Efforts to Identify and Address the Causes and Disparities Related to the Increase in Liver Cancer
Overview

Epidemiology

Risk Factors
- Alcohol
- Hepatitis B and C

Health Disparities
Liver Cancer Epidemiology

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Cancer Epidemiologist
Cancer Prevention and Control Section
Liver Cancer: Nationwide Trend

Incidence Rate has Increased 69% Over the Last 16 Years.
Mortality Rate has Increased 47% Over the Last 16 Years.

Source: Centers for Disease Control and Prevention, US Cancer Statistics
Liver Cancer: Michigan Trends

- **Incidence** increased in males by 28.2% and females by 27.3%.
  - Males aged 60-64 increased by 165.6% and females aged 70-74 increased by 39.8%.

- **Mortality** increase in males by 21.2% and females by 27.3%.
  - Males aged 60-64 increased by 146.1% and females aged 70-74 increased by 103.1%.

Source: Michigan Cancer Surveillance Program, Division of Vital Records and Health Statistics
Liver Cancer: Michigan Fast Stats

- Incidence (2015): 6.7 per 100,000 people
  - Estimated 1,200 cases in 2018
  - Median Age at Diagnosis: 64 Years
- Mortality (2016): 6.3 per 100,000 people
  - Estimated 880 Deaths in 2018
  - Sixth Highest for Cancer Related Deaths
  - Median Age at Death: 67 Years
- Five-Year Survival: 17.7%
- Diagnosed at Localized Stage: 41.2%
  - Percent of Surviving: 31.3%
- Diagnosed at Distant Stage: 19.1%
  - Percent of Surviving: 2.4%

Source: Michigan Cancer Surveillance Program, Division of Vital Records and Health Statistics
Liver Cancer: By Race in Michigan, 2011-2015 NIH

Source: National Cancer Institute, State Cancer Profiles
Liver 101

- Essential organ
- Breaks down and stores nutrients
- Makes substance that causes blood to clot
- Helps with the production of bile
- Helps with breaking down toxic waste
Liver Cancer

- Primary Liver cancer
  - Hepatocellular carcinoma
  - Intrahepatic cholangiocarcinoma (bile duct cancer)
  - Angiosarcoma and hemangiosarcoma
  - Hepatoblastoma
- Secondary liver cancer (more common)
Liver Cancer: Signs and Symptoms

- Weight loss
- Loss of appetite
- Enlarged liver
- Pain in the abdomen
- Swelling in the abdomen
- Jaundice
- High blood calcium levels

Source: American Cancer Society
Liver Cancer: Screening

**Average Risk**
- No recommended screening tests at this time

**High Risk**
- Alpha-fetoprotein blood tests and ultrasound exams every 6 to 12 months
- Many patients with early stages of liver cancer have normal AFP levels

Source: American Cancer Society
Stages of Progression

Fatty Liver: Reversible

Chronic injury:
- Viral infection
- Alcohol
- NASH
- Autoimmune disorders
- Cholestatic disorders
- Metabolic diseases

Genetic polymorphisms
- Epigenetic marks
- Cofactors (such as obesity and alcohol)

5–50 years

Liver transplant

Liver failure
- Portal hypertension

Normal liver

Inflammatory damage
- Matrix deposition
- Parenchymal cell death
- Angiogenesis

Early fibrosis

Disrupted architecture
- Loss of function
- Aberrant hepatocyte regeneration

Cirrhosis

Resolution

Regression

- Removal of underlying cause
- Anti-fibrotic drug or cell therapy

Hepatocellular carcinoma
Factors Contributing to Liver Cancer Incidence in the U.S.

