Regional differences in mortality rates and characteristics of decedents with hepatitis B listed as a cause of death, United States, 2000–2019

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NASTAD Virtual Learning Collaborative  
April 19, 2023
Background
Background

- **Hepatitis B**
  - Can lead to cirrhosis and hepatocellular carcinoma, resulting in premature death
  - Has been associated with elevated mortality rates from all causes\(^1\)

- **Stable** US hepatitis B-listed death rate during 1999-2019\(^2\)

- US hepatitis B-listed death rates highest among decedents who were
  - Aged >55 years, Non-Hispanic Asian/Pacific Islander, and male\(^2\)

- Published hepatitis B mortality reports lack information on decedent place of birth, comorbidities, and underlying vs contributing causes of death

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Study Rationale and Objectives

- Examination of hepatitis B mortality sub-nationally can identify differences in mortality rates and decedent characteristics.

- Study objectives:
  - To analyze state-level hepatitis B-listed death counts, rates, and characteristics of decedents
  - To examine the distribution of sociodemographic characteristics, median age at death, and UCOD among US-born and non-US-born decedents with hepatitis B-listed deaths
Methods
# Data Source and Definitions

- **Data Source:** Restricted-use US Multiple Cause of Death data, 2000–2019
- **Causes of Death**
  - *International Statistical Classification of Diseases, Tenth Revision (ICD-10)*

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underlying COD (n=1)</td>
<td>Disease or injury that <em>initiated</em> the chain of morbid events leading directly to death</td>
</tr>
<tr>
<td>Non-underlying COD (n&lt;19)</td>
<td>Immediate cause, conditions leading to immediate cause, and any other significant condition which unfavorably influenced the course of the morbid process and thus contributed to the fatal outcome</td>
</tr>
<tr>
<td>Hepatitis B-listed death</td>
<td>≥1 ICD-10 code indicative of hepatitis B (<em>B16, B17.0, B18.0, and B18.1</em>) listed as the UCOD of a CCOD</td>
</tr>
<tr>
<td>Hepatitis D virus coinfection death</td>
<td>Hepatitis B-listed death with ≥1 ICD-10 code indicative of hepatitis D (<em>B16.0, B16.1, B17.0, and B18.0</em>) present as any COD</td>
</tr>
<tr>
<td>Hepatitis C virus coinfection death</td>
<td>Hepatitis B-listed death with ≥1 ICD-10 code indicative of hepatitis C (<em>B17.1 and B18.2</em>) present as any COD</td>
</tr>
<tr>
<td>HIV coinfection death</td>
<td>Hepatitis B-listed death with ≥1 ICD-10 code indicative of HIV (<em>B20–B24</em>) present as any COD</td>
</tr>
<tr>
<td>US-born (USB)</td>
<td>Birth in any of 50 US states or DC</td>
</tr>
<tr>
<td>Non-US-born (NUSB)</td>
<td>Birth in the remainder of the world</td>
</tr>
</tbody>
</table>

Link to NVSS mortality data: https://www.cdc.gov/nchs/nvss/deaths.htm
Statistical Analyses

- Hepatitis B-listed death **state-level** analyses
  - Hepatitis B-listed death **counts** and age-adjusted **rates**\(^1,2\)
  - **Median age** at hepatitis B-listed death
  - Distribution of **US birthplace status**
  - Distribution of **HCV, HIV, and HDV coinfection status**

  - Distribution of
    - Sociodemographic characteristics (sex, age, year of birth, and race/ethnicity)
    - UCOD categories\(^3\) (for decedents who had hepatitis B listed as a CCOD)

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2. [https://seer.cancer.gov/stdpopulations/](https://seer.cancer.gov/stdpopulations/)
Results

Among 17,483 (6.5%) hepatitis B-listed deaths,
- 24.6% (4,297) were with HCV infection
- 5.5% (961) were with HIV infection
- 1.7% (295) were with both HCV and HIV infection
- 0.03% (6) deaths included HDV infection

*Condition was listed as the underlying or a contributing cause of death.*
Age-adjusted hepatitis B-listed death rates in 50 states and DC, United States, 2010–2019

- **Death rates in 12 states** significantly surpassed the national death rate (0.47)
  - Primarily coastal and Appalachian states
  - DC (high, 1.78), HI, OK, CA, TN, WV, MS, OR, WA, LA, KY, and NY (Adjusted P<.05)

- **Death rates were lowest** in
  - MT (0.14) followed by ID and IL (0.21 for both)

- **US median age (IQR)** at hepatitis B-listed death: 60.0 (53.0-69.0) years.

