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Texas Cancer Registry

CPRIT

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Trends in Liver Cancer and Hepatocellular Carcinoma in Texas, 1995 - 2010

Texas Cancer Registry, Cancer Epidemiology and Surveillance Branch
Texas Department of State Health Services

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What is Liver Cancer?

"Liver cancer" – Cancers that originate in the tissues of the liver (not metastatic).

Most common liver cancers:

1. Hepatocellular carcinoma (HCC)
   - > 90% of liver cancers diagnosed in Texas[3]
2. Intrahepatic cholangiocarcinomas (ICC)
   - Bile duct[1,2]
   - 8% of liver cancers diagnosed in Texas[3]

[1] London WT, McGlynn KA (2006). Liver Cancer. In Schottenfeld D, Fraumeni JF (Eds.) Cancer Epidemiology and Prevention (pp. 763-786). New York, NY: Oxford.

[2]American Cancer Society (2012). Detailed Guide – Liver Cancer. Accessed May 17, 2013 at http://www.cancer.org/Cancer/LiverCancer/DetailedGuide/index

[3]Texas Department of State Health Services, Cancer Epidemiology and Surveillance Branch, Texas Cancer Registry, Incidence – Texas, 1995-2010, Cut-off 11/30/12, SEER*Prep 2.5.2 (Confidential)

What is Liver Cancer? (continued)

- Both HCC and ICC have increased in incidence; in some populations by more than 100%.[1] US (SEER) data show an average annual increase of almost 4% per year from 1995 forward.
- Because risk factors for HCC and ICC are different, remaining analysis will focus on HCC.

[1]London WT, McGlynn KA (2006). Liver Cancer. In Schottenfeld D, Fraumeni JF (Eds.) Cancer Epidemiology and Prevention (pp. 763-786). New York, NY: Oxford.

Hepatocellular Carcinoma
Risk Factors

Known risk factors for HCC[1,2]

Chronic hepatitis C infection	Major cause
Chronic hepatitis B infection	Major cause
Alcohol induced liver disease	Major cause
Non-specific cirrhosis	
Iron storage diseases such as hemochromatosis	
Mycotoxin or androgen exposure	
Diabetes	Highly associated but causality debated. Recent research suggests obesity & diabetes may become more important factors in HCC trends[3]

[1] London WT, McGlynn KA (2006). Liver Cancer. In Schottenfeld D, Fraumeni JF (Eds.) Cancer Epidemiology and Prevention (pp. 763-786). New York, NY: Oxford.

[2] Jaltekruse SF, McGlynn KA, Reichman ME (2009). Hepatocellular Carcinoma Incidence, Mortality and Survival Trends in the United States from 1975 to 2005. Journal of Clinical Oncology. 1485-1491.

[3] El_Serag HB (2004). Hepatocellular Carcinoma: Recent Trends in the United States. Gastroenterology .S27-S34.

Liver Cancer Incidence and Mortality (all Liver Cancers) in Texas and the US (SEER)

- Liver Cancer is the 14th most commonly diagnosed cancer in the US (SEER)[1] and in Texas.[2]

  2,489 Texans are expected to be diagnosed in 2013[4]

  - 73% male

- Liver cancer is the 8th most common cause of cancer deaths in the US (SEER)[3] and 6th in Texas.[3]

  1,987 Texans are expected to die in 2013[4]

  - 69% male

[1]SEER*Stat, "Incidence – SEER 13 Regs Research Data, Nov 2012 Sub (1992-2010)"

[2] Texas Department of State Health Services, Cancer Epidemiology and Surveillance Branch, Texas Cancer Registry, Incidence – Texas, 1995-2010, Cut-off 11/30/12, SEER*Prep 2.5.2 (Confidential)

[3]SEER*Stat, "Mortality – All COD, Aggregated with State, Total U.S. (1990-2010)"

[4]Texas Department of State Health Services. (2013) Cancer Epidemiology and Surveillance Branch. Expected New Cancer Cases and Deaths by Primary Site, Texas, 2013. Accessed 5/17/2013 at http://www.dshs.state.tx.us/tcr/statisticalData/Expected-Numbers-of-Cancer-Cases-and-Deaths-Texas-2013.aspx

Why do we care about liver cancer?