Liver Cancer: Risk Factors

- Chronic Viral Hepatitis (Hep-B or Hep-C)
  - Male Sex
  - Cirrhosis
  - Obesity
- Heavy Alcohol Use
  - Type 2 Diabetes
  - Smoking
  - Aflatoxins
- Race

Source: American Cancer Society
Alcohol

Patrick Hindman, MPH, BSN
Alcohol Epidemiologist
Lifecourse Epidemiology and Genomics Division
Definitions

- Excessive drinking- includes binge drinking, heavy drinking, and any drinking by pregnant women or people younger than age 21.
  - Binge drinking- the most common form of excessive drinking
    - 4 drinks or more on an occasion for women
    - 5 drinks or more on an occasion for men
  - Heavy drinking
    - 8 drinks or more per week for women
    - 15 or more drinks per week for men

Reference: [https://www.cdc.gov/alcohol/factsheets/alcohol-use.htm](https://www.cdc.gov/alcohol/factsheets/alcohol-use.htm)
Alcohol and Health

- Roughly 88,000 people die from alcohol related causes annually, making it the 3rd leading cause of preventable death in the United States.

- In 2015, there were 78,529 liver disease deaths among those aged 12 and over; 47 percent involved alcohol.

- Not only is alcohol a risk factor for cancer of the liver, but it can also be associated with cancer of the breast, mouth, throat, esophagus, and colon.

References: [https://www.cdc.gov/alcohol/fact-sheets/alcohol-use.htm](https://www.cdc.gov/alcohol/fact-sheets/alcohol-use.htm)  
Alcohol and Liver Related Mortality

- Alcohol-attributable deaths due to excessive alcohol use:
  - National statistics
    - Alcoholic liver disease- 14,695
    - Liver cancer- 998
    - Liver cirrhosis, unspecified- 7,847
  - Michigan statistics
    - Alcoholic liver disease- 499
    - Liver cancer- 36
    - Liver cirrhosis, unspecified- 282

Alcohol as a Risk Factor

- Alcohol use is one of the most common risk factors for cancer among adults in the United States.
  - 56% of adults drink alcohol
  - 67% of adult drinkers exceed guidelines for moderate alcohol use
  - 17% of adults binge drink
  - 6% of adults are heavy drinkers
- Drinking among young people is also common.
  - 35% of high school students drink alcohol
  - 21% of high school students binge drink

Alcohol Trends in MI: Binge Drinking

Reference:
https://www.cdc.gov/brfss/brfssprevalence/
Binge Drinking by Gender

Reference:
https://www.cdc.gov/brfss/brfssprevalence/
Alcohol Trends in MI: Heavy Drinking

Reference:
https://www.cdc.gov/brfss/brfssprevalence/
Heavy Drinking by Gender

Heavy Drinking in Adults by Gender, MI, BRFSS, 2007-2016

Reference:
https://www.cdc.gov/brfss/brfssprevalence/
Alcohol Trends Among MI Youth

Currently Drank Alcohol, MI, YRBS, 1997-2017

Reference:
Prevention Efforts

- The Community Guide for excessive alcohol consumption-
  - Electronic screening and brief interventions
  - Privatization of retail alcohol sales
  - Responsible beverage service training
  - Dram shop liability
  - Over-service law enforcement initiatives
  - Maintaining limits on hours and days of sale
  - Increasing alcohol taxes
  - Regulation of outlet density
  - Enhanced enforcement of laws prohibiting sales to minors

Viral Hepatitis

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Viral Hepatitis Epidemiologist and Viral Hepatitis Prevention Coordinator
Healthcare Associated Infection, Body Art Licensure, Tuberculosis, and Viral Hepatitis Section
Outline

1. Viral Hepatitis Epidemiology
   - Chronic Hepatitis B
   - Chronic Hepatitis C

2. Opportunities to Treat HBV and Cure HCV Infection

3. Viral Hepatitis Outcomes
   - Viral Hepatitis Hospitalizations
   - Viral Hepatitis Liver Transplants
   - Liver Cancer
Viral Hepatitis Epidemiology
Chronic Hepatitis B Cases Per 100,000 in Michigan, 2012-2017

