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Comparative Burden and Attributable Risk of Hepatocellular Carcinoma in China versus G20 Nations from 1990 to 2040: A Joinpoint Regression and Bayesian Age-Period-Cohort Modeling Study

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Abstract

Hepatocellular carcinoma (HCC) is a principal contributor to cancer-related deaths globally, presenting significant public health and economic challenges. This investigation presents a detailed examination of the spatial and temporal progression, associated risk factors, and projected trajectories of HCC burden in China and G20 nations spanning the period from 1990 to 2040. Leveraging data from the Global Burden of Disease 2023 study, we applied descriptive statistical methods, Joinpoint regression analysis, Bayesian age-period-cohort (BAPC) modeling, ARIMA forecasting techniques, and risk factor decomposition. Findings revealed that while the absolute count of HCC cases rose, largely attributable to demographic aging, the age-standardized incidence and mortality rates (ASIR and ASMR) exhibited a downward trend from 1990 to 2023. This reduction was more pronounced in China compared to the G20 average, despite China's rates continuing to exceed the group mean. Notable inequalities were identified, with higher burdens observed among males, older populations, and G20 countries with lower socioeconomic status. A transition in the etiological profile was evident: the proportion of cases attributable to hepatitis B virus (HBV) declined, whereas the fraction linked to metabolic dysfunction-associated fatty liver disease (MAFLD) rose significantly. Projections for 2040, generated through integrated BAPC-ARIMA models, anticipate a persistent decrease in age-standardized rates. Scenario modeling indicated that enhanced control of primary risk factors—including HBV, HCV, alcohol use, tobacco consumption, and MAFLD—could markedly hasten this decline. In summary, despite advancements, the HCC burden remains substantial, with a growing contribution from metabolic risks. These results highlight the necessity for precise, resource-adapted preventive measures, with particular emphasis on addressing MAFLD and existing inequalities, to effectively reduce the future impact of HCC.

Keywords: Hepatocellular carcinoma, Disease burden, Risk factors, Forecasting, G20 countries

Introduction

Hepatocellular carcinoma (HCC) constitutes a major worldwide health issue, ranking among the most common and fatal cancers. As the primary histological subtype of liver cancer, HCC is distinguished by its rapid progression, unfavorable clinical outcomes, and considerable financial strain on medical infrastructures. The therapeutic approach to HCC is inherently complex, frequently requiring coordinated care from multiple specialties due to the common presence of concurrent chronic liver conditions, which directly affect treatment feasibility and

patient prognosis [1] Although contemporary treatment modalities continue to advance, they are hampered by challenges such as detection at advanced stages, frequent tumor recurrence, and heterogeneous patient responses, reinforcing the critical demand for better early screening and more efficacious, tailored therapies [2,3]

The epidemiology of HCC displays considerable variation across different regions and time periods, primarily influenced by the prevalence of its key causative agents. For decades, persistent infection with hepatitis B virus (HBV) and hepatitis C virus (HCV) has been the foremost global cause of HCC, responsible for a large percentage of incidents [4] Nonetheless, a significant epidemiological shift is occurring, characterized by a swift increase in the impact of metabolic dysfunction-associated fatty liver disease (MAFLD), formerly known as non-alcoholic fatty liver disease (NAFLD). MAFLD is now established as the most widespread chronic liver disorder and a key factor in HCC development, especially in Western countries, and is expected to emerge as a leading etiology for liver cirrhosis and cancer globally [5,6] This evolving etiological landscape, combined with the ongoing effects of alcohol intake and tobacco use, creates a multifaceted and changing risk environment that differs among populations and across decades.

Substantial research efforts have been dedicated to understanding the burden, risk factors and therapeutic strategies for hepatocellular carcinoma (HCC). Epidemiological research has established its patterns of occurrence and death, while clinical studies have progressed diagnostic protocols, classification frameworks such as the Barcelona Clinic Liver Cancer (BCLC) system, and therapeutic options from surgery and liver transplantation to systemic treatments like immune checkpoint inhibitors [2,7] Additionally, the application of multi-omics methodologies—spanning genomics, transcriptomics, and radiomics—is transforming the discipline, facilitating more accurate prediction of outcomes, identification of biomarkers, and enhanced comprehension of the tumor's biological context [8,9] For example, prognostic tools that combine clinical, radiological, and molecular information are under development to predict relapse and patient survival, in line with the principles of precision medicine [10,11]

Notwithstanding these developments, significant uncertainties remain regarding the global impact of HCC. Numerous prior investigations are limited by a narrow geographic scope or by providing only descriptive accounts of past trends without incorporating predictive estimates. There is a scarcity of longitudinal, comparative studies that concurrently evaluate the changing burden in countries with varying economic levels while analyzing the shifting influence of principal adjustable risk determinants. In particular, a systematic, direct comparison of HCC burden trends between China—a nation with a longstanding high rate of

viral hepatitis—and the G20 group, which encompasses a range of economic stages and risk exposures, is currently absent. Furthermore, although the growing significance of metabolic risks such as metabolic dysfunction-associated fatty liver disease (MAFLD) is recognized, a thorough, quantitative examination of how the contribution of these factors has changed over time across different population groups and countries is not sufficiently investigated. This limitation hinders the development of refined, evidence-based prevention strategies that can adapt to changing epidemiological patterns.

To overcome these limitations, this research implements a rigorous, multi-phase analytical strategy using the extensive Global Burden of Disease (GBD) 2023 dataset. The methodological rigor is founded on the combination of sophisticated statistical methods to offer a comprehensive and prospective outlook. We apply descriptive analyses and Joinpoint regression to outline long-term trends and detect important turning points in burden indicators. To separate the intricate influences of age, time period, and birth cohort on occurrence and death rates, we use Bayesian Age-Period-Cohort (BAPC) analysis. Additionally, autoregressive integrated moving average (ARIMA) models are utilized to forecast future burden trends up to 2040. A key aspect of our work involves calculating the population-attributable fractions for major risks, including hepatitis B virus (HBV), hepatitis C virus (HCV), alcohol consumption, tobacco use, and MAFLD, enabling an evaluation of their relative importance and changes over time.

The main goals of this study are threefold. First, we intend to methodically describe the spatial and temporal changes in HCC burden—including new cases, deaths, existing cases, and disability-adjusted life years (DALYs)—in China and among G20 nations from 1990 onward. Second, we aim to measure and contrast the burden attributable to key modifiable risk factors, exploring variations by gender, age, and national economic development, and recording changes in the leading causes over decades. Lastly, by integrating historical data analysis with model-driven predictions, we project future trajectories. This study aims to forecast the trajectory of the hepatocellular carcinoma (HCC) burden through 2040 based on current trends. The primary objective is to produce robust, comparative data to guide the formulation of precise, economically efficient, and forward-looking national and international policies for HCC prevention, early diagnosis, and management. This effort seeks to mitigate the substantial global health burden imposed by HCC.

Materials and Methods

Data Sources

The analysis was conducted using data from the Global Burden of Disease (GBD) 2023 study. This database undergoes a rigorous, standardized quality assurance protocol, which includes validation of data, imputation for missing values, and harmonization across different geographical regions. It offers extensive estimates of disease burden for 195 countries and territories, with its reliability confirmed through international peer review. The investigation focused on China and the 19 other member countries of the G20. The time frame was segmented into two distinct intervals: 1990–2023 for retrospective trend analysis and 2024–2040 for prospective forecasting.

The following metrics were selected for evaluation: (1) Absolute measures of burden (counts of new hepatocellular carcinoma [HCC] cases, deaths, prevalent cases, and total Disability-Adjusted Life Years [DALYs]); (2) Relative burden measures (age-standardized incidence rate [ASIR], age-standardized mortality rate [ASMR], age-standardized prevalence rate [ASPR], and age-standardized DALY rate [ASDR]); and (3) Risk factor attribution metrics (Population Attributable Fractions [PAFs] and the corresponding DALYs linked to five specific risks: substance use disorders, high alcohol intake, elevated body mass index [BMI], high fasting plasma glucose, and smoking). All variable definitions and data retrieval processes strictly followed the official GBD 2023 study protocols.

Study Design and Analytical Methods

A three-stage analytical strategy was adopted, comprising “historical trend evaluation,” “stratified attribution decomposition,” and “future scenario projection.” The detailed methodological approaches are described below:

Descriptive Statistical Analysis

Data were stratified by sex, age group (20 categories ranging from under 5 years to 95 years and older), and national economic level (high-income and upper-middle-income). Categorical variables were summarized as frequencies (percentages), while continuous variables were expressed as mean $\pm$ standard deviation or median (interquartile range). Annual percentage changes, cumulative change percentages, and male-to-female ratios were calculated to quantify temporal shifts in disease burden and population characteristics.

Joinpoint Regression Analysis

Temporal patterns in age-standardized rates from 1990 to 2023 were analyzed using Joinpoint Regression Software (version 4.9.1). Significant inflection points in trends were detected via permutation tests. The Annual Percent Change (APC) for each identified segment and the Average Annual Percent Change (AAPC) for the entire observation period were calculated. The precision of these estimates was assessed using 95% confidence intervals (CI), with a significance threshold of $P < 0.05$.

Bayesian Age-Period-Cohort (BAPC) Model

The independent effects of age, calendar period (5-year intervals), and birth cohort (10-year intervals) on incidence risk were separated using models implemented with the bayesAPC package in R. Parameter estimation was performed via Markov Chain Monte Carlo (MCMC) simulation (10,000 iterations following a 2,000-iteration burn-in phase). Model convergence was verified using Gelman-Rubin diagnostics (with a potential scale reduction factor < 1.1), and model adequacy was evaluated through posterior predictive checks.

Future Disease Burden Projection

A composite forecasting approach was utilized, integrating an “ARIMA model with a BAPC model.” The ARIMA model (with parameters $p=2$, $d=1$, $q=1$ selected based on the Akaike Information Criterion) captured short-term linear trends, whereas the BAPC model addressed long-term non-linear patterns. Projections from both models were merged using a weighted average, with weights (ARIMA: 0.4, BAPC: 0.6) determined by their respective model fit R^2 statistics. Two future scenarios were simulated: a baseline scenario (maintaining current intervention intensities) and an enhanced intervention scenario (strengthened management of the five specified risk factors). Burden estimates for the period 2024–2040 were produced. The predictive performance of the model was evaluated by calculating the Mean Absolute Error (MAE) and Root Mean Square Error (RMSE).

Analysis of Population Attributable Risk

The influence of the five specified risk factors was assessed by calculating Population Attributable Fractions (PAFs) based on the Global Burden of Disease 2023 methodology. The relative risk (RR) estimates applied were: substance use disorders (3.2), high alcohol intake (2.3), high body mass index (2.1), elevated fasting plasma glucose (1.8), and smoking (1.8). Subgroup analyses were carried out by sex, age group (under 50, 50–69, 70 years and

older), and national income level. Annual percentage changes in PAFs were determined, and possible interaction effects among factors were examined.

Statistical Methods and Data Quality Control

All statistical computations were performed using R software (version 4.3.1), with specific packages including dplyr and joinpointR. The quality control protocol consisted of the following steps: (1) Exclusion of data entries with a reliability score lower than 0.6; (2) Use of multiple imputation (5 imputations) for variables where missing data constituted less than 5% of records; (3) Verification of data accuracy through double-entry procedures, with agreement confirmed by a Kappa statistic exceeding 0.95; (4) Conduct of sensitivity analyses to test the stability of the results; and (5) Adjustment of rates by age standardization to control for confounding effects related to the age distribution of the population.

Result

Comprehensive Analysis of HCC Disease Burden in China and G20 Nations (1990–2023)

Magnitude of Absolute Burden and Temporal Dynamics

Between 1990 and 2023, the absolute burden of hepatocellular carcinoma (HCC) in both China and G20 nations demonstrated a consistent upward trend (Figure 1A–D). In China, the annual incidence count rose from 100,087 (95% Uncertainty Interval [UI]: 82,278–122,823) in 1990 to 165,113 (95% UI: 126,764–210,288) in 2023, marking an approximate 65% increase (Table 1). Similarly, the annual incidence in G20 countries increased from 183,161 (95% UI: 162,237–208,915) to 379,276 (95% UI: 322,431–438,038). Annual mortality in China grew from 92,324 (95% UI: 75,963–113,246) to 143,499 (95% UI: 111,314–181,615), while in G20 nations, it escalated from 165,927 (95% UI: 146,681–189,913) to 326,015 (95% UI: 278,965–373,462) (Figure 1A–B). Disability-Adjusted Life Years (DALYs) and prevalent cases exhibited parallel growth, indicating a persistent expansion of the absolute disease burden (Figure 1C–D).

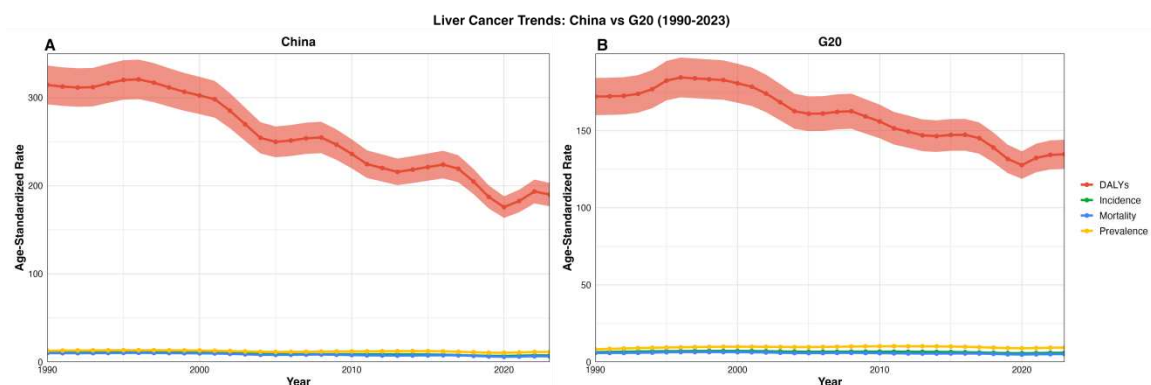


Figure 1: Temporal trends in absolute burden (incidence, mortality, DALYs, prevalence) of hepatocellular carcinoma in China and G20 countries, 1990–2023.

Patterns in Age-Standardized Rates and Global Context

Following age adjustment, all rate indicators in China continued to exceed the G20 average, despite showing downward trajectories over the study duration (Table 1). In 2023, China's age-standardized incidence rate (ASIR) was 14.69 per 100,000 (95% UI: 12.00–17.38), substantially higher than the G20 average of 8.66 per 100,000 (95% UI: 7.10–10.22). From 1990 to 2023, the Estimated Annual Percentage Change (EAPC) for ASIR in China was -1.36 (95% CI: -1.52 to -1.20); for the age-standardized mortality rate (ASMR), it was -1.60 (95% CI: -1.78 to -1.42); and for the age-standardized DALY rate (ASDR), it was -1.77 (95% CI: -1.95 to -1.59). These reductions were more pronounced than those in G20 countries (EAPCs of -0.50 , -0.52 , and -0.91 , respectively). Notably, the age-standardized prevalence rate (ASPR) in G20 nations displayed a marginal increase (EAPC: 0.33 , 95% CI: 0.18 – 0.48), while China experienced a slight decrease (EAPC: -0.57 , 95% CI: -0.72 to -0.42).