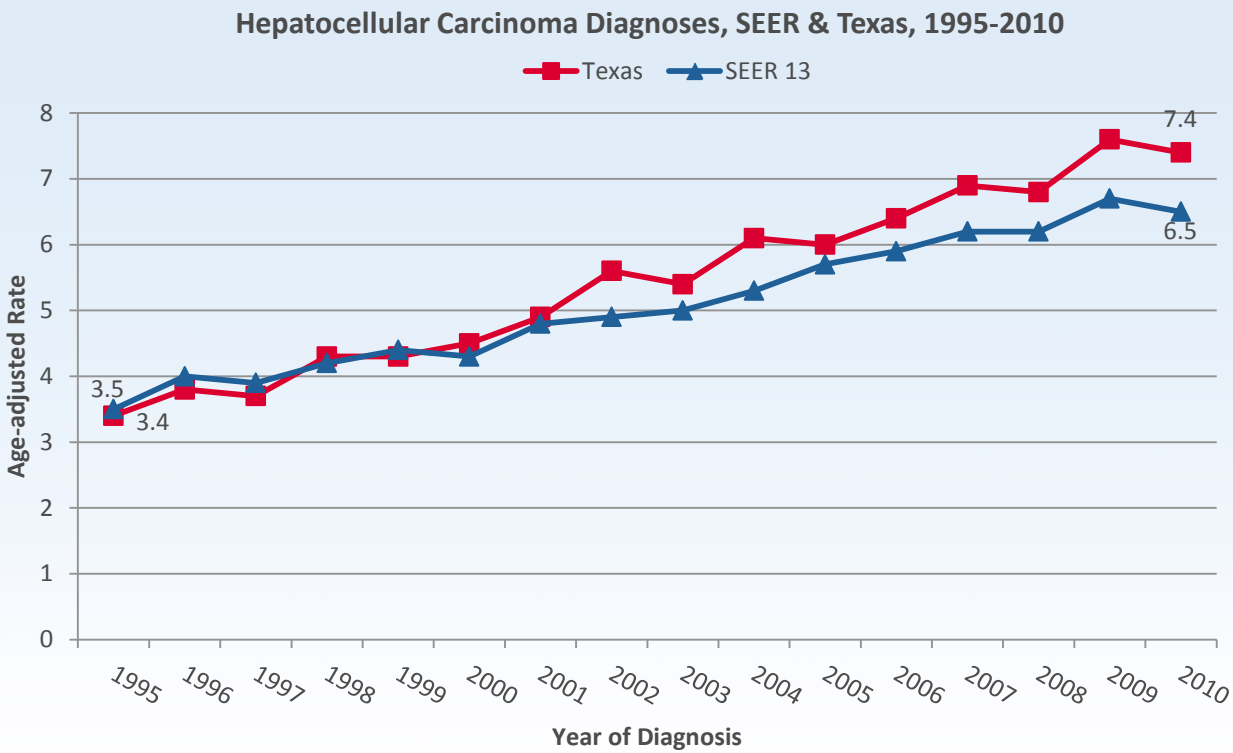
- Liver cancer rare; but survival rates "exceedingly poor"[1]
  - Accounts for 1.3% of all new cancer cases but 2.6% of all cancer deaths[1]
  - Five-year survival in Texas and nationally is 15-16%, compared to 63-68% for all types of cancer combined.[2,3]
- Incidence increasing in Texas and nationally for all types of liver cancer, including HCC
- Time trends differ by sex, race-ethnicity, age

[1]London WT, McGlynn KA (2006). Liver Cancer. In Schottenfeld D, Fraumeni JF (Eds.) Cancer Epidemiology and Prevention (pp. 763-786). New York, NY: Oxford.

[2]Texas Department of State Health Services. (2013) Cancer Epidemiology and Surveillance Branch. "Five-Year Cause-Specific Cancer Survival for Malignant Cancers Diagnosed 2001-2008 and followed through December 2009". Accessed 5/16/2013 at http://www.dshs.state.tx.us/tcr/Texas-Cancer-Registry---Cause-Specific-Cancer-Survival.aspx.

