Published in final edited form as:

Cancer. 2019 March 01; 125(5): 726–734. doi:10.1002/cncr.31869.

Trends in Liver Cancer Mortality in the United States: Dual Burden Among Foreign- and US-Born Persons

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Abstract

BACKGROUND: Since the mid-1980s, the burden of liver cancer in the United States has doubled, with 31,411 new cases and 24,698 deaths occurring in 2014. Foreign-born individuals may be more likely to die of liver cancer than individuals in the general US-born population because of higher rates of hepatitis B infection, a low socioeconomic position, and language barriers that limit the receipt of early cancer detection and effective treatment.

METHODS: To determine whether liver cancer mortality rates were higher among foreign-born individuals versus US-born individuals in the United States, population-based cancer mortality data were obtained from the National Center for Health Statistics of the Centers for Disease Control and Prevention. Annual population estimates were obtained from the US Census Bureau's American Community Survey. Age-adjusted mortality rates and rate ratios (RRs) for liver cancer stratified by birth place were calculated, and the average annual percent change (AAPC) was used to evaluate trends.

RESULTS: A total of 198,557 deaths from liver and intrahepatic bile duct cancer were recorded during 2005–2014, and 16% occurred among foreign-born individuals. Overall, foreign-born individuals had a 24% higher risk of liver cancer mortality than US-born individuals (RR, 1.24; 95% confidence interval [CI], 1.22–1.25). Foreign-born individuals did not have any significant

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AUTHOR CONTRIBUTIONS

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CONFLICT OF INTEREST DISCLOSURES

The authors made no disclosures.

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

changes in liver cancer mortality rates overall, but among US-born individuals, liver cancer mortality rates significantly increased (AAPC, 2.7; 95% CI, 2.1–3.3).

CONCLUSIONS: Efforts that address the major risk factors for liver cancer are needed to help to alleviate the health disparities observed among foreign-born individuals and reverse the increasing trend observed in the US-born population.

Keywords

cancer; foreign-born; hepatitis B; hepatitis C; liver; liver and intrahepatic bile duct; liver cancer; mortality; mortality rates; nativity status; US-born

INTRODUCTION

Since the mid-1980s, the liver cancer mortality rate in the United States has doubled,[1] with 31,411 new cases and 24,698 deaths occurring in 2014.[2] In the US population, liver cancer mortality rates are significantly increasing for nearly all sex, age, and race/ethnicity group stratifications.[3,4] Globally, chronic infection with hepatitis B virus (HBV) or hepatitis C virus (HCV) is the major cause of liver cancer[3,5]; however, in the United States, obesity, chronic HCV infection, excessive alcohol consumption, and tobacco use are the leading causes of liver cancer.[6]

Foreign-born individuals represent a rapidly growing segment of the general US population, and from 1970 to 2010, the foreign-born population increased from 9.6 to 40.0 million individuals.[7] This group is also more likely to develop and die of liver cancer than US-born individuals.[8] According to their country of origin, HBV infection rates in the foreign-born population can range from 1 to 33 times the rates observed in the general US-born population, whereas their risk of HCV infection is lower than or similar to the risk for their US-born counterparts.[9–12] Barriers such as limited English proficiency, an undocumented status, a mistrust or fear of an unfamiliar health care system, busy work schedules, and a low socioeconomic position all hinder foreign-born individuals from proper diagnosis and treatment, and this increases their risk of developing and dying of liver cancer.[13,14] Although other studies have evaluated excess liver cancer mortality risk in the foreign-born population, the work is not contemporary[8] or has been limited in geographic area or the race/ethnicity of the participants.[15,16] We analyzed the most recent 10-year national mortality rate data (2005–2014) to provide current liver cancer mortality estimates by birth place, sex, and race/ethnicity and to determine the extent to which these rates are changing over time.

MATERIALS AND METHODS

Data Sources

Population-based cancer mortality data were obtained from the National Center for Health Statistics. The National Center for Health Statistics receives demographic and vital statistics from the National Vital Statistics System. The National Vital Statistics System collects information on sex, race, ethnicity, birth place, age at death, state of residence, and cause of death from death certificates filed in each state. Individuals whose death certificates stated

that they were born in 1 of the 50 states, the District of Columbia, or the US territories were categorized as US-born. Remaining cases with a recorded place of birth were categorized as foreign-born.[17] Mortality data were selected with code C22 from the *International Classification of Diseases, Tenth Revision*, to identify all liver and intrahepatic bile duct cancers (called liver cancer in this article). A total of 200,925 deaths from liver cancer were recorded between 2005 and 2014. Cases with no recorded place of birth (1.2%) were excluded from all analyses.

