Liver and Intrahepatic Bile Duct Cancer in Texas

Prepared by the Texas Cancer Registry
Texas Department of State Health Services

November 2018

Background

- Liver cancer incidence and mortality rates have been increasing in the US population over the past 10 years.
- Risk factors for liver cancer include chronic hepatitis B virus (HBV) or hepatitis C virus (HCV) infections, obesity, heavy alcohol use, cigarette smoking and diabetes.
- This statistical report describes incidence and mortality rates for liver cancer in Texas and replicates some of the analyses described in a recent publication on trends in liver cancer mortality in the United States.[1] This report also compares cancer rates and trends in Texas to the United States.

Implications for Public Health Practice:

- Efforts to identify and treat those living with HBV or HCV and to increase vaccination rates for HBV may reduce the burden of liver cancer.
- Strategies to decrease rates of obesity, heavy alcohol use, cigarette smoking, and diabetes may reduce the liver cancer burden.

[1] Xu, J. 2018. NCHS Data Brief, No.314.

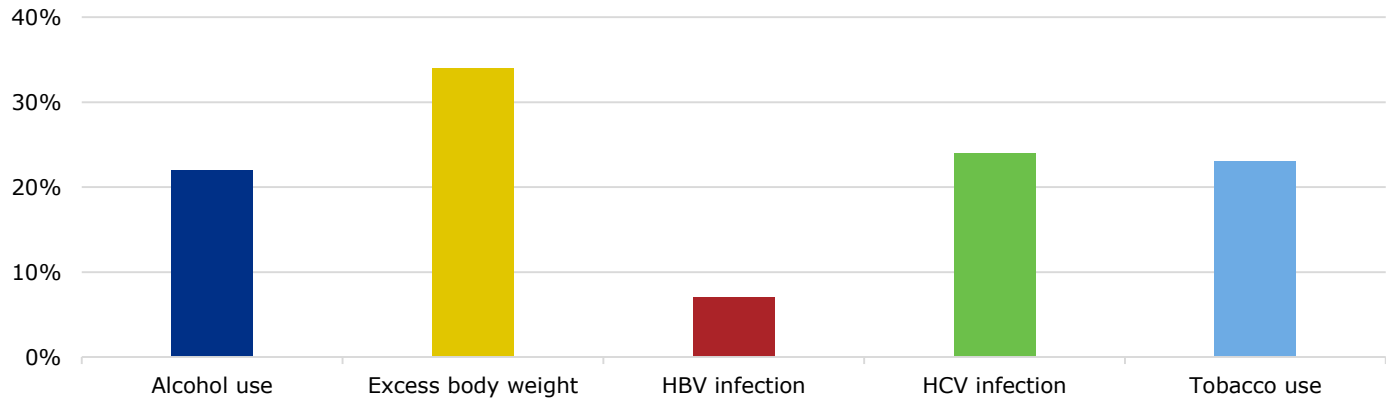
Liver Cancer Overview

- In 2018, an estimated 3,714 Texans will be diagnosed with liver cancer. It is the ninth most common cancer diagnosed in males in Texas.
- In 2018, an estimated 2,532 Texans will die from liver cancer. It is the sixth most common cause of cancer death in Texas (fourth for males, seventh for females).
- Liver cancer has low survival compared to other cancers.
  - 26% of Texans diagnosed with localized liver cancer survive for five years.
  - 11% of Texans diagnosed with regional liver cancer survive for five years.
  - 4% of Texans diagnosed with distant liver cancer survive for five years.

Liver Cancer Risk Factors

- Up to 63% of liver cancer cases are associated with potentially modifiable risk factors.
- Risk factors include hepatitis B (HBV) or hepatitis C (HCV) infection, liver cirrhosis, tobacco use, obesity, and diabetes.

Percent of Liver Cancer Cases Attributed to Select Risk Factors [1]



- Liver cirrhosis is caused by heavy alcohol use, non-alcoholic fatty liver disease (associated with obesity), and certain types of autoimmune disease or inherited metabolic conditions.

[1] Islami et al. 2018. CA Cancer J. Clin.

Hepatitis B and C Viruses

- 24% of liver cancer cases are attributed to HCV infection, and 7% are attributed to HBV infection.[1]
- In the US, hepatitis C virus (HCV) infection is more common than hepatitis B virus (HBV) infection, and is more common among males than females. HCV and HBV are spread via contaminated needles and unprotected sex. In the past, it was spread through blood transfusions and organ transplants because donated blood and organs weren't screened for these viruses.
- Liver cancer rates have been increasing since the 1980s, especially in people born between 1945-1965. This group had an elevated risk of acquiring a hepatitis infection before preventative measures, such as blood screening, were introduced.
- About 75% of the 3.5 million people in the US estimated to be infected with HCV are part of this age group, and fewer than half of those infected are aware of their infection. Therefore, testing for HCV is recommended for those born between 1945-1965.

[1] Islami et al. 2018. CA Cancer J. Clin.

Definitions and Abbreviations

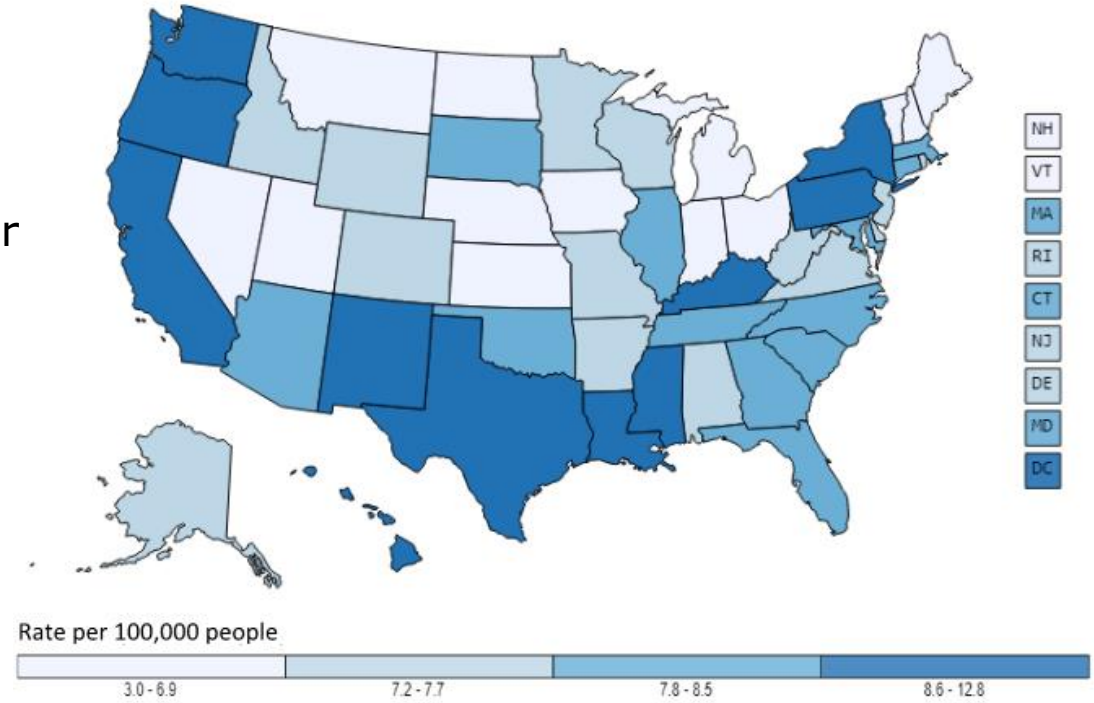
- **Age-adjusted incidence rate (incidence rate):** number of new cases diagnosed per 100,000 people per year. Numbers are age-adjusted to allow for comparison between populations with different age compositions.
- **Age-adjusted mortality rate (mortality rate):** number of deaths per 100,000 people where the cause of death was recorded as liver or intrahepatic bile duct cancer. Numbers are age-adjusted to allow for comparison between populations with different age compositions.
- **Annual percent change (APC):** measures the trend over time, such as how quickly (or slowly) a cancer incidence rate has increased or decreased over a given time period. For example, an APC of 2.0% over 10 years means that there was a 2% increase in incidence rate per year. APCs were calculated using Joinpoint which fits a least squares regression line to the natural logarithm of the age-adjusted rates. The slope is tested for a significant difference from 0. For instances where the APC changed over the 15-year time frame, separate APCs were reported for each time period, and an average APC over 15-years was calculated to allow for comparison.
- **Racial/ethnic group acronyms:** Non-Hispanic (NH), Asian/Pacific Islander (A/PI)

Liver Cancer Incidence in Texas, 2001-2015

Incidence Rate Trends by Sex, Age, Race/Ethnicity, and County

Liver Cancer Incidence Rates, 2015

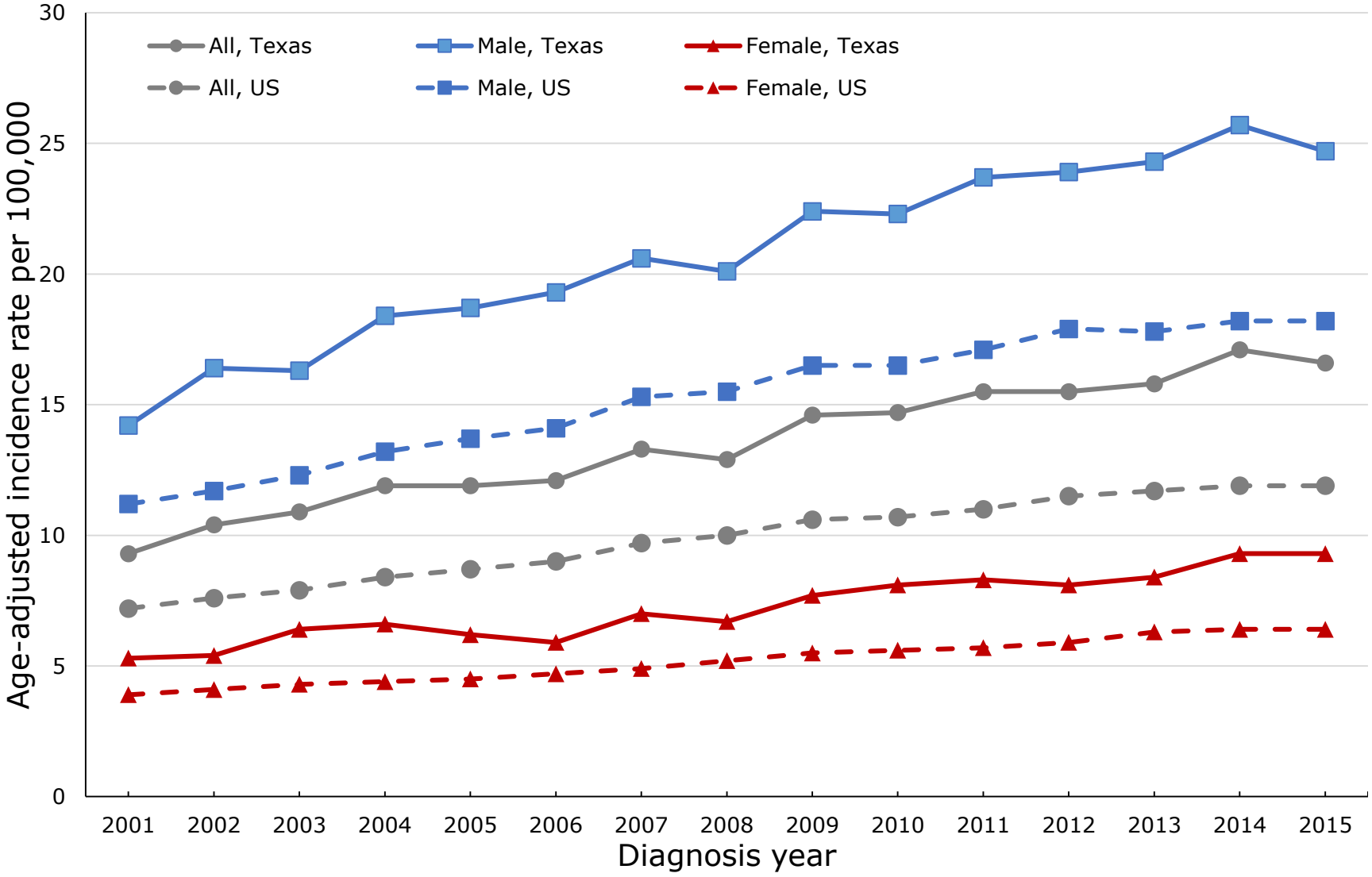
- In 2015, Texas had the highest liver cancer incidence rate of all US states,* with 11.6 cases per 100,000 people of all ages.†
- The incidence rate for the entire US was 8.3 cases per 100,000 people.