Chronic Hepatitis B Cases per 100,000 Persons, Michigan, 2012-2017

<table>
<thead>
<tr>
<th>Year</th>
<th>Michigan Cases</th>
<th>Michigan (Rate per 100,000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012</td>
<td>1416</td>
<td>14.33</td>
</tr>
<tr>
<td>2013</td>
<td>1130</td>
<td>11.43</td>
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<tr>
<td>2014</td>
<td>1142</td>
<td>11.55</td>
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<tr>
<td>2015</td>
<td>1076</td>
<td>10.89</td>
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<tr>
<td>2016</td>
<td>1283</td>
<td>12.93</td>
</tr>
<tr>
<td>2017</td>
<td>1237</td>
<td>12.46</td>
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</tbody>
</table>
Chronic Hepatitis B Cases per 100,000 Population By Gender, Michigan, 2012-2017

Males are more likely to be impacted by Hepatitis B than females

<table>
<thead>
<tr>
<th>Year</th>
<th>Male</th>
<th>Male Incidence</th>
<th>Female</th>
<th>Female Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012</td>
<td>713</td>
<td>14.71</td>
<td>701</td>
<td>13.92</td>
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<tr>
<td>2013</td>
<td>691</td>
<td>14.25</td>
<td>437</td>
<td>8.68</td>
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<tr>
<td>2014</td>
<td>645</td>
<td>13.3</td>
<td>495</td>
<td>9.83</td>
</tr>
<tr>
<td>2015</td>
<td>645</td>
<td>13.3</td>
<td>431</td>
<td>8.56</td>
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<tr>
<td>2016</td>
<td>745</td>
<td>15.28</td>
<td>538</td>
<td>10.66</td>
</tr>
<tr>
<td>2017</td>
<td>714</td>
<td>14.62</td>
<td>522</td>
<td>10.33</td>
</tr>
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</table>
Asian and African Americans are disproportionately impacted by Hepatitis B than Caucasians.
Chronic Hepatitis C Cases per 100,000 Persons in MI, 2012-2017

<table>
<thead>
<tr>
<th>Year</th>
<th>Michigan Cases</th>
<th>Rate per 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012</td>
<td>8,005</td>
<td>80.99</td>
</tr>
<tr>
<td>2013</td>
<td>6,719</td>
<td>67.98</td>
</tr>
<tr>
<td>2014</td>
<td>8,233</td>
<td>83.30</td>
</tr>
<tr>
<td>2015</td>
<td>7,833</td>
<td>79.25</td>
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<tr>
<td>2016</td>
<td>11,883</td>
<td>119.76</td>
</tr>
<tr>
<td>2017</td>
<td>12,062</td>
<td>121.49</td>
</tr>
</tbody>
</table>
# Chronic Hepatitis C Cases per 100,000 Population by Gender, Michigan, 2012-2017

### Chronic Hepatitis C Cases per 100,000 Population by Gender in Michigan, 2012-2017

<table>
<thead>
<tr>
<th>Year</th>
<th>Male Cases</th>
<th>Male Incidence</th>
<th>Female Cases</th>
<th>Female Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012</td>
<td>5,170</td>
<td>106.64</td>
<td>2,791</td>
<td>55.43</td>
</tr>
<tr>
<td>2013</td>
<td>4,299</td>
<td>88.67</td>
<td>2,400</td>
<td>47.66</td>
</tr>
<tr>
<td>2014</td>
<td>5,215</td>
<td>107.57</td>
<td>3,000</td>
<td>59.58</td>
</tr>
<tr>
<td>2015</td>
<td>4,873</td>
<td>100.51</td>
<td>2,943</td>
<td>58.44</td>
</tr>
<tr>
<td>2016</td>
<td>6,946</td>
<td>142.42</td>
<td>4,906</td>
<td>97.23</td>
</tr>
<tr>
<td>2017</td>
<td>6,973</td>
<td>142.80</td>
<td>5,054</td>
<td>100.18</td>
</tr>
</tbody>
</table>

Males are more likely to be impacted by Hepatitis B than females.