- **Significantly younger** median age at death in KY, WV, TN, OH, and MS (red)
  - Range: 54.0-59.0 years

- **Significantly older** median age at hepatitis B-listed death (yellow)
  - CA (63.0 years)

*Adjusted P<.05, statistically different death rate than the overall death rate*
Compared to non-US-born decedents, **US-born decedents (63.3%) were more frequently**

<table>
<thead>
<tr>
<th>Category</th>
<th>US-born</th>
<th>Non-US-born</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aged 45–64 years</td>
<td>60%</td>
<td>46%</td>
</tr>
<tr>
<td>Born 1945–1965</td>
<td>66%</td>
<td>54%</td>
</tr>
<tr>
<td>Non-Hispanic, White</td>
<td>67%</td>
<td>11%</td>
</tr>
<tr>
<td>Non-Hispanic, Black</td>
<td>25%</td>
<td>9%</td>
</tr>
<tr>
<td>Had HCV, HIV, or HDV co-infection</td>
<td>39%</td>
<td>9%</td>
</tr>
</tbody>
</table>

Distribution of US birthplace status among hepatitis B-listed deaths, United States, 2010–2019

<table>
<thead>
<tr>
<th>% of Hepatitis B-listed Deaths by US birthplace</th>
<th>No.</th>
<th>Jurisdiction</th>
</tr>
</thead>
<tbody>
<tr>
<td>*<em>Significantly</em> higher % <strong>NUSB vs national distribution</strong></td>
<td>7</td>
<td>CA (64.7%), MN, HI, NY, MA, WA, NJ (47.1%)</td>
</tr>
<tr>
<td><strong>Higher % of NUSB vs national distribution (not significant)</strong></td>
<td>3</td>
<td>CT (44.0%), RI, IL (38.4%)</td>
</tr>
<tr>
<td><strong>At national % (USB 63%, NUSB 37%)</strong></td>
<td>3</td>
<td>UT, OR, NV</td>
</tr>
<tr>
<td><em><em>Significantly</em> higher % of USB than national distribution</em>*</td>
<td>22</td>
<td>MS (95.2%), KY, TN, LA, IN, AR, SC, OH, OK, MI, GA, MO, NC, DC, ME, KS, NM, IA, PA, AZ, TX, and FL (70.6%)</td>
</tr>
<tr>
<td><strong>Higher % of USB than national distribution but not significantly</strong></td>
<td>7</td>
<td>AK (73.9%), ID, MD, WI, CO, NE, VA (64.4%)</td>
</tr>
</tbody>
</table>

*P<.05 vs overall national distribution.
US birthplace data for Alabama, Delaware, Montana, New Hampshire, North Dakota, South Dakota, Vermont, West Virginia, and Wyoming were not displayed because at least 1 cell (either US-born or non-US-born) had fewer than 10 deaths.
Distribution of underlying causes of death by birthplace of hepatitis B-listed decedents, United States, 2010–2019

- There was **no difference** in the frequency with which “hepatitis B” was listed as the **UCOD** among US- and non-US-born hepatitis B-listed decedents (Both ~30%, P=.24)

- For decedents with **hepatitis B** listed as a **CCOD**,
  - Liver cancer was **more frequently** listed as UCOD among **non-US decedents** compared with US-born decedents (53.7% vs 20.6%, P<.001)
  - Several conditions **more frequently*** listed as UCOD among **US-born** (Table)

<table>
<thead>
<tr>
<th>Underlying cause of death when hepatitis B listed as contributing cause of death</th>
<th>US Born</th>
<th>Non-US Born</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver cancer</td>
<td>20.6%</td>
<td>53.7%</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>3.5%</td>
<td>0.7%</td>
</tr>
<tr>
<td>Other viral hepatitis</td>
<td>0.8%</td>
<td>0.1%</td>
</tr>
<tr>
<td>Liver, alcohol</td>
<td>10.2%</td>
<td>3.3%</td>
</tr>
<tr>
<td>Liver, non-alcohol</td>
<td>5.5%</td>
<td>3.8%</td>
</tr>
<tr>
<td>HIV</td>
<td>8.2%</td>
<td>1.8%</td>
</tr>
<tr>
<td>Circulatory</td>
<td>12.6%</td>
<td>7.1%</td>
</tr>
<tr>
<td>Respiratory</td>
<td>4.6%</td>
<td>1.6%</td>
</tr>
<tr>
<td>Injuries/trauma</td>
<td>3.7%</td>
<td>1.0%</td>
</tr>
<tr>
<td>Mental/behavioral</td>
<td>2.1%</td>
<td>0.8%</td>
</tr>
<tr>
<td>Other</td>
<td>6.4%</td>
<td>4.5%</td>
</tr>
</tbody>
</table>