[3] American Cancer Society (2013). Cancer Facts & Figures 2013. Accessed 5/16/2013 at http://www.cancer.org/research/cancerfactsfigures/cancerfactsfigures/cancer-facts-figures-2013

Hepatocellular Carcinoma Trends in Texas and the US (SEER)



Texas
16 Year PC = 120.8%
APC = 5.4%*

SEER
16 Year PC = 86.2%
APC = 4.3%*

PC = Percentage Change
APC = Annual Percentage Change

*The APC is significantly different from zero ($p<0.05$)

Rates are per 100,000 and age-adjusted to the 2000 US Standard Population (19 age groups - Census P25-1130) standard.
Percent changes were calculated using 1 year for each end point; APCs were calculated using weighted least squares method.

Data Sources: Texas Department of State Health Services, Cancer Epidemiology and Surveillance Branch, Texas Cancer Registry, Incidence – Texas, 1995-2010, Cut-off 11/30/12, SEER*Prep 2.5.2 and Incidence – SEER 13 Regs Research Data, Nov 2011 Sub.

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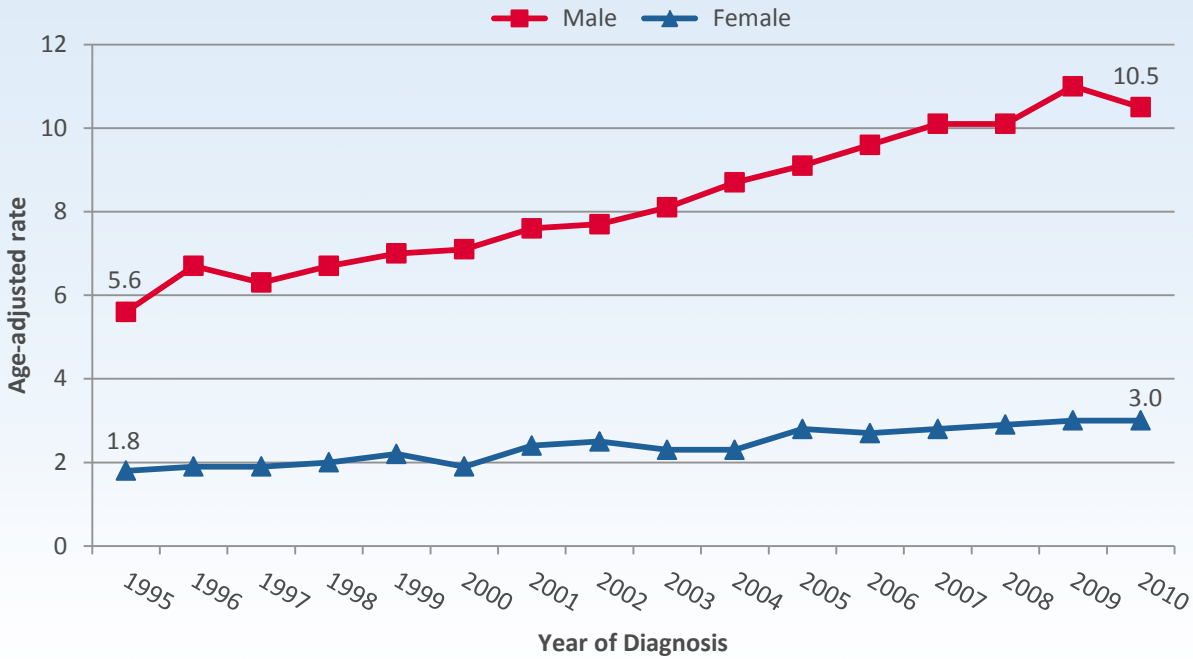
Hepatocellular Carcinoma Trends in Texas by Sex

Hepatocellular Carcinoma Incidence, Texas, 1995-2010, by Sex



Men
16 Year PC = 86.5%
APC = 4.3%*

Women
16 Year PC = 70.1%
APC = 3.6%*

PC = Percentage Change
APC = Annual Percentage Change

*The APC is significantly different from zero ($p<0.05$)

Rates are per 100,000 and age-adjusted to the 2000 US Standard Population (19 age groups - Census P25-1130) standard.
Percent changes were calculated using 1 year for each end point; APCs were calculated using weighted least squares method.

Data Source: Texas Department of State Health Services, Cancer Epidemiology and Surveillance Branch, Texas Cancer Registry, Incidence – Texas, 1995-2010, Cut-off 11/30/12, SEER*Prep 2.5.2.