Case Definition Change, 2016*
Chronic Hepatitis C Cases per 100,000 by Race and Ethnicity in Michigan, 2012-2017

Case Definition Change, 2016*

African American Incidence
Caucasian Incidence
All Other Races Incidence
Similar to HBV, African Americans are more likely to be impacted by HCV than Caucasians.
Opportunities to Treat HBV and Cure HCV Infection
**HBV Cure Cascade (Worldwide)**

**FIGURE 1. Care cascade* for hepatitis B treatment, by World Health Organization region, 2016**

- **Western Pacific**
- **South-East Asia**
- **European**
- **Eastern Mediterranean**
- **American**
- **African**

*Hepatitis B diagnosis and treatment status*:
- **Infected**
- **Infection diagnosed**
- **On treatment**
- **Viral suppression achieved**

HBV Treatment Study

![Graph showing cumulative probability of survival for Tenofovir and Placebo treatments.](image)

- **Tenofovir**
  - Number of patients: 27
  - Follow up in 90 days: 24, 19, 14, 11, 10, 10

- **Placebo**
  - Number of patients: 13
  - Follow up in 90 days: 24, 19, 14, 11, 10, 10

- *P value <0.05 (Log rank test)*
HCV Cure Cascade (U.S.)

- Chronic HCV-Infected* 100%
- Diagnosed and Aware† 50%
- Access to Outpatient Care‡ 43%
- HCV RNA Confirmed§ 27%
- Underwent Liver Biopsy¶ 17%
- Prescribed HCV Treatment¶¶ 16%
- Achieved SVR** 9%

* Chronic HCV-Infected; N=3,500,000.
† Calculated as estimated number chronic HCV-infected (3,500,000) x estimated percentage diagnosed and aware of their infection (49.8%); n=1,743,000.
‡ Calculated as estimated number diagnosed and aware (1,743,000) x estimated percentage with access to outpatient care (86.9%); n=1,514,667.
§ Calculated as estimated number with access to outpatient care (1,514,667) x estimated percentage HCV RNA confirmed (62.9%); n=952,726.
¶ Calculated as estimated number with access to outpatient care (1,514,667) x estimated percentage who underwent liver biopsy (38.4%); n=581,632.
¶¶ Calculated as estimated number with access to outpatient care (1,514,667) x estimated percentage prescribed HCV treatment (36.7%); n=555,883.
** Calculated as estimated number prescribed HCV treatment (555,883) x estimated percentage who achieved SVR (58.8%); n=326,859.

Note: Only non-VA studies are included in the above HCV treatment cascade.
### Proportion of Clients Receiving Test Type by Sex, 2017

#### Female
- **HCV Antibody**: 4572 (100.0%)
- **HCV RNA**: 2312 (50.6%)
- **HCV Genotype**: 762 (16.7%)

#### Male
- **HCV Antibody**: 6150 (100.0%)
- **HCV RNA**: 3322 (54.0%)
- **HCV Genotype**: 1543 (23.6%)
Proportion of Clients Receiving Test Type by Race, 2017

**White**
- HCV Antibody: 5500 (100.0%)
- HCV RNA: 3298 (59.4%)
- HCV Genotype: 1403 (25.3%)

**Black / African-American**
- HCV Antibody: 1641 (100.0%)
- HCV RNA: 848 (51.7%)
- HCV Genotype: 339 (20.7%)
HCV cure can improve liver inflammation and fibrosis...

**Figure 3 - Liver Stiffness Treatments in Patients Treated with Direct-Acting Antiviral Therapy**

This study enrolled 70 patients who received direct-acting antiviral therapy for chronic HCV infection. This graphic shows liver stiffness measurement at baseline, end-of-treatment, and 12-month posttreatment. Overall, 48.6% of the patients had a 30% or greater improvement in the liver stiffness measurement (at end of follow-up compared with baseline).

... Reduce risk of death, including liver-related and non-liver-related deaths...