Rank	State	Incidence Rate per 100,000	Case Count	Population
1	Texas	11.6	3,329	27,429,639
2	New Mexico	11.0	286	2,080,328
3	Hawaii	10.8	205	1,425,157
4	Louisiana	10.1	584	4,668,960
5	California	9.7	4,268	38,993,940

* The District of Columbia's incidence rate (12.8) was higher than any US state's.
† Rate includes cases identified from death certificates.
Image source: https://gis.cdc.gov/Cancer/USCS/DataViz.html

Liver Cancer Incidence Rate Trends by Sex



Liver Cancer Incidence Rate Trends by Sex

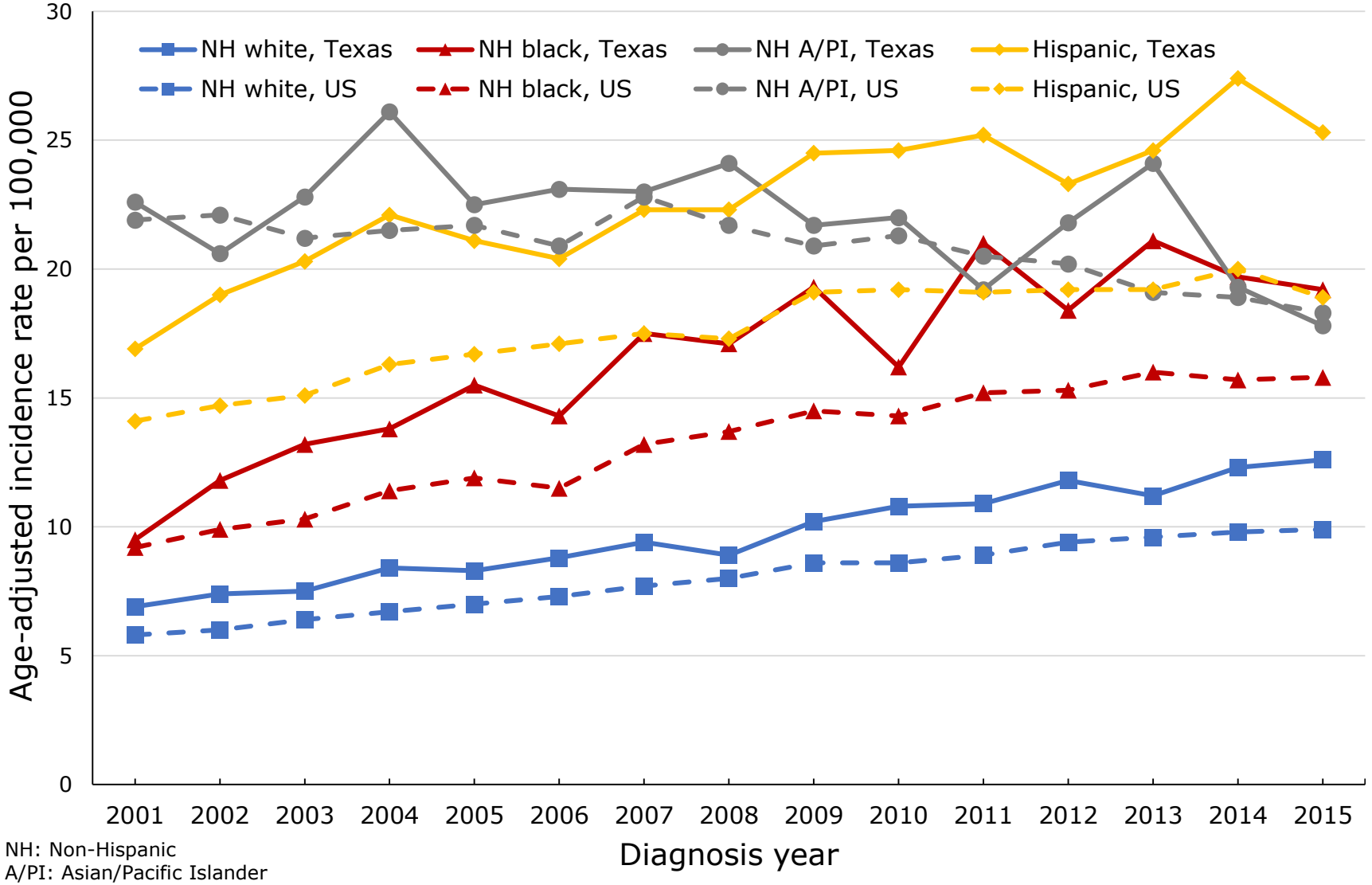
- In Texas, the overall incidence rate of liver cancer in adults ages 25 years and over significantly increased by an average of 3.9% per year from 9.3 cases per 100,000 in 2001 to 16.6 cases per 100,000 in 2015. During the same time period, the overall US rate increased by an average of 3.8% per year.

- In Texas males, liver cancer incidence rates significantly increased by 5.0% per year from 2001 to 2009, then by 2.1% per year from 2009-2015, with an average increase of 3.8% per year. The US rate increased by 4.9% per year until 2009, then by 1.9% per year.

- In Texas females, liver cancer incidence rates significantly increased by 3.9% per year. During the same time period, the overall US rate increased by 3.8% per year.

- Incidence rates were more than two times higher for males than females, and rates were higher in Texas than in the overall US population from 2001-2015.

Liver Cancer Incidence Rate Trends by Race/Ethnicity

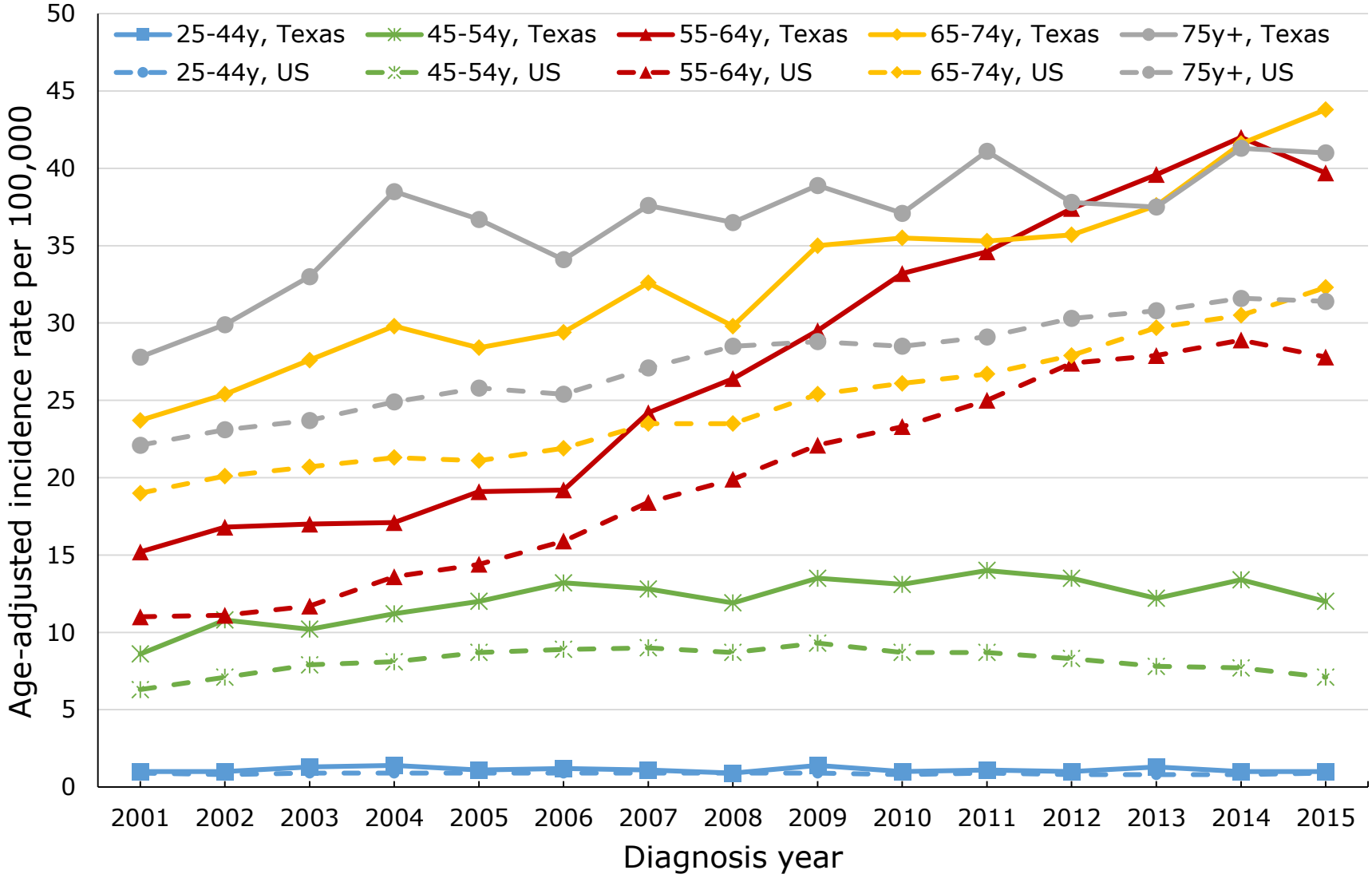


NH: Non-Hispanic
A/PI: Asian/Pacific Islander

Liver Cancer Incidence Rate Trends by Race/Ethnicity

- In Texas, between 2001 and 2008 the liver cancer incidence rate in adults ages 25 years and over was highest for non-Hispanic (NH) Asian/Pacific Islanders (A/PI).
- From 2009 onwards, the incidence rate was highest in Hispanics.
- Across all years, the liver cancer incidence rate was lowest in NH whites.
- Between 2001-2015, liver cancer incidence rates significantly increased by 2.5% per year in Hispanics, 4.3% per year in NH whites, and 4.1% per year in NH blacks.
- Rates showed a significant decline in NH A/PI of 1.4% per year.
- The incidence rates by race/ethnicity for the overall US showed similar trends.