Joinpoint regression analysis detected several significant turning points in the trajectories of age-standardized rates (Figure 2A–D). ASIR, ASMR, and ASDR in China showed phased declines, with the pace of reduction generally accelerating post-inflection; in contrast, ASPR exhibited relatively stable changes. Segmented trends for various metrics in G20 countries paralleled those in China but with less pronounced overall declines. Continuous temporal curves further illustrated that although all age-standardized rates in China persistently surpassed those in G20 nations throughout the period, the absolute disparity between the two gradually diminished over time (Figure 3A–D).

Table 1: Age-standardized rates and Estimated Annual Percentage Changes (EAPC) for hepatocellular carcinoma in China and G20 countries in 1990 and 2023.

Location	Measure	All-ages cases		Age-standardized rates		1990–2023 EAPC (95%CI)
		1990 (95%UI)	2023 (95%UI)	1990 (per 100,000,95%UI)	2023 (per 100,000,95%UI)	
China	Incidence	100,087 (82,278–122,823)	165,113 (126,764–210,288)	18.41 (15.01–21.81)	14.69 (12.00–17.38)	-1.36 (-1.52 to -1.20)
	Mortality	92,324 (75,963–113,246)	143,499 (111,314–181,615)	17.41 (14.25–20.57)	11.34 (9.29–13.39)	-1.60 (-1.78 to -1.42)
	DALYs	3,113,534 (2,565,476–3,825,173)	4,055,012 (3,133,971–5,172,064)	400.39 (328.32–472.46)	422.70 (346.62–498.78)	-1.77 (-1.95 to -1.59)
	Prevalence	124,810 (102,642–160,149)	239,407 (183,748–303,862)	15.07 (12.36–17.78)	17.85 (14.64–21.06)	-0.57 (-0.72 to -0.42)
G20	Incidence	183,161 (162,237–208,915)	379,276 (322,431–438,038)	10.32 (8.45–12.19)	8.66 (7.10–10.22)	-0.50 (-0.63 to -0.37)
	Mortality	165,927 (146,681–189,913)	326,015 (278,965–373,462)	8.66 (7.09–10.23)	6.68 (5.46–7.90)	-0.52 (-0.65 to -0.39)
	DALYs	5,142,180 (4,516,499–5,943,459)	8,339,747 (7,135,993–9,643,069)	273.10 (223.94–322.26)	269.18 (220.73–317.63)	-0.91 (-1.05 to -0.77)
	Prevalence	241,715 (210,799–291,634)	579,932 (471,246–702,539)	10.89 (8.91–12.87)	14.47 (11.86–17.08)	0.33 (0.18 to 0.48)

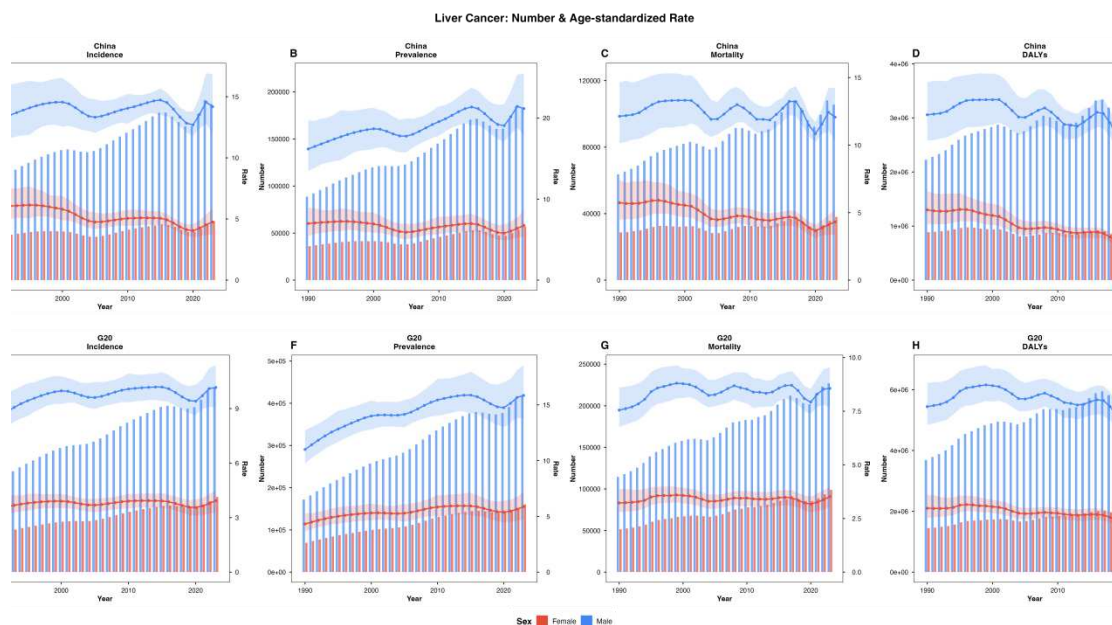


Figure 2: Segmented trends in age-standardized rates of hepatocellular carcinoma in China and G20 countries analyzed using Joinpoint regression, 1990–2023.

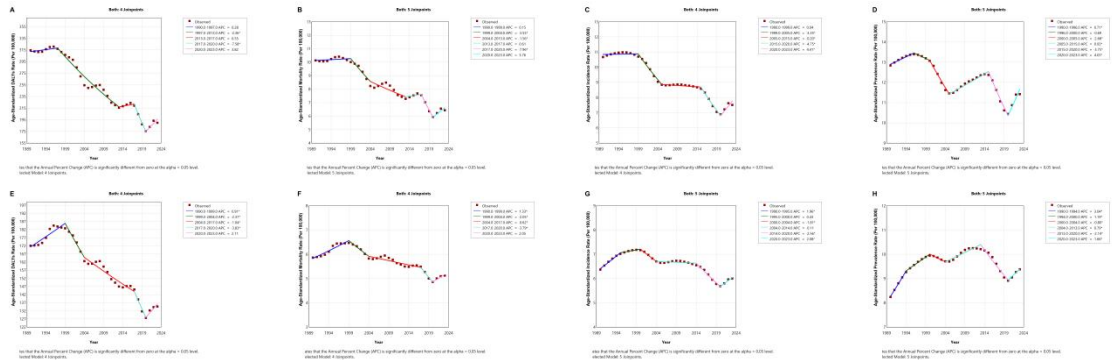


Figure 3: Trends in age-standardized rates of hepatocellular carcinoma in China and G20 countries, 1990–2023.

Gender-Based Differences in Disease Burden

The HCC burden displayed marked gender heterogeneity. From 1990 to 2023, all age-standardized rates were considerably higher in males than females, with gender ratios consistently ranging from 2.5:1 to 3.5:1 (Figure 4A–D). In 2023, the ASIR for males in China was 11.47 per 100,000 (95% UI: 9.79–13.57) compared to 3.58 per 100,000 (95% UI: 2.82–4.34) for females; in G20 countries, the rates were 11.99 per 100,000 (95% UI: 10.62–13.37) for males and 4.30 per 100,000 (95% UI: 3.62–4.98) for females (Table 2). Although age-standaWhile age-standardized rates demonstrated a decline for both sexes, the reduction was more substantial among females. The estimated annual percentage change (EAPC) for the age-standardized incidence rate (ASIR) in Chinese females was -2.28 (95% CI: -2.47 to -2.08), compared to -1.02 (95% CI: -1.17 to -0.88) in males. Comparable trends were noted for the age-standardized mortality rate (ASMR) and the age-standardized disability-adjusted life year rate (ASDR). Examination of the absolute case numbers by sex revealed that males constituted more than 70% of all cases, a proportion that showed minimal variation over the study duration (Figure 5A–B).

Table 2: Sex-specific burden metrics and Estimated Annual Percentage Changes (EAPC) for hepatocellular carcinoma in China and G20 nations, 1990–2023.

Location	Measure	Sex	Number (95%UI)		Estimated Annual Percentage Change (EAPC) (95%CI)	ASR(per 100,000,95%UI)		Estimated Annual Percentage Change (EAPC) (95%CI)
			1990	2023		1990	2023	
China	Incidence	Both	100088 (87198-116766)	165113 (143144-190095)	-1.39 (-1.54-1.23)	10.68 (9.28-12.44)	7.52 (6.58-8.64)	-1.39 (-1.54-1.23)
		Female	30293 (23734-39074)	41449 (32343-51070)	-2.28 (-2.47-2.08)	6.63 (5.18-8.64)	3.58 (2.82-4.34)	-2.28 (-2.47-2.08)

	Male	69795 (58652-83675)	123664 (104594-147266)	-1.02 (-1.17-0.88)	14.64 (12.24-17.60)	11.47 (9.79-13.57)	-1.02 (-1.17-0.88)
	Both	92325 (80178-108028)	143500 (126372-163697)	-1.64 (-1.81-1.47)	10.13 (8.78-11.87)	6.44 (5.72-7.37)	-1.64 (-1.81-1.47)
	Female	28710 (22549-37186)	37967 (29589-45635)	-2.49 (-2.68-2.30)	6.45 (5.06-8.34)	3.20 (2.51-3.83)	-2.49 (-2.68-2.30)
Mortality	Male	63615 (53441-76516)	105533 (90312-124799)	-1.29 (-1.46-1.12)	13.81 (11.51-16.70)	9.73 (8.41-11.45)	-1.29 (-1.46-1.12)
	Both	3113535 (2707540-3642279)	4055010 (3543092-4675076)	-1.85 (-2.01-1.69)	314.36 (273.45-367.36)	189.99 (166.57-219.32)	-1.85 (-2.01-1.69)
	Female	888538 (715367-1119841)	886698 (718827-1065121)	-3.00 (-3.19-2.81)	185.61 (148.61-235.90)	79.02 (64.72-94.53)	-3.00 (-3.19-2.81)
DALYs	Male	2224997 (1879379-2661182)	3168312 (2720503-3807928)	-1.43 (-1.59-1.27)	436.81 (368.51-523.66)	299.65 (257.39-358.88)	-1.43 (-1.59-1.27)
	Both	124811 (107080-147769)	239406 (204266-281545)	-0.58 (-0.72-0.43)	12.84 (11.05-15.17)	11.42 (9.73-13.39)	-0.58 (-0.72-0.43)
	Female	36095 (28183-46263)	56914 (45236-72999)	-1.38 (-1.57-1.19)	7.66 (5.95-9.82)	5.35 (4.26-6.65)	-1.38 (-1.57-1.19)
Prevalence	Male	88716 (74098-107982)	182492 (154227-220166)	-0.25 (-0.38-0.13)	17.79 (14.80-21.64)	17.43 (14.72-20.99)	-0.25 (-0.38-0.13)
	Both	183160 (167979-203454)	379276 (338543-413447)	-0.50 (-0.65-0.34)	6.37 (5.83-7.08)	6.01 (5.35-6.55)	-0.50 (-0.65-0.34)
	Female	54964 (47367-67601)	109474 (91411-124794)	-0.72 (-0.87-0.57)	3.65 (3.15-4.47)	3.21 (2.68-3.65)	-0.72 (-0.87-0.57)
Incidence	Male	128197 (114791-144784)	269802 (240598-302473)	-0.41 (-0.57-0.26)	9.36 (8.41-10.54)	9.05 (8.09-10.13)	-0.41 (-0.57-0.26)
	Both	165925 (151399-186306)	326012 (295151-354995)	-0.68 (-0.83-0.52)	5.86 (5.37-6.58)	5.12 (4.64-5.58)	-0.68 (-0.83-0.52)
	Female	51392 (44436-61896)	98871 (84603-111566)	-0.87 (-1.01-0.73)	3.44 (2.98-4.13)	2.84 (2.43-3.20)	-0.87 (-1.01-0.73)
Mortality	Male	114533 (102535-130352)	227141 (203379-253525)	-0.60 (-0.76-0.45)	8.56 (7.68-9.76)	7.64 (6.87-8.49)	-0.60 (-0.76-0.45)
	Both	5142177 (4680764-5766709)	8339747 (7587576-9160872)	-1.04 (-1.18-0.89)	172.10 (156.71-193.17)	134.69 (122.24-148.05)	-1.04 (-1.18-0.89)
	Female	1449551 (1231715-1757383)	2180859 (1898391-2455416)	-1.38 (-1.50-1.25)	94.44 (80.29-114.40)	66.72 (58.08-75.39)	-1.38 (-1.50-1.25)
DALYs	Male	3692626 (3280146-4234471)	6158888 (5428503-6951608)	-0.91 (-1.07-0.76)	253.33 (226.22-288.20)	205.89 (180.90-232.30)	-0.91 (-1.07-0.76)
	Both	241714 (216963-277813)	579934 (497491-679186)	0.14 (-0.04-0.33)	8.24 (7.41-9.42)	9.38 (8.11-10.98)	0.14 (-0.04-0.33)
	Female	69607 (58540-85348)	160670 (129114-	-0.05 (-0.24-0.15)	4.57 (3.85-5.57)	4.92 (3.95-	-0.05 (-0.24-0.15)

e		197184)			5.95)	
Male	172108 (151959-199678)	419264 (365110-490733)	0.22 (0.04-0.40)	12.17 (10.78-14.04)	14.18 (12.34-16.59)	0.22 (0.04-0.40)

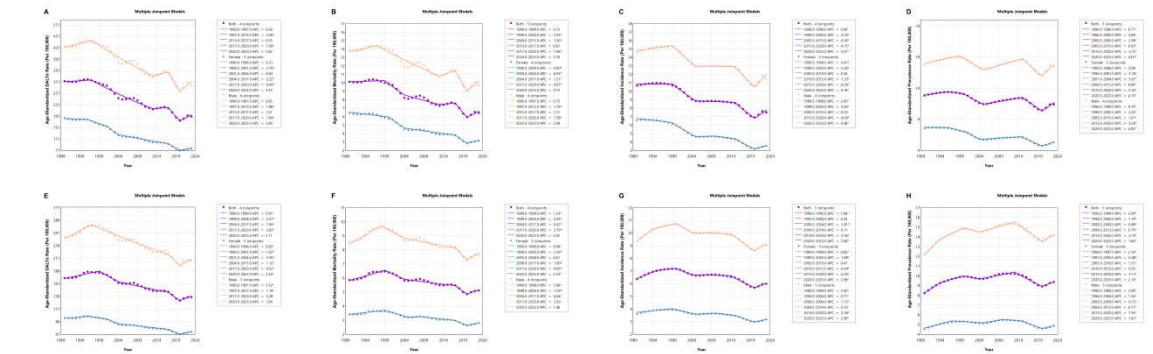


Figure 4: Sex disparities in age-standardized rates of hepatocellular carcinoma in China and G20 countries, 1990–2023.