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Comparison of Hepatocellular Carcinoma Trends in Men Texas and US (SEER)

- HCC rates ↑ since 1995 in both Texas and US (SEER)
- Texas rates ↑ more rapidly than US (SEER) rates

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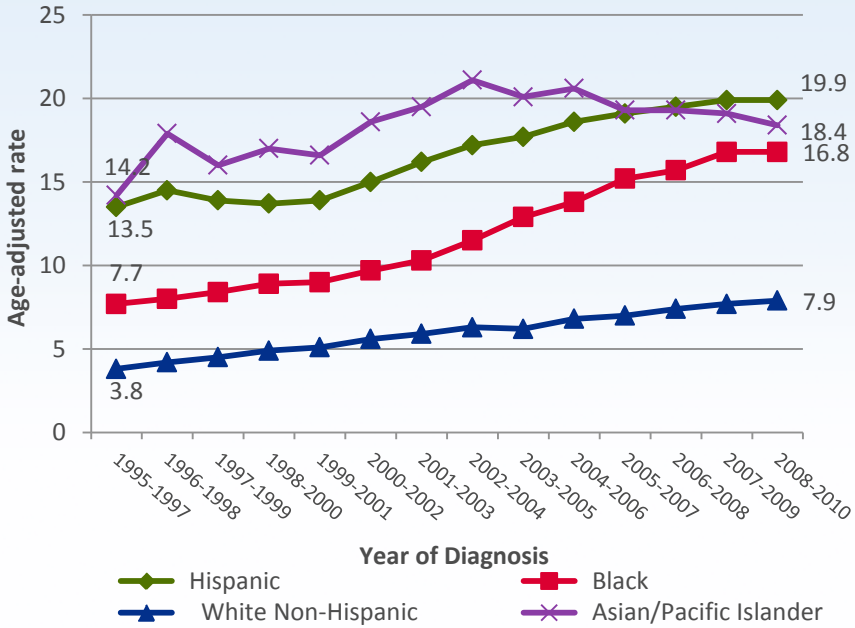
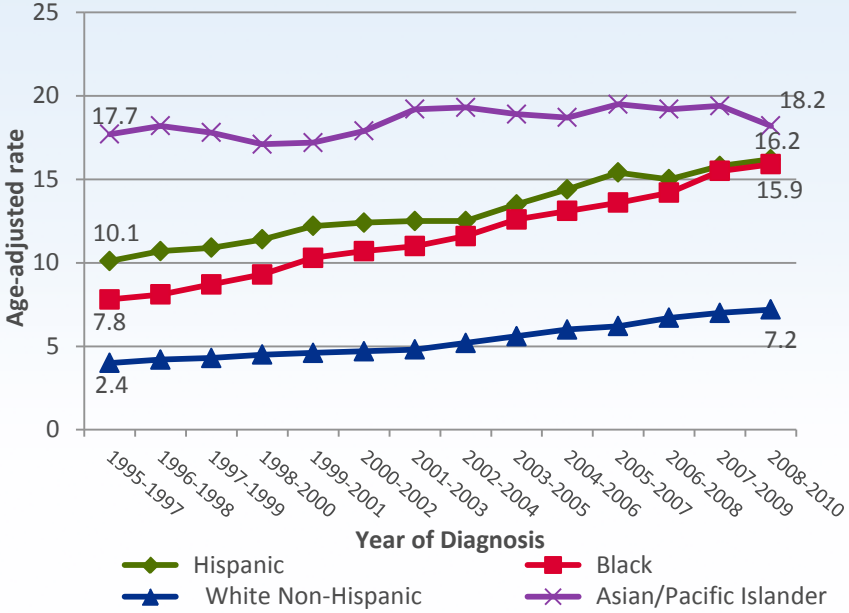
Male Hepatocellular Carcinoma Incidence Trends, 1995-2010, 3-Year Moving Averages, by Race/Ethnicity



US (SEER)
Male Hepatocellular Carcinoma Incidence Trends, 1995-2010, 3-Year Moving Averages, by Race/Ethnicity



Rates are per 100,000 and age-adjusted to the 2000 US Standard Population (19 age groups - Census P25-1130) standard.

