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

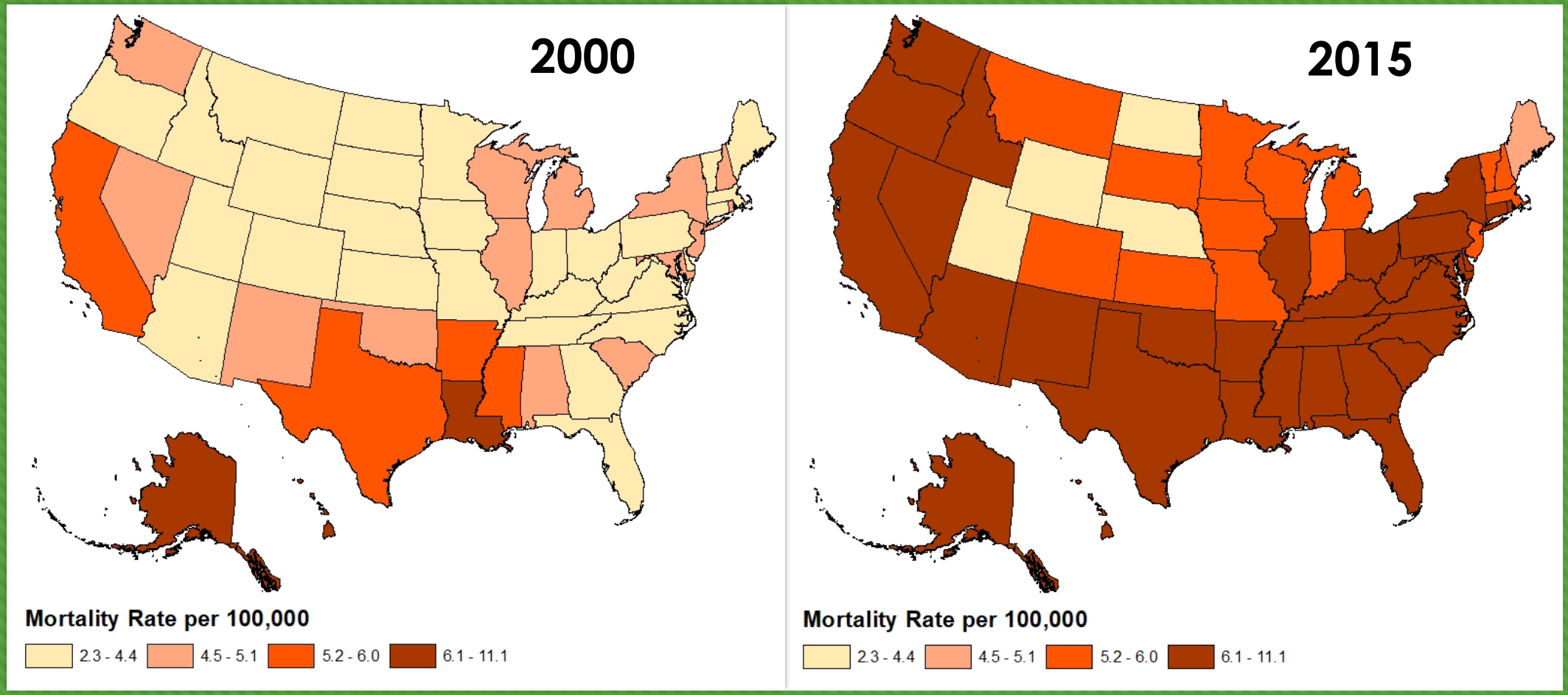
Health Disparities

Liver Cancer Epidemiology

Taylor Seaton, MS

Cancer Epidemiologist

Cancer Prevention and Control Section

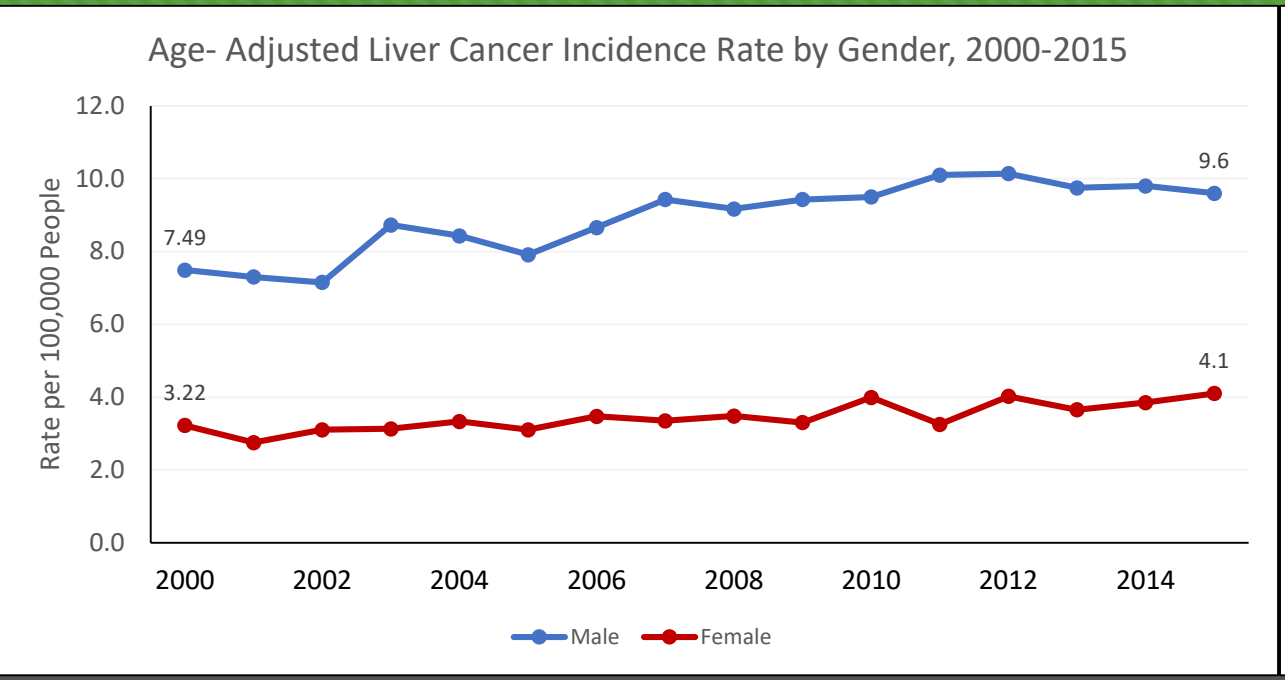


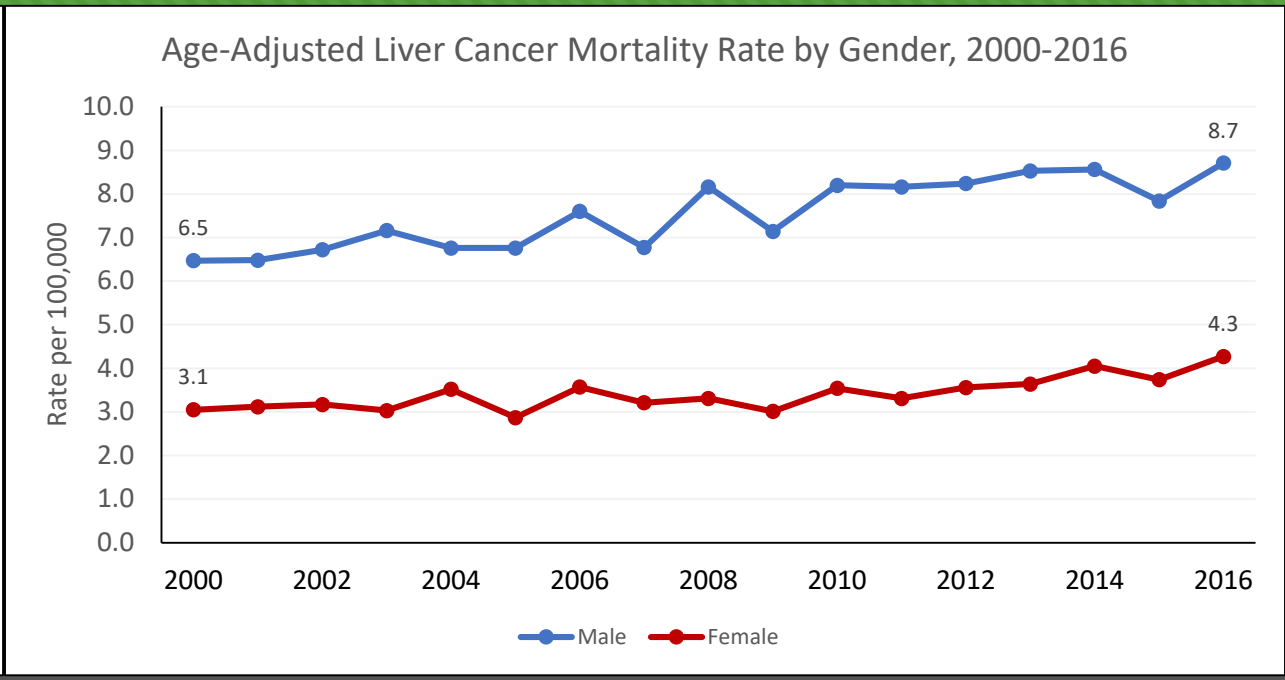
Liver Cancer: Nationwide Trend

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





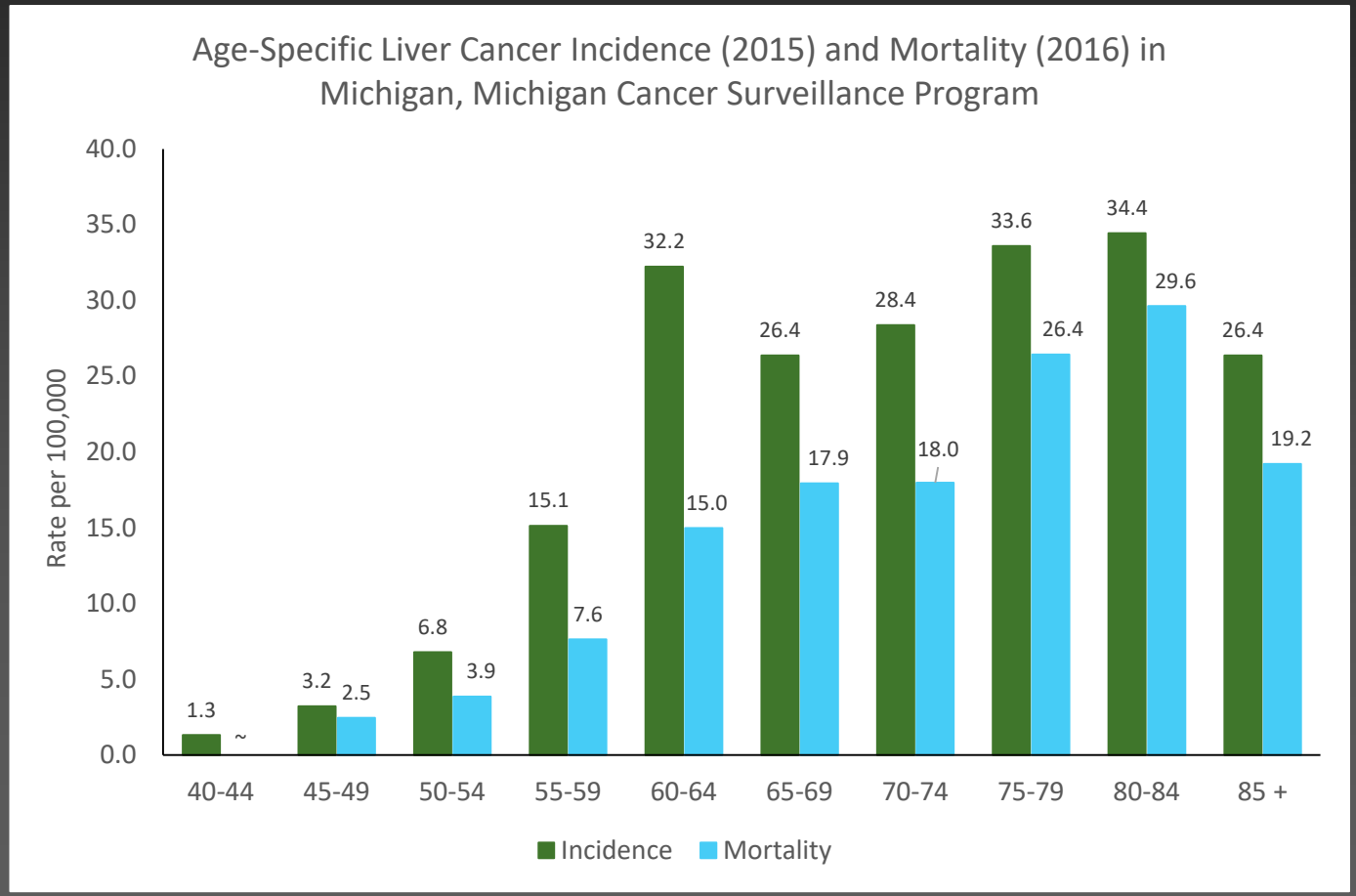
