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Letters to the editor

Comment on "burden of disease and risk factors for primary liver cancer by etiology in the United States, 1990–2021: Results from the global burden of disease study, 2021"

Dear Editor,

We read with great interest the study by Wang et al. [1], which analyzed recent temporal trends in the causes of liver cancer (LC) in the United States from 1990 to 2021 and predicted future trends. Although the study provides valuable epidemiological insights into LC in the United States, its assessment of the temporal trend of the disease primarily relies on the linear regression model estimated annual percent change (EAPC), which assumes a linear trend in the disease over time. However, the actual changes in disease burden often follow nonlinear or stage-specific patterns, making it crucial to adopt more scientific, rigorous, and accurate methods to quantify the true epidemiological burden trend of LC in the United States.

To investigate whether the burden of LC in the United States during this period follows a linear or nonlinear trend, we employed the segmented joinpoint model recommended by the National Cancer Institute, using the average annual percent change (AAPC) as the metric [2]. Compared to traditional linear regression methods, AAPC effectively captures the nonlinear characteristics of disease burden over time, particularly in the presence of trend fluctuations or phase-specific changes. By calculating the average annual change rate for each time segment, AAPC can reveal the dynamic variations in LC burden across different periods, helping to identify key change points and trend reversals. Moreover, the weighted average nature of AAPC allows for more accurate trend assessments in diverse epidemiological contexts, providing reliable evidence for forecasting future LC burden and formulating public health policies.

The comparison between the results of the AAPC and the EAPC for LC burden in the United States reveals both similarities and differences in trend estimations (Table 1 and Fig. 1). Both AAPC and EAPC show a general increase in the burden of LC across the various etiologies, with similar patterns observed in the incidence, prevalence, mortality, and disability-adjusted life years rates. However, the key difference lies in the magnitude of the trends. The EAPC results consistently reflect higher rates of change compared to the AAPC, particularly in the case of HCV and MASLD-associated LC. This suggests that both AAPC and EAPC have distinct advantages in capturing LC trends.

In conclusion, both AAPC and EAPC offer valuable insights into understanding the burden of LC. EAPC is used to estimate the annualized percent change under the assumption of linear growth in disease trends, especially when the trend is relatively stable. AAPC is more flexible for nonlinear trends and is suitable for analyzing complex disease trends. Each method has its own strengths in different contexts, and together, they offer a more comprehensive understanding of the disease burden trends. Therefore, it is recommended that future studies combine both methods to accurately assess and interpret the evolving patterns of LC burden. We appreciate the opportunity to reflect on these methods and believe that these insights will contribute to strengthening the assessment work in future global disease burden studies.

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Table 1
AAPC for incidence, prevalence, mortality, and DALYs of liver cancer (LC) due to four causes in the United States, 1990–2021.

Cause	ASIR of AAPC (95% CI)	ASPR of AAPC (95% CI)	ASMR of AAPC (95% CI)	ASDR of AAPC (95% CI)
HBV-associated LC	2.33 (2.30 to 2.35)	2.90 (2.88 to 2.92)	1.98 (1.87 to 2.06)	1.79 (1.68 to 1.87)
HCV-associated LC	2.89 (2.85 to 2.91)	3.48 (3.43 to 3.51)	2.52 (2.42 to 2.59)	2.48 (2.40 to 2.54)
MASLD-associated LC	3.09 (3.04 to 3.13)	3.71 (3.67 to 3.74)	2.71 (2.64 to 2.77)	2.74 (2.66 to 2.81)
Alcohol-associated LC	2.91 (2.86 to 2.94)	3.55 (3.50 to 3.59)	2.54 (2.43 to 2.66)	2.58 (2.50 to 2.68)

AAPC, annual average percentage change; ASIR, age-standardized incidence rate; ASPR, age-standardized prevalence rate; ASMR, age-standardized mortality rate; ASDR, age-standardized disability-adjusted life years rate; HBV, hepatitis B virus; HCV, hepatitis C virus; LC, liver cancer; MASLD, metabolic dysfunction-associated steatotic liver disease.

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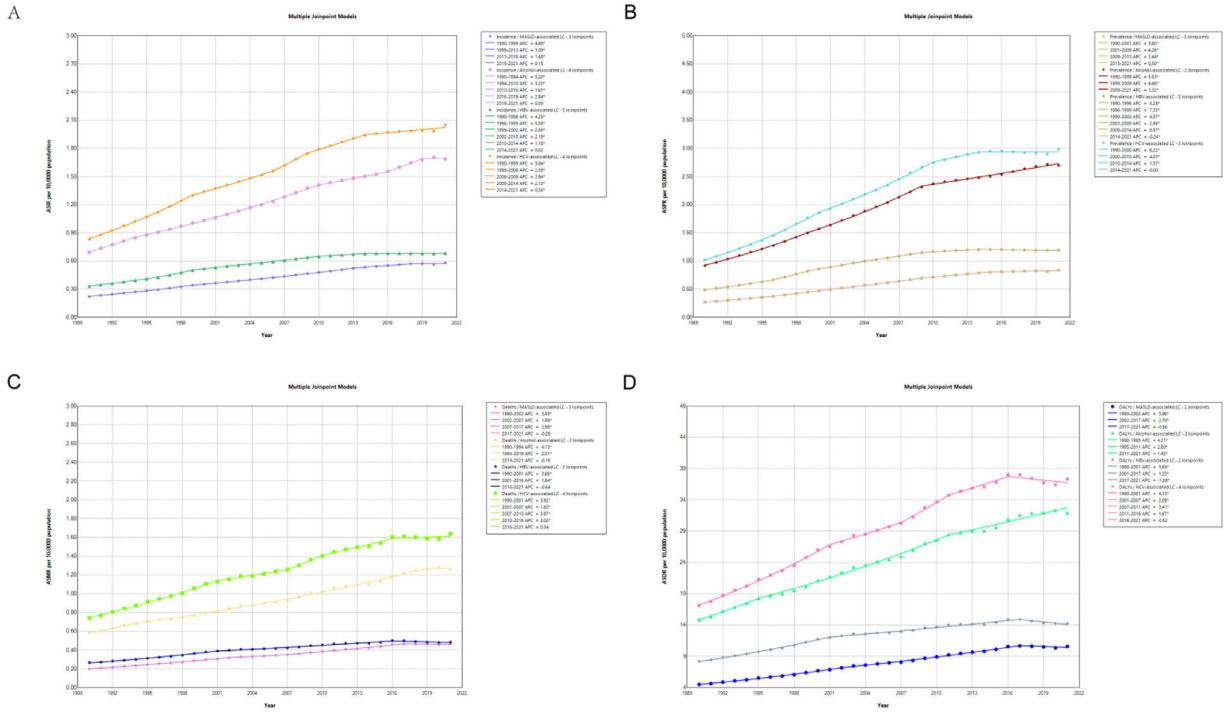

Fig. 1. Visualization of AAPC for incidence, prevalence, mortality, and DALYs of LC due to four causes in the United States, 1990–2021.AAPC, annual average percentage change; ASIR, age-standardized incidence rate; ASPR, age-standardized prevalence rate; ASMR, age-standardized mortality rate; ASDR, age-standardized disability-adjusted life years rate; HBV, hepatitis B virus; HCV, hepatitis C virus; LC, liver cancer; MASLD, metabolic dysfunction-associated steatotic liver disease.

Declaration of competing interest

None.

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[2] National Cancer Institute, "AAPC definition,"accessed August 16, 2025, https://surveillance.cancer.gov/help/joinpoint/tech-help/frequently-asked-questions/aapc-definition.

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