Annual population estimates were obtained from the US Census Bureau's American Community Survey (ACS). The ACS is a continuous national survey of randomly selected households and collects detailed information on the US population, including information on birth place.[18] Information is collected regardless of residency status, so legal and undocumented individuals are surveyed and represented in the estimates.[19] Because of this, the ACS is often used as a detailed source of information for the immigrant population in the United States.[17] The ACS also provides 5-, 3-, and 1-year estimates of the US population and provides public-use microdata sample files that can be used to estimate the US population with social, housing, and demographic characteristics. We obtained the annual ACS public-use microdata sample files from 2005 to 2014 and estimated the US-born and foreign-born populations for age, race/ethnicity, and sex subgroups with the provided person weights.

Statistical Analysis

Mortality data from the National Center for Health Statistics and population estimates from the ACS for 2005–2014 were formatted with software from the Surveillance, Epidemiology, and End Results (SEER) program (SEER*Prep, version 2.5.3) to create a SEER*Stat database. Performing age adjustments to the 2000 US standard population, we calculated age-adjusted mortality rates for liver cancer among US- and foreign-born individuals. Rate ratios (RRs), standard errors, and 95% confidence intervals (CIs) were calculated with SEER*Stat (version 8.3.4).

The National Cancer Institute's Joinpoint trend analysis software (version 4.5.0.1) was used to evaluate the annual percent change (APC) and average annual percent change (AAPC) in mortality rates from 2005 to 2014 by birth place (US- vs foreign-born) after stratification by sex, age, and race/ethnicity. APCs were calculated with a maximum of 1 joinpoint. The Monte Carlo permutation method was used to test whether the APC or AAPC was significantly different from 0.

RESULTS

Comparing Liver Cancer Mortality Rates: Foreign-Born Versus US-Born

From 2005 to 2014, 31,097 deaths from liver cancer were recorded for the foreign-born population, whereas 167,460 deaths were recorded among the US-born. Differences in liver cancer mortality rates by birth place, sex, race/ethnicity, and age groups are displayed in Table 1. Overall, foreign-born individuals had a higher risk of liver cancer mortality than US-born individuals (RR, 1.24; 95% CI, 1.22–1.25). This pattern remained after

stratification by sex with an RR of 1.17 (95% CI, 1.15–1.19) for males and with an RR of 1.44 (95% CI, 1.42–1.48) for females. With stratification by sex and race/ethnicity, foreign-born males who were non-Hispanic Asian/Pacific Islander (API; RR, 1.71; 95% CI, 1.59–1.84) had higher mortality rates than US-born non-Hispanic APIs. In contrast, foreign-born men who were non-Hispanic black (RR, 0.61; 95% CI, 0.57–0.66) or Hispanic (RR, 0.52; 95% CI, 0.51–0.54) had a significantly lower risk of death than US-born individuals of the same race/ethnicity. Non-Hispanic white and non-Hispanic API foreign-born women had higher liver cancer mortality rates than their US-born counterparts (RR for non-Hispanic whites, 1.16; 95% CI, 1.11–1.20; RR for non-Hispanic APIs, 1.56; 95% CI, 1.41–1.73). Foreign-born women who were non-Hispanic black (RR, 0.91; 95% CI, 0.83–0.99) or Hispanic (RR, 0.92; 95% CI, 0.88–0.96) had a significantly lower risk of death than their US-born counterparts. Foreign-born men and women had significantly higher mortality rates in most age groups examined than US-born men and women with the exception of men 50 to 64 years old.

Trends in Liver Cancer Mortality Rates

Overall, liver cancer mortality rates significantly increased in the United States from 2005 to 2014 (AAPC, 2.2; 95% CI, 1.0–3.4; Table 2). In general, rates significantly increased among men and women, among individuals 50 years old or older, and among non-Hispanic whites, non-Hispanic blacks, and Hispanics. Notably, the largest increases overall were observed among men and women aged 50 to 64 years, with identical increases in men (AAPC, 3.9; 95% CI, 2.9–4.8) and women (AAPC, 3.9; 95% CI, 2.6–5.3).

Among foreign-born individuals overall, no significant changes were observed in liver cancer mortality rates from 2005 to 2014 (AAPC, 0.5; 95% CI, −1.5 to 2.6; Table 2). When they were stratified by sex, a significant increase in mortality rates was observed among men overall (AAPC, 1.2), with rates specifically increasing among men aged 50 to 64 years (AAPC, 1.5) and men aged ≥80 years (AAPC, 2.5) and among men of non-Hispanic white race/ethnicity (AAPC, 2.1). Among foreign-born women, no significant increases in mortality rates were observed overall, by age, or by race/ethnicity stratifications.

Liver cancer mortality rates significantly increased from 2005 to 2014 among US-born individuals (AAPC, 2.7; 95% CI, 2.1–3.3; Table 2). Among US-born men, liver cancer mortality rates significantly increased overall (AAPC, 2.7), with rates specifically increasing among men 50 years old or older and among non-Hispanic white, non-Hispanic black, and Hispanic men (Fig. 1). The trends for US-born women varied; significant increases were observed overall (AAPC, 2.1), among women 50 to 79 years old (AAPC for 50–64 years, 4.5; AAPC for 65–79 years, 2.1), and among non-Hispanic white women (AAPC, 2.0) and non-Hispanic black women (AAPC, 2.3; Fig. 2 and Table 2).