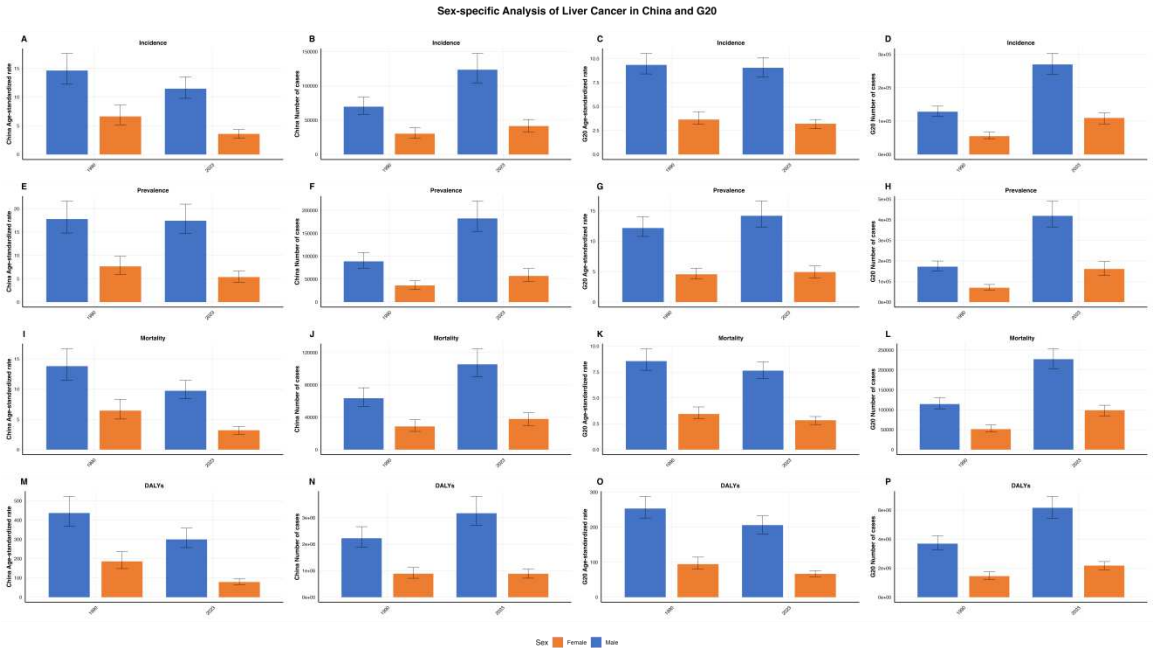


Figure 5: Temporal shifts in sex-specific standardized rates and the sex distribution of the absolute burden for hepatocellular carcinoma in China and G20 nations.

Analysis of Heterogeneity in HCC Burden Among Population Subgroups

Age-Specific Patterns

Age serves as a pivotal factor influencing the burden of HCC. Three-dimensional distribution analyses indicated a temporal shift in the peak incidence toward older age brackets in both

China and G20 countries, signifying an aging pattern in the disease burden (Figure 6A–B). Cross-sectional data from 2023 illustrated that age-specific incidence, mortality, and DALY rates rose exponentially with advancing age, reaching their zenith in the population aged 70 years and above. Rates for all age categories in China surpassed those observed in G20 countries (Figure 7A–C). Sex-age distribution pyramids further clarified that males exhibited higher incidence rates across every age group, with the most marked sex disparity evident among middle-aged and older adults (Figure 8A–B).

A comparative temporal assessment from 1990 to 2023 revealed that age-specific incidence and mortality rates decreased in the majority of age groups within China. The most pronounced declines were identified in individuals under 50 years old. Conversely, for certain age groups over 75 years, a clear downward trend was absent, and a marginal increase was even observed (Figure 9A–B). A similar overall declining pattern was seen across age groups in G20 nations, although improvements were likewise constrained in the older populations (Figure 10A–B).

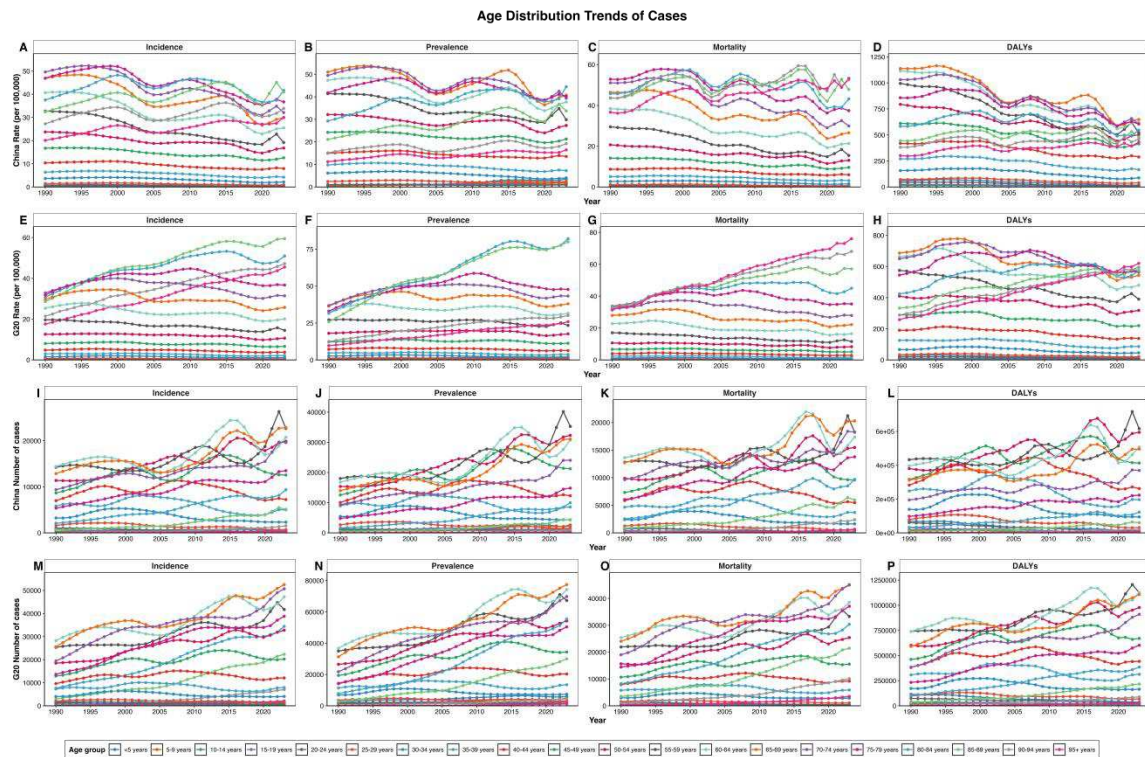


Figure 6: Three-dimensional representation of the age-time-burden relationship for hepatocellular carcinoma in China and G20 countries, 1990–2023.

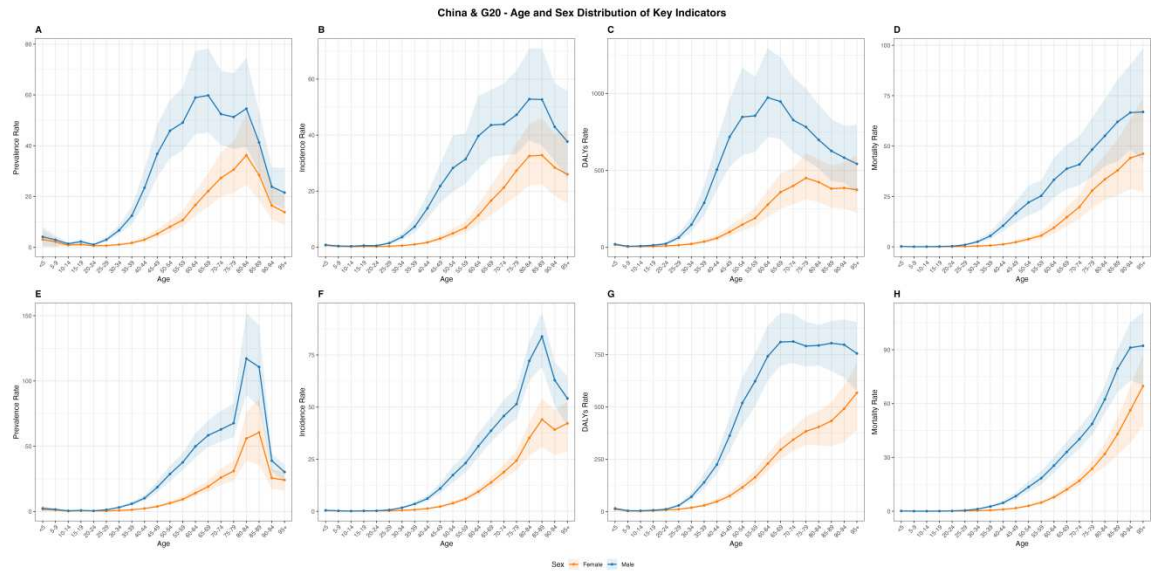


Figure 7: Age-specific incidence, mortality, and DALY rates for hepatocellular carcinoma in China and G20 countries for the year 2023.



Figure 8: Sex-age pyramids depicting the burden of hepatocellular carcinoma in China and G20 nations.

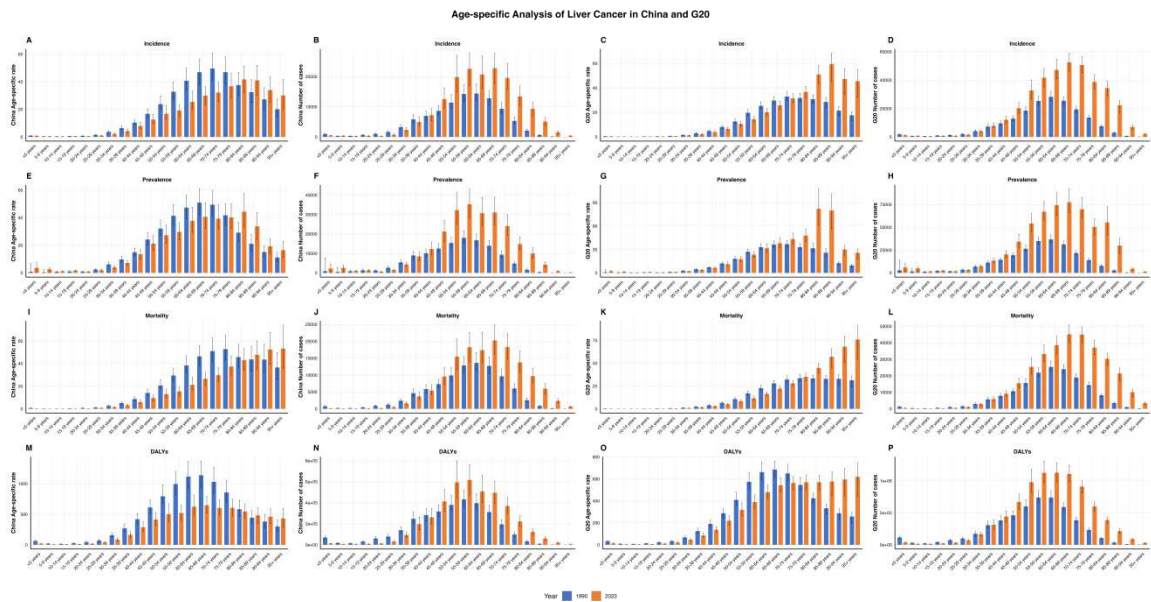


Figure 9: Temporal changes in the incidence and mortality burden of hepatocellular carcinoma across various age groups in China, 1990–2023.

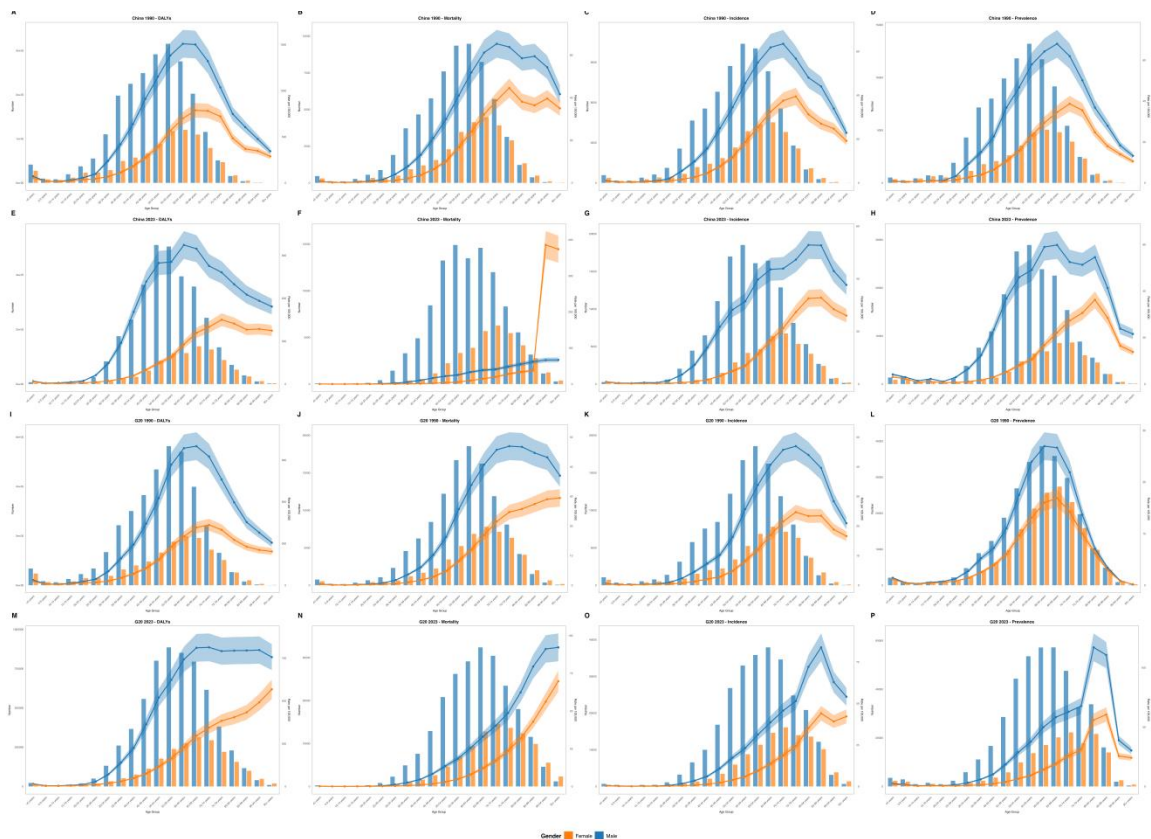


Figure 10: Temporal changes in the burden of hepatocellular carcinoma across different age groups in G20 countries, 1990–2023.

Correlation Between Economic Development and Disease Burden Within G20 Nations

Among G20 countries, a significant inverse correlation was observed between the economic level and the burden of HCC (Figure 11A–D). When categorized according to World Bank income classifications, the group of lower-middle-income countries displayed the highest age-standardized incidence, mortality, DALY, and prevalence rates. In contrast, the high-income country group exhibited the lowest rates, demonstrating a distinct gradient. These findings imply that nations with lower economic development levels shoulder a disproportionately greater HCC burden.