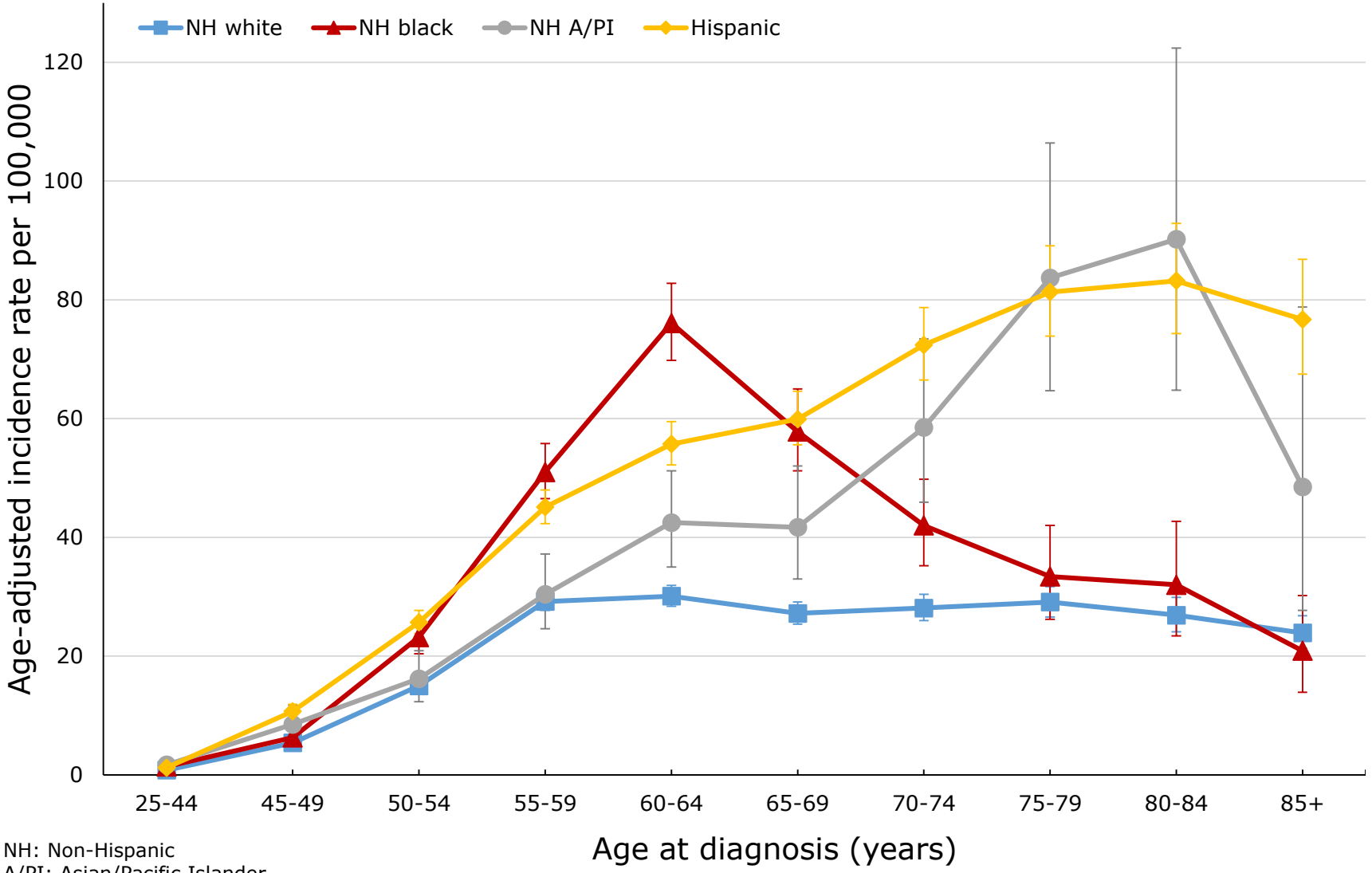
Liver Cancer Incidence Rate Trends by Age at Diagnosis



Liver Cancer Incidence Rate Trends by Age at Diagnosis

- For ages 25-44 years in Texas, rates remained stable from 2001-2015 (non-significant annual percent change [APC] of -0.6%).
- For ages 45-54 years in Texas, rates significantly increased from 2001-2006 by 7.2% per year, followed by a non-significant decrease of 0.1% per year from 2009-2015.
- For ages 55-64 years in Texas, rates significantly increased by 9.4% from 2001-2013, and then remained stable from 2013-2015 (non-significant decrease of 1%).
- For ages 65-74 years in Texas, rates significantly increased by 3.9% per year.
- For ages 75 years and over, rates significantly increased by 9.3% from 2001-2004, and by 1% from 2004-2015.
- Trends were similar for the overall US population, but a smaller average increase was seen for ages 45-54 years (1%), 55-64 years (7.4%), and 65-74 years (3.6%).

Liver Cancer Incidence Rates in Texas by Age and Race/Ethnicity, 2011-2015

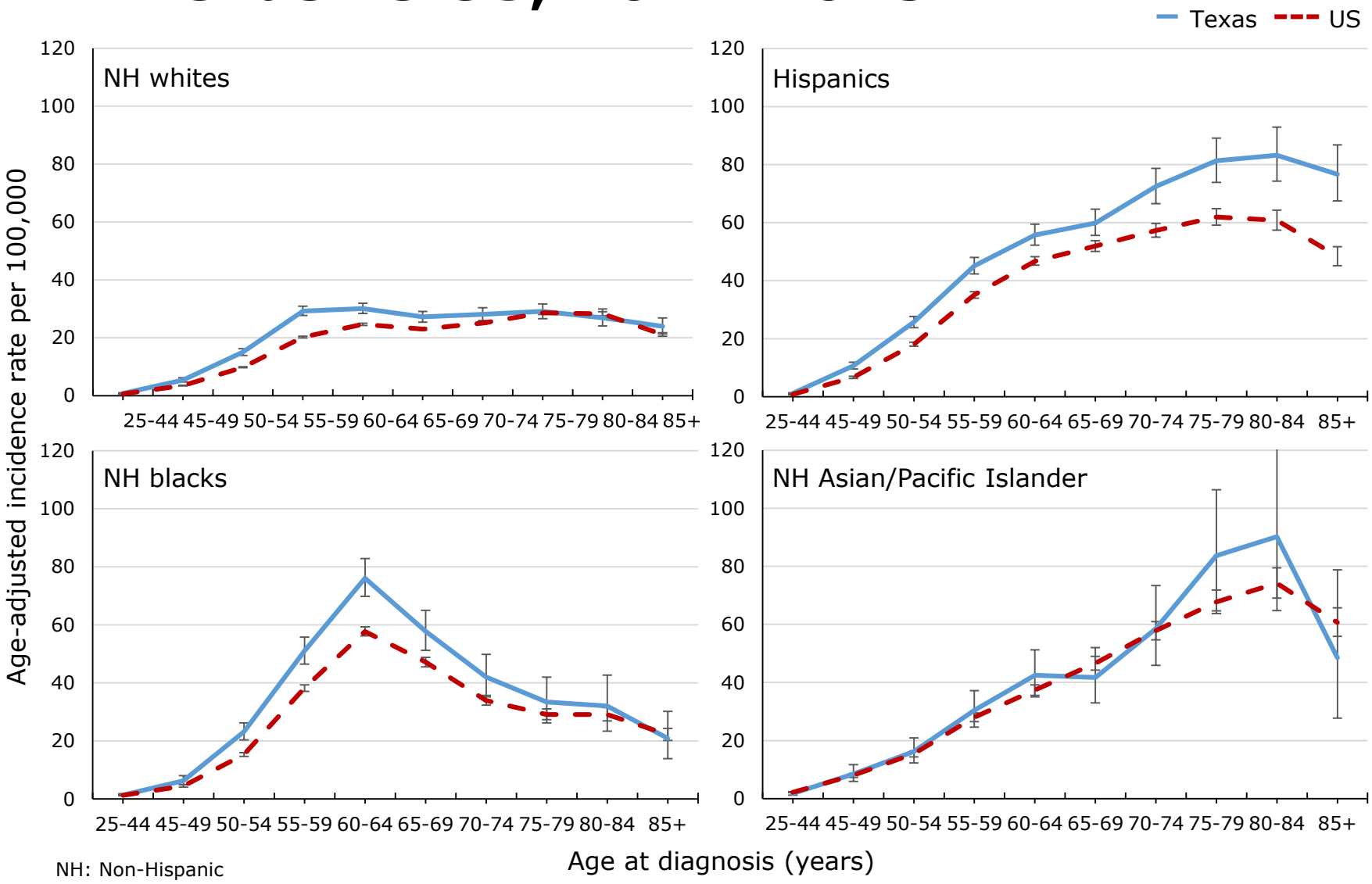


NH: Non-Hispanic
A/PI: Asian/Pacific Islander

Liver Cancer Incidence Rates in Texas by Age and Race/Ethnicity, 2011-2015

- In non-Hispanic (NH) whites, liver cancer rates increased until age 60-64 years, then stabilized.
- In NH blacks, liver cancer rates increased until age 60-64 years, then declined.
- In Hispanics, liver cancer rates increased until age 80-84 years.
- In NH Asian/Pacific Islanders (A/PI), liver cancer rates increased until age 80-84 years, but confidence intervals were large (indicating less stability in the estimate).
- For ages 50-69 years, liver cancer rates were highest for Hispanics and NH blacks, with NH blacks having the highest rate for ages 55-64 years.
- For ages 70-74 years and 85 years and older, rates were highest for Hispanics, while for ages 75-84 years rates were similarly high for Hispanics and NH A/PI.