- **Incidence** increased in males by 28.2% and females by 27.3%.
  - Males aged 60-64 increased by165.6% and females aged 70-74 increased by 39.8%.

- **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

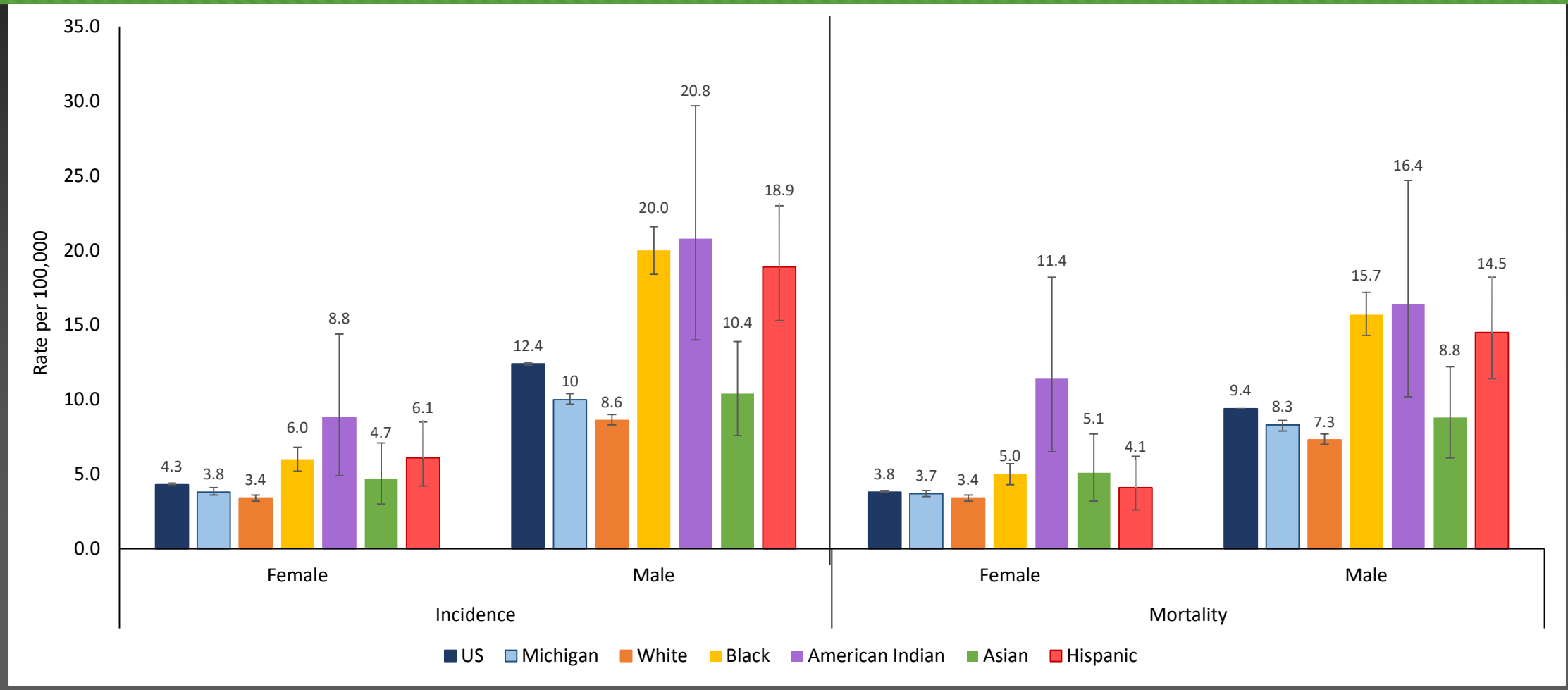
Liver Cancer: Michigan Fast Stats

- 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

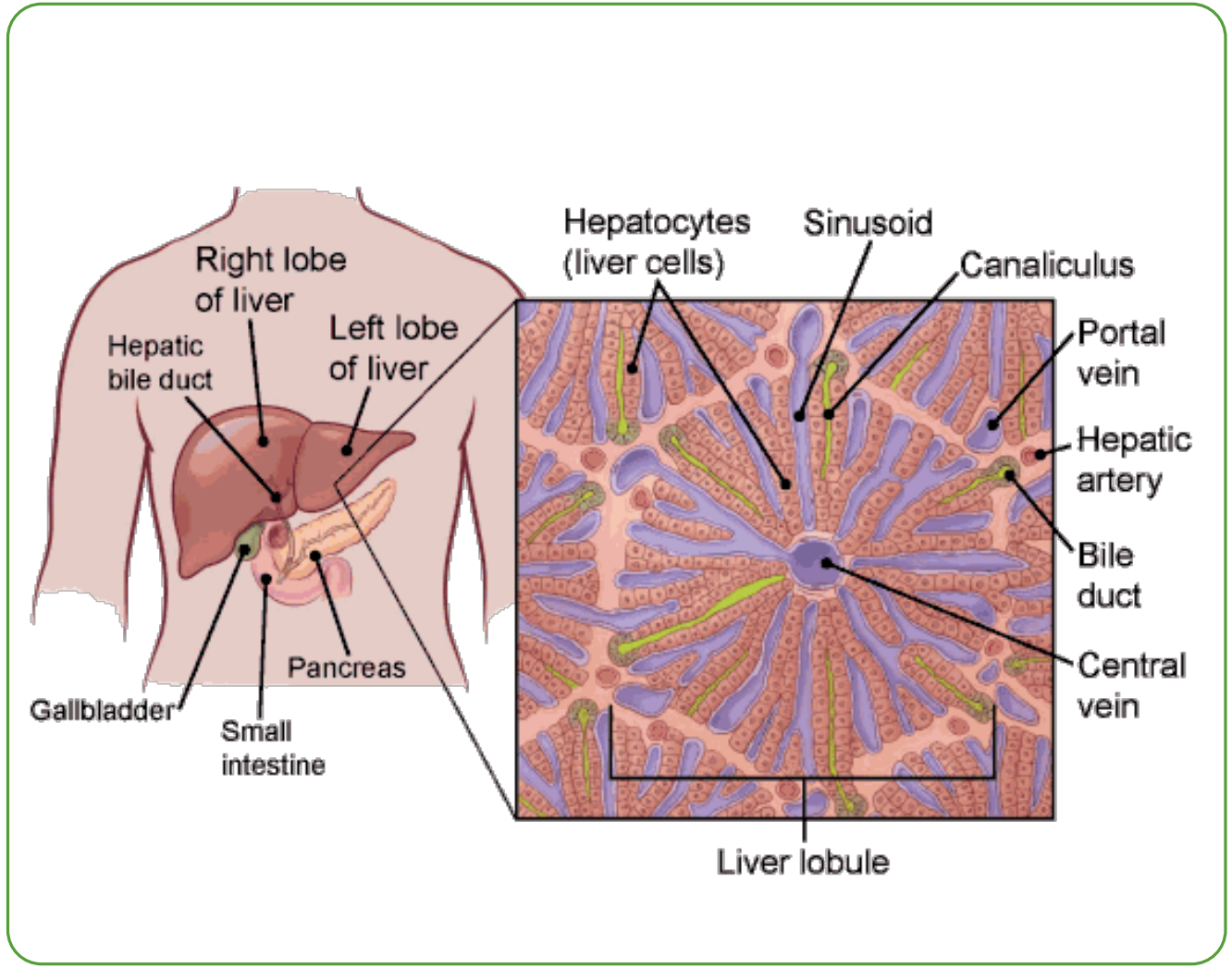
Liver Cancer: By Race in Michigan, 2011-2015 NIH