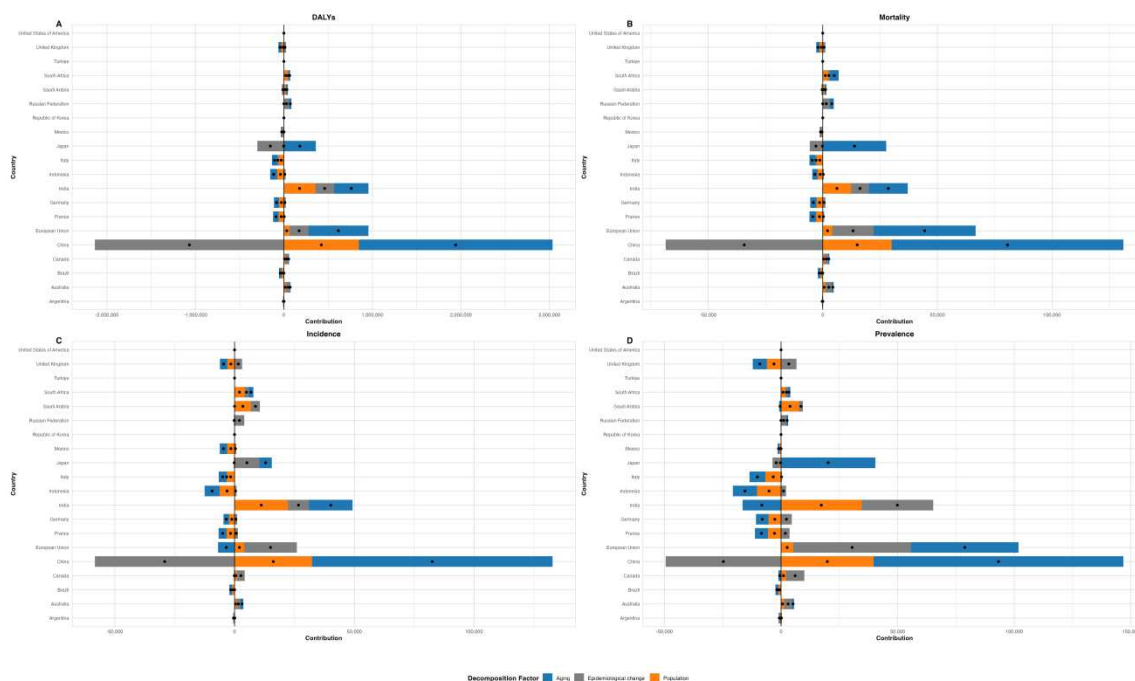


Figure 11: Analysis of hepatocellular carcinoma burden according to economic level among G20 countries.

Attribution Analysis of Risk Factors for HCC DALYs

Summary of Primary Contributing Risk Factors

Analysis of the Population Attributable Fraction (PAF) pinpointed five principal modifiable risk factors contributing to HCC DALYs: Hepatitis B virus (HBV) infection, alcohol use, tobacco smoking, metabolic dysfunction-associated steatotic liver disease (MASLD), and Hepatitis C virus (HCV) infection (Figure 13A–D). The relative ranking of these risk factors in terms of their contribution to mortality, incidence, and prevalence was largely consistent. Sex-stratified analyses revealed distinct risk factor profiles for DALYs (Figure 12A–B). Among males in

China, alcohol consumption, smoking, and hepatitis B virus (HBV) were the three leading contributors to DALYs. In contrast, among Chinese females, the primary contributors were HBV, metabolic dysfunction-associated steatotic liver disease (MASLD), and hepatitis C virus (HCV). The sex-specific attribution patterns observed in G20 nations were largely congruent with those identified in China.

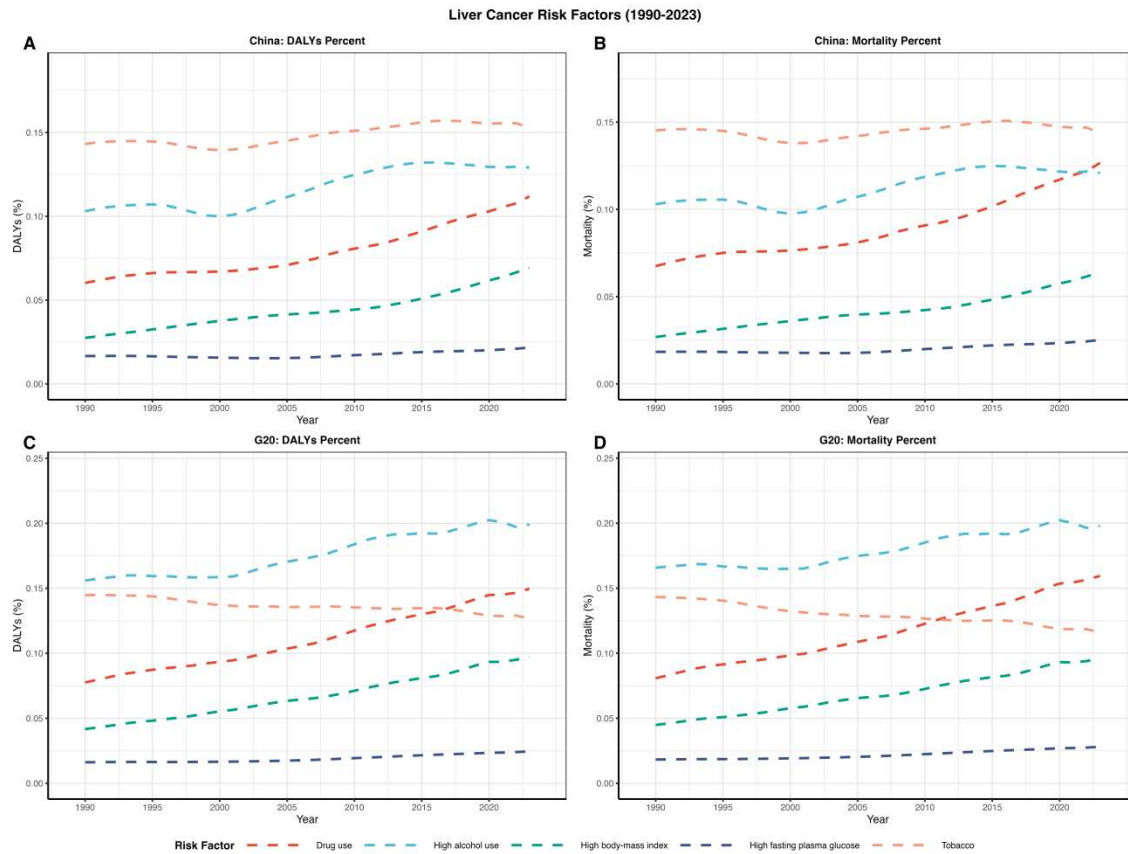


Figure 12: Sex-disaggregated analysis of attributable risk factors for hepatocellular carcinoma DALYs in China and G20 countries, 1990–2023.

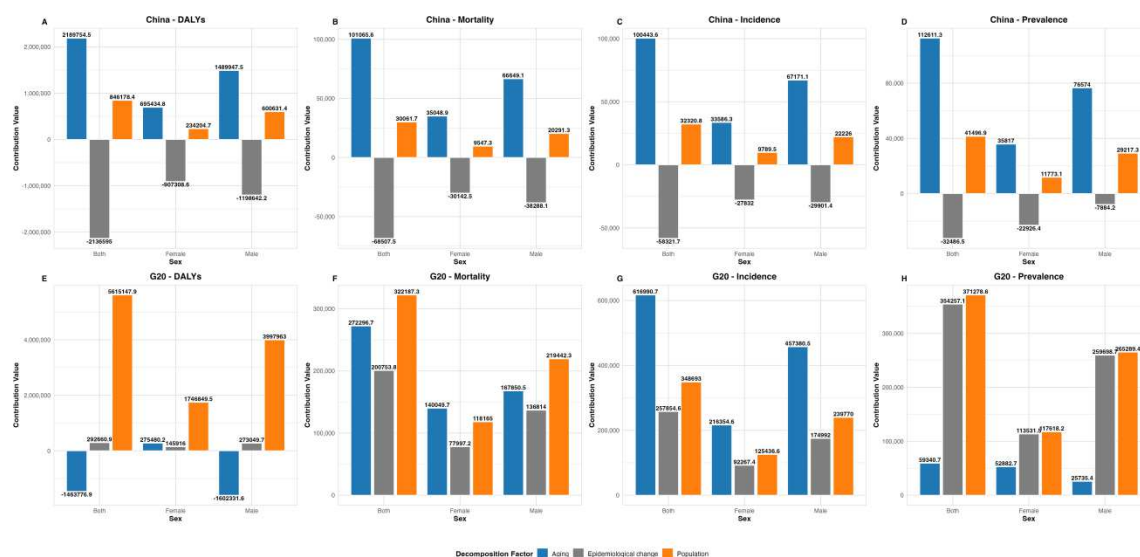


Figure 13: Population Attributable Fractions (PAFs) and risk factor driver decomposition for hepatocellular carcinoma DALYs, mortality, incidence, and prevalence.

Age-Specific Distribution and Temporal Dynamics of Attributable Risk Factors

The proportional contributions of different risk factors to DALYs exhibited considerable variation across age groups (Figure 14A–B). In individuals under 50 years of age, HBV and HCV were responsible for a predominant share of attributable burden. With advancing age, the contributions from alcohol consumption, smoking, and MASLD progressively increased, emerging as significant attribution sources in the population aged 70 years and older. This age-dependent pattern was consistently observed in both China and G20 countries.

From 1990 to 2023, the composition of attributable risk factors underwent significant changes (Figure 15A–B). In China, the attributable fraction for HBV demonstrated a continuous decline, whereas that for MASLD rose markedly. The proportions attributed to alcohol use and tobacco smoking remained relatively stable. The evolution of the attribution composition in G20 countries mirrored the trend in China, collectively indicating a substantial shift in the etiological spectrum of HCC: the relative significance of metabolic risk factors is becoming increasingly pronounced, while the contribution of viral factors is progressively decreasing.

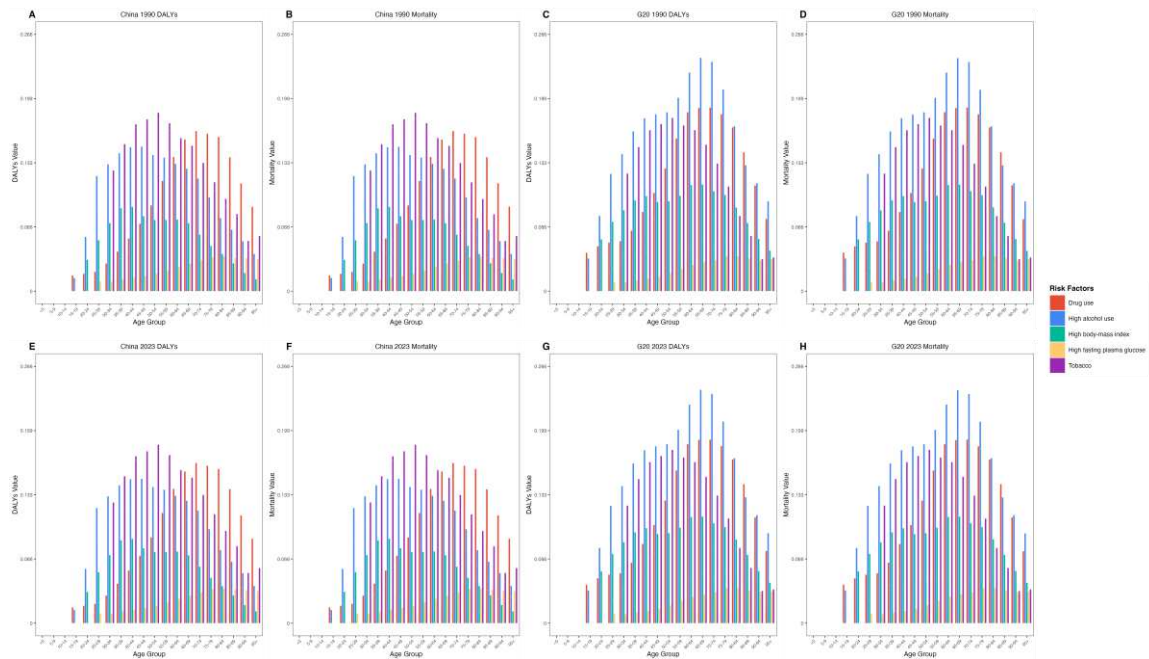


Figure 14: Age-specific distribution of attributable risk factors for hepatocellular carcinoma DALYs in China and G20 countries.

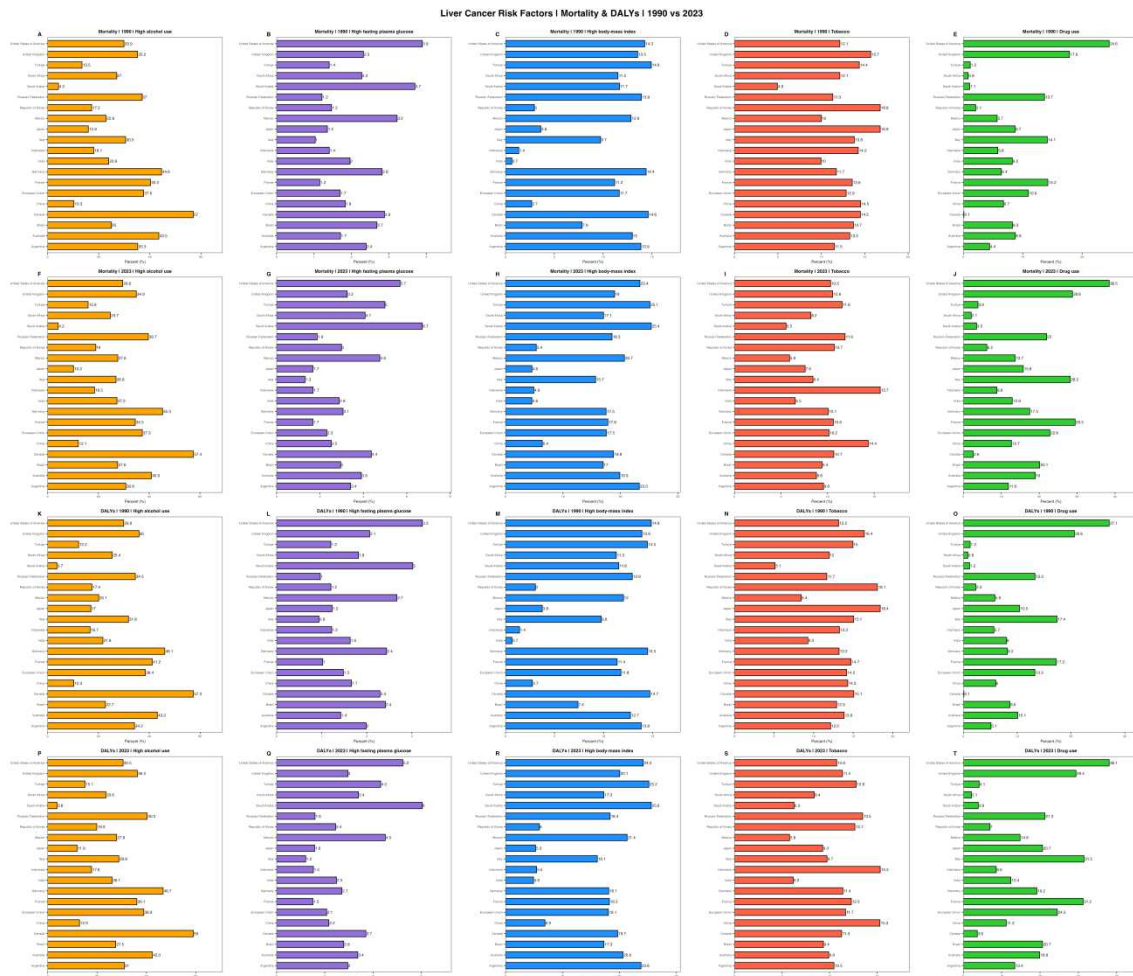


Figure 15: Trends in the composition of major attributable risk factors for hepatocellular carcinoma in China and G20 countries, 1990–2023.