Liver Cancer Incidence Rates in Texas vs US, 2011-2015



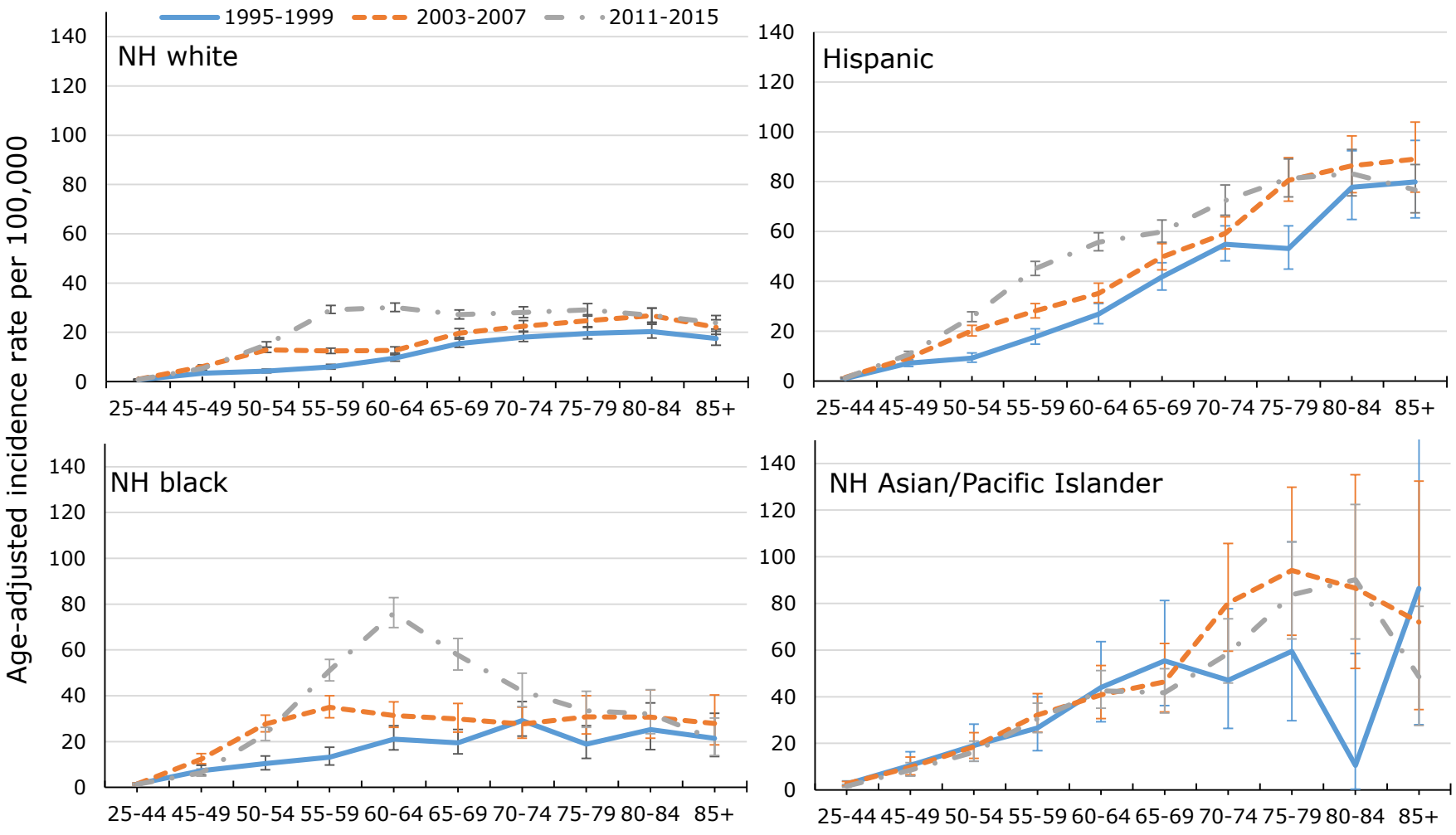
NH: Non-Hispanic

Liver Cancer Incidence Rates in Texas vs US, 2011-2015

- Incidence rates of liver cancer tended to be higher in Texas than in the overall US population, but patterns varied by age and race/ethnicity.

- Higher rates of liver cancer in Texas compared to the overall US may be due to higher rates of risk factors and/or differences in the age/race/ethnicity structure of the population.

Liver Cancer Incidence Rates in Texas by Race/Ethnicity for Year Intervals

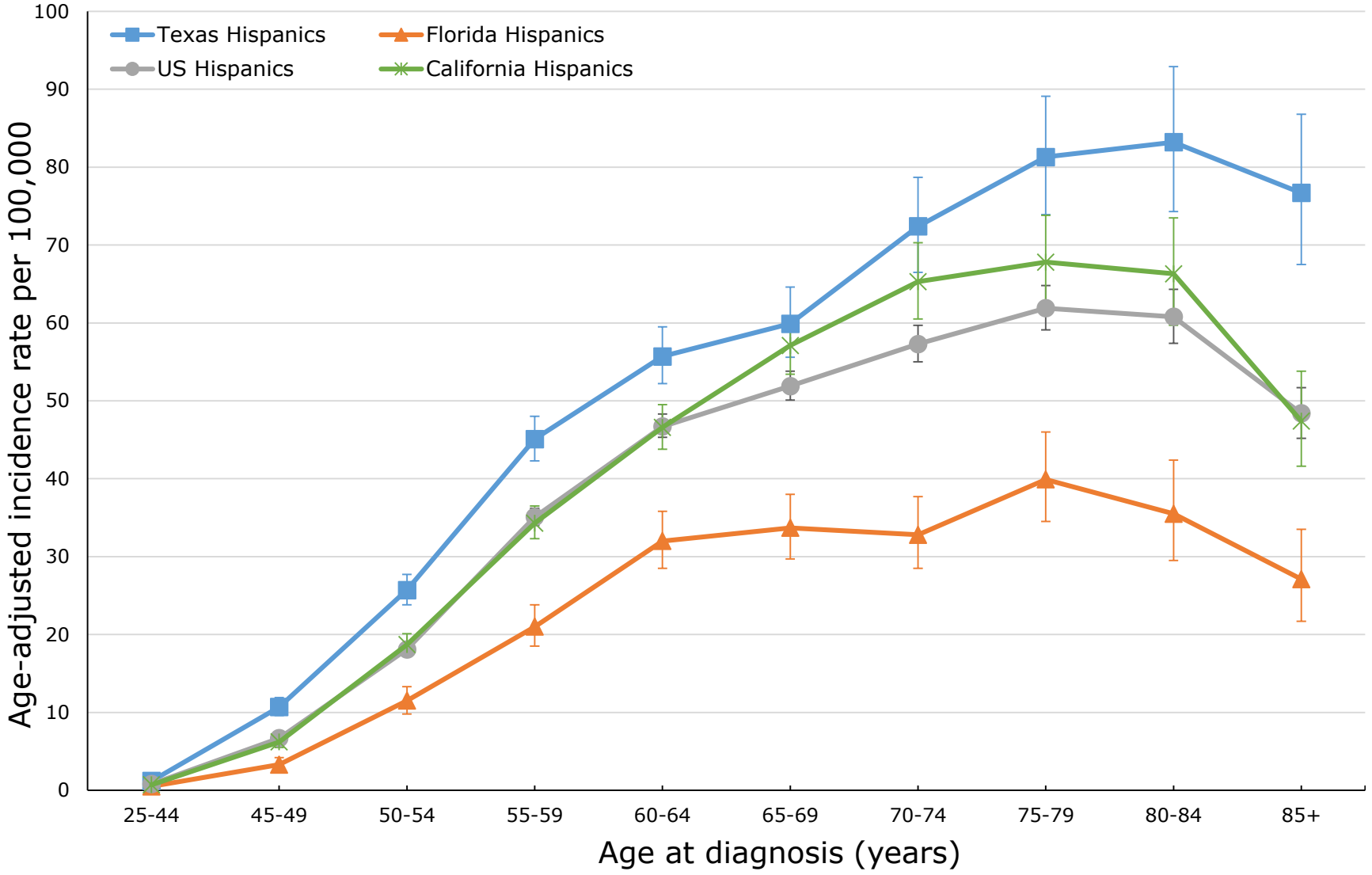


NH: Non-Hispanic

Liver Cancer Incidence Rates in Texas by Race/Ethnicity for Year Intervals

- When compared among three 5-year cohorts representing the early (1995-1999), middle (2003-2007), and late (2011-2015) time periods of available data, liver cancer incidence rates were generally higher for the most recent time period across most ages, but trends varied by race/ethnicity.
- The largest percentage increase between 1995-1999 and 2011-2015 in non-Hispanic (NH) whites, NH blacks, and Hispanics was for ages 50-64 years.
- For NH blacks there was a sharp increase in incidence rates for ages 60-69 years during 2011-2015.

Liver Cancer Incidence Rates in Hispanics, 2011-2015



Liver Cancer Incidence Rates in Hispanics, 2011-2015

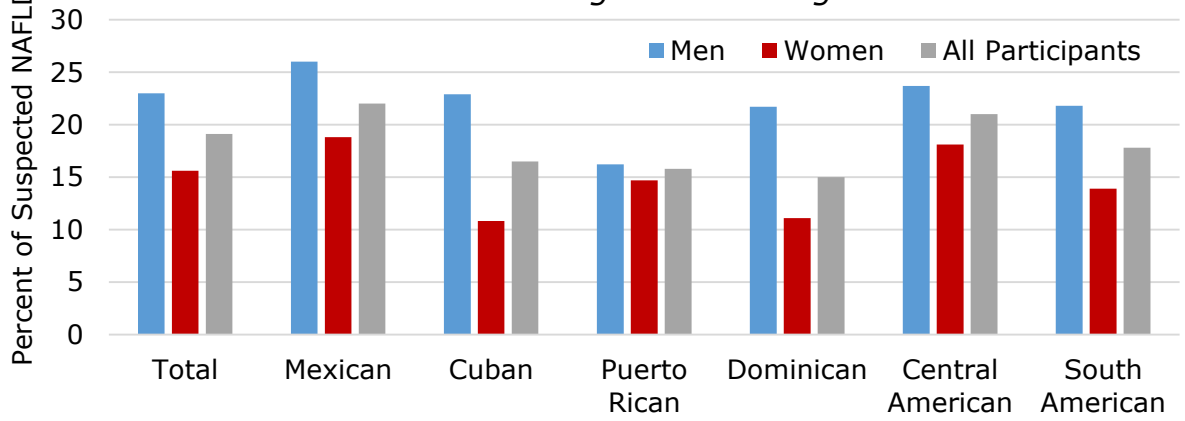
- The incidence rate of liver cancer is particularly high among Hispanics, which likely contributes to the overall high rate in Texas compared to the US average.
- Rates are also higher in Texas Hispanics compared to Hispanics in the overall US, Florida, and California.
- One reason could be differences in Hispanic ethnicity and nativity between states. Texas Hispanics are predominantly of Mexican origin (87%), and 71% are US-born. By comparison, 14% of Florida Hispanics and 83% of Californian Hispanics are of Mexican origin, with 53% and 64% US-born respectively. In the overall US population, 63% of Hispanics are of Mexican origin, and 65% of are US-born.
- Cancer rates are known to differ among Hispanic subgroups and between those who were US-born vs foreign-born. Mexican Americans have higher liver cancer mortality rates compared to other Hispanic subgroups in the US, although rates in Puerto-Rican Hispanics are also high.[1,2] Liver cancer incidence and mortality rates are higher in US-born Hispanic males than in foreign-born Hispanic males.[1,3]

[1] Pinheiro, et al. 2017. BMC Cancer,17:478.
[2] Pinheiro, et al. 2017. Cancer Epidemiol. Biomarkers Prev.,26:376-382.
[3] Setiawan, et al. 2016. Cancer, 122:1444-1452.

Non-Alcoholic Fatty Liver Disease and Hepatitis C Virus in Hispanics

- The higher prevalence of non-alcoholic fatty liver disease (NAFLD) in Mexican Americans, particularly among males that were US-born, compared to other Hispanic subgroups has been suggested as one possible explanation for the high rate of liver cancer in Texas Hispanics.[1-3] Both genetic and demographic/behavioral risk factors are likely to contribute to this increased risk.