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 cholangiocarinoma (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

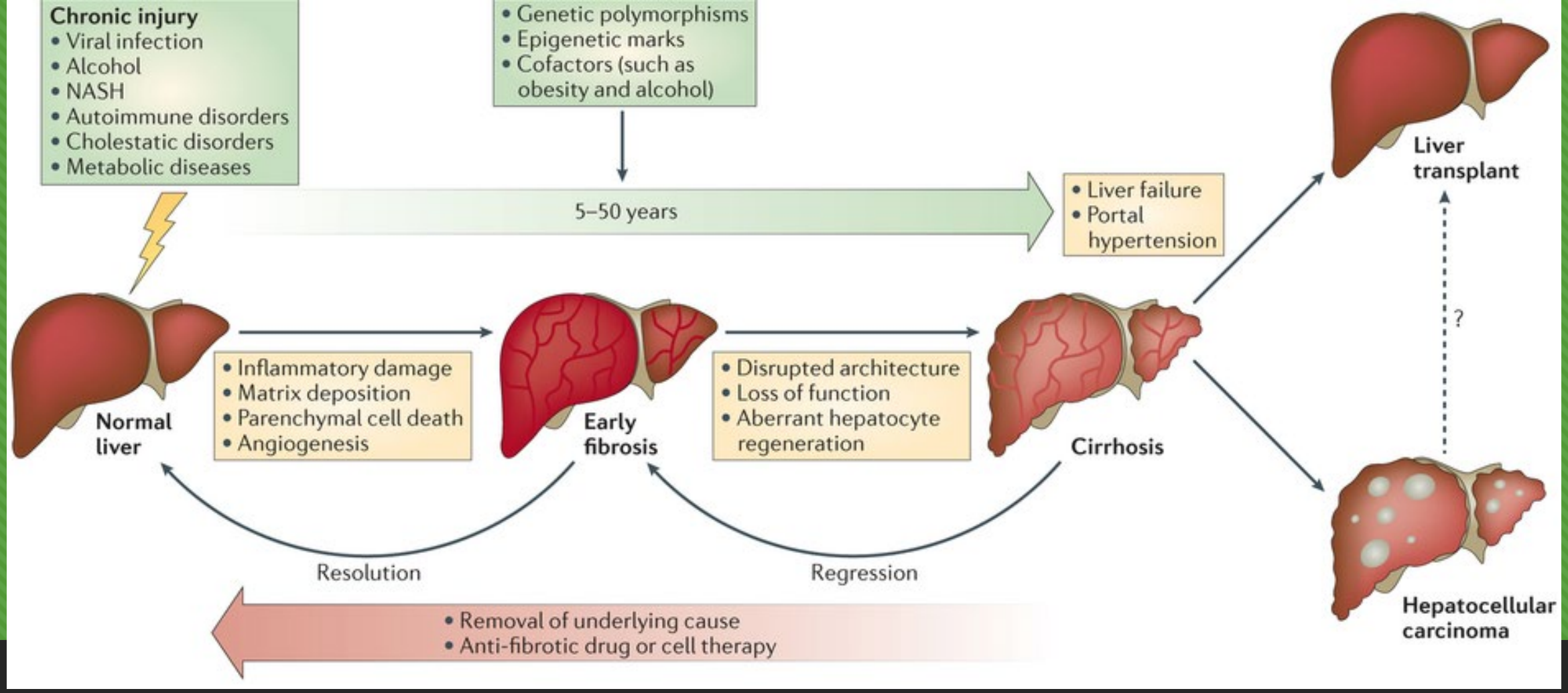
Average Risk

- 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

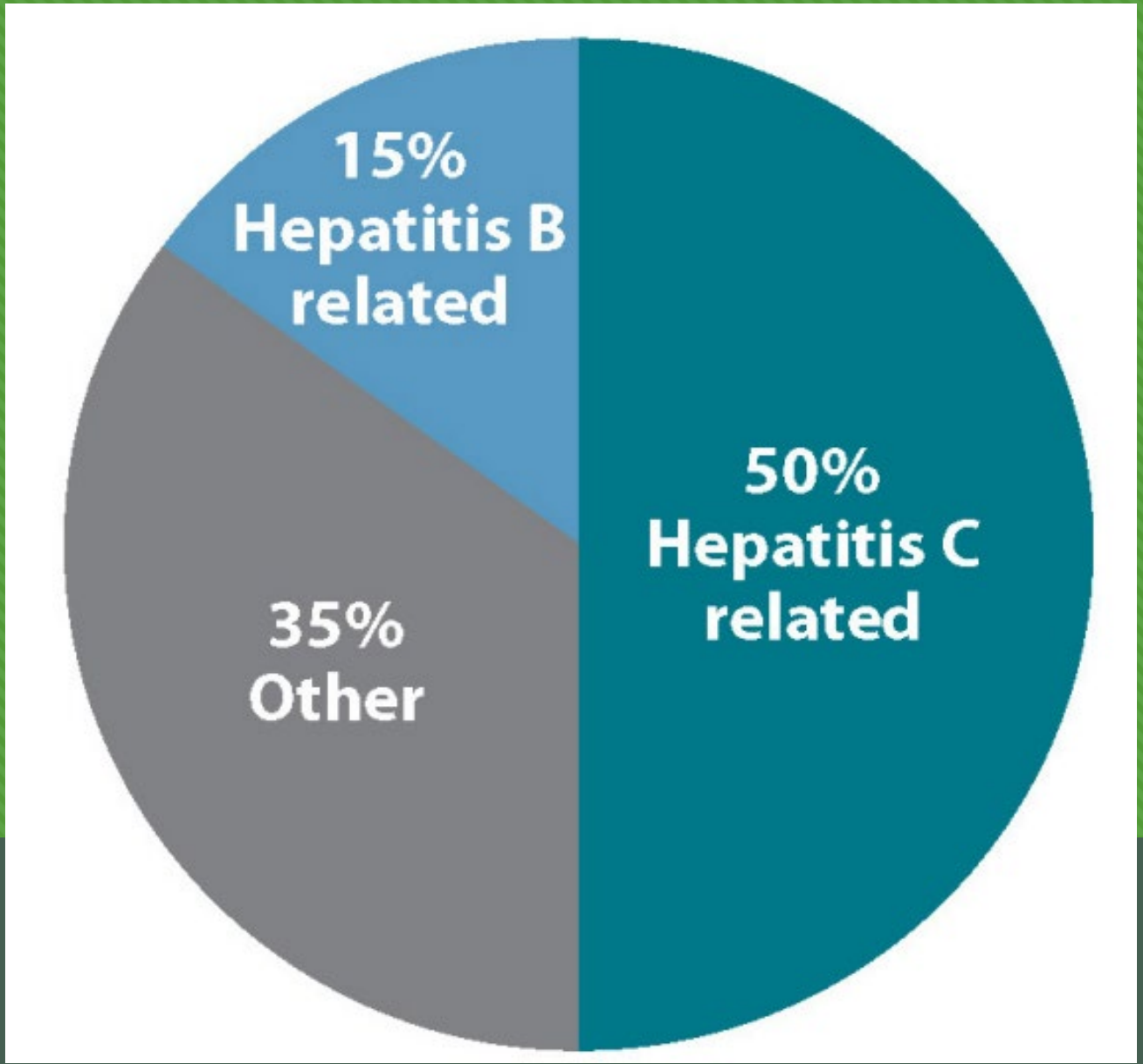
Source: American Cancer Society



Stages of Progression

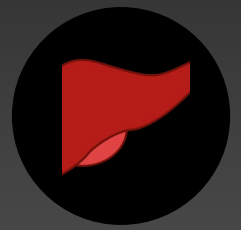
Fatty Liver: Reversible

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



Source: https://www.cdc.gov/nchhstp/newsroom/docs/factsheets/viral-hep-liver-cancer.pdf

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/fact-sheets/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.niaaa.nih.gov/alcohol-health/overview-alcohol-consumption/alcohol-facts-and-statistics

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

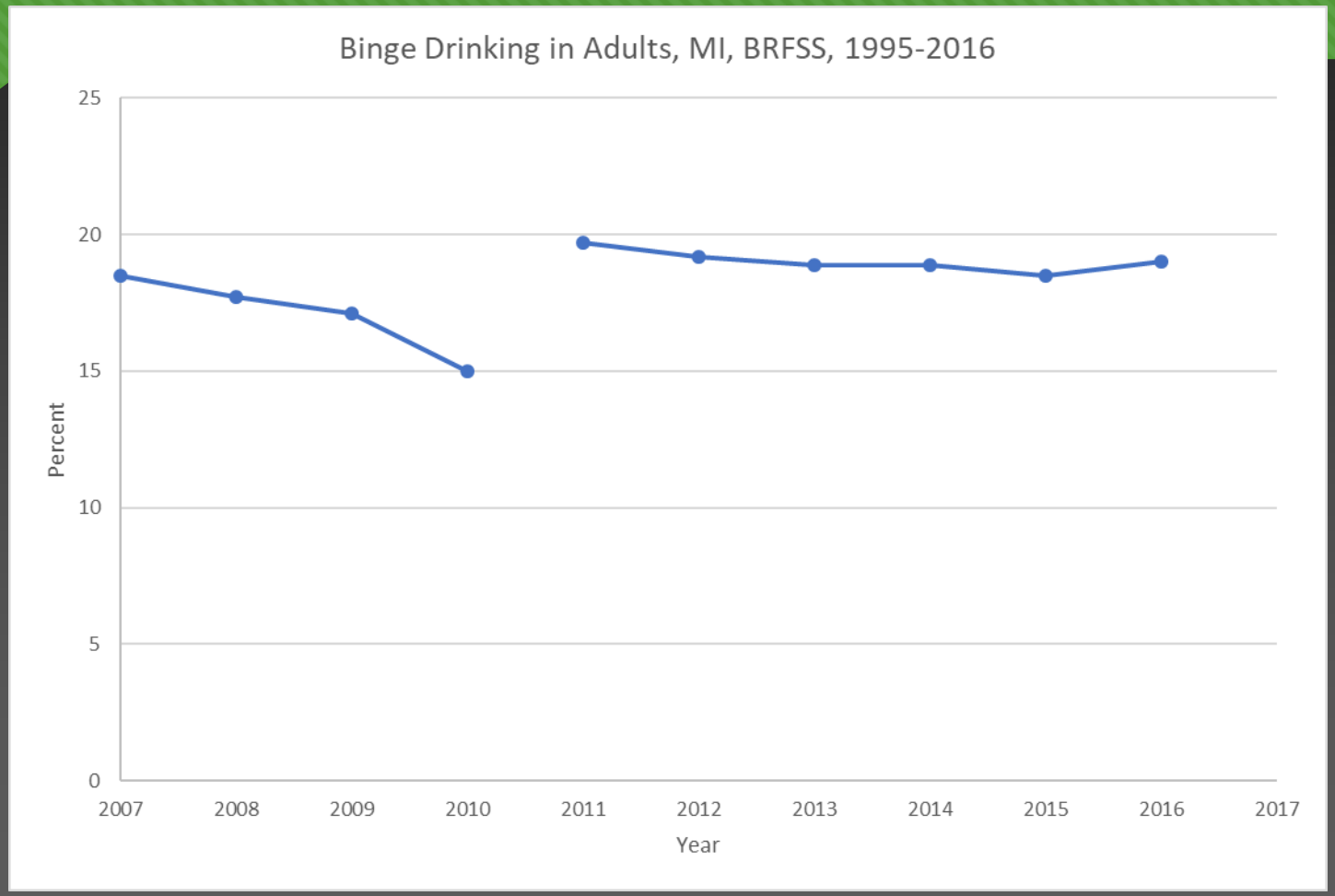
Reference:
https://nccd.cdc.gov/DPH_ARDI/Default/Default.aspx