DISCUSSION

Foreign-born individuals in the United States have an elevated risk of liver cancer mortality in comparison with the US-born population; however, their risk varies by age, sex, and race/ethnicity. In both foreign- and US-born populations, liver cancer mortality rates were higher for men than women and for older individuals than younger age groups. The findings from

this study are consistent with other studies that have found higher liver cancer mortality rates among foreign-born individuals,[8] men,[3] and older age groups[3,4,20,21] in comparison with their respective counterparts. When we analyzed trends over time, we found that the foreign-born population had few significant changes in liver cancer mortality rates, whereas a significant increasing trend was observed in the US-born population for most race/ethnicities, age groups, and sex stratifications.

Although foreign-born individuals generally had an elevated risk of liver cancer mortality, when they were stratified by ethnicity and sex, foreign-born non-Hispanic APIs were the only foreign-born group to have significantly higher liver cancer mortality for both sexes in comparison with their US-born counterparts. The high risk of liver cancer mortality observed among foreign-born APIs is likely to be partially explained by an elevated risk of acquiring an HBV infection before their immigration to the United States.[22] HBV infection rates among foreign-born individuals can range from 1 to 33 times the observed rates among the general US-born population according to their country of origin and subsequent HBV vaccination rates.[9,10] As childhood HBV vaccination rates continue to improve globally, it is likely that the liver cancer mortality rates among foreign-born individuals in the United States will decline.[3] In contrast to foreign-born APIs, foreign-born Hispanic and non-Hispanic black men had significantly lower rates of liver cancer mortality than their US-born counterparts. This may partly be explained by the higher rates of metabolic disorders, alcoholic liver disease, and HCV infection among US-born Hispanic men in comparison with their foreign-born counterparts,[22] and it is likely that a similar trend is occurring among US-born non-Hispanic blacks.[8] In contrast to previous work, this study did not find a significant decrease in liver cancer mortality rates among US- or foreign-born APIs.[3,4] Although this finding could be due to fluctuating mortality rates, these rates should be monitored and elucidated to improve interventions in this population.

Notably, our study also shows a continuation of the rapidly rising trend in liver cancer mortality rates in the US-born population. In the current study, liver cancer mortality rates significantly increased for nearly all sex, age, and race/ethnicity groups in the US-born population, and this aligned with previous findings.[3,4] It is likely that this increase will continue, and it has been estimated that by 2030, liver cancer will the third leading cause of cancer mortality among men and women.[23] Because of the limited treatment options available after diagnosis, the 5-year relative survival rate of patients with liver cancer is only 14.8%.[24] To alleviate the higher liver cancer mortality burden observed among foreign-born individuals and reverse the increasing trend observed in the US-born population, a combination of behavioral change programs for weight management, smoking cessation, reductions in alcohol consumption, and risk reduction for people who inject drugs as well as screening and treatment efforts for HBV and HCV will be needed.

Chronic infection with HBV or HCV is a well- documented risk factor for the development of liver cancer; currently in the United States, upward of 2.2 million individuals have chronic HBV,[10,25] and 3.5 million have an HCV infection.[26] HBV vaccination is 80% to 100% effective in preventing disease. For patients with chronic HBV, early diagnosis and treatment can reduce the risk of liver cancer by 50% to 80%.[27,28] There are curative treatment options for HCV infection that can reduce the risk of liver cancer by 75%.[29,30]

Improved hepatitis screening, HBV vaccination, and hepatitis treatment services for at-risk groups would help to alleviate the growing burden of liver cancer in the United States. The Centers for Disease Control and Prevention and the US Preventive Services Task Force both currently recommend HBV and HCV testing for individuals at high risk for infection. For HBV infection, foreign-born individuals whose country of origin has an HBV infection prevalence higher than 2% are considered a high-risk group.[31] For HCV, the following factors are associated with a high risk of infection: current or past injection drug use, long-term hemodialysis, a blood transfusion before 1992, high-risk sexual behaviors, and birth between 1945 and 1965.