Projected Trends in HCC Burden (2024–2040)

BAPC Model Projections (Age-Period-Cohort Effect Scenario)

Projections derived from the Bayesian Age-Period-Cohort (BAPC) model indicate that from 2024 to 2040, age-standardized mortality and DALY rates for HCC in both China and G20 countries are expected to continue declining. However, absolute rates in China are projected to remain elevated compared to G20 nations (Figure 16A–B). Sex-stratified projections suggest that age-standardized incidence and mortality rates will persist at higher levels in males than in females, with both sexes exhibiting a gradual downward trajectory (Figure 16C–F). Projections for age-standardized prevalence rates (ASPR) also indicate higher rates in males, though trends are relatively flat (Figure 16G–H). Detailed projected values and corresponding 95% confidence intervals for various metrics are provided in Tables 3 and 4.

Table 3: BAPC model projections for age-standardized rates of hepatocellular carcinoma in China (2024–2040) under the Age-Period-Cohort effect scenario.

Location	Year	Age-standardized Mortality rate, per 100,000 people (95%CI)			Age-standardized DALYs rate, per 100,000 people (95%CI)		
		Both	Male	Female	Both	Male	Female
China	2024	7.29(6.72-7.85)	10.49(9.61-11.37)	3.68(3.4-3.97)	211.66(194.73-228.59)	311.43(282.96-339.9)	89.19(82.11-96.28)
	2025	7.31(6.35-8.28)	10.31(8.95-11.66)	3.77(3.24-4.31)	213.84(186.41-241.26)	307.49(267.39-347.59)	90.71(78.77-102.65)
	2026	7.34(5.87-8.81)	10.13(8.18-12.09)	3.86(3.01-4.72)	216.02(174.85-257.2)	303.54(248.21-358.87)	92.25(73.95-110.56)
	2027	7.36(5.3-9.42)	9.95(7.32-12.59)	3.95(2.72-5.19)	218.15(160.7-275.6)	299.49(226.52-372.46)	93.79(67.89-119.7)
	2028	7.38(4.66-10.11)	9.77(6.4-13.14)	4.04(2.37-5.72)	220.14(144.25-296.04)	295.3(202.97-387.62)	95.3(60.7-129.9)
	2029	7.4(3.95-10.85)	9.59(5.45-13.74)	4.13(1.96-6.3)	222.03(125.71-318.35)	290.97(178.01-403.93)	96.79(52.45-141.12)
	2030	7.42(3.19-11.65)	9.41(4.46-14.36)	4.22(1.5-6.95)	223.87(105.27-342.47)	286.6(152-421.2)	98.28(43.2-153.36)
	2031	7.43(2.37-12.5)	9.23(3.45-15.02)	4.32(0.98-7.65)	225.7(83.04-368.37)	282.21(125.17-439.25)	99.8(32.97-166.63)
	2032	7.45(1.49-13.41)	9.05(2.42-15.69)	4.41(0.41-8.42)	227.45(59.04-395.86)	277.74(97.69-457.8)	101.31(21.76-180.87)
	2033	7.46(0.57-14.35)	8.87(1.38-16.37)	4.5(-0.23-9.23)	229.04(33.35-424.73)	273.15(69.7-476.59)	102.79(9.57-196.01)
	2034	7.46(-0.4-15.33)	8.69(0.33-17.05)	4.6(-0.92-10.11)	230.5(6.05-454.95)	268.44(41.37-495.51)	104.24(-3.57-212.06)
	2035	7.47(-1.42-16.36)	8.51(-0.71-17.74)	4.69(-1.66-11.05)	231.9(-22.79-486.58)	263.69(12.86-514.53)	105.7(-17.67-229.07)
	2036	7.47(-2.47-17.42)	8.33(-1.75-18.42)	4.79(-2.47-12.05)	233.26(-53.11-519.62)	258.94(-15.72-533.6)	107.17(-32.73-247.08)
	2037	7.47(-3.56-18.51)	8.16(-2.79-19.1)	4.88(-3.34-13.11)	234.52(-84.86-553.91)	254.14(-44.24-552.52)	108.65(-48.74-266.03)
	2038	7.47(-4.69-19.63)	7.97(-3.81-19.76)	4.98(-4.27-14.23)	235.61(-117.94-589.16)	249.23(-72.6-571.07)	110.08(-65.69-285.84)
	2039	7.46(-5.85-20.77)	7.79(-4.81-20.4)	5.07(-5.26-15.41)	236.53(-152.27-625.33)	244.23(-100.68-589.15)	111.47(-83.56-306.51)
	2040	7.45(-7.04-21.94)	7.61(-5.8-21.02)	5.17(-6.31-16.65)	237.36(-187.81-662.53)	239.21(-128.39-606.82)	112.87(-102.39-328.12)
	2024	6.06(5.8-6.33)	9.03(8.6-9.45)	3.34(3.22-3.47)	160.89(153.95-167.84)	246.16(234.53-257.8)	79.46(75.99-82.92)
	2025	6.17(5.7-6.65)	9.16(8.41-9.91)	3.44(3.19-3.69)	164.58(152.38-176.77)	251.38(231.6-271.16)	81.7(75.69-87.71)
	2026	6.29(5.54-7.04)	9.3(8.13-10.46)	3.54(3.12-3.95)	168.34(149.24-187.43)	256.7(226.15-287.25)	83.99(74.61-93.38)
G20	2027	6.4(5.33-7.48)	9.43(7.78-11.08)	3.64(3.03-4.24)	172.08(144.7-199.46)	261.96(218.5-305.41)	86.31(72.84-99.78)
	2028	6.51(5.06-7.96)	9.56(7.35-11.77)	3.74(2.91-4.57)	175.76(138.82-212.7)	267.08(208.77-325.4)	88.65(70.43-106.87)
	2029	6.62(4.76-8.49)	9.68(6.85-12.52)	3.84(2.75-4.93)	179.46(131.71-227.2)	272.19(197.13-347.24)	91.04(67.4-114.68)
	2030	6.73(4.4-9.06)	9.81(6.29-13.33)	3.94(2.57-5.32)	183.18(123.41-242.96)	277.29(183.67-370.92)	93.48(63.75-123.2)
	2031	6.85(4.01-9.69)	9.94(5.68-14.2)	4.05(2.35-5.75)	186.98(113.95-260.02)	282.49(168.46-396.52)	95.97(59.48-132.46)
	2032	6.96(3.57-10.35)	10.07(5-15.13)	4.16(2.1-6.21)	190.74(103.26-278.21)	287.58(151.41-423.76)	98.48(54.55-142.41)
	2033	7.07(3.09-11.05)	10.19(4.26-16.11)	4.27(1.83-6.71)	194.4(91.33-297.48)	292.49(132.49-452.5)	101.02(48.96-153.08)
	2034	7.18(2.56-11.8)	10.3(3.46-17.14)	4.38(1.51-7.25)	198.07(78.18-317.95)	297.35(111.77-482.92)	103.6(42.69-164.51)

2035	7.29(2-12.59)	10.42(2.61-18.23)	4.49(1.17-7.82)	201.76(63.84-339.67)	302.19(89.29-515.08)	106.23(35.73-176.74)
2036	7.4(1.39-13.42)	10.54(1.7-19.37)	4.61(0.79-8.43)	205.49(48.29-362.69)	307.07(65.07-549.08)	108.91(28.05-189.77)
2037	7.51(0.73-14.29)	10.65(0.74-20.56)	4.73(0.37-9.09)	209.13(31.5-386.77)	311.79(39.06-584.52)	111.6(19.64-203.57)
2038	7.61(0.03-15.19)	10.75(-0.28-21.78)	4.85(-0.08-9.78)	212.62(13.46-411.79)	316.25(11.28-621.21)	114.29(10.46-218.12)
2039	7.71(-0.71-16.13)	10.84(-1.36-23.04)	4.97(-0.57-10.51)	216.06(-5.8-437.92)	320.57(-18.22-659.35)	117(0.51-233.49)
2040	7.81(-1.49-17.11)	10.93(-2.48-24.35)	5.09(-1.11-11.28)	219.52(-26.28-465.32)	324.84(-49.42-699.11)	119.78(-10.23-249.78)

Table 4: BAPC model projections for age-standardized rates of hepatocellular carcinoma in G20 countries (2024–2040) under the Age-Period-Cohort effect scenario.

Location	Year	Age-standardized Prevalence rate, per 100,000 people (95%CI)			Age-standardized Incidence rate, per 100,000 people (95%CI)		
		Both	Male	Female	Both	Male	Female
China	2024	11.35(10.36-12.34)	16.72(15.23-18.21)	5.46(4.97-5.95)	8.32(7.8-8.83)	12.17(11.39-12.96)	4.08(3.83-4.34)
	2025	11.28(10.02-12.54)	16.42(14.65-18.19)	5.51(4.82-6.19)	8.39(7.62-9.15)	12.08(11.04-13.12)	4.19(3.75-4.63)
	2026	11.22(9.61-12.84)	16.14(14-18.28)	5.55(4.61-6.5)	8.46(7.36-9.56)	11.99(10.62-13.37)	4.3(3.62-4.98)
	2027	11.17(9.13-13.21)	15.87(13.28-18.45)	5.61(4.35-6.87)	8.53(7.04-10.02)	11.9(10.13-13.67)	4.41(3.44-5.38)
	2028	11.13(8.6-13.65)	15.61(12.52-18.7)	5.67(4.05-7.28)	8.6(6.66-10.54)	11.81(9.6-14.01)	4.52(3.22-5.83)
	2029	11.09(8.03-14.14)	15.37(11.74-19)	5.73(3.71-7.74)	8.67(6.24-11.1)	11.71(9.03-14.38)	4.63(2.95-6.32)
	2030	11.06(7.43-14.69)	15.14(10.93-19.36)	5.8(3.35-8.25)	8.74(5.77-11.71)	11.61(8.43-14.79)	4.75(2.64-6.86)
	2031	11.05(6.81-15.29)	14.94(10.11-19.77)	5.88(2.94-8.81)	8.81(5.26-12.36)	11.52(7.81-15.23)	4.87(2.29-7.45)
	2032	11.04(6.15-15.94)	14.75(9.29-20.22)	5.96(2.51-9.42)	8.88(4.71-13.06)	11.43(7.17-15.68)	4.99(1.89-8.09)
	2033	11.05(5.47-16.63)	14.59(8.45-20.72)	6.06(2.04-10.08)	8.95(4.12-13.79)	11.33(6.5-16.16)	5.11(1.45-8.78)
	2034	11.07(4.76-17.39)	14.44(7.61-21.26)	6.16(1.53-10.79)	9.02(3.49-14.56)	11.23(5.82-16.64)	5.24(0.96-9.52)
	2035	11.11(4.03-18.2)	14.31(6.77-21.86)	6.27(0.98-11.57)	9.09(2.81-15.37)	11.14(5.12-17.15)	5.36(0.42-10.31)
	2036	11.17(3.26-19.07)	14.21(5.92-22.51)	6.4(0.38-12.42)	9.17(2.11-16.23)	11.04(4.41-17.67)	5.5(-0.17-11.16)
	2037	11.24(2.47-20.02)	14.14(5.06-23.22)	6.54(-0.26-13.34)	9.24(1.36-17.13)	10.95(3.69-18.21)	5.63(-0.81-12.07)
	2038	11.34(1.63-21.04)	14.09(4.18-23.99)	6.7(-0.95-14.34)	9.32(0.58-18.06)	10.86(2.96-18.76)	5.77(-1.5-13.04)
	2039	11.45(0.76-22.14)	14.06(3.3-24.83)	6.87(-1.7-15.43)	9.39(-0.25-19.02)	10.76(2.21-19.31)	5.91(-2.25-14.07)
G20	2040	11.59(-0.15-23.34)	14.06(2.39-25.73)	7.05(-2.52-16.62)	9.46(-1.11-20.04)	10.67(1.46-19.88)	6.05(-3.05-15.16)
	2024	10.26(9.7-10.82)	15.58(14.73-16.43)	5.38(5.07-5.68)	7.03(6.78-7.28)	10.59(10.17-11.01)	3.75(3.63-3.87)
	2025	10.35(9.59-11.11)	15.72(14.57-16.87)	5.44(5.01-5.86)	7.18(6.77-7.59)	10.8(10.13-11.46)	3.86(3.64-4.08)
	2026	10.44(9.41-11.47)	15.87(14.31-17.43)	5.5(4.92-6.08)	7.33(6.71-7.95)	11(10.03-11.98)	3.97(3.62-4.31)
	2027	10.54(9.18-11.89)	16.02(13.97-18.06)	5.56(4.79-6.34)	7.49(6.62-8.36)	11.21(9.86-12.57)	4.07(3.57-4.58)
	2028	10.63(8.9-12.36)	16.16(13.56-18.77)	5.63(4.64-6.62)	7.64(6.48-8.8)	11.42(9.63-13.21)	4.19(3.51-4.87)

2029	10.72(8.58-12.86)	16.31(13.08-19.54)	5.69(4.46-6.93)	7.8(6.31-9.28)	11.63(9.36-13.91)	4.3(3.42-5.18)
2030	10.82(8.23-13.41)	16.46(12.55-20.36)	5.76(4.26-7.26)	7.96(6.11-9.81)	11.84(9.03-14.66)	4.42(3.3-5.53)
2031	10.92(7.84-14)	16.61(11.97-21.25)	5.83(4.04-7.62)	8.12(5.87-10.37)	12.06(8.65-15.47)	4.54(3.17-5.91)
2032	11.02(7.42-14.62)	16.77(11.34-22.19)	5.9(3.8-7.99)	8.28(5.6-10.97)	12.28(8.22-16.34)	4.66(3.01-6.31)
2033	11.12(6.96-15.28)	16.92(10.66-23.18)	5.97(3.54-8.4)	8.45(5.29-11.6)	12.49(7.74-17.25)	4.78(2.83-6.74)
2034	11.22(6.48-15.97)	17.08(9.93-24.23)	6.04(3.25-8.82)	8.61(4.95-12.28)	12.71(7.21-18.21)	4.91(2.62-7.2)
2035	11.33(5.96-16.7)	17.24(9.15-25.33)	6.11(2.95-9.27)	8.78(4.57-12.99)	12.92(6.62-19.23)	5.04(2.39-7.7)
2036	11.44(5.41-17.47)	17.41(8.33-26.49)	6.19(2.63-9.75)	8.95(4.15-13.75)	13.15(5.99-20.3)	5.18(2.13-8.23)
2037	11.55(4.82-18.27)	17.58(7.45-27.71)	6.27(2.29-10.24)	9.12(3.7-14.54)	13.36(5.31-21.42)	5.31(1.84-8.79)
2038	11.66(4.21-19.11)	17.76(6.53-28.98)	6.34(1.92-10.77)	9.29(3.21-15.37)	13.58(4.57-22.59)	5.45(1.52-9.38)
2039	11.78(3.56-20)	17.94(5.56-30.31)	6.42(1.53-11.32)	9.46(2.68-16.24)	13.79(3.77-23.8)	5.59(1.17-10.01)
2040	11.9(2.88-20.92)	18.12(4.54-31.71)	6.51(1.13-11.89)	9.63(2.11-17.14)	14(2.93-25.07)	5.73(0.79-10.68)