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

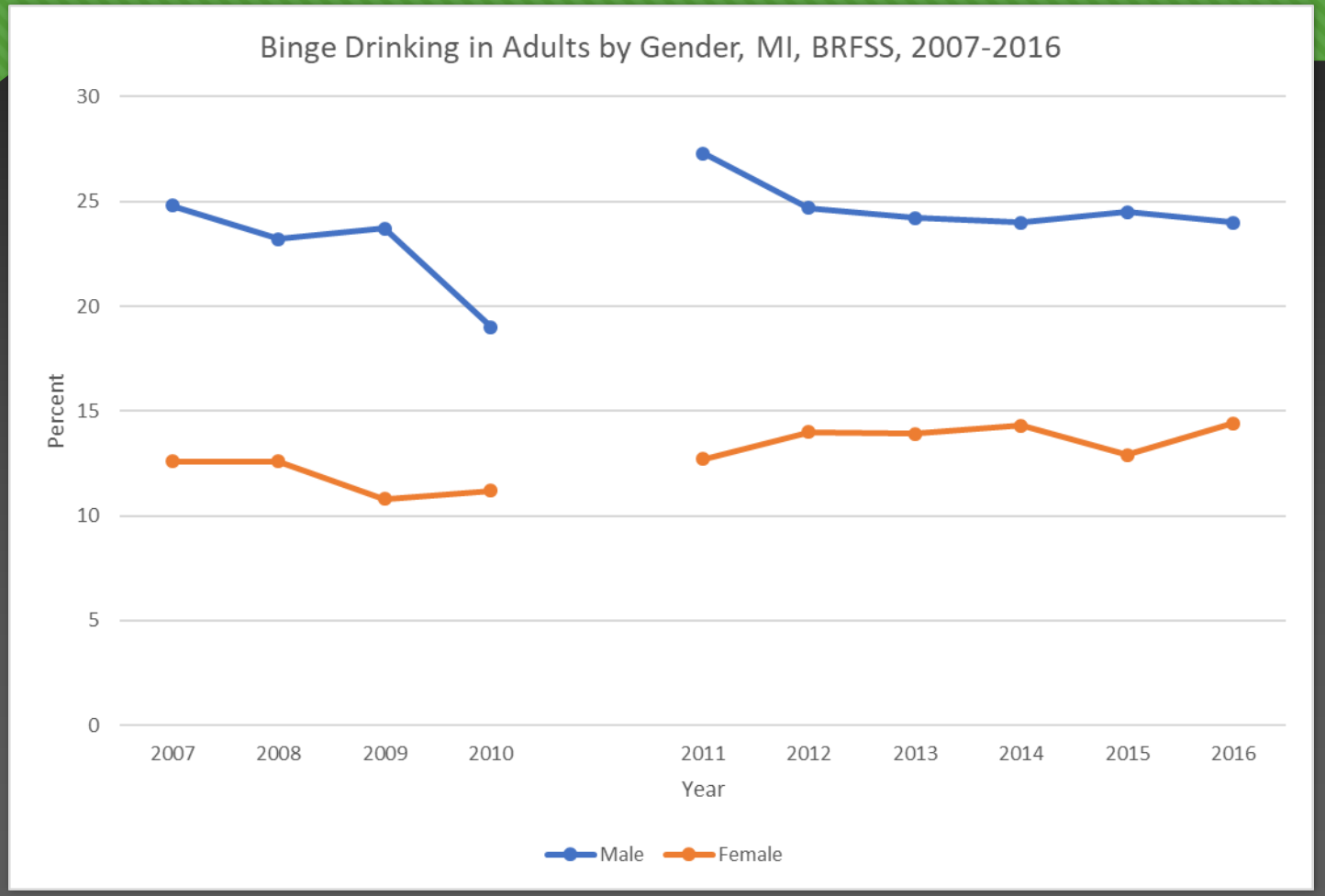
Reference:
https://www.cdc.gov/cancer/dcpc/prevention/policies_practices/alcohol/index.htm

Alcohol Trends in MI: Binge Drinking



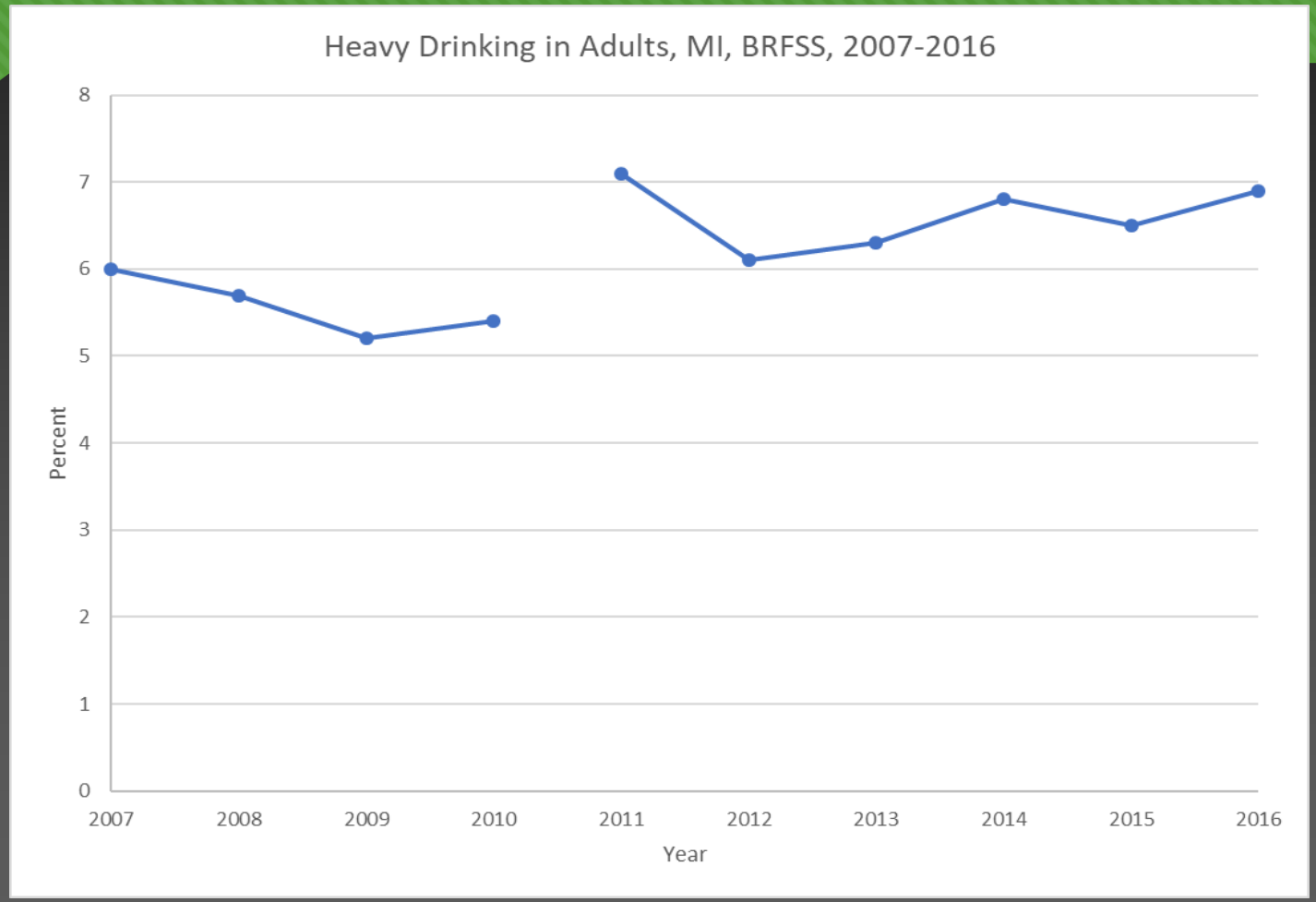
Reference:
https://www.cdc.gov/brfss/brfssprevalence/