- Compared to non-US-born hepatitis B-listed decedents, US-born decedents had a significantly* younger median age at death for the following UCOD conditions:

<table>
<thead>
<tr>
<th>Cause of Death</th>
<th>US Born</th>
<th>Non-US Born</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis B</td>
<td>59 yrs</td>
<td>63 yrs</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>58 yrs</td>
<td>62 yrs</td>
</tr>
<tr>
<td>Liver, non-alcohol</td>
<td>59 yrs</td>
<td>65 yrs</td>
</tr>
<tr>
<td>Circulatory</td>
<td>62 yrs</td>
<td>68 yrs</td>
</tr>
<tr>
<td>Respiratory</td>
<td>63 yrs</td>
<td>73 yrs</td>
</tr>
<tr>
<td>Diabetes</td>
<td>61 yrs</td>
<td>65 yrs</td>
</tr>
<tr>
<td>Injuries/trauma</td>
<td>56 yrs</td>
<td>64 yrs</td>
</tr>
</tbody>
</table>

Medians age at death and underlying COD among decedents with and without hepatitis B, 2010–2019

- Overall and for most UCOD categories, both US-born and non-US born hepatitis B-listed decedents had a significantly younger median age at death when compared to decedents who did not have hepatitis B listed at death.

- Most frequently listed UCOD categories among both US-born and non-US-born hepatitis B decedents were:
  - Hepatitis B (USB: 30.2%, NUSB: 29.4%)
  - Liver cancer (USB: 14.4%, NUSB: 37.9%)
  - Non-liver cancers (USB: 11.4%, NUSB: 11.7%)

- Most frequently UCOD categories among decedents who did NOT have hepatitis B listed:
  - Circulatory conditions (30.9%) and non-liver cancers (21.7%)
Hepatitis B-listed Death Rate Changes from 2000-2009 to 2010-2019

- National hepatitis B-listed death rate **declined** by 19.0%, from 0.58 deaths/100,000 population during 2000–2009 to 0.47 deaths/100,000 population during 2010–2019.

- State-level death rates **significantly decreased** in:
  - CT (-45.8%), PA, NC, MD, VA, LA, TX, MI, IL, GA, WA, FL, CA, and NY (-18.7%)

- State-level death rates **significantly increased** in:
  - WV (+83.8%) and KY (+69.4%)
Discussion
Limitations

- Variability in provider reporting of conditions leading to death
- Underestimation of the true hepatitis B mortality burden due to under-diagnosis of hepatitis B\(^1\)
- American Indian and Alaska Native persons are often misclassified as other race groups on their death certificate, resulting in underreporting of conditions\(^2\)

# Conclusions & Public Health Relevance

## Main Finding

<table>
<thead>
<tr>
<th></th>
<th>Interpretation/Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hepatitis B-listed death rates</strong></td>
<td>were significantly higher in 12 coastal and Appalachian states.</td>
</tr>
<tr>
<td><strong>Baseline estimates of state and regional level hepatitis B deaths can be used to identify high mortality burden areas and inform state public health and elimination efforts.</strong></td>
<td></td>
</tr>
</tbody>
</table>

- Significant *increases* in hepatitis B-listed death rate were observed exclusively in WV and KY.

- These states have also experienced high death rate from all causes and pronounced declines in life expectancy (e.g., opioid deaths).
- Support universal hepatitis B vaccination and harm reduction efforts.

<table>
<thead>
<tr>
<th><strong>US-born decedents</strong></th>
<th>constituted 63% of all hepatitis B-listed deaths.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Contrary to published NHANES prevalence data indicating more non-US-born persons living with chronic hepatitis B, US-born decedents constituted most hepatitis B-listed deaths.</strong></td>
<td></td>
</tr>
</tbody>
</table>

- Significantly *younger median age* at death occurred in KY, WV, TN, OH, and MS where most decedents were US-born.
- Significantly *older median age* at death occurred among California decedents, who were predominantly non-US-born.
- Hepatitis B-listed decedents had a significantly *younger median age* at death when compared to non-hepatitis B-listed decedents.