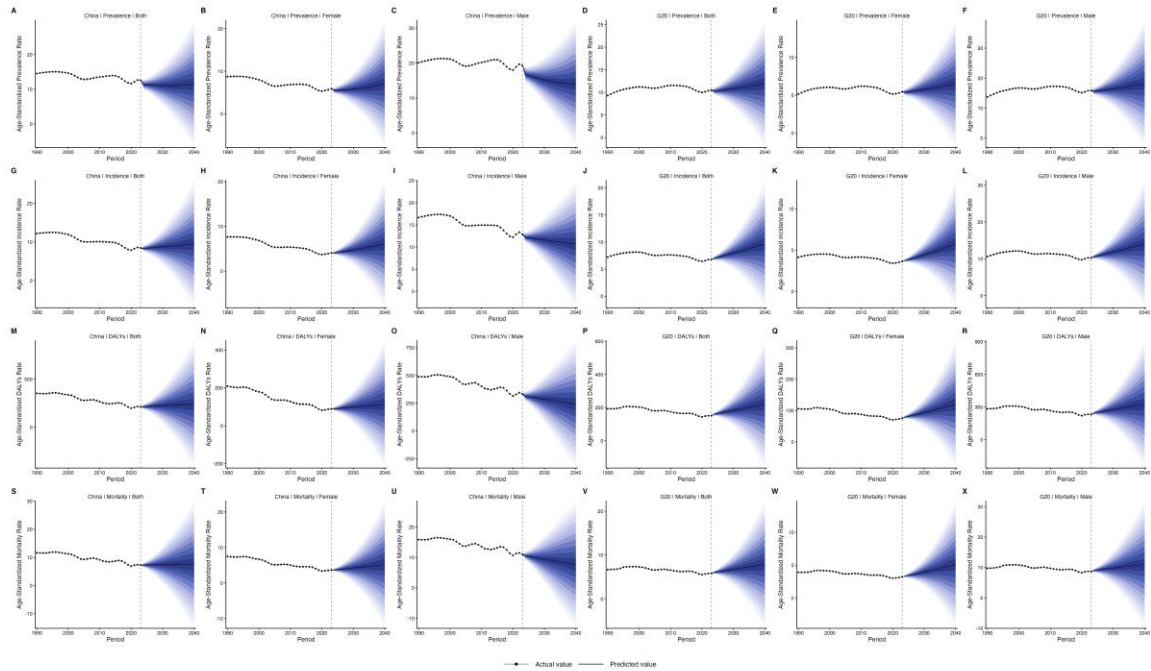


Figure 16: Projections for hepatocellular carcinoma burden in China and G20 countries from 2024 to 2040, derived from the BAPC model (Age-Period-Cohort effect scenario).

ARIMA Model Projections (Baseline Scenario)

Baseline projections generated by the Autoregressive Integrated Moving Average (ARIMA) model showed strong concordance with the results from the BAPC model (Figure 17A–H). In

China, the age-standardized mortality rate (ASMR) is projected to decrease from 5.74 per 100,000 in 2024 to 3.61 per 100,000 in 2040. Similarly, the age-standardized DALY rate (ASDR) is expected to decline from 175.61 per 100,000 to 100.34 per 100,000 (Table 5). G20 countries are also projected to follow a similar downward trend, albeit with a comparatively smaller magnitude of decline (Table 6). Sex-stratified projections further reinforce the established pattern of a higher disease burden in males. The directional agreement of results from these two independent modeling approaches underscores the robustness of the projections. The application of multiple modeling techniques strengthens the reliability of the predictive findings.

Table 5: Forecasted age-standardized incidence rates for hepatocellular carcinoma in China (2024–2040) based on the ARIMA model under the baseline scenario.

Location	Year	Age-standardized Mortality rate, per 100,000 people (95%CI)			Age-standardized DALYs rate, per 100,000 people (95%CI)		
		Both	Male	Female	Both	Male	Female
China	2024	5.74(5.48-6.01)	8.83(8.37-9.29)	3.2(3.03-3.36)	175.61(167.47-183.76)	286.99(270.9-303.08)	77.36(73.53-81.19)
	2025	4.97(4.35-5.59)	8.11(7.09-9.13)	3.07(2.69-3.45)	160.3(141.84-178.76)	282.62(250.76-314.48)	72.3(63.14-81.46)
	2026	4.75(3.74-5.75)	7.95(6.51-9.39)	2.88(2.29-3.46)	151.92(125.16-178.67)	278.26(236.17-320.34)	65.75(51.45-80.05)
	2027	5.08(3.83-6.32)	8.22(6.58-9.85)	2.69(1.96-3.41)	151.38(120.13-182.63)	273.89(223.62-324.16)	59.78(41.73-77.83)
	2028	5.42(4.08-6.76)	8.48(6.77-10.19)	2.54(1.73-3.36)	153.93(120.86-186.99)	269.52(212.22-326.82)	55.51(35.24-75.79)
	2029	5.32(3.94-6.71)	8.43(6.69-10.17)	2.45(1.59-3.32)	153.97(120.04-187.9)	265.15(201.6-328.71)	52.86(31.37-74.34)
	2030	4.82(3.38-6.26)	8.07(6.27-9.87)	2.39(1.49-3.29)	149.19(114.3-184.09)	260.79(191.54-330.03)	50.91(28.64-73.18)
	2031	4.33(2.78-5.88)	7.65(5.73-9.56)	2.32(1.39-3.26)	141.25(104.63-177.86)	256.42(181.91-330.93)	48.71(25.69-71.73)
	2032	4.2(2.5-5.9)	7.38(5.32-9.43)	2.24(1.26-3.22)	133.52(94.43-172.6)	252.05(172.63-331.47)	45.71(21.75-69.67)
	2033	4.37(2.55-6.18)	7.31(5.13-9.49)	2.13(1.1-3.16)	128.31(86.71-169.91)	247.68(163.64-331.73)	41.95(16.8-67.1)
	2034	4.5(2.62-6.38)	7.34(5.07-9.6)	2.01(0.93-3.09)	125.56(81.99-169.13)	243.32(154.89-331.74)	37.85(11.39-64.32)
	2035	4.34(2.42-6.27)	7.29(4.97-9.62)	1.89(0.76-3.02)	123.51(78.52-168.51)	238.95(146.35-331.55)	33.87(6.14-61.59)
	2036	3.97(1.99-5.95)	7.12(4.73-9.5)	1.78(0.61-2.96)	120.42(74.25-166.58)	234.58(137.98-331.18)	30.25(4.43-59.08)
	2037	3.65(1.58-5.71)	6.87(4.41-9.32)	1.68(0.47-2.9)	115.72(68.33-163.11)	230.22(129.78-330.65)	27(-2.77-56.77)
	2038	3.55(1.39-5.71)	6.64(4.1-9.17)	1.59(0.34-2.84)	110.14(61.32-158.95)	225.85(121.72-329.98)	23.91(-6.7-54.52)
	2039	3.61(1.37-5.85)	6.48(3.86-9.1)	1.49(0.2-2.78)	104.79(54.4-155.18)	221.48(113.78-329.18)	20.77(-10.66-52.19)
	2040	3.61(1.32-5.91)	6.38(3.68-9.08)	1.39(0.07-2.71)	100.34(48.41-152.27)	217.11(105.96-328.27)	17.45(-14.81-49.71)
G20	2024	5.11(4.96-5.27)	7.52(7.29-7.76)	2.9(2.82-2.99)	134.27(130.07-138.47)	202.14(195.53-208.74)	67.49(65.61-69.37)
	2025	5.09(4.76-5.42)	7.52(7-8.04)	2.93(2.74-3.12)	133.71(124.46-142.96)	202.5(187.74-217.25)	67.71(63.44-71.98)
	2026	5.08(4.58-5.57)	7.52(6.73-8.31)	2.94(2.65-3.22)	133.33(119.37-147.3)	202.5(179.88-225.11)	66.92(60.32-73.52)
	2027	5.07(4.46-5.68)	7.52(6.53-8.51)	2.93(2.56-3.3)	133.2(115.42-150.97)	202.5(174.13-230.87)	66.13(57.83-74.43)
	2028	5.07(4.37-5.78)	7.52(6.36-8.68)	2.92(2.49-3.36)	133.21(112.51-153.92)	202.5(169.35-235.64)	65.34(55.64-75.05)
	2029	5.07(4.3-5.85)	7.52(6.22-8.82)	2.92(2.43-3.4)	133.29(110.27-156.3)	202.5(165.19-239.81)	64.56(53.62-75.49)
	2030	5.08(4.24-5.91)	7.52(6.09-8.95)	2.92(2.38-3.45)	133.35(108.39-158.3)	202.5(161.44-243.55)	63.77(51.73-75.8)
	2031	5.08(4.19-5.97)	7.52(5.97-9.07)	2.91(2.34-3.49)	133.38(106.68-160.08)	202.5(158.01-246.98)	62.98(49.93-76.03)
	2032	5.08(4.13-6.02)	7.52(5.86-9.18)	2.92(2.3-3.53)	133.38(105.05-161.72)	202.5(154.82-250.17)	62.19(48.21-76.17)
	2033	5.08(4.08-6.07)	7.52(5.75-9.28)	2.92(2.27-3.56)	133.38(103.47-163.28)	202.5(151.84-253.15)	61.4(46.54-76.26)
	2034	5.08(4.03-6.12)	7.52(5.66-9.38)	2.92(2.24-3.6)	133.37(101.95-164.79)	202.5(149.02-255.97)	60.61(44.92-76.31)
	2035	5.08(3.98-6.17)	7.52(5.56-9.47)	2.92(2.2-3.63)	133.36(100.49-166.23)	202.5(146.34-258.65)	59.83(43.35-76.3)
	2036	5.08(3.94-6.22)	7.52(5.47-9.56)	2.92(2.17-3.66)	133.36(99.09-167.62)	202.5(143.78-261.21)	59.04(41.81-76.27)

2037	5.08(3.89-6.26)	7.52(5.39-9.65)	2.92(2.14-3.69)	133.36(97.76-168.96)	202.5(141.33-263.66)	58.25(40.3-76.2)
2038	5.08(3.85-6.3)	7.52(5.31-9.73)	2.92(2.11-3.72)	133.36(96.47-170.25)	202.5(138.98-266.01)	57.46(38.82-76.1)
2039	5.08(3.81-6.34)	7.52(5.23-9.81)	2.92(2.09-3.75)	133.36(95.23-171.49)	202.5(136.71-268.28)	56.67(37.36-75.98)
2040	5.08(3.77-6.38)	7.52(5.15-9.88)	2.92(2.06-3.77)	133.36(94.03-172.69)	202.5(134.52-270.48)	55.88(35.93-75.84)

Table 6: Forecasted age-standardized incidence rates for hepatocellular carcinoma in G20 nations (2024–2040) based on the ARIMA model under the baseline scenario.

Location	Year	Age-standardized Prevalence rate, per 100,000 people (95%CI)			Age-standardized Incidence rate, per 100,000 people (95%CI)		
		Both	Male	Female	Both	Male	Female
China	2024	11.06(10.86-11.26)	16.55(16.21-16.88)	5.57(5.47-5.66)	7.21(7.03-7.39)	10.44(10.15-10.73)	3.63(3.55-3.71)
	2025	10.65(10.05-11.25)	15.89(14.91-16.87)	5.69(5.43-5.95)	7.07(6.55-7.58)	9.68(8.83-10.52)	3.57(3.36-3.78)
	2026	10.41(9.38-11.45)	15.82(14.23-17.4)	5.69(5.22-6.16)	6.97(6.16-7.77)	9.58(8.23-10.93)	3.41(3.03-3.79)
	2027	10.4(9.01-11.79)	16.13(14.14-18.11)	5.57(4.87-6.27)	6.87(5.85-7.89)	9.89(8.24-11.55)	3.19(2.63-3.74)
	2028	10.52(8.88-12.16)	16.45(14.24-18.66)	5.36(4.45-6.27)	6.77(5.58-7.97)	10.13(8.34-11.92)	2.95(2.24-3.65)
	2029	10.66(8.86-12.46)	16.55(14.21-18.9)	5.12(4.04-6.19)	6.68(5.33-8.02)	10.04(8.17-11.91)	2.73(1.91-3.55)
	2030	10.75(8.83-12.66)	16.46(13.99-18.93)	4.88(3.68-6.09)	6.58(5.1-8.06)	9.71(7.76-11.67)	2.57(1.68-3.47)
	2031	10.76(8.75-12.76)	16.32(13.71-18.93)	4.71(3.43-5.99)	6.48(4.87-8.09)	9.39(7.31-11.46)	2.48(1.54-3.42)
	2032	10.72(8.61-12.82)	16.25(13.47-19.02)	4.6(3.27-5.93)	6.38(4.66-8.1)	9.22(7-11.43)	2.44(1.47-3.4)
	2033	10.67(8.46-12.87)	16.26(13.33-19.2)	4.57(3.21-5.93)	6.28(4.45-8.11)	9.18(6.83-11.53)	2.42(1.44-3.4)
	2034	10.64(8.32-12.95)	16.32(13.24-19.4)	4.58(3.2-5.96)	6.19(4.25-8.12)	9.16(6.7-11.62)	2.41(1.41-3.4)
	2035	10.63(8.2-13.06)	16.36(13.15-19.57)	4.62(3.22-6.02)	6.09(4.06-8.12)	9.07(6.52-11.62)	2.37(1.36-3.39)
	2036	10.64(8.11-13.17)	16.36(13.04-19.69)	4.65(3.22-6.08)	5.99(3.87-8.11)	8.91(6.27-11.54)	2.3(1.26-3.34)
	2037	10.66(8.04-13.29)	16.34(12.9-19.79)	4.65(3.18-6.11)	5.89(3.68-8.11)	8.73(6-11.45)	2.19(1.11-3.26)
	2038	10.67(7.96-13.39)	16.32(12.76-19.88)	4.61(3.09-6.12)	5.8(3.5-8.09)	8.58(5.76-11.39)	2.05(0.93-3.17)
	2039	10.67(7.88-13.47)	16.32(12.64-19.99)	4.52(2.95-6.09)	5.7(3.32-8.08)	8.47(5.56-11.38)	1.9(0.73-3.07)
	2040	10.67(7.79-13.55)	16.32(12.54-20.11)	4.41(2.78-6.04)	5.6(3.14-8.06)	8.37(5.37-11.37)	1.76(0.54-2.97)
G20	2024	9.33(9.24-9.41)	14.01(13.85-14.17)	5.11(5.07-5.15)	6(5.93-6.07)	8.76(8.64-8.87)	3.28(3.26-3.31)
	2025	9.15(8.89-9.42)	13.8(13.26-14.33)	5.3(5.18-5.41)	6(5.77-6.23)	8.4(8.02-8.78)	3.32(3.25-3.4)
	2026	8.97(8.47-9.48)	13.58(12.51-14.66)	5.45(5.24-5.67)	5.99(5.56-6.42)	8.15(7.45-8.85)	3.33(3.17-3.48)
	2027	8.88(8.12-9.64)	13.37(11.64-15.1)	5.55(5.22-5.89)	5.99(5.32-6.65)	8.04(7.03-9.06)	3.31(3.05-3.57)
	2028	8.89(7.9-9.87)	13.15(10.67-15.64)	5.59(5.15-6.04)	5.98(5.05-6.91)	8.02(6.74-9.31)	3.28(2.92-3.64)
	2029	8.96(7.81-10.1)	12.94(9.62-16.26)	5.57(5.01-6.12)	5.98(4.76-7.19)	8(6.47-9.53)	3.25(2.8-3.71)
	2030	9.03(7.76-10.3)	12.73(8.5-16.96)	5.48(4.85-6.12)	5.97(4.43-7.51)	7.91(6.16-9.67)	3.23(2.7-3.76)
	2031	9.07(7.71-10.43)	12.51(7.3-17.73)	5.36(4.67-6.05)	5.97(4.09-7.84)	7.77(5.77-9.77)	3.22(2.63-3.81)