Globally, chronic HBV and HCV infections account for a majority of liver cancer cases, but in the United States, the risk factors for liver cancer have been gradually changing.[3,10] Historically in the United States, HBV or HCV infections were the leading cause of liver cancer mortality. However, with the implementation of the childhood HBV vaccine and with the elimination of HCV from the nation's blood supply, the prevalence of these infections in the United States has declined, whereas the incidence and mortality rate of liver cancer continue to increase.[6] In a recent study, Makarova-Rusher et al[6] calculated the population attributable fraction (PAF) for each of the major risk factors for liver cancer and showed how each risk factor contributed to the overall liver cancer burden in the United States. Their work found that metabolic disorders, including obesity, were responsible for 32% of the liver cancer burden in the United States, and they were followed by HCV (PAF, 20.5%), alcohol (PAF, 13.4%), smoking (PAF, 9%), HBV (PAF, 4.3%), and genetic disorders (PAF, 1.5%); these findings were consistent with another study.[32] These results highlight that despite the low liver cancer risk conferred by some risk factors (eg, metabolic disorders or smoking), because of the high prevalence of these conditions in the population, they can account for a substantial number of cancer cases.

The main strength of this study is that it combines validated data from multiple sources to provide the most up-to-date comprehensive examination of liver cancer mortality rates by place of birth for the entire US population over the past decade. In addition, because the place of birth is frequently missing from cancer incidence data, this analysis approach provides the only way to accurately estimate the burden of cancer in the immigrant population at a national level, with only 1.2% of cases missing data for the place of birth. One limitation of this study is that mortality data were based on information obtained from death certificates, and this may have resulted in the undercounting of liver cancer deaths if the causes of death were not fully recorded. In addition, cancers frequently metastasize and spread to the liver, and this leaves the possibility that metastasized cancers from other sites could have been recorded as primary liver cancer. These issues were likely eliminated with the trend analysis because these issues are likely to occur at a constant rate over time.[33] In addition, we did not have access to all variables relevant to liver cancer mortality (specifically, socioeconomic attributes, etiologic risk factors, and health insurance status). Finally, we did not differentiate between hepatocellular carcinoma and intrahepatic bile duct cancer in this article because of concerns about misclassification.[34,35]

In summary, foreign-born individuals in the United States have an elevated risk of liver cancer mortality in comparison with the US-born population. However, although the liver

cancer mortality rates among foreign-born individuals have remained fairly stable from 2005 to 2014, the mortality rates among US-born individuals have significantly increased for nearly all race and sex subgroups. Efforts to address the major risk factors for liver cancer are needed to address the health disparities observed among foreign-born individuals and reverse the increasing trend observed in the US-born population.

FUNDING SUPPORT

No specific funding was disclosed.

We thank Jessica King and Trevor Thompson for their help in building the data set for this article.

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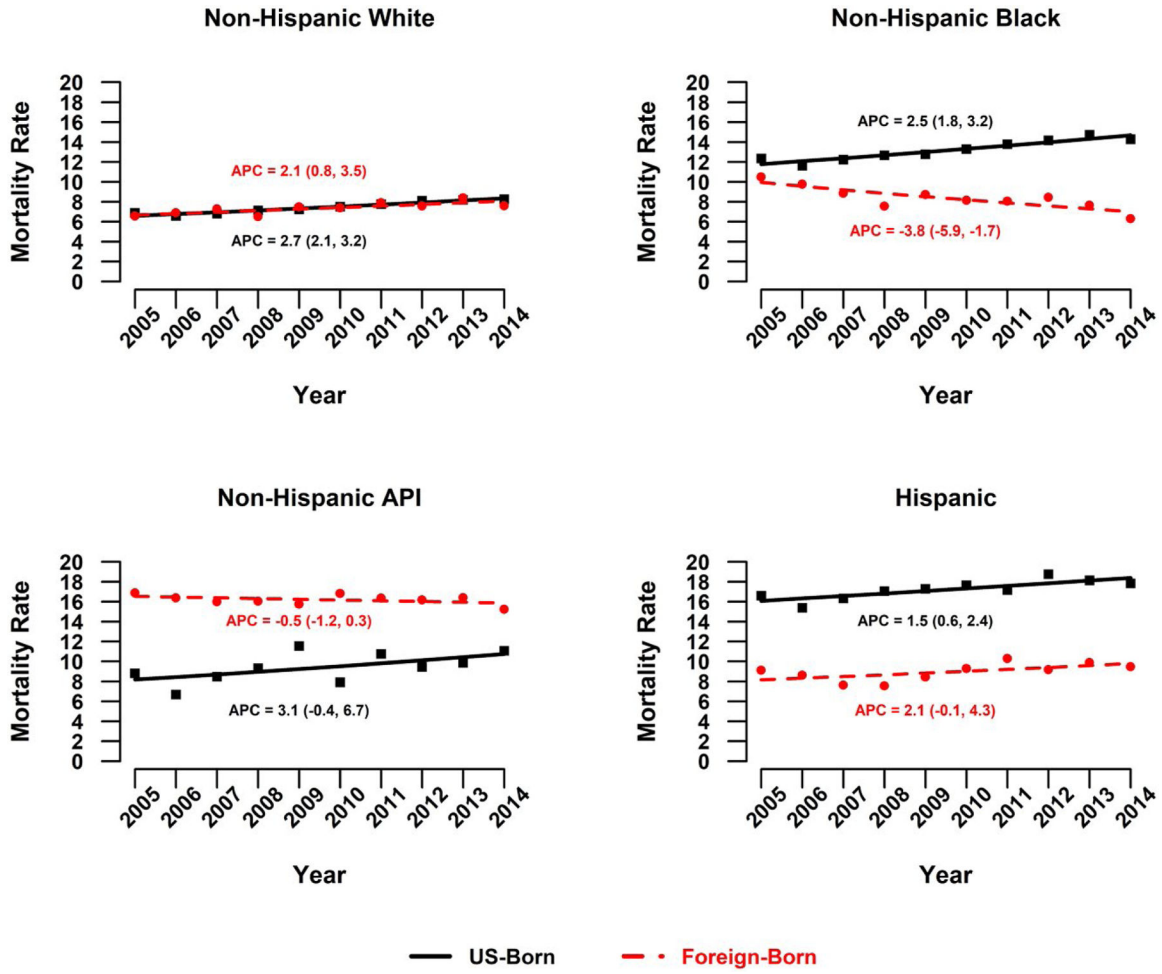