Data Sources: Texas Department of State Health Services, Cancer Epidemiology and Surveillance Branch, Texas Cancer Registry, Incidence – Texas, 1995-2010, Cut-off 11/30/12, SEER*Prep 2.5.2. and Incidence – SEER 13 Regs Research Data, Nov 2012 Sub.

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Comparison of Hepatocellular Carcinoma Trends in Men Texas and US (SEER) (continued)

- Rates increased >2X 1995-2010 in all race/ethnic groups except Hispanics and A/PI
- APC's ↑ significantly for all races/ethnicities except A/PI in Texas and the US (SEER)
- APC for all races combined is significantly higher for Texas than the US (SEER)

Hepatocellular Carcinoma Incidence Trends in Men, Percentage Change, 1995-2010, Texas and US (SEER), by Race/Ethnicity

	Texas		US (SEER)	
Race/Ethnicity	Total Percent Change	Annual Percent Change (APC)	Total Percent Change	Annual Percent Change (APC)
All Races Combined	117.7	5.3 *	86.5	4.3 *
Non-Hispanic White	118.2	5.3 *	102.2	4.8 *
Black	135.0	6.7 *	134.2	5.6 *
Hispanic (any race)	74.2	3.3 *	94.3	3.8 *
Asian/Pacific Islander	65.0	1.4	1.3	0.5

* The APC is significantly different from zero ($p<0.05$)

Data Sources: Texas Department of State Health Services, Cancer Epidemiology and Surveillance Branch, Texas Cancer Registry, Incidence – Texas, 1995-2009, Cut-off 11/30/12, SEER*Prep 2.5.2. and
Incidence – SEER 13 Regs Research Data, Nov 2012 Sub.

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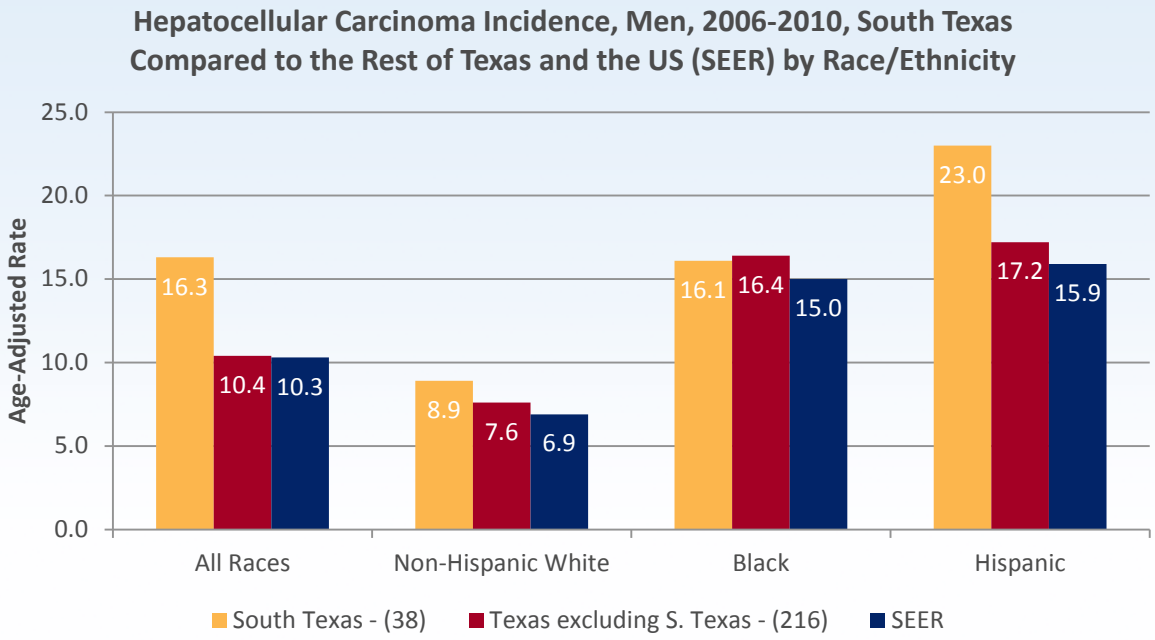
Comparison of Hepatocellular Carcinoma in Men in the South Texas Region

- Hispanics in the 38 South Texas Counties have a significantly higher incidence rate of HCC than Hispanics in the remainder of Texas (216 counties) and Hispanics in the US (SEER)
- Non-Hispanic whites in South Texas have a significantly higher rate than non-Hispanic whites in the US (SEER)



Rates are per 100,000 and age-adjusted to the 2000 US Standard Population (19 age groups - Census P25-1130) standard.