2032	9.07(7.64-10.5)	12.3(6.04-18.56)	5.21(4.49-5.94)	5.96(3.72-8.2)	7.61(5.33-9.88)	3.22(2.58-3.85)
2033	9.06(7.56-10.55)	12.09(4.72-19.46)	5.07(4.33-5.81)	5.96(3.33-8.58)	7.46(4.88-10.03)	3.22(2.55-3.9)
2034	9.05(7.5-10.59)	11.87(3.33-20.41)	4.95(4.21-5.69)	5.95(2.92-8.98)	7.34(4.45-10.22)	3.23(2.53-3.93)
2035	9.06(7.48-10.65)	11.66(1.9-21.42)	4.87(4.13-5.6)	5.95(2.49-9.4)	7.23(4.02-10.45)	3.24(2.52-3.97)
2036	9.1(7.48-10.71)	11.45(0.4-22.49)	4.83(4.09-5.57)	5.94(2.05-9.83)	7.14(3.59-10.68)	3.25(2.5-4)
2037	9.14(7.51-10.78)	11.23(-1.14-23.6)	4.83(4.09-5.58)	5.94(1.59-10.28)	7.03(3.15-10.9)	3.25(2.47-4.03)
2038	9.18(7.54-10.82)	11.02(-2.73-24.77)	4.88(4.13-5.64)	5.93(1.11-10.75)	6.91(2.69-11.13)	3.25(2.45-4.06)
2039	9.21(7.56-10.85)	10.8(-4.37-25.98)	4.96(4.2-5.72)	5.93(0.61-11.24)	6.78(2.21-11.35)	3.25(2.42-4.09)
2040	9.22(7.58-10.87)	10.59(-6.06-27.24)	5.05(4.29-5.81)	5.92(0.1-11.74)	6.65(1.71-11.6)	3.25(2.39-4.11)



Figure 17: Projections for hepatocellular carcinoma burden in China and G20 countries from 2024 to 2040, derived from the ARIMA model (Baseline scenario).

Projections Under an Optimized Intervention Scenario

When modeling an optimized intervention scenario characterized by the intensified control of five primary modifiable risk factors—hepatitis B virus (HBV), hepatitis C virus (HCV), alcohol use, tobacco smoking, and metabolic dysfunction-associated steatotic liver disease (MASLD)—the rate of decrease for all age-standardized metrics was markedly accelerated relative to the baseline scenario (Figure 18A–H). Using the age-standardized mortality rate (ASMR) as an illustration, the extent of reduction in China under this enhanced intervention framework was greater than that projected under the baseline conditions. A comparable pattern of accelerated decline was observed across G20 countries (Tables 7–8). Comparative evaluations of age-standardized incidence (ASIR), death (ASDR), and

prevalence (ASPR) rates uniformly suggest that the adoption of comprehensive, reinforced intervention measures has the potential to achieve substantial decreases in the disease burden over the coming twenty years.

Table 7: Projected age-standardized rates for hepatocellular carcinoma in China under the optimized intervention scenario (2024–2040).

Location	Year	Age-standardized Mortality rate, per 100,000 people (95%CI)			Age-standardized DALYs rate, per 100,000 people (95%CI)		
		Both	Male	Female	Both	Male	Female
China	2024	6.34(5.91-6.78)	9.43(8.71-10.16)	3.31(3.04-3.57)	186.55(173.85-199.25)	290.56(270.05-311.06)	81.01(74.92-87.1)
	2025	6.27(5.37-7.16)	9.19(7.69-10.68)	3.41(2.83-4.00)	183.09(154.72-211.46)	281.35(235.65-327.04)	83.00(69.39-96.62)
	2026	6.20(4.82-7.59)	8.99(6.66-11.32)	3.52(2.54-4.49)	179.62(132.16-227.09)	272.14(195.72-348.56)	85.00(62.22-107.78)
	2027	6.15(4.26-8.04)	8.82(5.64-12.01)	3.63(2.20-5.05)	176.16(106.68-245.64)	262.93(151.08-374.78)	86.99(53.65-120.34)
	2028	6.12(3.73-8.50)	8.69(4.65-12.74)	3.73(1.80-5.66)	172.70(78.63-266.77)	253.72(102.29-405.15)	88.99(43.83-134.14)
	2029	6.08(3.21-8.96)	8.59(3.70-13.47)	3.84(1.35-6.32)	169.24(48.24-290.24)	244.51(49.73-439.29)	90.98(32.90-149.06)
	2030	6.06(2.71-9.41)	8.50(2.78-14.21)	3.95(0.86-7.03)	165.78(15.69-315.86)	235.30(-6.29-476.89)	92.97(20.94-165.01)
	2031	6.04(2.24-9.84)	8.43(1.91-14.94)	4.05(0.33-7.77)	162.32(-18.85-343.49)	226.09(-65.53-517.72)	94.97(8.01-181.93)
	2032	6.02(1.78-10.27)	8.37(1.09-15.65)	4.16(-0.24-8.56)	158.86(-55.28-373.00)	216.88(-127.81-561.58)	96.96(-5.82-199.74)
	2033	6.01(1.35-10.67)	8.32(0.29-16.35)	4.27(-0.85-9.38)	155.39(-93.49-404.28)	207.67(-192.95-608.30)	98.96(-20.50-218.42)
	2034	6.00(0.93-11.07)	8.28(-0.46-17.03)	4.37(-1.49-10.23)	151.93(-133.40-437.26)	198.47(-260.82-657.75)	100.95(-36.00-237.90)
	2035	5.99(0.54-11.45)	8.25(-1.18-17.69)	4.48(-2.16-11.12)	148.47(-174.92-471.86)	189.26(-331.29-709.81)	102.94(-52.28-258.16)
	2036	5.99(0.16-11.81)	8.23(-1.87-18.33)	4.58(-2.87-12.04)	145.01(-218.00-508.02)	180.05(-404.27-764.36)	104.94(-69.30-279.17)
	2037	5.98(-0.21-12.17)	8.21(-2.53-18.94)	4.69(-3.61-12.99)	141.55(-262.57-545.66)	170.84(-479.65-821.32)	106.93(-87.03-300.90)
	2038	5.98(-0.55-12.51)	8.19(-3.16-19.54)	4.80(-4.38-13.97)	138.09(-308.58-584.75)	161.63(-557.35-880.61)	108.92(-105.46-323.31)
	2039	5.97(-0.89-12.83)	8.18(-3.77-20.12)	4.90(-5.17-14.98)	134.63(-355.99-625.24)	152.42(-637.29-942.14)	110.92(-124.56-346.40)
	2040	5.97(-1.21-13.15)	8.17(-4.35-20.69)	5.01(-6.00-16.02)	131.17(-404.74-667.07)	143.21(-719.42-1005.84)	112.91(-144.31-370.14)
G20	2024	5.15(4.96-5.34)	7.65(7.34-7.96)	2.91(2.82-3.01)	135.03(129.63-140.44)	204.90(196.35-213.45)	68.56(66.20-70.92)
	2025	5.18(4.76-5.60)	7.66(7.14-8.18)	2.96(2.77-3.16)	135.33(123.87-146.79)	204.11(186.45-221.77)	70.41(65.13-75.69)
	2026	5.21(4.50-5.91)	7.67(6.94-8.39)	3.01(2.70-3.31)	135.59(117.36-153.82)	203.46(176.01-230.92)	72.25(63.42-81.08)
	2027	5.23(4.21-6.26)	7.67(6.74-8.60)	3.04(2.63-3.45)	135.81(110.39-161.24)	202.95(165.47-240.42)	74.09(61.16-87.02)
	2028	5.26(3.87-6.65)	7.68(6.55-8.80)	3.07(2.55-3.59)	136.01(103.16-168.86)	202.53(155.06-250.00)	75.94(58.43-93.44)
	2029	5.29(3.50-7.08)	7.68(6.37-8.99)	3.09(2.46-3.72)	136.18(95.80-176.55)	202.19(144.91-259.48)	77.78(55.26-100.30)
	2030	5.31(3.09-7.54)	7.68(6.19-9.17)	3.11(2.38-3.84)	136.32(88.41-184.24)	201.92(135.09-268.75)	79.62(51.69-107.56)
	2031	5.34(2.66-8.02)	7.68(6.02-9.35)	3.12(2.29-3.95)	136.45(81.05-191.85)	201.70(125.63-277.77)	81.47(47.75-115.19)

2032	5.37(2.20-8.54)	7.69(5.86-9.51)	3.13(2.21-4.06)	136.56(73.77-199.36)	201.52(116.55-286.49)	83.31(43.45-123.17)
2033	5.40(1.71-9.08)	7.69(5.70-9.67)	3.14(2.13-4.16)	136.66(66.59-206.73)	201.38(107.84-294.91)	85.15(38.83-131.48)
2034	5.42(1.20-9.65)	7.69(5.55-9.83)	3.15(2.04-4.26)	136.74(59.54-213.94)	201.26(99.49-303.03)	87.00(33.89-140.10)
2035	5.45(0.67-10.24)	7.69(5.40-9.97)	3.16(1.97-4.35)	136.81(52.64-220.99)	201.17(91.48-310.86)	88.84(28.65-149.03)
2036	5.48(0.11-10.85)	7.69(5.26-10.12)	3.16(1.89-4.43)	136.88(45.88-227.87)	201.09(83.80-318.39)	90.68(23.12-158.25)
2037	5.51(-0.47-11.49)	7.69(5.13-10.25)	3.16(1.81-4.52)	136.93(39.29-234.58)	201.03(76.41-325.65)	92.52(17.31-167.74)
2038	5.53(-1.08-12.14)	7.69(5.00-10.38)	3.17(1.74-4.59)	136.98(32.85-241.11)	200.99(69.31-332.66)	94.37(11.23-177.50)
2039	5.56(-1.70-12.82)	7.69(4.87-10.51)	3.17(1.67-4.67)	137.02(26.57-247.47)	200.95(62.47-339.42)	96.21(4.90-187.53)
2040	5.59(-2.34-13.52)	7.69(4.75-10.63)	3.17(1.60-4.74)	137.06(20.45-253.67)	200.91(55.88-345.95)	98.05(-1.69-197.80)

Table 8: Projected age-standardized rates for hepatocellular carcinoma in G20 countries under the optimized intervention scenario (2024–2040).

Location	Year	Age-standardized Prevalence rate, per 100,000 people (95%CI)			Age-standardized Incidence rate, per 100,000 people (95%CI)		
		Both	Male	Female	Both	Male	Female
China	2024	11.44(11.10-11.78)	17.21(16.60-17.81)	5.59(5.42-5.77)	7.40(7.09-7.72)	11.18(10.68-11.68)	3.71(3.57-3.85)
	2025	11.45(10.75-12.15)	16.98(15.62-18.34)	5.83(5.45-6.22)	7.29(6.59-7.99)	10.94(9.91-11.97)	3.83(3.52-4.14)
	2026	11.46(10.38-12.54)	16.75(14.47-19.03)	6.07(5.43-6.72)	7.18(6.00-8.35)	10.75(9.15-12.35)	3.96(3.43-4.48)
	2027	11.47(10.00-12.94)	16.52(13.19-19.86)	6.32(5.37-7.26)	7.06(5.35-8.78)	10.60(8.41-12.78)	4.08(3.31-4.85)
	2028	11.48(9.62-13.34)	16.30(11.78-20.81)	6.56(5.27-7.84)	6.95(4.63-9.27)	10.48(7.72-13.24)	4.20(3.17-5.24)
	2029	11.49(9.25-13.72)	16.07(10.26-21.88)	6.80(5.15-8.45)	6.83(3.85-9.82)	10.38(7.06-13.70)	4.33(2.99-5.66)
	2030	11.49(8.88-14.10)	15.84(8.64-23.05)	7.04(4.99-9.09)	6.72(3.02-10.43)	10.30(6.43-14.17)	4.45(2.80-6.11)
	2031	11.49(8.53-14.46)	15.61(6.92-24.31)	7.28(4.81-9.75)	6.61(2.13-11.08)	10.24(5.84-14.64)	4.57(2.58-6.57)
	2032	11.50(8.19-14.80)	15.39(5.11-25.66)	7.52(4.60-10.44)	6.49(1.21-11.78)	10.19(5.28-15.09)	4.70(2.34-7.06)
	2033	11.50(7.87-15.13)	15.16(3.21-27.11)	7.76(4.36-11.16)	6.38(0.24-12.52)	10.15(4.76-15.54)	4.82(2.08-7.57)
	2034	11.50(7.56-15.45)	14.93(1.24-28.63)	8.00(4.11-11.90)	6.27(-0.78-13.31)	10.12(4.26-15.98)	4.95(1.80-8.09)
	2035	11.50(7.25-15.75)	14.70(-0.82-30.23)	8.24(3.83-12.66)	6.15(-1.83-14.14)	10.09(3.78-16.40)	5.07(1.50-8.64)
	2036	11.50(6.97-16.04)	14.48(-2.95-31.90)	8.49(3.53-13.44)	6.04(-2.92-15.00)	10.07(3.33-16.81)	5.19(1.19-9.20)
	2037	11.51(6.69-16.32)	14.25(-5.15-33.65)	8.73(3.21-14.24)	5.92(-4.05-15.90)	10.05(2.90-17.21)	5.32(0.86-9.77)
	2038	11.51(6.42-16.59)	14.02(-7.42-35.46)	8.97(2.87-15.07)	5.81(-5.21-16.84)	10.04(2.49-17.60)	5.44(0.52-10.37)
	2039	11.51(6.16-16.85)	13.80(-9.75-37.34)	9.21(2.51-15.91)	5.70(-6.41-17.81)	10.03(2.09-17.97)	5.57(0.16-10.97)
	2040	11.51(5.91-17.10)	13.57(-12.15-39.29)	9.45(2.13-16.77)	5.58(-7.65-18.81)	10.02(1.71-18.33)	5.69(-0.22-11.60)
G20	2024	9.49(9.34-9.63)	14.25(14.01-14.48)	5.08(5.00-5.16)	6.04(5.93-6.16)	9.02(8.83-9.21)	3.31(3.25-3.37)
	2025	9.58(9.27-9.88)	14.32(13.79-14.84)	5.23(5.05-5.42)	6.08(5.83-6.33)	9.00(8.57-9.42)	3.40(3.27-3.53)