Binge Drinking by Gender



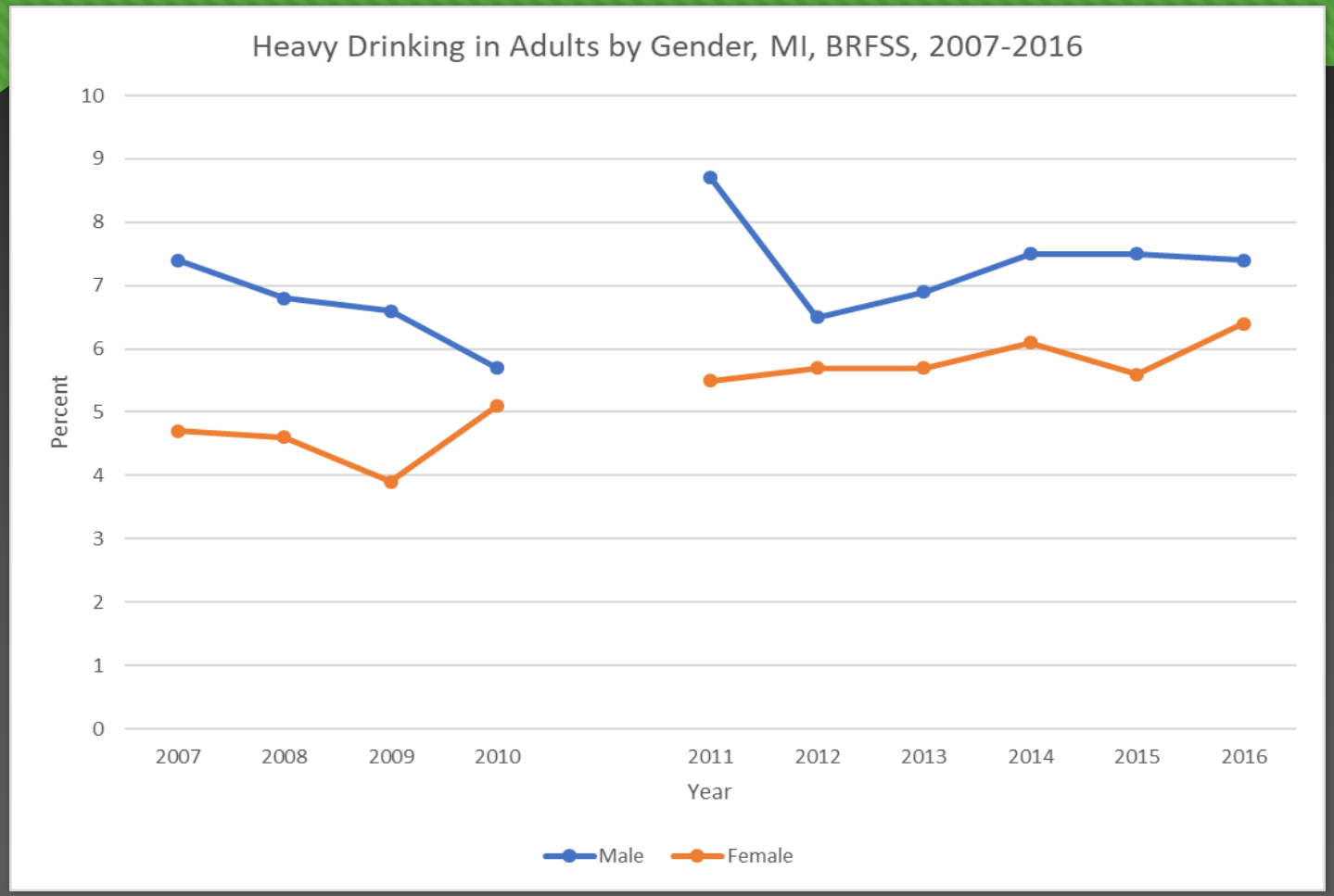
Reference:
https://www.cdc.gov/brfss/brfssprevalence/

Alcohol Trends in MI: Heavy Drinking



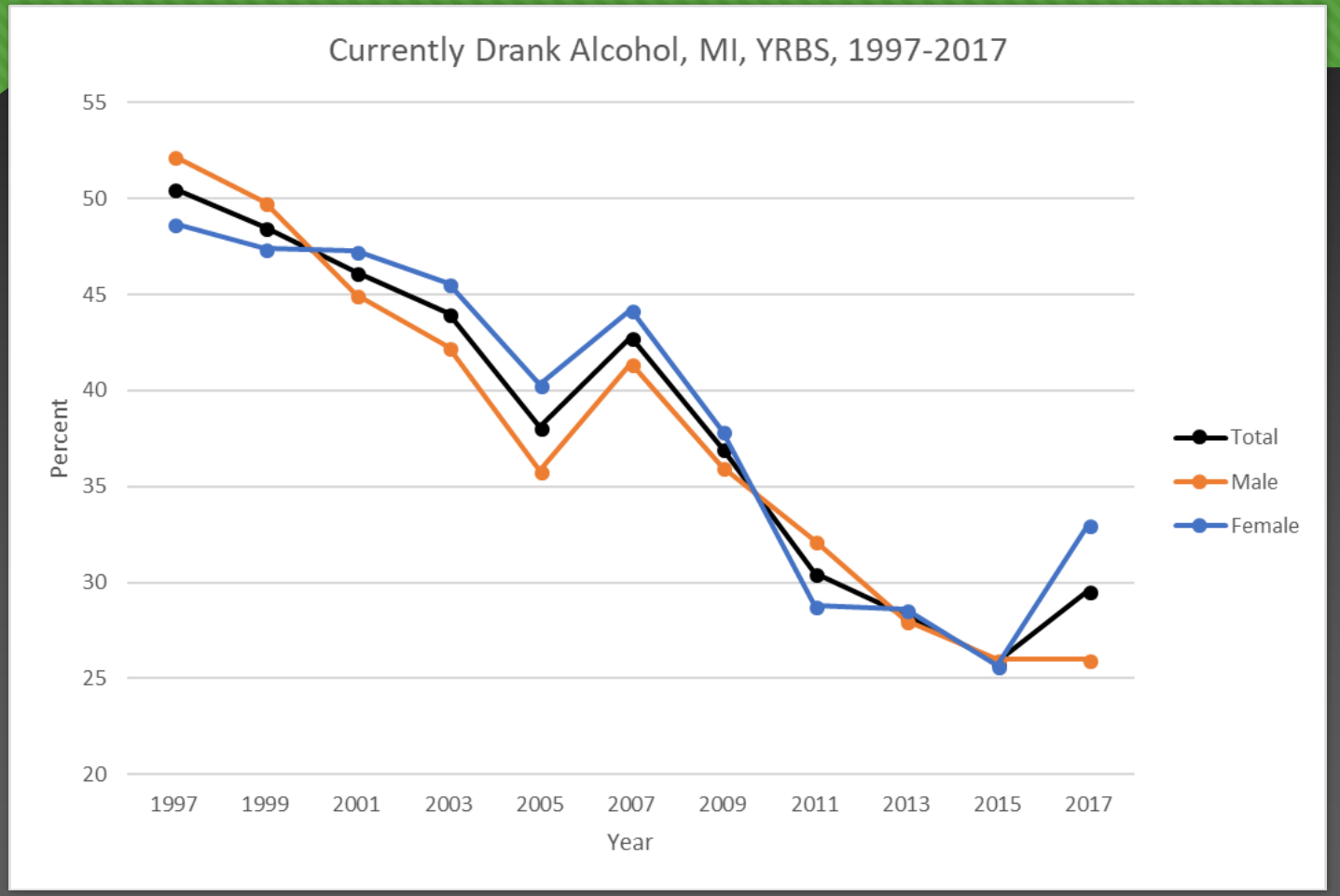
Reference:
https://www.cdc.gov/brfss/brfssprevalence/

Heavy Drinking by Gender



Reference:
https://www.cdc.gov/brfss/brfssprevalence/

Alcohol Trends Among MI Youth



Reference:
https://nccd.cdc.gov/youthonline/App/Results.aspx?LID=MI

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

Reference: https://www.thecommunityguide.org/topic/excessive-alcohol-consumption

Viral Hepatitis

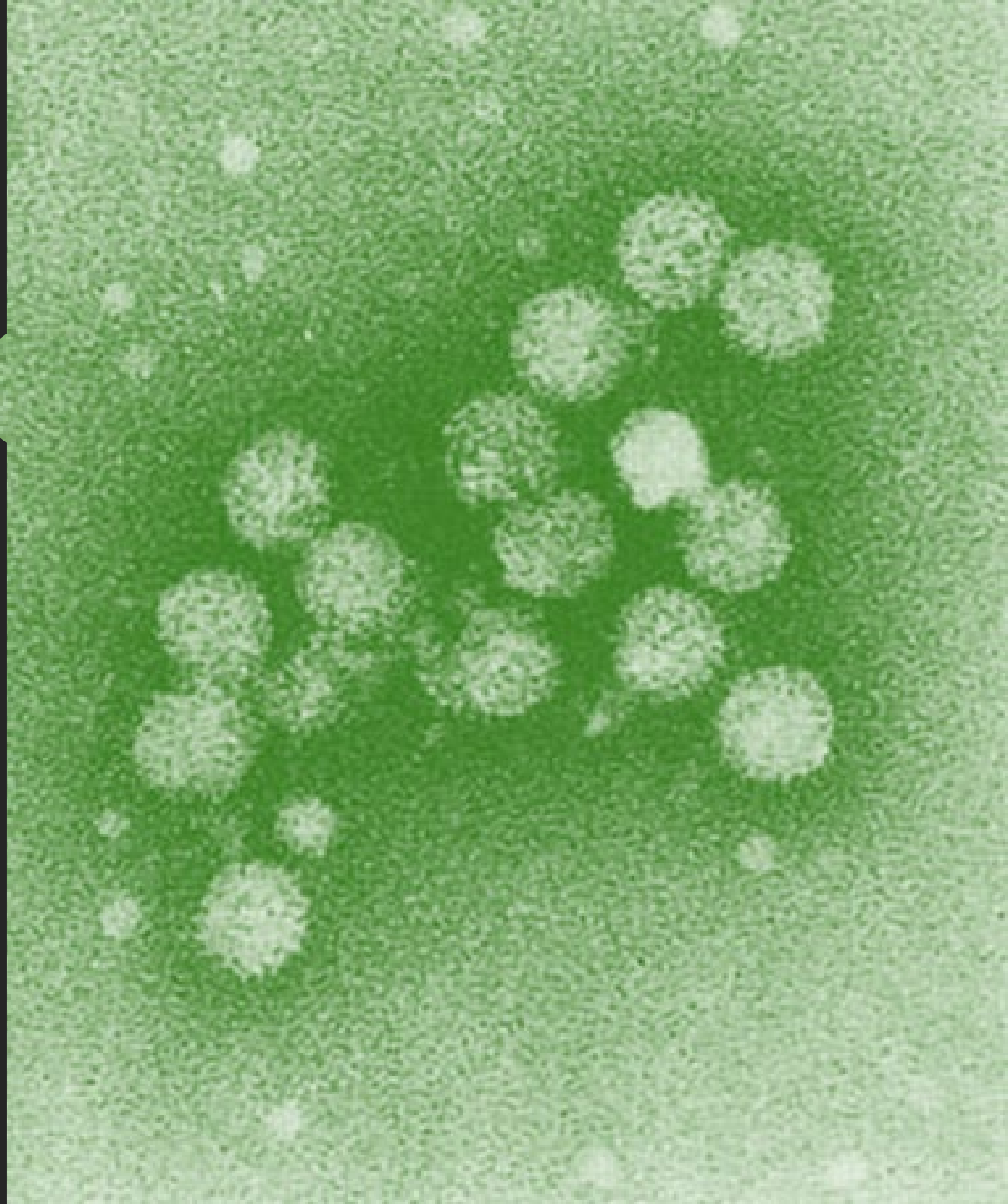
Marjorie Oswald, MPH and Teresa Wong, MPH