Figure 1.

APCs in liver cancer mortality rates among men by nativity status: United States, 2005–2014. APC indicates annual percent change; API, Asian/Pacific Islander.

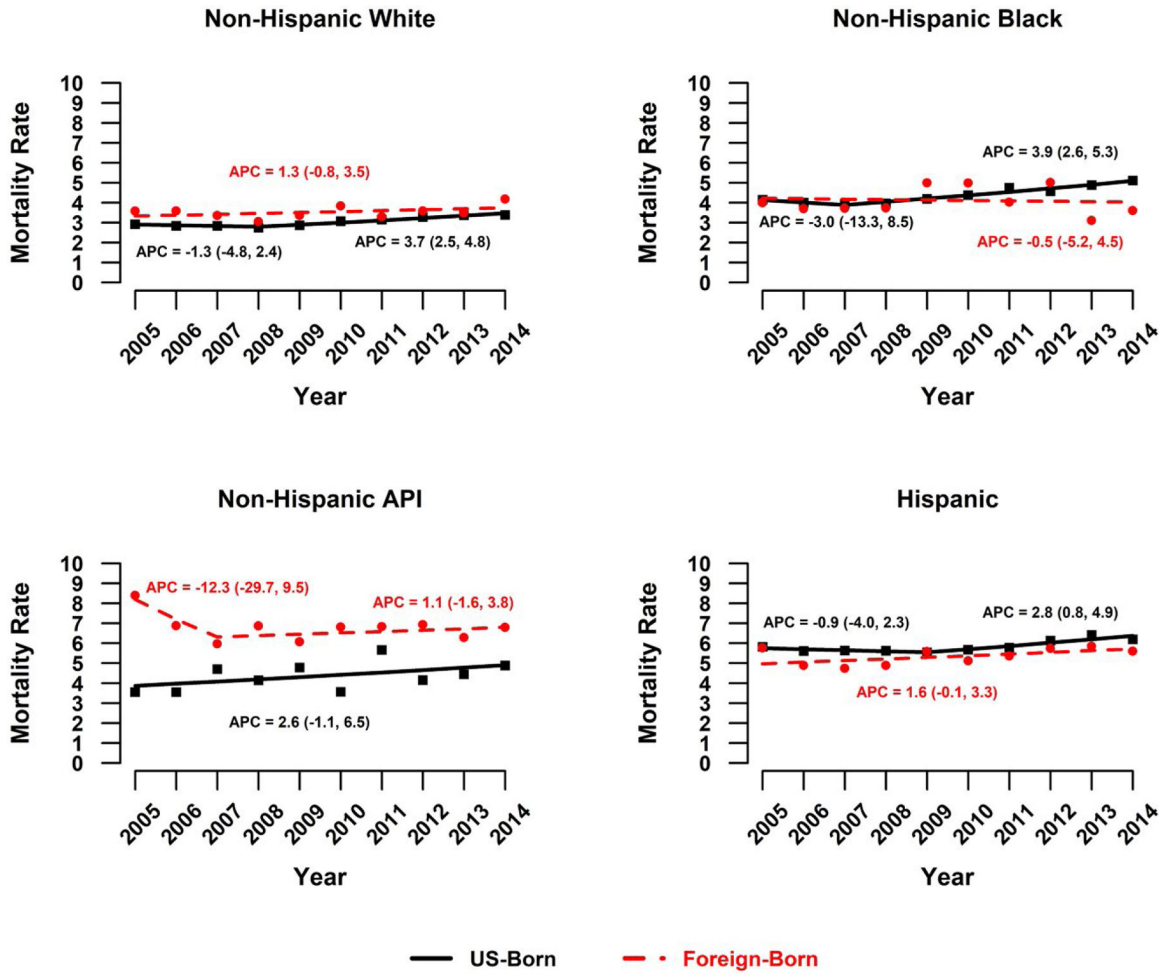

Figure 2.