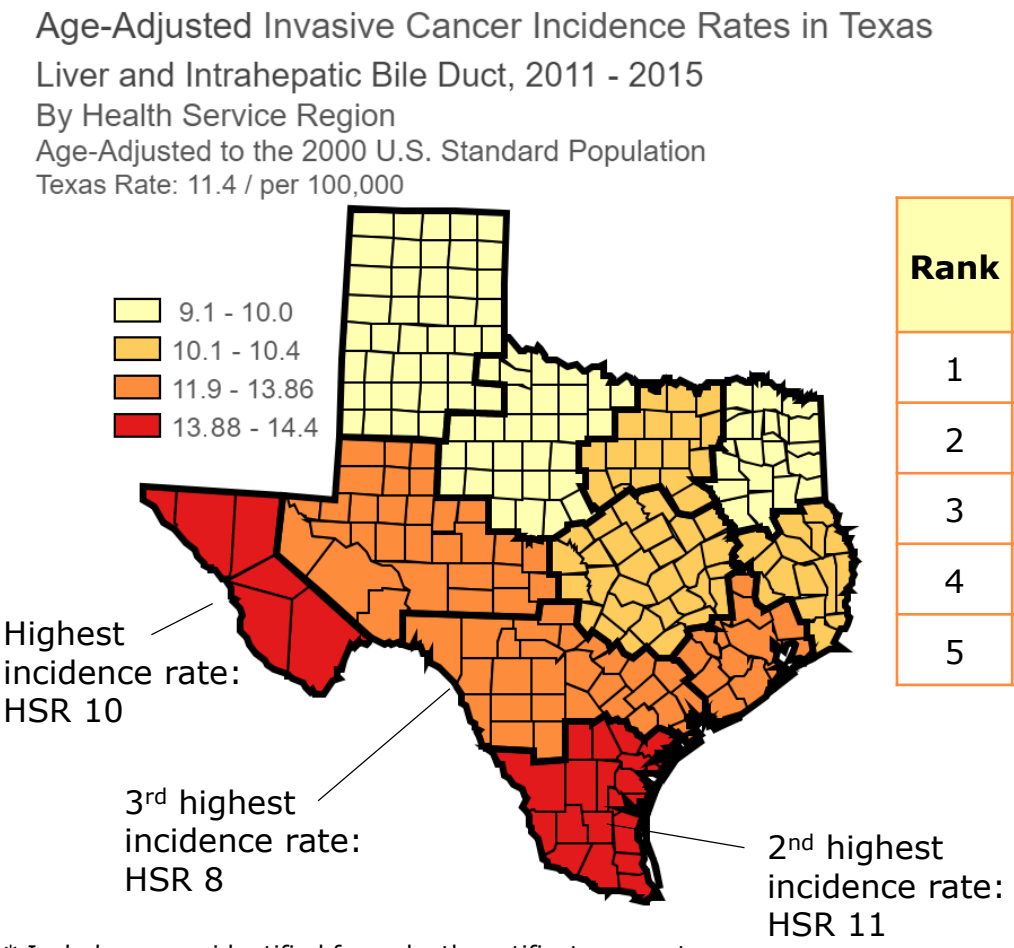
Age-Standardized Prevalence of NAFLD by Hispanic Ethnicity after Excluding Other Etiologies.[4]



- Different rates of hepatitis C virus (HCV) infection between Hispanic subgroups may also contribute to the variation in liver cancer rates between states. The overall prevalence rate of HCV in Texas Hispanics was recently estimated to be similar to that in California Hispanics.[5] However, another study on US Hispanics found that the HCV prevalence rate in Mexican Americans was lower than that in Puerto Ricans in the US mainland, but higher than that in Central American, Cuban, and South American Hispanics.[6]

[1] Setiawan, et al. 2016. Cancer, 122:1444-1452.
[2] Islami, et al. 2017. CA Cancer J Clin. 67:273-289.
[3] Kallwitz, et al. 2015. Clin. Gastroenterol. Hepatol. 13:569-576.
[4] Adapted from Kallwitz, et al. 2015. Clin. Gastroenterol. Hepatol. 13:569-576.
[5] Hall, et al. 2018. BMC Infect. Dis. 18:224.
[6] Kuniholm, et al. 2014. J. Infect. Dis. 209:1585-1590.

Liver Cancer Incidence Rates* by Health Service Region (all ages), 2011-2015



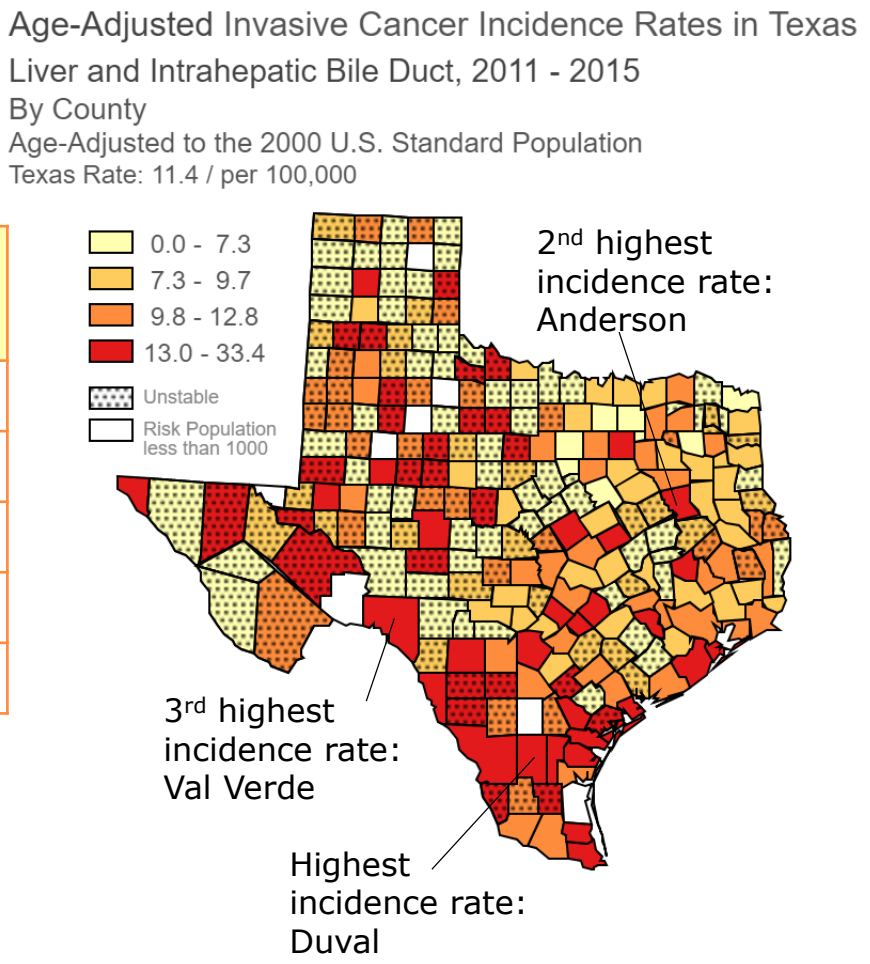
Rank	Health Service Region	Incidence Rate per 100,000	Cases	Population
1	HSR 10	14.4	586	4,271,558
2	HSR 11	13.88	1416	10,943,969
3	HSR 08	13.86	2048	13,794,458
4	HSR 06	12.0	3791	32,537,709
5	HSR 09	11.9	385	3,049,451

* Includes cases identified from death certificates or autopsy

Image from TCR Web Query Tool: https://www.cancer-rates.info/tx/

Liver Cancer Incidence Rates* by County (all ages), 2011-2015

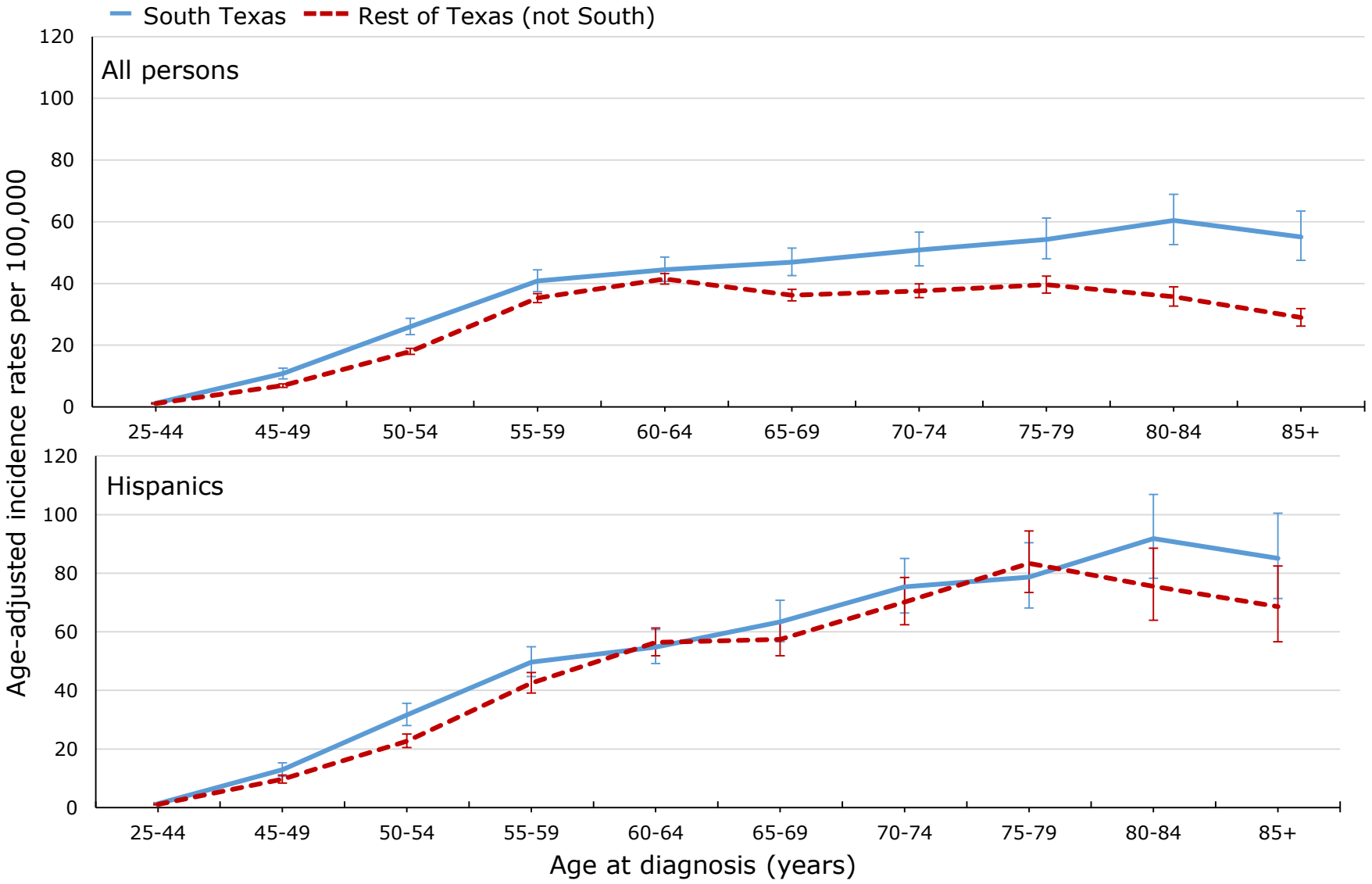
Rank	County	Incidence Rate per 100,000	Cases	Population
1	Duval	29.4	20	57,918
2	Anderson	28.1	100	289,475
3	Val Verde	20.2	51	244,376
4	Maverick	18.9	49	281,740
5	Jim Wells	18.5	43	207,499