2026	9.66(9.16-10.15)	14.39(13.51-15.27)	5.39(5.08-5.69)	6.12(5.70-6.54)	8.97(8.26-9.67)	3.49(3.28-3.71)
2027	9.72(9.04-10.41)	14.46(13.17-15.74)	5.54(5.09-5.99)	6.16(5.55-6.78)	8.94(7.91-9.98)	3.59(3.28-3.90)
2028	9.79(8.89-10.68)	14.53(12.78-16.27)	5.70(5.09-6.30)	6.20(5.37-7.03)	8.92(7.52-10.32)	3.68(3.26-4.10)
2029	9.84(8.73-10.95)	14.60(12.35-16.84)	5.85(5.07-6.63)	6.24(5.17-7.31)	8.89(7.09-10.69)	3.77(3.24-4.31)
2030	9.89(8.57-11.21)	14.67(11.89-17.45)	6.00(5.04-6.97)	6.28(4.95-7.61)	8.87(6.64-11.10)	3.87(3.20-4.53)
2031	9.93(8.39-11.46)	14.74(11.38-18.09)	6.16(4.99-7.33)	6.32(4.71-7.92)	8.84(6.15-11.53)	3.96(3.16-4.76)
2032	9.96(8.22-11.71)	14.81(10.84-18.77)	6.31(4.93-7.69)	6.35(4.46-8.25)	8.81(5.63-12.00)	4.05(3.11-5.00)
2033	10.00(8.04-11.96)	14.88(10.27-19.49)	6.47(4.86-8.07)	6.39(4.19-8.60)	8.79(5.09-12.49)	4.15(3.05-5.24)
2034	10.03(7.85-12.20)	14.94(9.66-20.23)	6.62(4.78-8.46)	6.43(3.91-8.96)	8.76(4.52-13.00)	4.24(2.98-5.49)
2035	10.05(7.67-12.43)	15.01(9.02-21.00)	6.78(4.69-8.86)	6.47(3.61-9.33)	8.74(3.93-13.54)	4.33(2.91-5.75)
2036	10.07(7.49-12.65)	15.08(8.36-21.81)	6.93(4.59-9.27)	6.51(3.29-9.72)	8.71(3.32-14.11)	4.42(2.83-6.02)
2037	10.09(7.31-12.87)	15.15(7.67-22.64)	7.09(4.48-9.69)	6.55(2.97-10.13)	8.69(2.68-14.69)	4.52(2.74-6.29)
2038	10.11(7.13-13.08)	15.22(6.95-23.50)	7.24(4.36-10.12)	6.59(2.63-10.54)	8.66(2.02-15.30)	4.61(2.65-6.57)
2039	10.12(6.95-13.29)	15.29(6.21-24.38)	7.39(4.23-10.56)	6.63(2.28-10.97)	8.63(1.34-15.93)	4.70(2.55-6.86)
2040	10.14(6.78-13.49)	15.36(5.44-25.29)	7.55(4.09-11.00)	6.66(1.92-11.41)	8.61(0.64-16.57)	4.80(2.45-7.15)

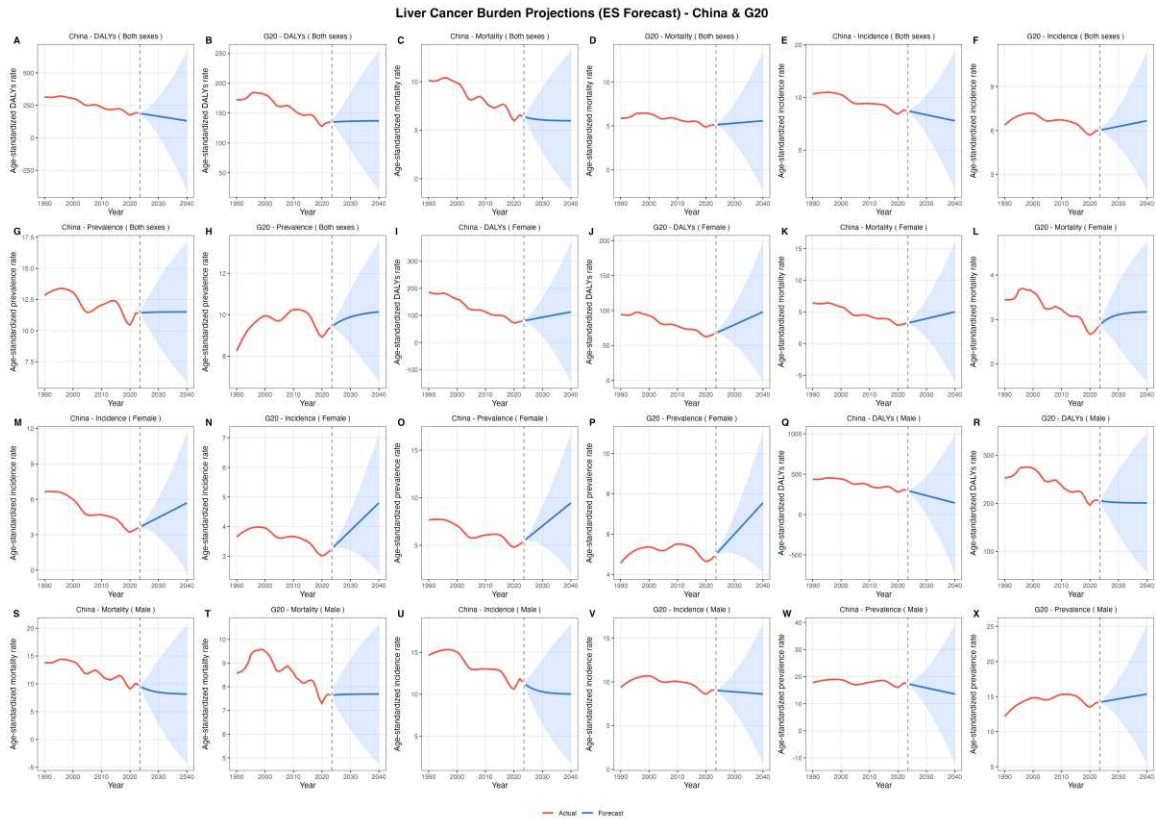


Figure 18: Comparative analysis of projected hepatocellular carcinoma burden under optimized intervention versus baseline scenarios for China and G20 countries, 2024–2040.

Discussion

Hepatocellular carcinoma (HCC) constitutes a significant worldwide public health issue, being a principal contributor to global cancer incidence and mortality. The disease prognosis is often unfavorable, primarily attributable to challenges in early diagnosis and the intricacies of treating advanced stages in the context of frequently impaired liver function [2]. The considerable economic impact of HCC, resulting from expensive therapeutic interventions and substantial premature life loss, highlights the pressing necessity for detailed epidemiological evaluations to guide effective health policy formulation [12]. Consequently, a nuanced comprehension of the changing burden of disease, influenced by an evolving profile of causative factors, is essential for refining prevention and management initiatives at national and international levels.

This investigation presents an exhaustive, multi-dimensional evaluation of the HCC burden from 1990 through 2040 in China and the G20 member states. By utilizing the authoritative Global Burden of Disease dataset within a consolidated analytical framework, our work outlines long-term spatial and temporal patterns, measures the impact of major modifiable risk factors, and forecasts future trends. Principal outcomes depict a complex scenario characterized by falling age-standardized rates concurrent with rising absolute case counts, pronounced disparities linked to demographic and socioeconomic factors, and a pivotal shift in the spectrum of attributable risks from infectious to metabolic etiologies. The subsequent discussion will interpret these central results, consider their implications for public health, and situate them within the wider context of HCC research and policy development.

Our results indicating that the age-standardized rates (ASRs) for hepatocellular carcinoma (HCC) in China have decreased more rapidly than the G20 average, with detectable inflection points, are consistent with and expand upon prior reports of improving HCC epidemiological trends in specific areas [13]. The more pronounced decline observed in China is likely reThe significant decline in age-standardized incidence and mortality rates for hepatocellular carcinoma (HCC) reflects the considerable public health impact of nationwide strategies, particularly the universal infant immunization against hepatitis B virus (HBV) launched in 1992 and the subsequent broadening of access to antiviral treatments. This focused suppression of a major viral cause has clearly modified the population-level risk landscape [14]. The joinpoint regression analysis offers further temporal detail, indicating that the turning points in the downward trend may align with the intensification of these specific public health measures or the adoption of new systemic treatments, including tyrosine kinase inhibitors and immune checkpoint blockers, which have enhanced survival and likely

influenced mortality patterns [2] However, the continuing increase in absolute case numbers, set against declining age-standardized rates, highlights a major challenge fueled by an aging population and overall demographic expansion. This pattern shows that while the risk per individual is being effectively reduced, the sheer growth in the size of the older population continues to drive the total clinical burden, requiring proactive health resource planning that considers this demographic momentum. The simultaneous occurrence of these trends underscores the intricate relationship between effective primary prevention and inevitable demographic changes.

The marked gender difference in HCC burden, with males experiencing a 2.5 to 3.5 times higher age-standardized risk, is a well-documented global finding, and our results confirm this pattern across the G20 countries [15] The biological basis for this disparity involves several factors, including variations in sex hormone activity, particularly pathways involving androgen receptors that can encourage liver cancer development, and a higher occurrence of key modifiable risk behaviors such as alcohol intake and tobacco smoking among men [14] Notably, our finding of a faster rate of decrease in age-standardized rates among women points to a differential effectiveness of public health interventions, potentially due to lower initial exposure to modifiable risks like alcohol or earlier interaction with healthcare services. Moreover, the observed trend toward an older age distribution of HCC cases, with the peak incidence moving to older groups and limited progress in the cohort aged 75 and above, presents a specific clinical dilemma. Elderly patients often have more advanced disease at diagnosis or may not be candidates for curative treatments because of coexisting medical conditions and diminished liver functional capacity, factors that make management more complex and constrain the benefits of therapeutic progress [7] This demographic evolution calls for the creation of geriatric oncology protocols and monitoring approaches designed for older, often frailer individuals with cirrhosis, where the potential benefits and risks of interventions require careful evaluation.

The strong negative association between a nation's level of economic development and its age-standardized HCC burden within the G20 emphasizes the powerful role of social health determinants. This gradient is likely rooted in inequalities in healthcare systems, availability of vaccination and antiviral drugs, quality of early detection programs, and varying exposure to environmental and lifestyle risk factors [16] Our detailed etiological attribution analysis provides a crucial additional dimension to this socioeconomic relationship. The documented shift from a predominance of infectious causes (HBV and HCV) to metabolic ones, specifically metabolic dysfunction-associated fatty liver disease (MAFLD), is a key observation. This transition parallels the global increase in obesity and metabolic syndrome

and indicates an evolving profile of underlying drivers for chronic liver disease [6] While viral hepatitis remains a critical concern. The increasing proportion of hepatocellular carcinoma (HCC) attributable to metabolic dysfunction-associated fatty liver disease (MAFLD) suggests a future epidemiological landscape where a greater number of HCC cases may develop in the absence of cirrhosis, thereby challenging conventional surveillance protocols that predominantly target cirrhotic populations [5] The observed variations in attribution patterns by sex and age—with metabolic factors constituting a more significant etiological component among females and older individuals—further highlight the necessity for prevention strategies that are specifically tailored to demographic profiles to address this shifting mosaic of causative factors.

Our integrated Bayesian age-period-cohort (BAPC) and autoregressive integrated moving average (ARIMA) modeling projects a continued, albeit gradual, decline in the age-standardized disease burden through 2040, offering a quantitative basis for long-term health policy formulation. This methodological synthesis, which combines the analysis of age-period-cohort effects with time-series forecasting, represents a progression beyond purely extrapolative models. It explicitly accounts for the complex interactions among generational shifts in risk, interventions specific to particular time periods, and the demographic process of population aging [13] The persistently elevated projected incidence rates in China, despite a historically steeper rate of decline, can be mechanistically explained by our attribution results: a dual etiological challenge persists, comprising the residual burden from historical cohorts exposed to hepatitis B virus (HBV) and the rising incidence of MAFLD-driven cases. This combination is likely to sustain a higher baseline burden compared to many other G20 nations [6] Importantly, our scenario analysis indicates that enhanced management of key modifiable risk factors—specifically MAFLD, alcohol consumption, and tobacco use—could significantly accelerate the rate of decline. This modeling work translates etiological understanding into actionable public health metrics, quantifying the potential gains in disability-adjusted life years (DALYs) averted and providing an economic rationale for prioritizing integrated prevention initiatives that target both established and emerging risk factors.

The analytical rigor of this study, which employs joinpoint regression, Bayesian age-period-cohort modeling, and ARIMA forecasting within the Global Burden of Disease (GBD) framework, provides a replicable template for comprehensive burden of disease assessment. A principal strength is the simultaneous application of these complementary models, which facilitates the separation of long-term generational trends from shorter-term temporal fluctuations—a distinction crucial for accurate forecasting and policy assessment [13] While

the GBD study ensures unparalleled comparability across different times and geographies, its dependence on modeled estimates requires cautious interpretation. For example, the attribution of burden to MAFLD is contingent upon the specific modeling assumptions and exposure definitions utilized within the GBD framework and may not fully encapsulate the complex, synergistic interactions between metabolic dysfunction and other risks, such as alcohol [5]. Furthermore, although robust, our predictive models inherently cannot account for unforeseen technological advancements, such as novel curative therapies or highly effective novel prevention strategies, which constitutes a fundamental limitation of all projections based on historical trends. Nonetheless, this multi-model approach strengthens the robustness of our conclusions and offers an adaptable framework for studying other malignancies where deciphering the interplay of age, period, and cohort effects is vital.

Notwithstanding the comprehensive nature of the analytical framework, several limitations of this study must be acknowledged. First, reliance on the GBD 2023 database, while ensuring standardized and comparable estimates, inherently incorporates the modeling assumptions and potential residual uncertainties from the original source data. This is particularly relevant for nations with incomplete vital registration or cancer surveillance systems, which may affect the precision of our national-level estimates and the inflection points identified through Joinpoint regression. Second, our predictive models, which integrate BAPC and ARIMA methodologies, operate under the assumption that historical trends and currentThe study outlines the changing patterns of hepatocellular carcinoma (HCC) burden in China and G20 countries from 1990 to 2040. Key observations reveal a reduction in age-standardized burden despite an increase in absolute case numbers, notable variations by sex, age, and economic status, and a shift in contributing risks from viral hepatitis to metabolic conditions such as metabolic dysfunction-associated fatty liver disease (MAFLD). Projections indicate a gradual decline in burden, which could be enhanced through focused management of risk factors. These findings offer essential evidence for developing tailored and proactive prevention approaches. Subsequent investigations should incorporate multi-omics and clinical information to clarify biological pathways and create adaptive, precise models for forecasting burden and assessing interventions.

Ethics Approval and Consent to Participate

This study was based on publicly available data from the Global Burden of Disease (GBD) 2023 study. All data used in this research were de-identified and aggregated at the population level, with no individual-level identifiable information included. Therefore,

additional ethical approval from the institutional review board and informed consent from participants were not required for this study.

Consent for Publication

All authors have read and approved the final version of this manuscript and consent to its publication in Cancer Cell International. All authors confirm that the content of this manuscript has not been published elsewhere in whole or in part, and is not under consideration for publication in any other journal.

Availability of Data and Materials

The datasets analyzed in this study are publicly available from the Global Burden of Disease 2023 study website (<https://vizhub.healthdata.org/gbd-results/>). All data generated or analyzed during this study are included in this published article.

Competing Interests

All authors are affiliated with Ningxia Medical University. The authors declare that they have no financial or non-financial competing interests related to the research presented in this manuscript. There are no commercial associations or financial relationships that could be construed as a potential conflict of interest.

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