Viral Hepatitis Epidemiologist and Viral Hepatitis Prevention Coordinator

Healthcare Associated Infection, Body Art Licensure, Tuberculosis, and Viral Hepatitis Section

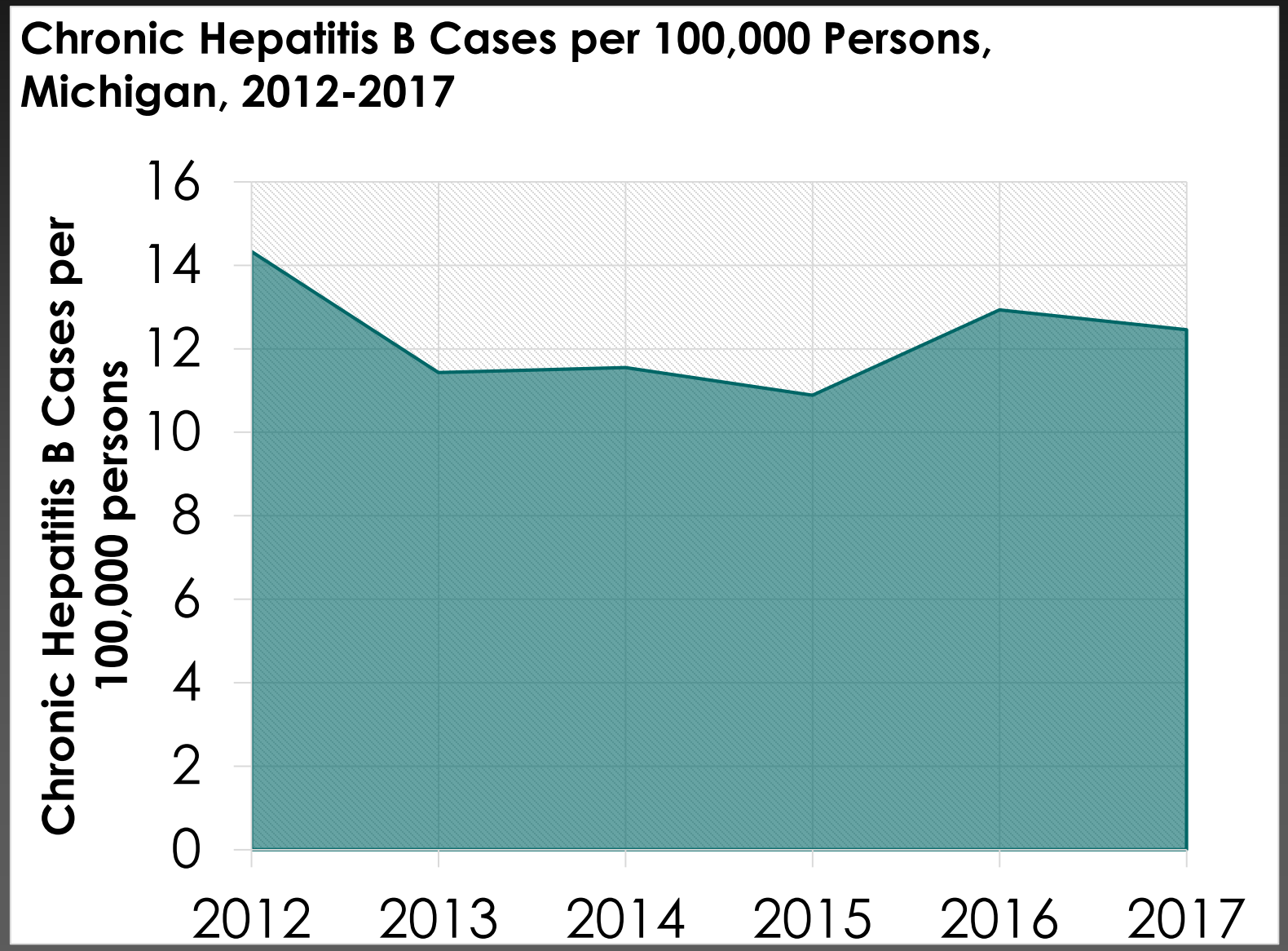
Outline

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

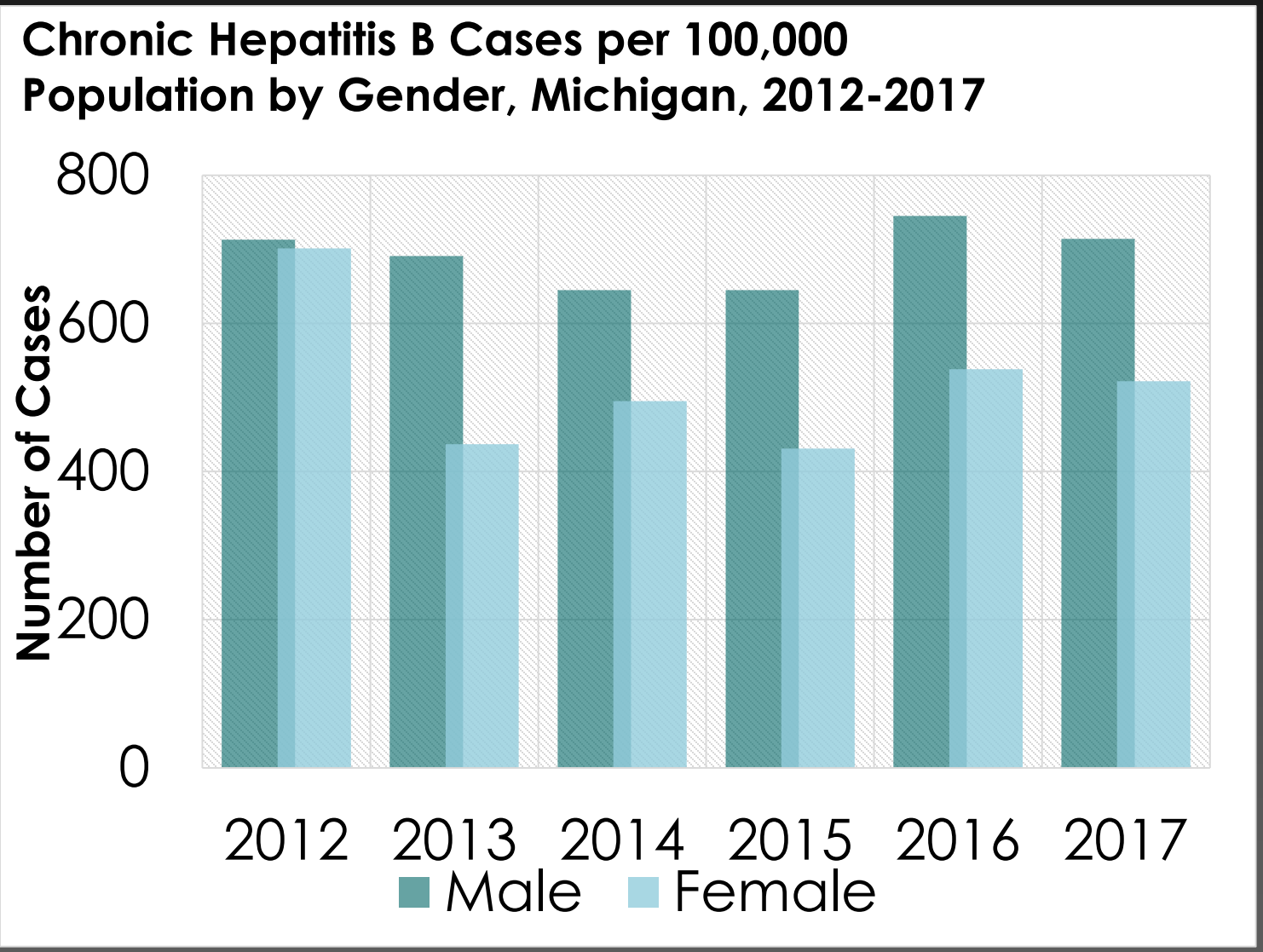
Chronic Hepatitis B Cases Per 100,000 in Michigan, 2012-2017