Figure 7 - Impact of SVR on Mortality Rates with DAA Therapy

... Decreases (but does not eliminate) incidence of hepatocellular carcinoma...
and reduces extrahepatic manifestations

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>No Treatment</th>
<th>Treatment without SVR</th>
<th>Treatment with SVR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mixed cryoglobulinemia</td>
<td>0.72</td>
<td>0.52</td>
<td>0.33</td>
</tr>
<tr>
<td>Glomerulonephritis</td>
<td>2.83</td>
<td>1.62</td>
<td>1.09</td>
</tr>
<tr>
<td>Porphyria cutanea tarda</td>
<td>0.52</td>
<td>0.37</td>
<td>0.16</td>
</tr>
<tr>
<td>Lichen planus</td>
<td>0.68</td>
<td>0.71</td>
<td>0.56</td>
</tr>
<tr>
<td>Non-Hodgkin’s lymphoma</td>
<td>0.91</td>
<td>0.55</td>
<td>0.43</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>21.6</td>
<td>17.0</td>
<td>13.9</td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>1.01</td>
<td>0.58</td>
<td>0.75</td>
</tr>
<tr>
<td>Stroke</td>
<td>9.14</td>
<td>4.64</td>
<td>5.10</td>
</tr>
</tbody>
</table>

**Figure 8 - HCV Treatment and Outcome of Extrahepatic Manifestations**

Viral Hepatitis Outcomes
Liver Transplants and Transplant Waitlist, Michigan, 1988-2017

- Transplants
- Transplant Waitlist
- Transplants + Waitlist
Invasive Cancers of the Liver and Intrahepatic Bile Ducts in Michigan by Gender, 2004-2015

Incidence Rate (per 100,000 persons)

- Total Population
- Male
- Female
Number of Chronic Hepatitis C Cases Reported to MDHHS by year, 18-29 years of age, 2000-2017

Change in case definition, 2016*
Many people waiting for livers

New livers are becoming available because of the opioid crisis, but many of these livers are infected with HCV

But because there is a cure for HCV, there is the possibility of using these organs for transplant with the patient’s consent
Next Step:
Increase HCV Screening and Treatment

- Expansion of harm reduction services
  - Syringe services programs
    - HBV Vaccination
    - HCV Testing and Linkage to Care
    - Sterile needles/syringes and drug preparation equipment

- Integrated HCV screening and linkage to care
  - MDHHS BOL HCV Automatic Reflex Testing
  - Gilead FOCUS Program Partner
  - MDHHS HCV Treatment Navigator

- Increase public awareness of HBV, HCV, and liver cancer
  - Liver Cancer Awareness Month
In Closing...

- African Americans are disproportionately impacted by HBV and HCV than Caucasian counterparts.
- For HBV and HCV, males are more widely impacted than females.
- Baby boomers and young adults have high rates of HCV.
- Liver cancer incidence and mortality are both increasing.
- Hepatitis B and C are leading causes of liver cancer.
- More efforts are needed to screen individuals for HCV and vaccinate individuals for HBV, and link to care and treatment those who are infected with HBV or HCV.
For more viral hepatitis surveillance data, visit: www.michigan.gov/hepatitis
Acknowledgements

- Joe Coyle, MPH
- Adam Hart, MPH
- Kim Kirkey, PhD, MPH
Thanks!

- Contact the Viral Hepatitis Unit:
  [MDHHS-Hepatitis@michigan.gov](mailto:MDHHS-Hepatitis@michigan.gov)
Health Disparities

Heidi Neumayer, MPH
Health Disparities Epidemiologist
Health Disparities Reduction and Minority Health Section
Concept Overview

- Health Equity
- Health Disparities
- Health Inequities
- Equity vs. Equality

Image Source: Robert Wood Johnson Foundation
## Monitoring Disparities

- **Pairwise Disparity**
  - Compares minority group to reference group
  - **Relative Difference** = Minority Estimate / White Estimate
  - **% Change in relative difference** = \[rac{(Time 2 - Time 1)}{Time 1}\] \* 100