Data Sources: Texas Department of State Health Services, Cancer Epidemiology and Surveillance Branch, Texas Cancer Registry, Incidence – Texas, 1995-2009, Cut-off 11/30/12, SEER*Prep 2.5.2. and Incidence – SEER 13 Regs Research Data, Nov 2012 Sub.

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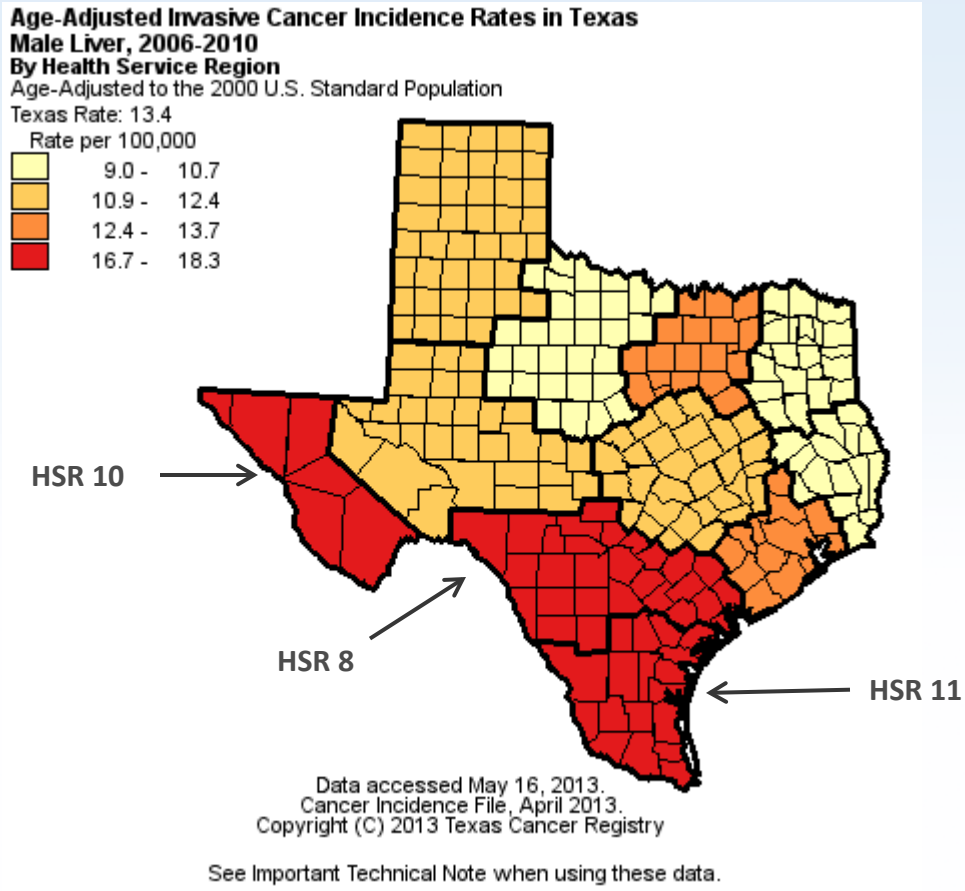
Comparison of Liver Cancer in Men by Race/Ethnicity and Region

- All of the 38 South Texas counties are contained with the 47 counties in HSRs 8 and 11
- HSRs 8, 10, and 11 all have liver cancer incidence rates significantly higher than the other HSRs