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

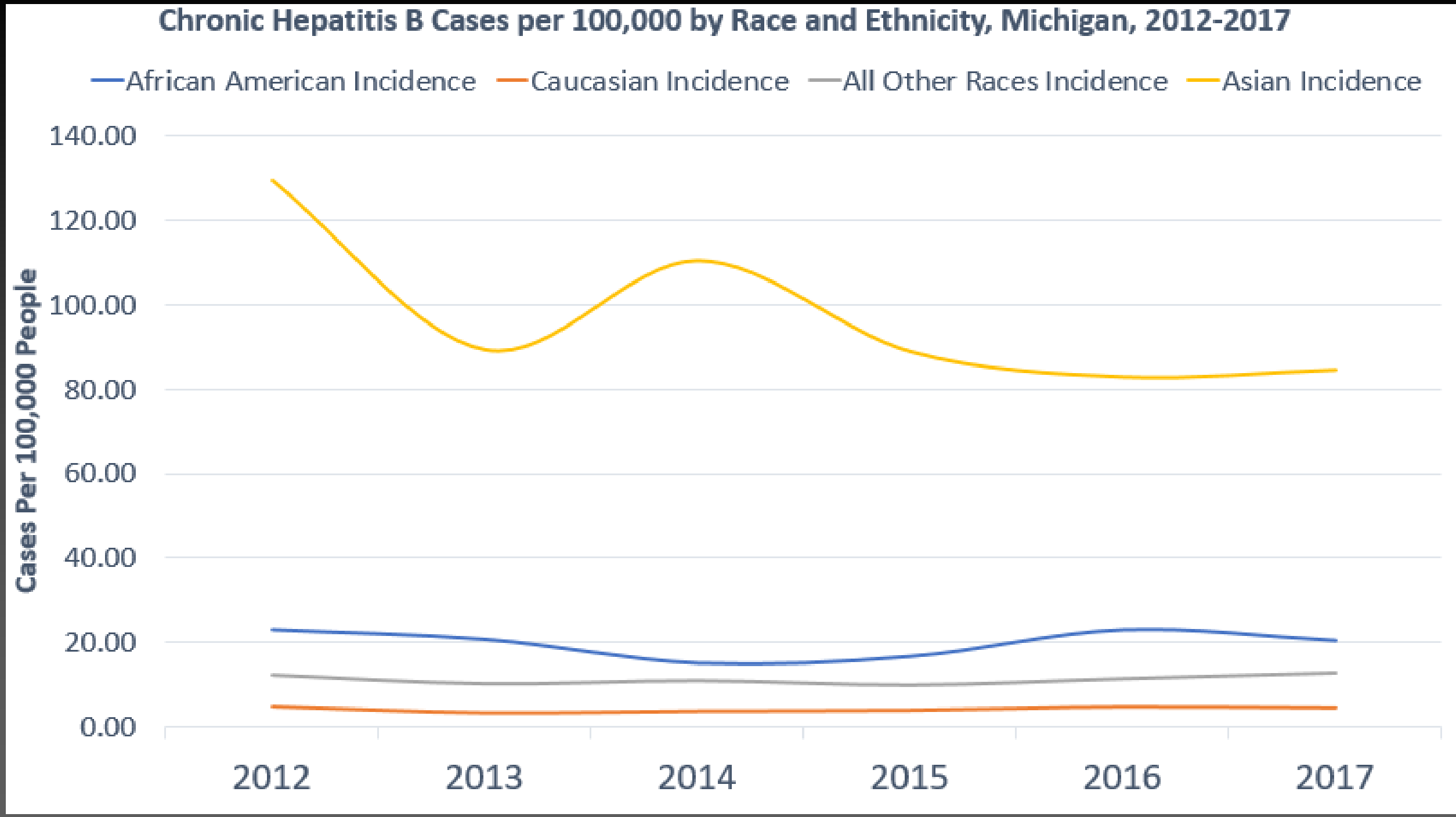
Year	Michigan Cases	Michigan (Rate per 100,000)
2012	1416	14.33
2013	1130	11.43
2014	1142	11.55
2015	1076	10.89
2016	1283	12.93
2017	1237	12.46

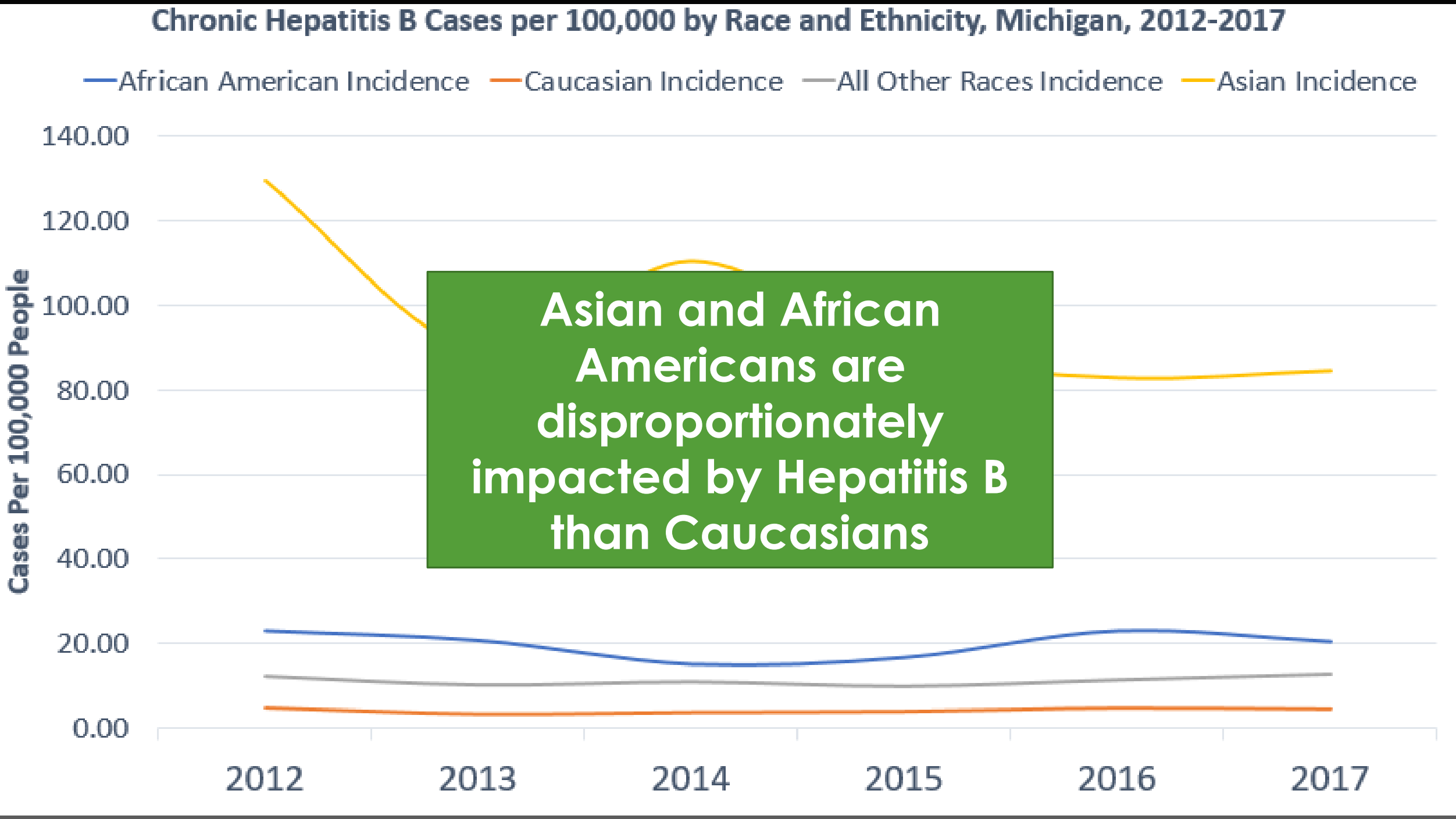
Chronic Hepatitis B Cases per 100,000 Population By Gender, Michigan, 2012-2017



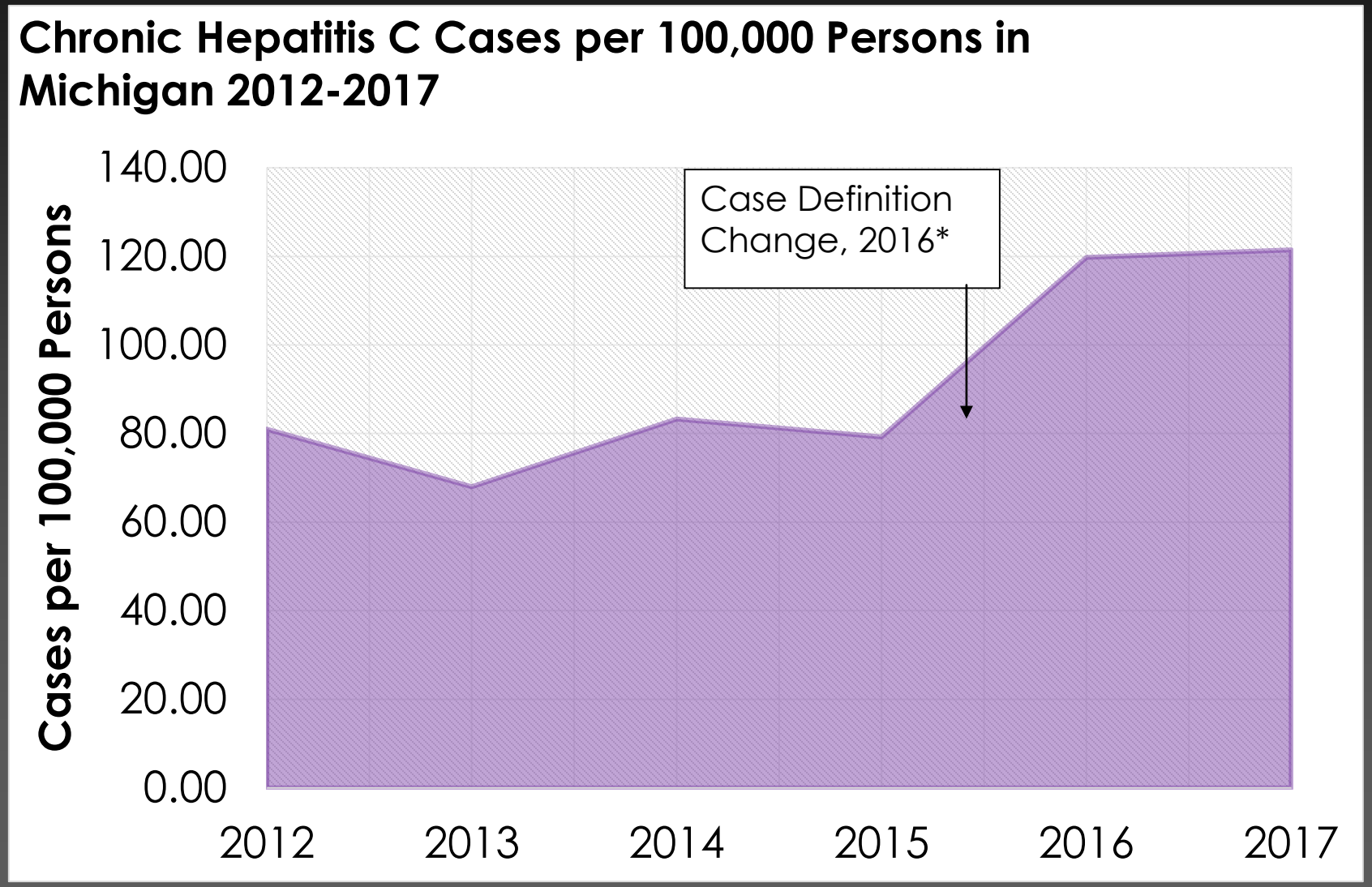
Males are more likely to be impacted by Hepatitis B than females