APCS in liver cancer mortality rates among women by nativity status: United States, 2005–2014. APC indicates annual percent change; API, Asian/Pacific Islander.

TABLE 1.

Liver Cancer Mortality Rates in the United States by Demographic Characteristics: 2005–2014

	US-Born		Foreign-Born		
	No. of Cases	**Average Annual Rate (95% CI)[a]**	**No. of Cases**	**Average Annual Rate (95% CI)[a]**	**Rate Ratio (95% CI)[b]**
Overall	167,460	5.69 (5.66–5.71)	31,097	7.04 (6.96–7.13)	1.24[c] (1.22–1.25)
Sex					
Male	113,666	8.49 (8.44–8.54)	19,312	9.92 (9.78–10.07)	1.17° (1.15–1.19)
Female	53,794	3.32 (3.29–3.35)	11,785	4.80 (4.71–4.89)	1.44[c] (1.42–1.48)
Age: male					
<35 y	715	0.11 (0.10–0.12)	225	0.20 (0.16–0.24)	1.73[c] (1.42–2.14)
35–49y	5,643	2.05 (1.99–2.10)	1,772	2.71 (2.58–2.84)	1.32[c] (1.25–1.40)
50–64y	49,996	20.48 (20.30–20.66)	6,871	17.24 (16.84–17.65)	0.84[c] (0.82–0.86)
65–79 y	39,344	34.46 (34.11–34.80)	7,250	45.60 (44.55–46.68)	1.32[c] (1.29–1.36)
>80 y	17,968	50.22 (49.48–50.96)	3,194	70.81 (68.37–73.31)	1.41[c] (1.36–1.46)
Age: female					
<35 y	524	0.08 (0.08–0.09)	102	0.12 (0.08–0.17)	1.39 (0.91–2.06)
35–49 y	2,205	0.80 (0.77–0.83)	583	0.90 (0.83–0.97)	1.12[c] (1.02–1.23)
50–64 y	13,520	5.20 (5.11–5.29)	2,447	5.55 (5.33–5.77)	1.07[c] (1.02–1.11)
65–79 y	20,263	15.07 (14.86–15.28)	5,027	23.80 (23.14–24.47)	1.58[c] (1.53–1.63)
>80 y	17,282	27.29 (26.88–27.70)	3,626	44.47 (43.03–45.94)	1.63[c] (1.57–1.69)
Race/ethnicity: male					
Non-Hispanic white	83,919	7.50 (7.44–7.55)	4,720	7.40 (7.18–7.62)	0.99 (0.96–1.02)
Non-Hispanic black	17,712	13.36 (13.16–13.58)	1,104	8.19 (7.64–8.77)	0.61[c] (0.57–0.66)
Non-Hispanic API	843	9.44 (8.80–10.12)	7,755	16.17 (15.79–16.56)	1.71[c] (1.59–1.84)
Hispanic	9.930	17.33 (16.97–17.69)	5,693	9.01 (8.75–9.27)	0.52[c] (0.51–0.54)
Race/ethnicity: female					
Non-Hispanic white	41,609	3.05 (3.02–3.08)	3,261	3.53 (3.40–3.66)	1.16[c] (1.11–1.20)

	US-Born		Foreign-Born		
	No. of Cases	Average Annual Rate (95% CI)[a]	No. of Cases	Average Annual Rate (95% CI)[a]	Rate Ratio (95% CI)[b]
Non-Hispanic black	7,389	4.43 (4.33–4.53)	622	4.03 (3.71–4.39)	0.91[c] (0.83–0.99)
Non-Hispanic API	457	4.32 (3.91–4.75)	3,826	6.73 (6.52–6.96)	1.56[c] (1.41–1.73)
Hispanic	3,706	5.87 (5.68–6.07)	4,048	5.39 (5.21–5.57)	0.92[c] (0.88–0.96)

Abbreviations: API, Asian/Pacific Islander; CI, confidence interval.

The liver cancer mortality rates include liver and intrahepatic bile duct cancers (C22). Values in columns may not sum to the total because of missing values. Underlying mortality rates were provided by the National Center for Health Statistics.

[a] Rates have been age-adjusted to the 2000 US standard population and are shown per 100,000.

[b] The US-born population was used as the reference group to generate rate ratios.

[c] $P < .05$.

TABLE 2.