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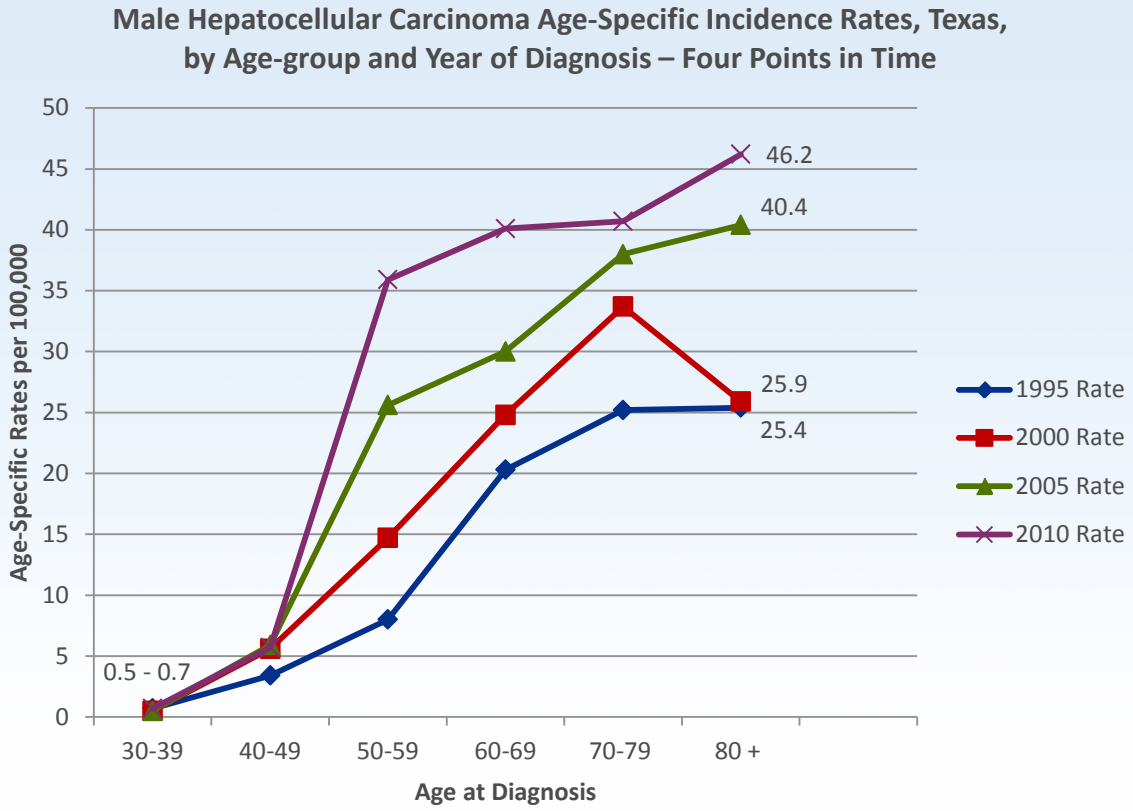
Age at diagnosis is shifting towards younger patients

- Literature reviews reveal that not only is the incidence of HCC increasing more rapidly in recent years, but that the ***age at diagnosis*** has been shifting toward younger patients.
- This shift has been occurring in both men and women of all race/ethnic groups.[1,2]
- This trend is true in Texas and the US as a whole.

[1] El_Serag HB (2004). Hepatocellular Carcinoma: Recent Trends in the United States. Gastroenterology .S27-S34.

[2] Jaltekruse SF, McGlynn KA, Reichman ME (2009). Hepatocellular Carcinoma Incidence, Mortality and Survival Trends in the United States from 1975 to 2005. Journal of Clinical Oncology. 1485-1491.

Comparison of Hepatocellular Carcinoma Diagnoses by Age Group



Data Source: Texas Department of State Health Services, Cancer Epidemiology and Surveillance Branch, Texas Cancer Registry, Incidence – Texas, 1995-2010, Cut-off 11/30/12, SEER*Prep 2.5.2.

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Possible Contributing Risk Factors: Hepatitis C (HCV) and Liver Cancer/Hepatocellular Carcinoma

According to the Centers for Disease Control and Prevention:[1]

- Persons born between 1945 and 1965 comprise approximately 27% of the US population.
- This cohort accounts for approximately *three-fourths* of all HCV infection in the US. It is estimated that 3.25% of the population born between 1945 and 1965 is chronically infected with HCV.
- HCV a major risk factor for liver cancer (including HCC)
- CDC recommends "one-time testing without prior ascertainment of HCV risk for persons born during 1945-1965".

