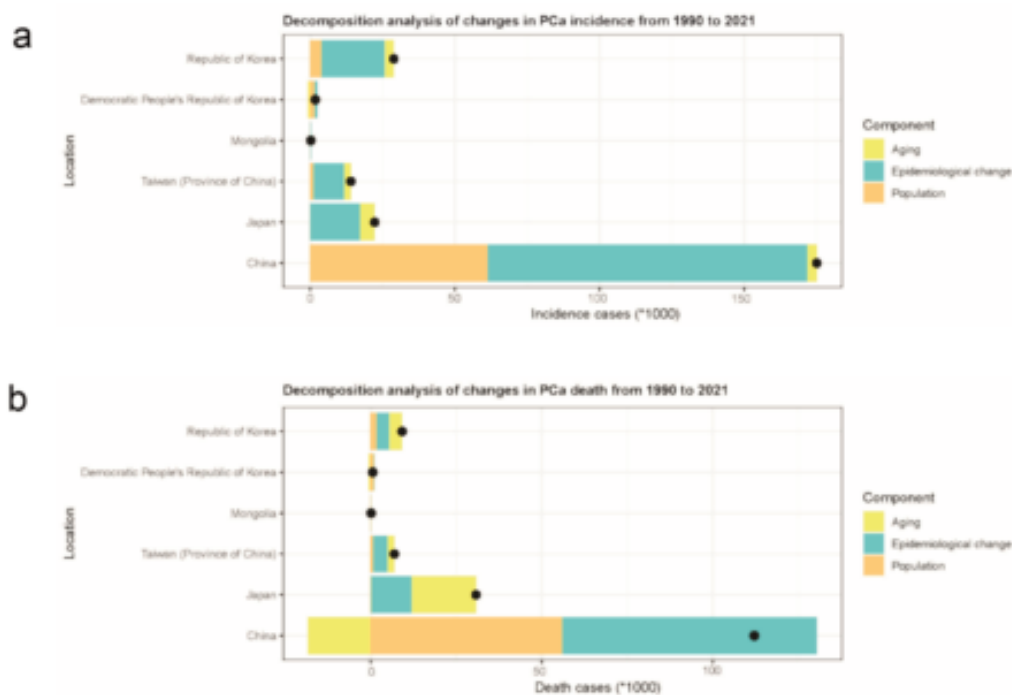


Figure 4. Decomposition analysis of prostate cancer from 1990 to 2021. A positive value indicates the factor that contributed to an increase in net burden, and a negative value indicates the factor that reduced the net burden; (a) incidence; (b) mortality; black dots represent the total impact of these three factors.

tors play a role in reducing the PCa burden. Led by the trajectories of the ASMR and ASDR, strengthening the development of economic and social education is, in theory, an approach to relieve the PCa burden for developing countries in East Asia. However, a study involving individuals with low-risk or localized PCa found that patients with higher incomes were more inclined to choose radical prostatectomy over nonsurgical treatment (Gray *et al.*, 2017). Despite a lack in conclusive evidence to prove radical prostatectomy is superior to other treatments for low-risk cases (Hoffman *et al.*, 2020), medical centres in East Asian regions with higher socioeconomic status should fulfil their duty to provide patients a comprehensive explanation of potential side effects and possible impacts on their quality of life before discussing the optimal plan with them.

Both in mainland China and Taiwan, decomposition analysis revealed that demographically adjusted epidemiological change was the primary factor contributing to the increase in the number of deaths (Figure 4a). Given that epidemiological changes were also the main driver behind the increase in incidence, the observed rise in death numbers can, at least partially, be attributed to an increase in incidence. However, it is essential to highlight the critical concerns that i) potential risk factors may accelerate PCa-related death and ii) the management of PCa may not keep up with the rising incidence of cases in mainland China and Taiwan. One study summarized that the rising levels of modern industry, air pollution, westernized lifestyles and shifting dietary patterns may be contributing factors to the rapid increase in PCa mortality rates in China (Zhang *et al.*, 2023). Therefore, mitigating these risk factors