* Includes cases identified from death certificates or autopsy

Image from TCR Web Query Tool: https://www.cancer-rates.info/tx/

Liver Cancer Incidence in South Texas, 2011-2015



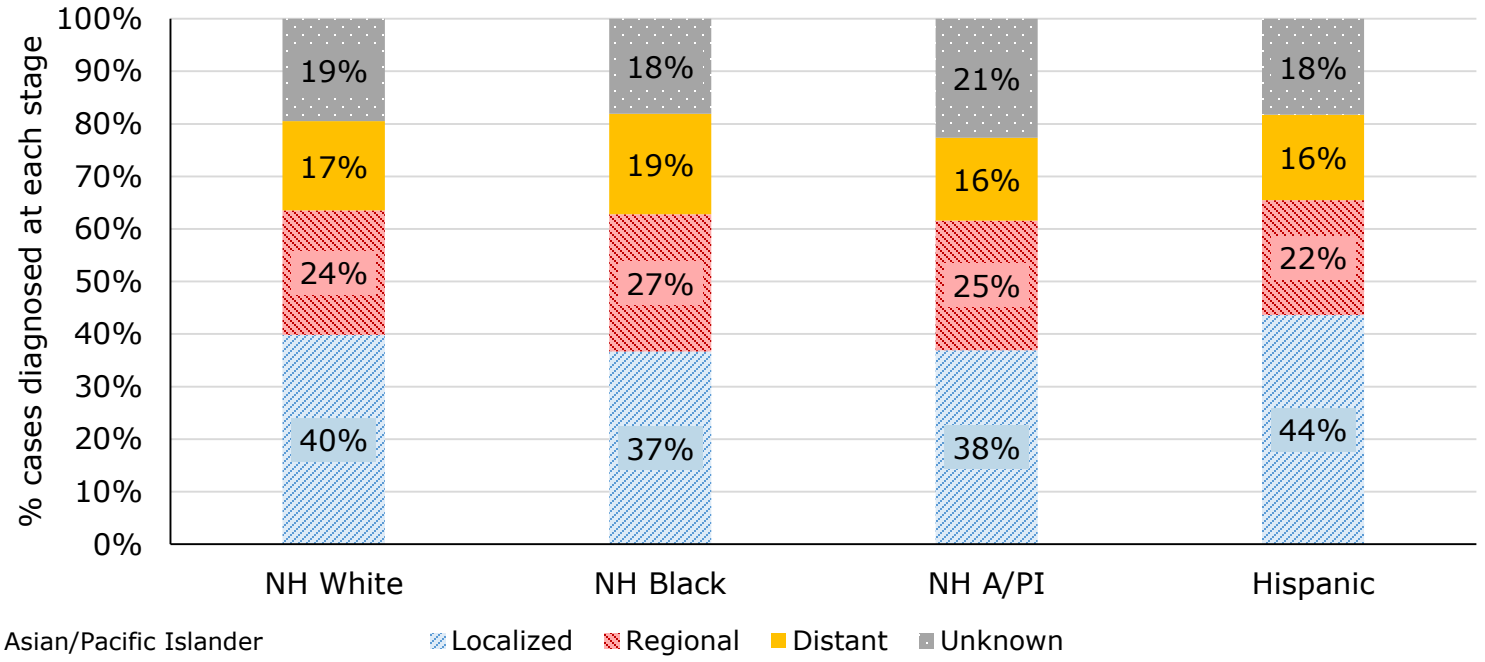
Liver Cancer Incidence in South Texas, 2011-2015

- The liver cancer incidence rate was significantly higher in South Texas than in the rest of Texas for most ages.
- For Hispanics, liver cancer incidence rates in South Texas were significantly higher than in the rest of Texas for ages 45-49, 50-54, 55-59 years (and overall). Rates also tended to be higher in South Texas for older age classes but not significantly so.
- This disparity in liver cancer incidence rates has been reported previously, and may be linked to the notably higher rates of obesity and diabetes (linked to non-alcoholic liver disease) in South Texas.[1,2] Some other cancer sites linked to overweight and obesity, including kidney, gallbladder, and endometrial cancers, also have higher incidence rates in South Texas[2].
- South Texas is also often considered to have higher HCV infection rates[3]. However, a recent estimate suggested the HCV infection rate in South Texas Mexican Americans may be comparable to that in the overall US Mexican-American population, although cases are more often undiagnosed[4].

[1] Ramirez, et al. 2014. PLOS One, 9:e99365
[2] South Texas Health Status Review
[3] Yalamanchili, et al. 2005. BUMC Proceedings, 18:3-6.
[4] Watt, et al. 2016. Epidemiol. Infect. 144:297-305.

Liver Cancer Incidence by Stage and Race/Ethnicity, 2011-2015

- During 2011-2015, 41% of liver cancer cases were diagnosed at the localized stage, 24% at the regional stage, and 17% at the distant stage. 18% were of unknown stage.
- The proportion of liver cancer tumors that were diagnosed at the localized stage was highest in Hispanics, and lowest in non-Hispanic (NH) blacks.
- The proportion of liver cancer tumors that were diagnosed at the regional or distant stage was highest in NH blacks, and lowest in Hispanics.

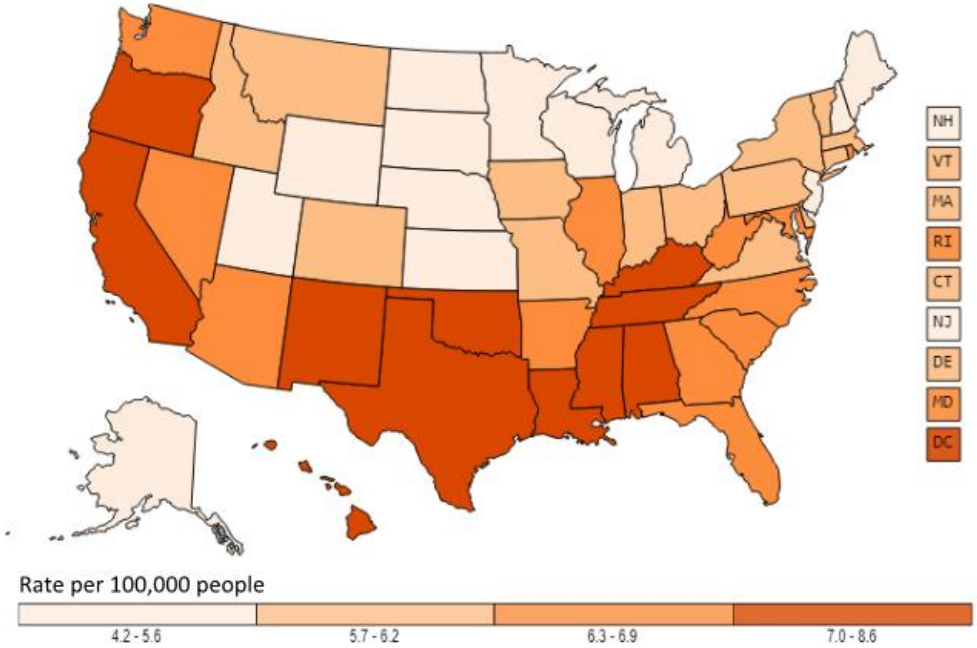


A/PI: Asian/Pacific Islander

Liver Cancer Mortality in Texas, 2001-2015

Mortality Rate Trends by Sex, Age, Race/Ethnicity, and County

Liver Cancer Mortality Rate, 2015

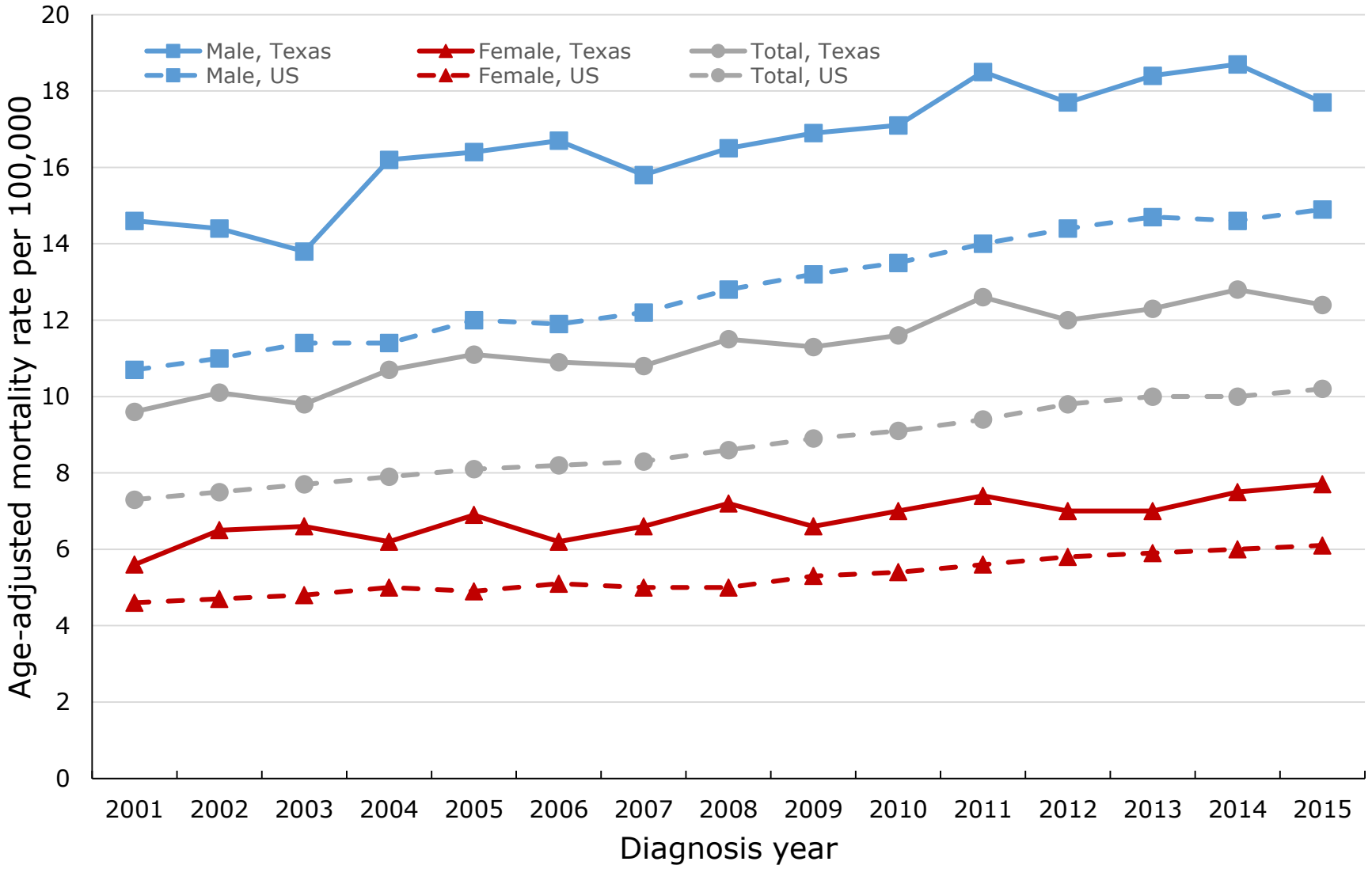


- In 2015, Texas had the fourth highest liver cancer mortality rate of all US states*, with 8.1 deaths per 100,000 people of all ages.†
- The mortality rate for the entire US was 6.6 deaths per 100,000 people.