[1]Centers for Disease Control and Prevention (2012). Morbidity and Mortality Weekly Report (MMWR). Recommendations for the Identification of Chronic Hepatitis C Virus Infection Among Persons Born During 1945-1965. Downloaded 8/16/2012 from: http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6104a1.htm

Possible Contributing Risk Factors: Diabetes Mellitus (DM) and Hepatocellular Carcinoma

While HCV, HBV, and various other diseases or conditions are recognized risk factors for HCC, in 15%-50% of HCC patients, no specific risk factor has been identified.[1,2]

In the past decade, a number of studies have examined the association of DM with HCC:

- Consensus that DM is associated with the development of HCC [1,2,3]
- No consensus that DM is independently associated with HCC in the absence of other risk factors[1,2,3]

[1] El Serag HB (2004). Hepatocellular Carcinoma: Recent Trends in the United States. Gastroenterology .S27-S34.

[2] Gao C, Yao SK (2009). Diabetes mellitus: a "true" independent risk factor for hepatocellular carcinoma? Hepatobiliary & Pancreatic Diseases International. Vol 8, No 5. 465-473.

[3] McGlynn KA, Quraishi S, Welzel TN, Davila JA, El Serag HB, Graubard BI (2010). Attributable risks for hepatocellular carcinoma in the United States. Presented at the American Association for Cancer Research 101st Annual Meeting 2010, April 17-21, 2010, Washington DC.

Possible Contributing Factors
Hepatocellular Carcinoma (continued)

A 2010 study calculated overall risks (attributable risk) after stratifying for race/ethnicity, gender, and time since diagnosis.[1]

- 63% of HCC was associated with one or more known risk factors:
  - DM was associated with 34% of cases
  - Alcohol-related disorders with 24%
  - Hepatitis C infection with 21%
  - Hepatitis B infection with 6%
  - Rare metabolic disorders with 3%
  - Obesity with 3%
- Associated risks varied by race/ethnicity and gender.

[1] McGlynn KA, Quraishi S, Welzel TN, Davila JA, El Serag HB, Graubard BI (2010). Attributable risks for hepatocellular carcinoma in the United States. Presented at the American Association for Cancer Research 101st Annual Meeting 2010, April 17-21, 2010, Washington DC.

Diabetes Mellitus (DM) and Hepatocellular Carcinoma – a Cautionary Note

Biases noted when researching DM associated HCC:

- Studying any association between DM and HCC is difficult[1]
  - Diabetes is a risk factor for nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH), which can lead to liver fibrosis, cirrhosis, and ultimately HCC.
  - However, cirrhosis and end-stage liver disease can cause glucose intolerance and diabetes.
  - Hepatitis C infection is associated with ↑ risk of DM.

- Case-control studies have been used in most of the research investigating associations between DM and HCC. Inferring causation can be problematic with this study design.[1]

- Additional and prospective studies are necessary to determine if DM is an independent risk factor for HCC.[1]

[1]Gao C, Yao SK (2009). Diabetes mellitus: a "true" independent risk factor for hepatocellular carcinoma? Hepatobiliary & Pancreatic Diseases International. Vol 8, No 5. 465-473.

Trends in Liver Cancer/Hepatocellular Carcinoma in Texas and the US, 1995-2010 In Summary

- Liver cancer/HCC is rare, but survival poor.
  - >90% of Texas liver cancers are HCC
- HCC incidence significantly higher in Texas Hispanics, blacks, and A/PI than in non-Hispanic whites.
  - Texans have significantly higher HCC rates than US (SEER)
  - Significantly higher HCC rates in Texas Hispanics versus US (SEER) driven by very high Hispanic rates in South Texas.
- Incidence ↑ in both the US and Texas
  - More rapidly in Texas than US
- Age at diagnosis shifting toward younger patients, both in Texas and US
- Primary risk factors are HCV and HBV, followed by alcohol.
  - Diabetes being explored as an important risk factor

Questions

38 "South Texas" Counties as Defined for the *South Texas Health Status Review**

Atascosa	Kerr
Bandera	Kinney
Bee	Kleberg
Bexar	La Salle
Brooks	Live Oak
Cameron	Maverick
Comal	McMullen
Dimmit	Medina
Duval	Nueces
Edwards	Real
Frio	San Patricio
Gillespie	Starr
Guadalupe	Uvalde
Hidalgo	Val Verde
Jim Hogg	Webb
Jim Wells	Willacy
Karnes	Wilson
Kendall	Zapata
Kenedy	Zavala

* A study conducted by the University of Texas Health Science Center, San Antonio in 2006 and updated in 2012.

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