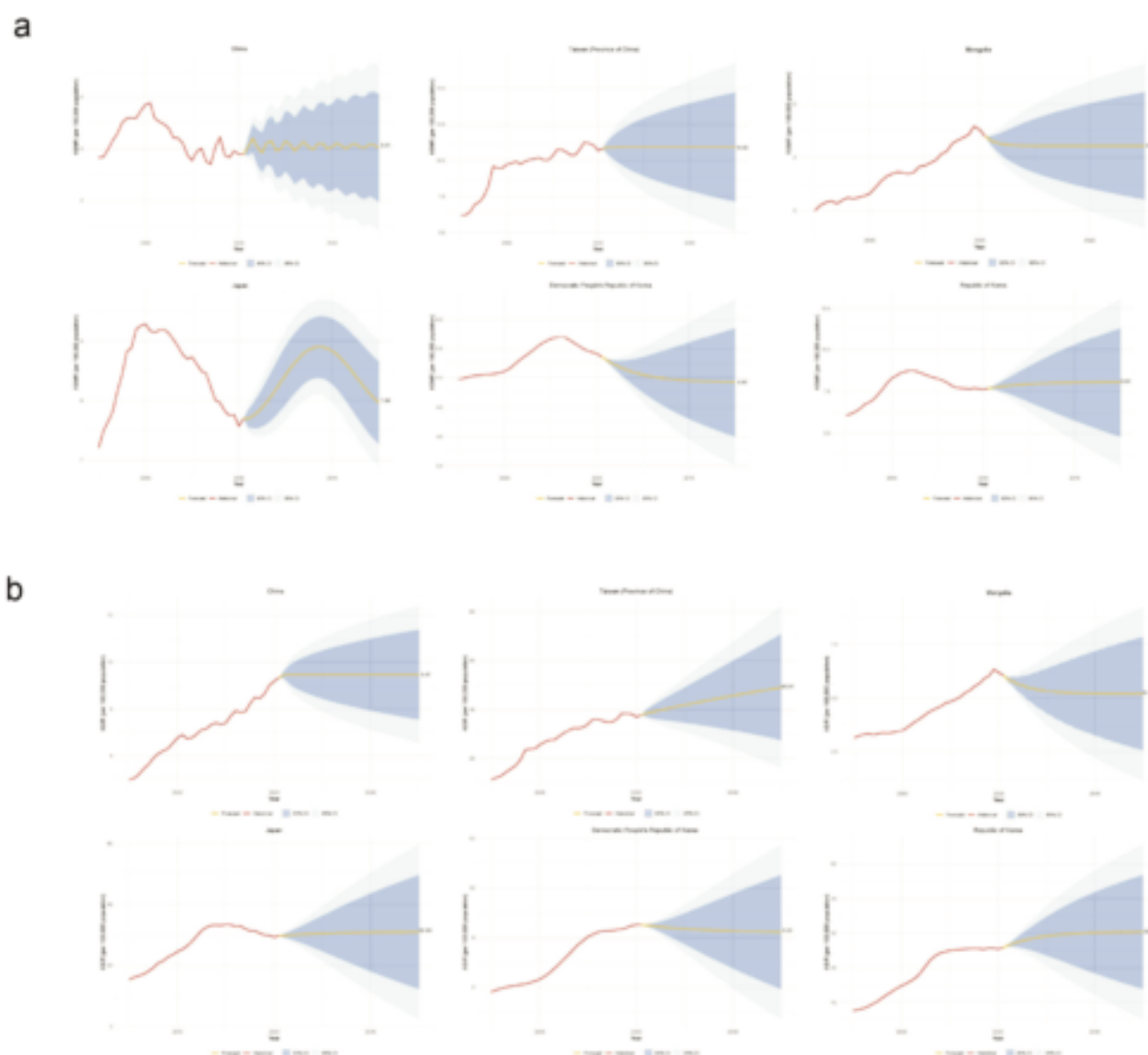


Figure 5. Predicted trends of PCa ASMR (a) and ASIR (b) in East Asia over next 30 years (2022–2050). The red line represents the historical trend of PCa during 1990–2021; the yellow line and shaded regions represent the predicted trend and its 95% CI, respectively. PCa, prostate cancer; ASIR, age-standardized incidence rate; ASMR, age-standardized disability-adjusted life-year rate; CI, confidence interval.

can become part of the policy to reduce the number of epidemiological change-attributed deaths.

The ARIMA analysis deduced that future trends in the ASMR and ASIR in most East Asian regions would be stable. However, the ASMR in Japan is expected to rise and peak in 2037. Decomposition analysis offers an interpretation of this situation revealing that population-aging was the primary driver of the increase in PCa mortality between 1990 and 2021. According to a demographic study, the proportion of people aged ≥ 65 years is expected to increase dramatically in the coming years, accounting for one-third of the total population by 2030 (Akiyama, 2020). Therefore, the rising trend in PCa ASMR in Japan is reasonable. To counterbalance the predicted rising ASDR, future medical resources and treatment strategies should be more inclined towards older patients, and revolutionary advances in therapeutic technologies should be encouraged.