Rank	State	Mortality Rate per 100,000	Death Count	Population
1	New Mexico	8.6	221	2,080,328
2	Louisiana	8.4	476	4,668,960
3	Hawaii	8.2	150	1,425,157
4	Texas	8.1	2,247	27,429,639
5	Mississippi	8.0	285	2,989,390

* The District of Columbia's incidence rate (8.6) was higher than any US state's except New Mexico.
† Rate includes cases identified from death certificates.
Image source: https://gis.cdc.gov/Cancer/USCS/DataViz.html

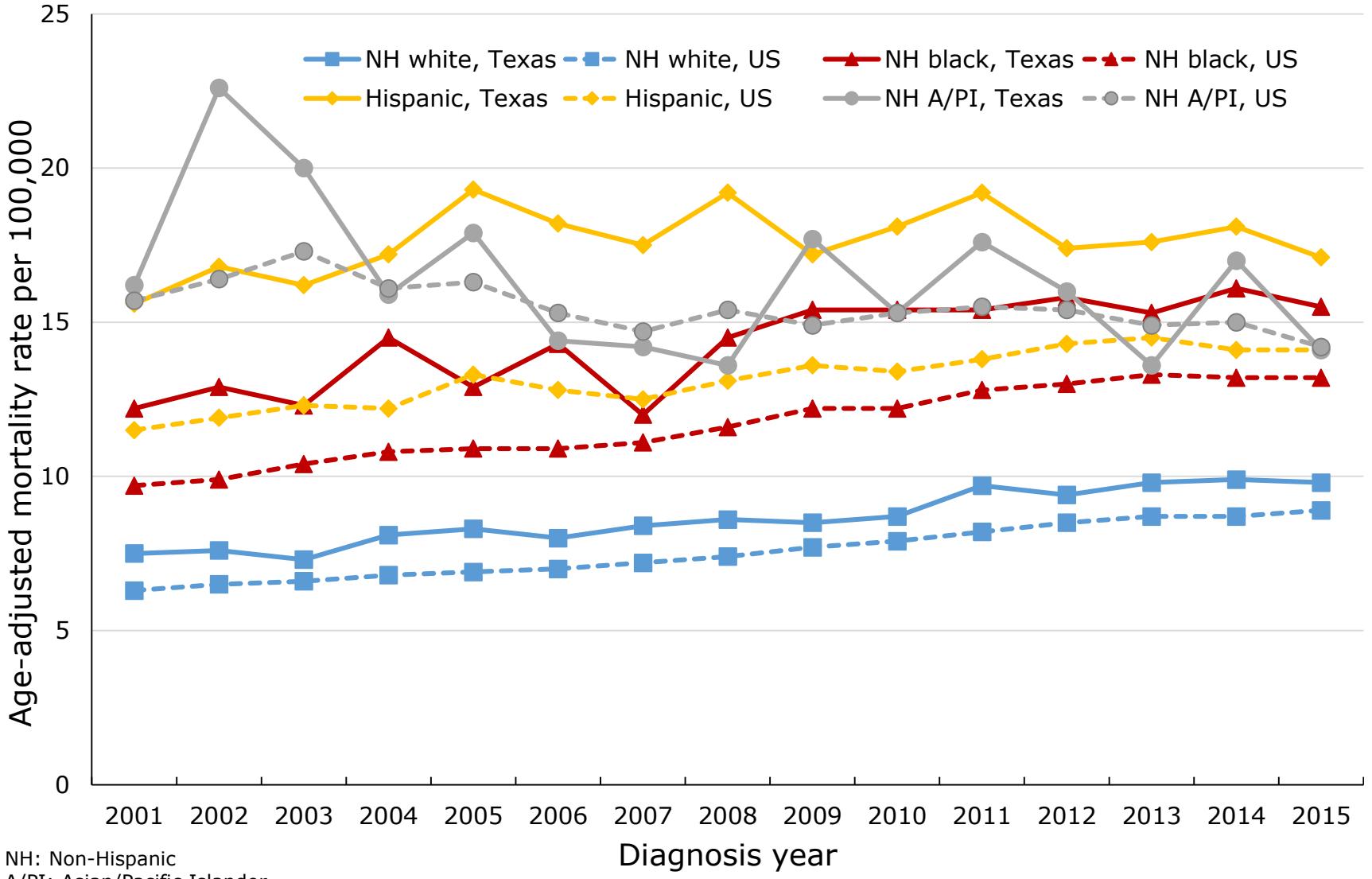
Liver Cancer Mortality Rate Trends by Sex



Liver Cancer Mortality Rate Trends by Sex

- The liver cancer mortality rate in Texas adults 25 years and older increased by 1.9% per year from 9.6 deaths per 100,000 in 2001 to 12.4 deaths per 100,000 in 2015 (a 29% increase over 15 years).
- In Texas, liver cancer mortality rates increased by 1.8% per year in males, and 1.5% per year in females. The overall US rate increased by 2.4% per year in males and 1.8% per year in females.
- In Texas, the liver cancer mortality rate in males ages 25 years and older was more than twice the rate in females.
- Liver cancer mortality rates were higher in Texas than the overall US population.

Liver Cancer Mortality Rate Trends by Race/Ethnicity

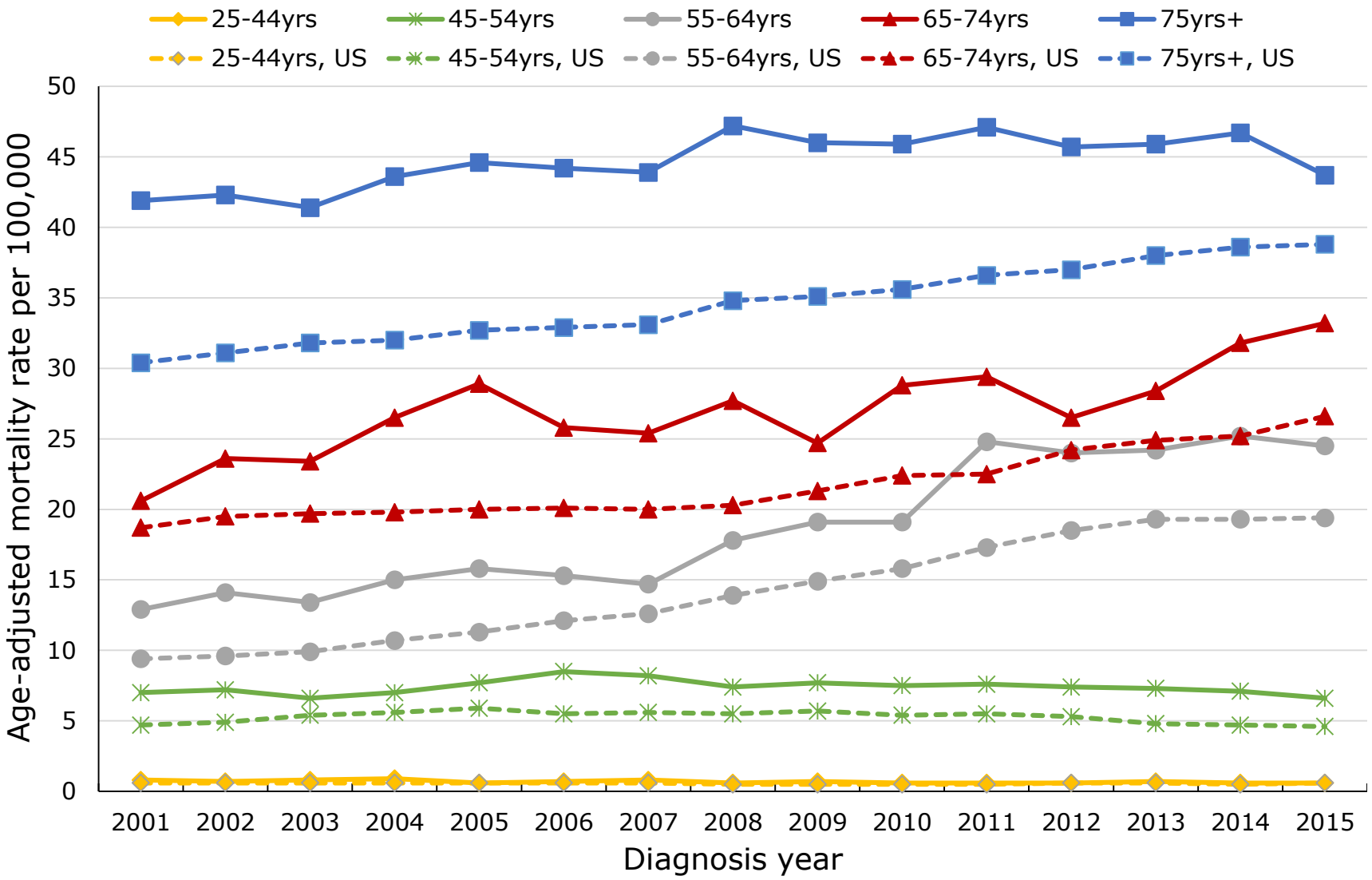


NH: Non-Hispanic
A/PI: Asian/Pacific Islander

Liver Cancer Mortality Rate Trends by Race/Ethnicity

- In Texas, during 2001-2003, liver cancer mortality rates in adults 25 years and older were highest for non-Hispanic (NH) Asian/Pacific Islander (A/PI), but from 2004 onwards, rates tended to be highest for Hispanics.
- NH whites had the lowest liver cancer mortality rate across all years.
- Liver cancer mortality rates significantly increased in NH whites (2.2% per year) and NH blacks (1.8% per year), but significantly decreased in NH A/PI (-1.5% per year). Rates remained stable in Hispanics (0.9% increase per year).
- The overall US rate increased by 2.4% per year in NH whites, 2.2% per year in NH blacks, and 1.5% per year in Hispanics, and decreased by 0.8% per year in NH A/PI.
- Liver cancer mortality rates were higher in Texas than in the overall US population for Hispanics, NH blacks, and NH whites. Rates in NH A/PI were variable with large confidence intervals but tended to be higher in Texas than in the overall US population.