- In the context of chronic hepatitis B, despite US-born persons having presumably a shorter duration of infection, they had a significantly younger median age at death.
Conclusions & Clinical Relevance

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<thead>
<tr>
<th>Main Finding</th>
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<tbody>
<tr>
<td>• Liver-related conditions were the most frequently listed UCOD among both US-born and non-US-born hepatitis B-listed decedents.</td>
<td>• US-born persons with hepatitis B may more frequently require diagnosis and management of viral coinfections, respiratory and cardiovascular conditions, non-viral liver disease, and addiction-related sequelae.</td>
</tr>
<tr>
<td>• Liver cancer was the predominant UCOD among non-US-born decedents. <em>(Nearly ½ had any cancer listed as UCOD.)</em></td>
<td>• These findings support universal adult hepatitis B screening and vaccination.</td>
</tr>
<tr>
<td>• Compared to non-US-born decedents, US-born decedents more frequently had non-hepatic conditions listed as UCOD.</td>
<td>• All persons with chronic hepatitis B need diagnosis and ongoing clinical management.</td>
</tr>
</tbody>
</table>
Work in Progress
Follow-up Questions

- Are there differences in social vulnerability indicators among hepatitis B decedents according to US- vs non-US birth, to state/county location?
- Is there a relationship between social vulnerability and mortality rates?
- Is there a relationship between social vulnerability and early hepatitis B-related mortality?
- Can identification of geolocation-specific social vulnerabilities among HBV decedents inform, focus, and improve public health interventions for persons living with CHB?
CDC ATSDR Social Vulnerability Index

- Social determinants of health (e.g., socioeconomic and health insurance status, minority status and language, access to housing and transportation) can affect access to health care and treatment, as well as patient-level outcomes for a variety of conditions.

- Social Vulnerability Index (SVI) was created by the CDC/ATSDR as a standardized metric that incorporates census tract- and county-level social determinants to identify and compare communities deemed vulnerable.

- We plan to merge SVI data with US MCOD data by county of residence.

DCIPHER Data Integration Project

- Web-based data platform used by many CDC programs for data integration, management, and analyses of public health surveillance data
- DVH plans to use DCIPHER for viral hepatitis case-based surveillance and mortality data
  - Jurisdictional health departments can access the platform to view their data and produce reports
- Integration of NNDSS and mortality data with SVI and other place-based SDOH datasets so jurisdictions can view their surveillance and mortality data in context of SDOH data sources
- Starting pilot with six health departments this month
- Anticipate to onboard other jurisdictions beginning later this year
CBC WONDER Mortality

- CDC Online query tool
- Aggregated data at the US, region, state, and county
- Examples:
  - CDC DVH Annual Viral Hepatitis Surveillance Reports

Table 3.8—Part 2 of 3
Numbers and rates* of deaths with hepatitis C virus infection listed as a cause of death† among residents, by demographic characteristics
United States, 2016-2020

Table 3.9
Rates* of death with hepatitis C virus infection listed as a cause of death† among residents, by state or jurisdiction
United States, 2020

Figure 3.8
Mortality in Hawai‘i

Higher Rates of Hepatitis B Deaths in Hawai‘i (2000-2020)

3 Times Higher
In 2019, Hep B mortality rate for Hawai‘i was 1.17 deaths per 100,000 compared to 0.42 per 100,000 for the United States.

Male Residents
Hep B mortality rates for male residents in Hawai‘i were up to 1.7 times state average from 2000 to 2020.

API Residents
Hep B mortality rates for Asian and Pacific Islander (API) residents were up to 1.4 times state average from 2000 to 2020.

In February 2023, the Hawai‘i Department of Health released Hawai‘i’s Hepatitis B Mortality and Liver Cancer, the first such report ever developed in the state. Below are the main report findings that demonstrate the importance of hepatitis elimination, in alignment with Hep Free 2030.

Higher rates of liver cancer mortality were also found when comparing Hawai‘i to the United States.

In Hawai‘i, higher rates were found among male and/or API residents as well.
Thank you!

Acknowledgement:
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Philip Spradling: pps9@cdc.gov

For more information, contact CDC
1-800-CDC-INFO (232-4636)

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.