The analysis of ASDR and possible risk factors illustrated that North Korea had the highest percentages of PCa DALYs attributable to a diet low in milk and calcium in East Asia, followed by mainland China and Taiwan. Consumption of food rich in calcium, such as milk may have a direct natural preventive correlation (Prentice, 2014). Although immediate changes in dietary habits may be challenging, educational efforts to promote adequate milk and other food rich in calcium can be considered; however,

these findings represent population-level associations, so such recommendations should be interpreted cautiously and should not be taken as evidence that increasing intake would reduce the burden of PCa. Besides, metaanalyses conducted by Aune *et al.* (2015) and Rahmati *et al.* (2018) reported that a higher intake of milk and calcium increases the risk of PCa, which suggests the necessity to provide different advice for PCa and non-PCa populations. In addition, Taiwan had the highest ASDR attributable to smoking in the whole study period, underscoring the importance of smoking cessation programs for patients with PCa in Taiwan.

Limitations

The present study has several limitations. First, the 95% CI was relatively wide in Mongolia across different analytical methods, indicating the suboptimal quality of the data. Therefore, the results for Mongolia should be interpreted with caution because of the lack of representativeness. Second, certain limitations are generally shared by all GBD studies. Due to the discrepancies in data collection and reporting systems among various regions, comparisons of estimated values across different locations may be affected, and population estimates in some regions are based on modelled projections due to the absence of recent demographic censuses (GBD 2021 Diseases and Injuries Collaborators, 2024); Qiu *et al.*, 2021). Finally, only three level risk factors were identified in

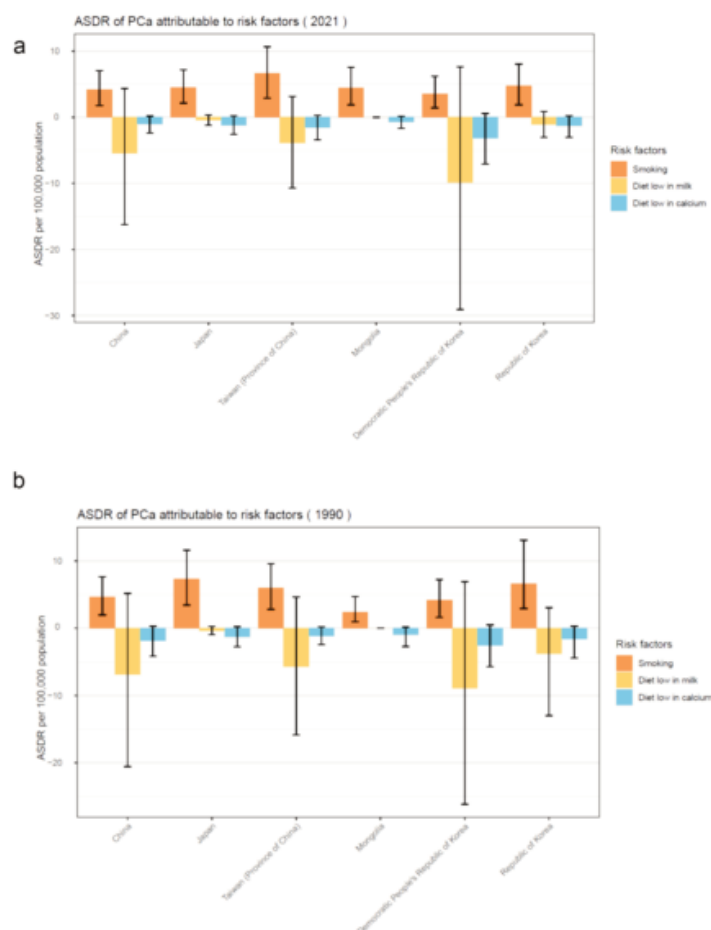


Figure 6. Comparison of the ASDR of PCa attributable to risk factors in 1990 and 2021. Negative values indicate deficiency caused by loss of health in the population, and positive values indicate burden caused by excessive exposure. PCa, prostate cancer; ASIR, age-standardized incidence rate; ASDR, age-standardized disability-adjusted life-year rate

GBD 2021 database, and the understanding of the attributable risk factors yielded by the current study might be incomplete.

Conclusions

This study revealed the complex landscape of PCa burden in East Asia. Although the overall trends of PCa ASIR, ASMR and ASDR in East Asia were favourable compared with the global situation, they remain a major concern among older people and future prospects are not optimistic for some regions. Future strategies designed to alleviate PCa burden must be tailored and aligned to the specific conditions of each region.

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Online supplementary materials

Table S1. The definitions of metrics and risk factors.

Table S2a. Percentage of the PCa incidence attributable to each component in decomposition analysis.

Table S2b. Percentage of the PCa death attributable.

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