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

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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 Texas³

2. Intrahepatic cholangiocarcinomas (ICC)
   - Bile duct¹,²
   - 8% of liver cancers diagnosed in Texas³


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)
Both HCC and ICC have increased in incidence; in some populations by more than 100%.\textsuperscript{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.

# Hepatocellular Carcinoma Risk Factors

<table>
<thead>
<tr>
<th>Known risk factors for HCC(^1,2)</th>
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</thead>
<tbody>
<tr>
<td>Chronic hepatitis C infection</td>
<td>Major cause</td>
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<tr>
<td>Chronic hepatitis B infection</td>
<td>Major cause</td>
</tr>
<tr>
<td>Alcohol induced liver disease</td>
<td>Major cause</td>
</tr>
<tr>
<td>Non-specific cirrhosis</td>
<td></td>
</tr>
<tr>
<td>Iron storage diseases such as hemochromatosis</td>
<td></td>
</tr>
<tr>
<td>Mycotoxin or androgen exposure</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>Highly associated but causality debated. Recent research suggests obesity &amp; diabetes may become more important factors in HCC trends(^3)</td>
</tr>
</tbody>
</table>

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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

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\(^2\)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)”

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

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Hepatocellular Carcinoma Trends in Texas and the US (SEER)

Hepatocellular Carcinoma Diagnoses, SEER & Texas, 1995-2010

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

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

*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.
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%*

*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.
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

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.
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

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Total Percent Change</th>
<th>Annual Percent Change (APC)</th>
<th>Total Percent Change</th>
<th>Annual Percent Change (APC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Races Combined</td>
<td>117.7</td>
<td>5.3 *</td>
<td>86.5</td>
<td>4.3 *</td>
</tr>
<tr>
<td>Non-Hispanic White</td>
<td>118.2</td>
<td>5.3 *</td>
<td>102.2</td>
<td>4.8 *</td>
</tr>
<tr>
<td>Black</td>
<td>135.0</td>
<td>6.7 *</td>
<td>134.2</td>
<td>5.6 *</td>
</tr>
<tr>
<td>Hispanic (any race)</td>
<td>74.2</td>
<td>3.3 *</td>
<td>94.3</td>
<td>3.8 *</td>
</tr>
<tr>
<td>Asian/Pacific Islander</td>
<td>65.0</td>
<td>1.4</td>
<td>1.3</td>
<td>0.5</td>
</tr>
</tbody>
</table>

* 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.
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)

Hepatocellular Carcinoma Incidence, Men, 2006-2010, South Texas Compared to the Rest of Texas and the US (SEER) by Race/Ethnicity

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>South Texas (38)</th>
<th>Texas excluding S. Texas (216)</th>
<th>SEER</th>
</tr>
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<tbody>
<tr>
<td>All Races</td>
<td>16.3</td>
<td>10.4</td>
<td>10.3</td>
</tr>
<tr>
<td>Non-Hispanic White</td>
<td>8.9</td>
<td>7.6</td>
<td>6.9</td>
</tr>
<tr>
<td>Black</td>
<td>16.1</td>
<td>16.4</td>
<td>15.0</td>
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<tr>
<td>Hispanic</td>
<td>23.0</td>
<td>17.2</td>
<td>15.9</td>
</tr>
</tbody>
</table>

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.
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
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.

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Comparison of Hepatocellular Carcinoma Diagnoses by Age Group

Male Hepatocellular Carcinoma Age-Specific Incidence Rates, Texas, by Age-group and Year of Diagnosis – Four Points in Time

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

According to the Centers for Disease Control and Prevention:

- 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”.

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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\(^1,2,3\)

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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.

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.\(^1\)

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*

<table>
<thead>
<tr>
<th>Atascosa</th>
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<td>Kenedy</td>
<td>Zavala</td>
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* A study conducted by the University of Texas Health Science Center, San Antonio in 2006 and updated in 2012.