Overall Trends in Liver Cancer Mortality Rates by Nativity Status, Sex, Age, and Race/Ethnicity in the United States: 2005–2014

	Trend 1			Trend 2			AAPC	
Group	**Years**	**APC**	**95% CI**	**Years**	**APC**	**95% CI**	**2005–2014**	**95% CI**
US- and foreign-born combined								
Overall	2005–2007	−0.84	−7.15 to 5.90	2007–2014	3.05[a]	2.25 to 3.85	2.17[a]	0.95 to 3.41
Sex								
Male	2005–2014	2.49[a]	1.94 to 3.03				2.49[a]	1.94 to 3.03
Female	2005–2008	−1.41	−3.97 to 1.23	2008–2014	3.58[a]	2.75 to 4.42	1.89[a]	1.10 to 2.70
Age: male								
<35 y	2005–2014	−2.48	−5.71 to 0.85				−2.48	−5.71 to 0.85
35–49 y	2005–2014	−2.81[a]	−3.96 to −1.64				−2.81[a]	−3.96 to −1.64
50–64y	2005–2012	5.24[a]	4.42 to 6.06	2012–2014	−0.87	−5.62 to 4.11	3.85[a]	2.87 to 4.84
65–79 y	2005–2007	−0.74	−5.04 to 3.75	2007–2014	2.82[a]	2.29 to 3.36	2.02[a]	1.20 to 2.85
≥80 y	2005–2014	1.75[a]	0.75 to 2.76				1.75[a]	0.75 to 2.76
Age: female								
<35 y	2005–2014	−0.22	−2.89 to 2.53				−0.22	−2.89 to 2.53
35–49 y	2005–2014	−0.17	−2.27 to 1.99				−0.17	−2.27 to 1.99
50–64 y	2005–2008	0.47	−3.88 to 5.02	2008–2014	5.72[a]	4.42 to 7.03	3.94[a]	2.61 to 5.29
65–79 y	2005–2007	−2.13	−5.78 to 1.66	2007–2014	2.95[a]	2.48 to 3.43	1.80[a]	1.09 to 2.52
≥80 y	2005–2007	−7.68	−15.69 to 1.09	2007–2014	2.86[a]	1.69 to 4.04	0.42	−1.26 to 2.12
Race/ethnicity: male								
Non-Hispanic white	2005–2014	2.65[a]	2.13 to 3.18				2.65[a]	2.13 to 3.18
Non-Hispanic black	2005–2014	2.06[a]	1.34 to 2.79				2.06[a]	1.34 to 2.79
Non-Hispanic API	2005–2014	0.17	−0.49 to 0.84				0.17	−0.49 to 0.84
Hispanic	2005–2014	1.59[a]	0.60 to 2.58				1.59[a]	0.60 to 2.58
Race/ethnicity: female								

	Trend 1			Trend 2			AAPC	
Group	**Years**	**APC**	**95% CI**	**Years**	**APC**	**95% CI**	**2005–2014**	**95% CI**
Non-Hispanic white	2005–2008	−1.50	−4.56 to 1.67	2008–2014	3.65[a]	2.64 to 4.68	1.91[a]	0.95 to 2.88
Non-Hispanic black	2005–2007	−2.10	−12.06 to 8.98	2007–2014	3.44[a]	2.16 to 4.74	2.18[a]	0.20 to 4.21
Non-Hispanic API	2005–2014	−0.26	−2.02 to 1.54				−0.26	−2.02 to 1.54
Hispanic	2005–2014	1.46[a]	0.37 to 2.57				1.46[a]	0.37 to 2.57
Foreign-born only								
Overall	2005–2007	−4.04	−14.25 to 7.38	2007–2014	1.86[a]	0.53 to 3.21	0.52	−1.53 to 2.61
Sex								
Male	2005–2014	1.15[a]	0.12 to 2.19				1.15[a]	0.12 to 2.19
Female	2005–2007	−7.23	−17.89 to 4.82	2007–2014	2.27[a]	0.86 to 3.69	0.08	−2.13 to 2.33
Age: male								
<35 y	2005–2014	−2.34	−8.64 to 4.40				−2.34	−8.64 to 4.40
35–49 y	2005–2014	−2.39[a]	−3.86 to −0.89				−2.39[a]	−3.86 to −0.89
50–64 y	2005–2014	1.46[a]	0.38 to 2.56				1.46[a]	0.38 to 2.56
65–79 y	2005–2014	0.85	−0.36 to 2.08				0.85	−0.36 to 2.08
≥80 y	2005–2014	2.53[a]	1.36 to 3.72				2.53[a]	1.36 to 3.72
Age: female								
<35 y	2005–2014	−11.51[a]	−18.33 to −4.12				−11.51[a]	−18.33 to −4.12
35–49 y	2005–2014	−3.18	−6.82 to 0.60				−3.18	−6.82 to 0.60
50–64 y	2005–2014	1.52	−0.50 to 3.58				1.52	−0.50 to 3.58
65–79 y	2005–2014	0.97	−0.58 to 2.55				0.97	−0.58 to 2.55
≥80 y	2005–2007	−11.02	−29.67 to 12.57	2007–2014	3.65[a]	0.84 to 6.54	0.19	−4.03 to 4.60
Race/ethnicity: male								
Non-Hispanic white	2005–2014	2.13[a]	0.80 to 3.48				2.13[a]	0.80 to 3.48
Non-Hispanic black	2005–2014	−3.82[a]	−5.88 to −1.71				−3.82[a]	−5.88 to −1.71
Non-Hispanic API	2005–2014	−0.45	−1.21 to 0.31				−0.45	−1.21 to 0.31
Hispanic	2005–2014	2.07	−0.09 to 4.28				2.07	−0.09 to 4.28

Cancer. Author manuscript; available in PMC 2020 March 01.