### Table: Relative Difference % Change 2011-2013, 2014-2016

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Black, non-Hispanic</td>
<td></td>
<td></td>
<td>2.00</td>
<td>2.16</td>
</tr>
<tr>
<td>Asian or Pacific Islander, non-Hispanic</td>
<td>1.48</td>
<td>1.70</td>
<td>1.79</td>
<td>1.90</td>
</tr>
<tr>
<td>American Indian or Alaska Native</td>
<td>2.6</td>
<td>2.95</td>
<td>1.77</td>
<td>2.04</td>
</tr>
<tr>
<td>Hispanic</td>
<td></td>
<td></td>
<td>1.43</td>
<td>1.15</td>
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<tr>
<td>Hispanic</td>
<td>2.00</td>
<td>2.16</td>
<td>1.63</td>
<td>1.58</td>
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<tr>
<td>Hispanic</td>
<td>2.00</td>
<td>2.16</td>
<td>1.63</td>
<td>1.58</td>
</tr>
</tbody>
</table>

### Diagram: Disease Prevalence

- **DISPARITY**
  - Time 1: 15%
  - Time 2: 28%
  - Reference
  - Minority
Population Disparity

- Index of Disparity
  - Average disparity between all subpopulations and the total population
- Between 2011-2013 and 2014-2016, the Index of Disparity decreased from 83.5% to 40.0% (equity improvement)

Index of Disparity

\[ ID = \frac{\left( \frac{\sum (r_n \times R)}{N} \right) - R}{R} \times 100 \]

- ID = Index of Disparity
- \( r_n \) = Estimate for Group n
- R = Estimate for Total Population
- N = Number of groups
Digging Deeper

Survival Differences
- 13.3% (12.7%-14.0%) 5-year survival rate for Blacks
- 15.6% (15.3%-15.9%) 5-year survival rate for Whites
- Previous literature has shown Blacks more likely to be diagnosed at regional or distant stages than Whites.

What is behind the differences in outcomes?
- Behavioral Risk Factors
- Access to Care
- Other Social Determinants of Health

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Years</th>
<th>NH Black: NH White Disparity</th>
<th>Years</th>
<th>NH Black: NH White Disparity</th>
<th>% Change</th>
<th>Disparity Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver and Intrahepatic Bile Duct (IHBD) Mortality</td>
<td>2009-2011</td>
<td>2.0</td>
<td>2012-2014</td>
<td>1.9</td>
<td>5.0%</td>
<td>-</td>
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<tr>
<td>Liver and IHBD Mortality Incidence</td>
<td>2009-2011</td>
<td>1.9</td>
<td>2012-2014</td>
<td>2.1</td>
<td>10.5%</td>
<td>+</td>
</tr>
<tr>
<td>Behavioral Risk Factors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Binge Drinking</td>
<td>2008-2010</td>
<td>0.6</td>
<td>2012-2014</td>
<td>0.7</td>
<td>16.7%</td>
<td>+</td>
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<tr>
<td>Heavy Drinking</td>
<td>2008-2010</td>
<td>0.5</td>
<td>2012-2014</td>
<td>0.5</td>
<td>0.0%</td>
<td>0</td>
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<td>Social Determinants</td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>No health care coverage</td>
<td>2008-2010</td>
<td>1.5</td>
<td>2012-2014</td>
<td>1.6</td>
<td>6.7%</td>
<td>+</td>
</tr>
<tr>
<td>No health care access due to cost</td>
<td>2008-2010</td>
<td>1.4</td>
<td>2012-2014</td>
<td>1.4</td>
<td>0.0%</td>
<td>0</td>
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<tr>
<td>No personal provider</td>
<td>2008-2010</td>
<td>1.6</td>
<td>2012-2014</td>
<td>1.4</td>
<td>12.5%</td>
<td>-</td>
</tr>
</tbody>
</table>
Challenges and Next Steps

Challenges
- Wide confidence intervals for smaller populations
- Aggregate years needed
- Age-adjustment
- Lack of data availability
- Subpopulation estimates differ from overarching population

Next Steps
- Increase data access and availability
  - Minority Behavioral Risk Factor Surveys
- Community Engagement
- Targeted Interventions
- Equity focused programming