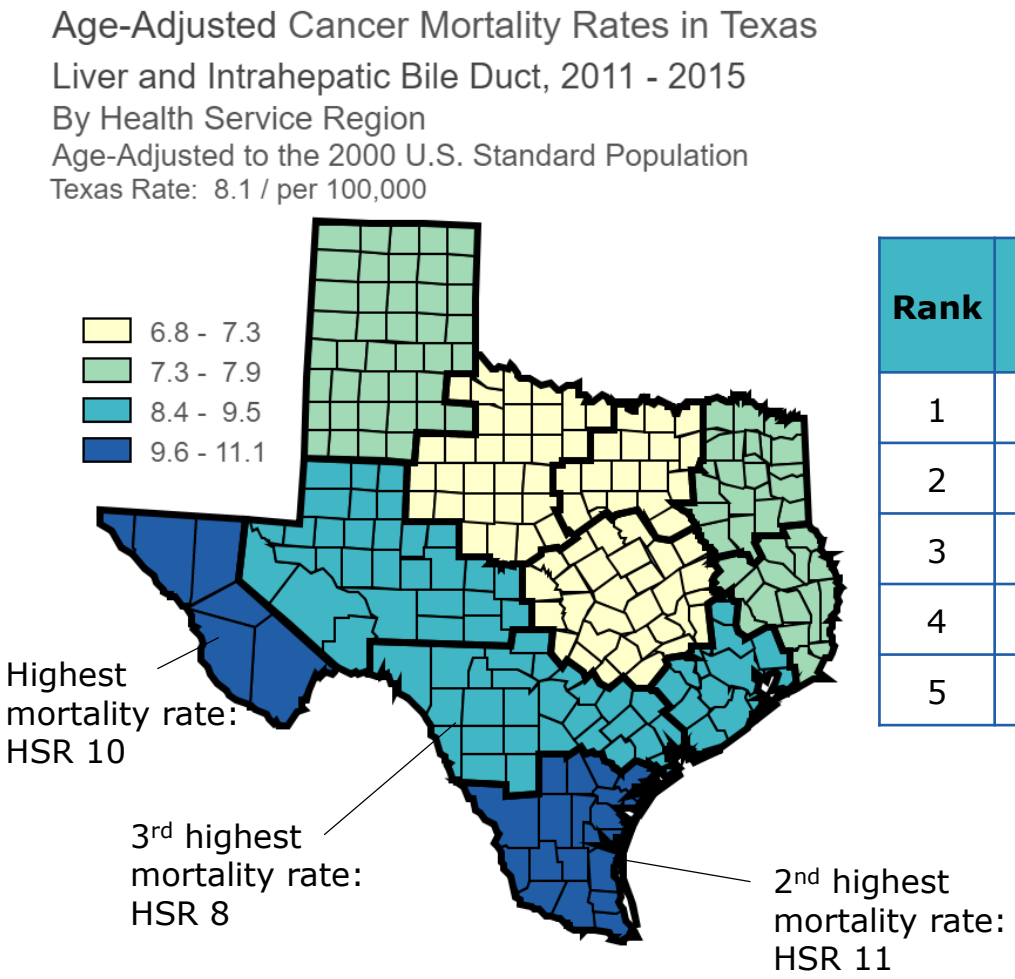
Liver Cancer Mortality Rate Trends by Age



Liver Cancer Mortality Rate Trends by Age

- For Texas adults 25-44 years of age, liver cancer mortality rates significantly declined by 2.2% per year from 2001-2015.
- For adults 45-54 years of age, mortality rates showed a non-significant tendency to decrease (-0.3% per year).
- Rates significantly increased from 2001-2015 by an average of 4.5% per year for ages 55-64 years, and 2.3% per year for ages 65-74 years.
- For ages 75 years and older there was a non-significant tendency to increase (0.5% per year).
- Liver cancer mortality rates were higher in Texas than in the overall US population for each age category.

Liver Cancer Mortality Rates by Health Service Region (all ages), 2011-2015



Rank	Health Service Region	Mortality Rate per 100,000	Deaths	Population
1	HSR 10	11.1	439	4,271,558
2	HSR 11	9.6	961	10,943,969
3	HSR 08	9.5	1382	13,794,458
4	HSR 09	8.8	276	3,049,451
5	HSR 06	8.4	2491	32,537,709

Image from TCR Web Query Tool: https://www.cancer-rates.info/tx/

Liver Cancer Mortality Rates by County (all ages), 2011-2015

Rank	County	Mortality Rate per 100,000	Deaths	Population
1	Anderson	32.5	115	289,475
2	Maverick	17.3	42	281,740
3	Jim Wells	16.4	38	207,499
4	San Patricio	15.2	56	330,341
5	Bee	13.2	21	163,096

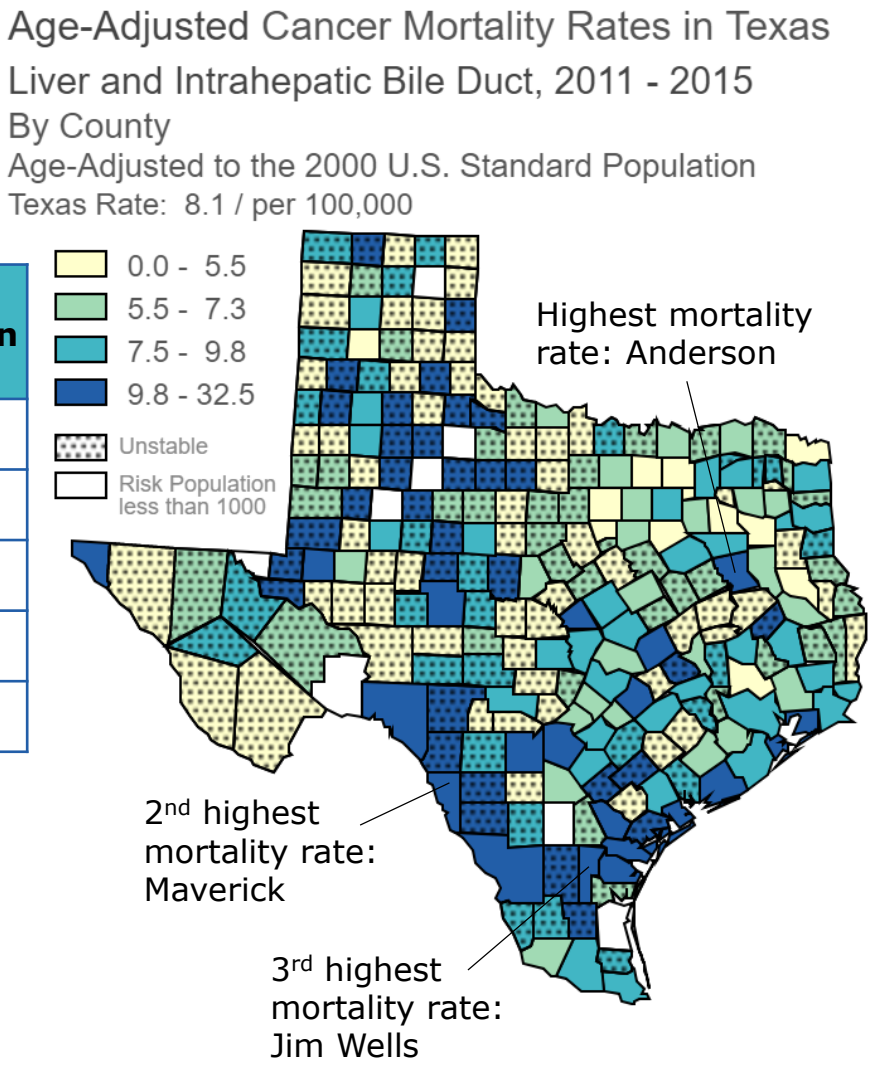


Image from TCR Web Query Tool: https://www.cancer-rates.info/tx/

Summary: Liver Cancer Incidence in Texas

- Texas was the state with the highest liver cancer incidence rate in 2015.
- Incidence rates increased significantly from 2001-2015, by an average of 3.8% per year in males and 3.9% per year in females.
- Incidence rates were twice as high in males than females.
- In 2015, liver cancer incidence rates were highest for Hispanics and lowest for non-Hispanic (NH) whites. From 2001-2015, rates increased in Hispanics, NH whites, and NH blacks but decreased in NH Asian/Pacific Islanders (A/PI).
- Liver cancer incidence rates increased significantly from 2001-2015 for all age groups over 44 years. The largest percentage increase from 2001-2015 was for ages 55-64 years (average annual percentage increase, 7.8%).
- Rates were higher in South Texas and the US/Mexico border regions.

Summary: Liver Cancer Mortality in Texas

- Texas had the 4th highest liver cancer mortality rate out of all states in 2015.
- Liver cancer mortality rates increased significantly from 2001-2015, by 1.8% per year in males, and 1.5% per year in females.
- Mortality rates were more than 2 times higher in males than females.
- In 2015, liver cancer mortality rate was highest for Hispanics and lowest for NH whites. From 2001-2015, liver cancer mortality rates increased for NH whites and NH blacks, decreased for NH A/PI, and remained stable for Hispanics.
- Liver cancer mortality rates increased significantly for age groups 55-64 years and 65-74 year. The largest percentage increase was for ages 55-64 years (4.5% per year).
- Rates were higher in South Texas and the US/Mexico border regions.

Technical Details: Data Sources

- *Texas incidence data*: Texas Cancer Registry SEER*Stat Database, 1995-2015 Incidence, created December 2017, based on NPCR-CSS Submission, cut-off 11/13/17.

- *Texas mortality data*: Texas Cancer Registry SEER*Stat Database, 1990-2015 Mortality, created January 2018.

- *US incidence data*: National Program of Cancer Registries and Surveillance, Epidemiology, and End Results SEER*Stat Database: NPCR and SEER Incidence – U.S. Cancer Statistics Public Use Research Database, Nov 2017 submission (2001-2015), US Department of HHS, CDCP and NCI. Released June 2018. Available at www.cdc.gov/cancer/public-use. Analyses were restricted to states that met the USCS publication criteria for 2001-2015; covering 51 states (including the District of Columbia) and 99% of the population in.

- *US mortality data*: Surveillance, Epidemiology, and End Results Program (www.seer.cancer.gov) SEER*Stat Database: Mortality - All COD, Aggregated Total U.S. (1990-2015) <Katrina/Rita Population Adjustment>, National Cancer Institute, DCCPS, Surveillance Research Program, released December 2017. Underlying mortality data provided by NCHS (www.cdc.gov/nchs).

Technical Details: Methods and Acronyms

Methods

- Age-adjusted rates were calculated using SEER*Stat, and were standardized to the 2000 US Standard population (19 age groups – Census P25-1130).
- Analyses were restricted to males and females ages 25 years and older, unless otherwise specified (<1% of liver cancer cases are found in ages less than 25 years). Age groups were defined as in Xu, 2018.
- Liver cancer statistics included intrahepatic bile duct cancer.
- Incidence rates exclude cases that were identified solely from death certificate or autopsy unless otherwise stated.
- Trends in rates (annual percent change, APC) were estimated using Joinpoint by fitting a least squares regression line to the natural logarithm of the age-adjusted rates.
- Small counts produced unstable rates for NH Native American/Alaska Natives and are therefore not presented.
- 95% confidence intervals around rates are presented.

Acronyms

- APC: Annual Percent Change.
- A/PI: Asian/Pacific Islander
- NH: Non-Hispanic

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