		Trend 1			Trend 2		AAPC	
Group	**Years**	**APC**	**95% CI**	**Years**	**APC**	**95% CI**	**2005–2014**	**95% CI**
Race/ethnicity: female								
Non-Hispanic white	2005–2014	1.32	−0.82 to 3.50				1.32	−0.82 to 3.50
Non-Hispanic black	2005–2014	−0.49	−5.24 to 4.50				−0.49	−5.24 to 4.50
Non-Hispanic API	2005–2007	−12.28	−29.74 to 9.52	2007–2014	1.06	−1.58 to 3.77	−2.07	−5.98 to 2.00
Hispanic	2005–2014	1.58	−0.08 to 3.27				1.58	−0.08 to 3.27
US-born only								
Overall	2005–2014	2.72[a]	2.11 to 3.34				2.72[a]	2.11 to 3.34
Sex								
Male	2005–2014	2.69[a]	2.14 to 3.25				2.69[a]	2.14 to 3.25
Female	2005–2008	−1.19	−4.27 to 1.99	2008–2014	3.74[a]	2.73 to 4.75	2.07[a]	1.11 to 3.04
Age: male								
<35 y	2005–2014	−1.76	−5.33 to 1.95				−1.76	−5.33 to 1.95
35–49 y	2005–2014	−3.16[a]	−4.61 to −1.70				−3.16[a]	−4.61 to −1.70
50–64 y	2005–2012	5.66[a]	4.90 to 6.43	2012–2014	−0.52	−4.94 to 4.11	4.26[a]	3.34 to 5.18
65–79 y	2005–2014	2.53[a]	1.95 to 3.11				2.53[a]	1.95 to 3.11
≥80 y	2005–2014	1.52[a]	0.43 to 2.62				1.52[a]	0.43 to 2.62
Age: female								
<35 y	2005–2014	0.61	−1.68 to 2.96				0.61	−1.68 to 2.96
35–49 y	2005–2014	0.56	−1.47 to 2.62				0.56	−1.47 to 2.62
50–64y	2005–2008	1.43	−3.35 to 6.43	2008–2014	6.08[a]	4.67 to 7.51	4.50[a]	3.05 to 5.98
65–79 y	2005–2008	−0.50	−1.97 to 0.99	2008–2014	3.38[a]	2.91 to 3.85	2.07[a]	1.62 to 2.52
≥80 y	2005–2007	−7.04	−15.95 to 2.82	2007–2014	2.42[a]	1.12 to 3.75	0.24	−1.62 to 2.13
Race/ethnicity: male								
Non-Hispanic white	2005–2014	2.67[a]	2.11 to 3.23				2.67[a]	2.11 to 3.23
Non-Hispanic black	2005–2014	2.47[a]	1.79 to 3.16				2.47[a]	1.79 to 3.16
Non-Hispanic API	2005–2014	3.07	−0.42 to 6.68				3.07	−0.42 to 6.68

	Trend 1			Trend 2			AAPC	
Group	**Years**	**APC**	**95% CI**	**Years**	**APC**	**95% CI**	**2005–2014**	**95% CI**
Hispanic	2005–2014	1.51[a]	0.63 to 2.39				1.51[a]	0.63 to 2.39
Race/ethnicity: female								
Non-Hispanic white	2005–2008	−1.29	−4.82 to 2.37	2008–2014	3.66[a]	2.49 to 4.84	1.98[a]	0.88 to 3.10
Non-Hispanic black	2005–2007	−2.99	−13.28 to 8.52	2007–2014	3.92[a]	2.56 to 5.29	2.34[a]	0.26 to 4.47
Non-Hispanic API	2005–2014	2.65	−1.07 to 6.51				2.65	−1.07 to 6.51
Hispanic	2005–2009	−0.89	−3.99 to 2.30	2009–2014	2.81[a]	0.78 to 4.88	1.15	−0.23 to 2.54

Abbreviations: AAPC, average annual percent change; APC, annual percent change; API, Asian/Pacific Islander; CI, confidence interval. The liver cancer mortality rates include liver and intrahepatic bile duct cancers (C22). A maximum of 1 joinpoint was allowed.

[a]The APC or AAPC was significantly different from 0 at $\alpha = .05$.