Year	Male	Male Incidence	Female	Female Incidence
2012	713	14.71	701	13.92
2013	691	14.25	437	8.68
2014	645	13.3	495	9.83
2015	645	13.3	431	8.56
2016	745	15.28	538	10.66
2017	714	14.62	522	10.33


Chronic Hepatitis B Cases per 100,000 by Race and Ethnicity, Michigan, 2012-2017
African American Incidence
Caucasian Incidence
All Other Races Incidence
Asian Incidence
Cases Per 100,000 People
140.00
120.00
100.00
80.00
60.00
40.00
20.00
0.00
2012
2013
2014
2015
2016
2017


Chronic Hepatitis B Cases per 100,000 by Race and Ethnicity, Michigan, 2012-2017
African American Incidence
Caucasian Incidence
All Other Races Incidence
Asian Incidence
Cases Per 100,000 People
140.00
120.00
100.00
80.00
60.00
40.00
20.00
0.00
2012
2013
2014
2015
2016
2017
Asian and African Americans are disproportionately impacted by Hepatitis B than Caucasians

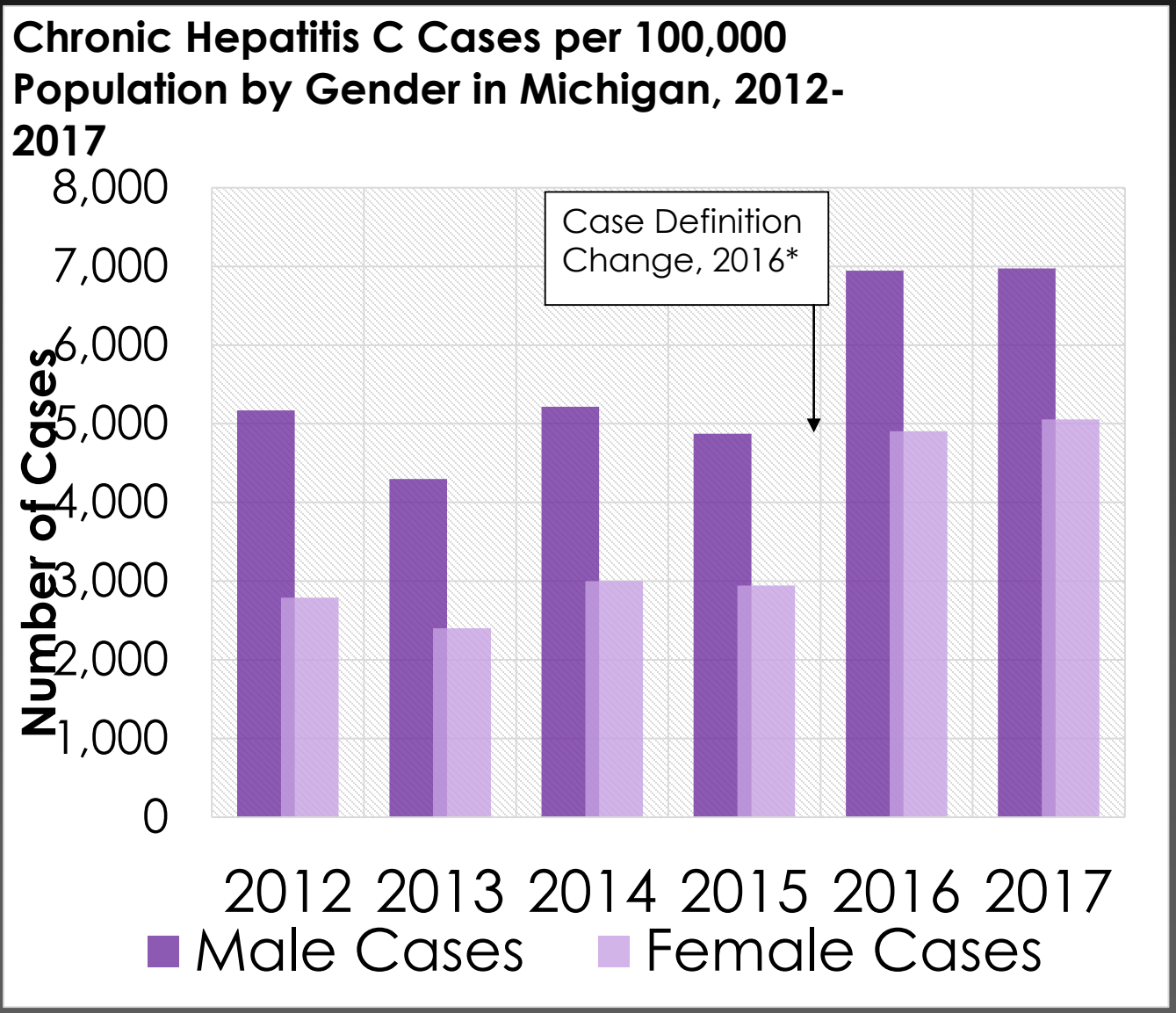
Chronic Hepatitis C Cases per 100,000 Persons in MI, 2012-2017



Chronic Hepatitis C Cases Per 100,000 Persons in Michigan, 2012-2017

Year	Michigan Cases	Rate per 100,000
2012	8,005	80.99
2013	6,719	67.98
2014	8,233	83.30
2015	7,833	79.25
2016	11,883	119.76
2017	12,062	121.49

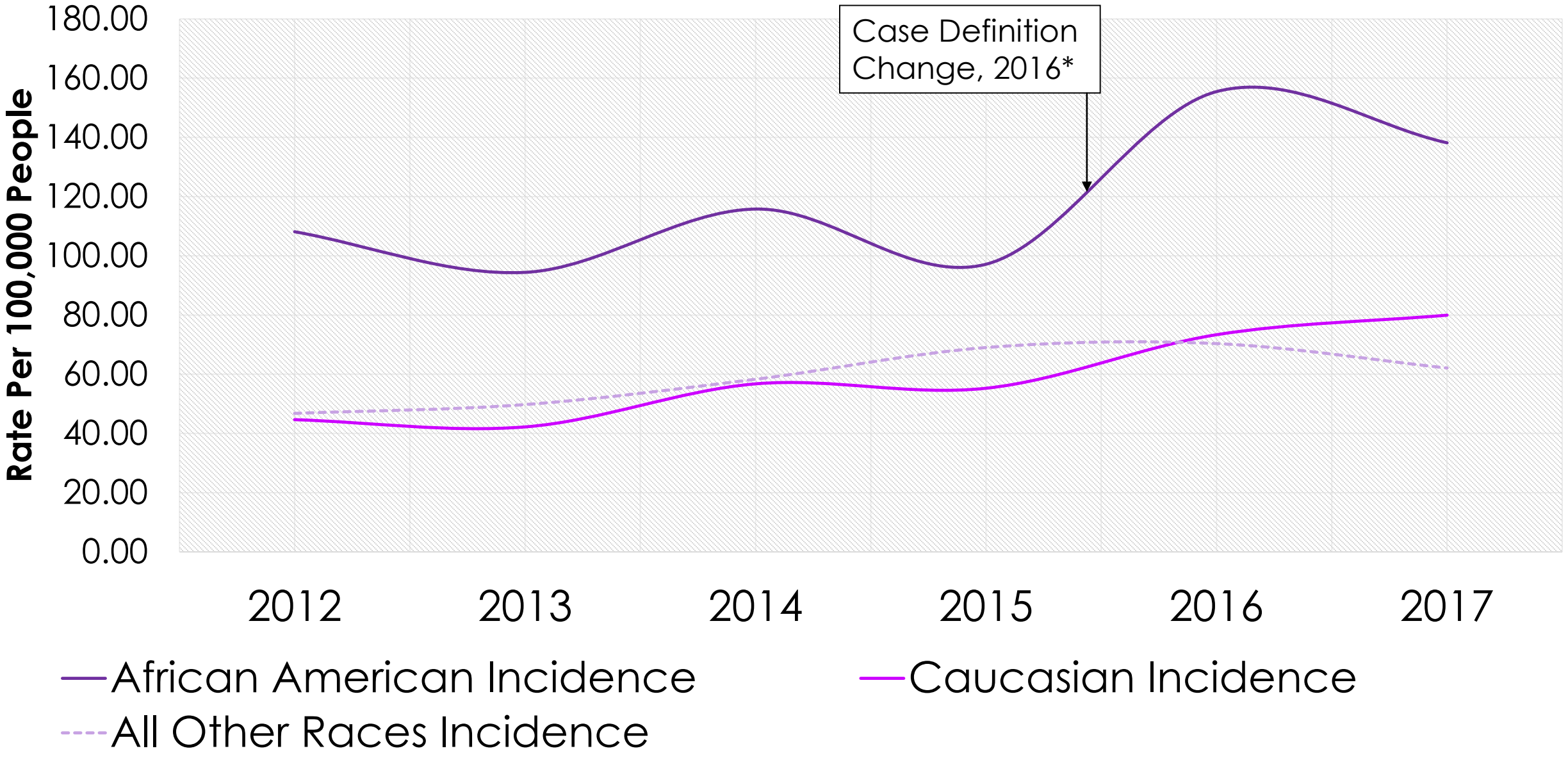
Chronic Hepatitis C Cases per 100,000 Population by Gender, Michigan, 2012-2017



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

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

Chronic Hepatitis C Cases per 100,000 by Race and Ethnicity in Michigan, 2012-2017



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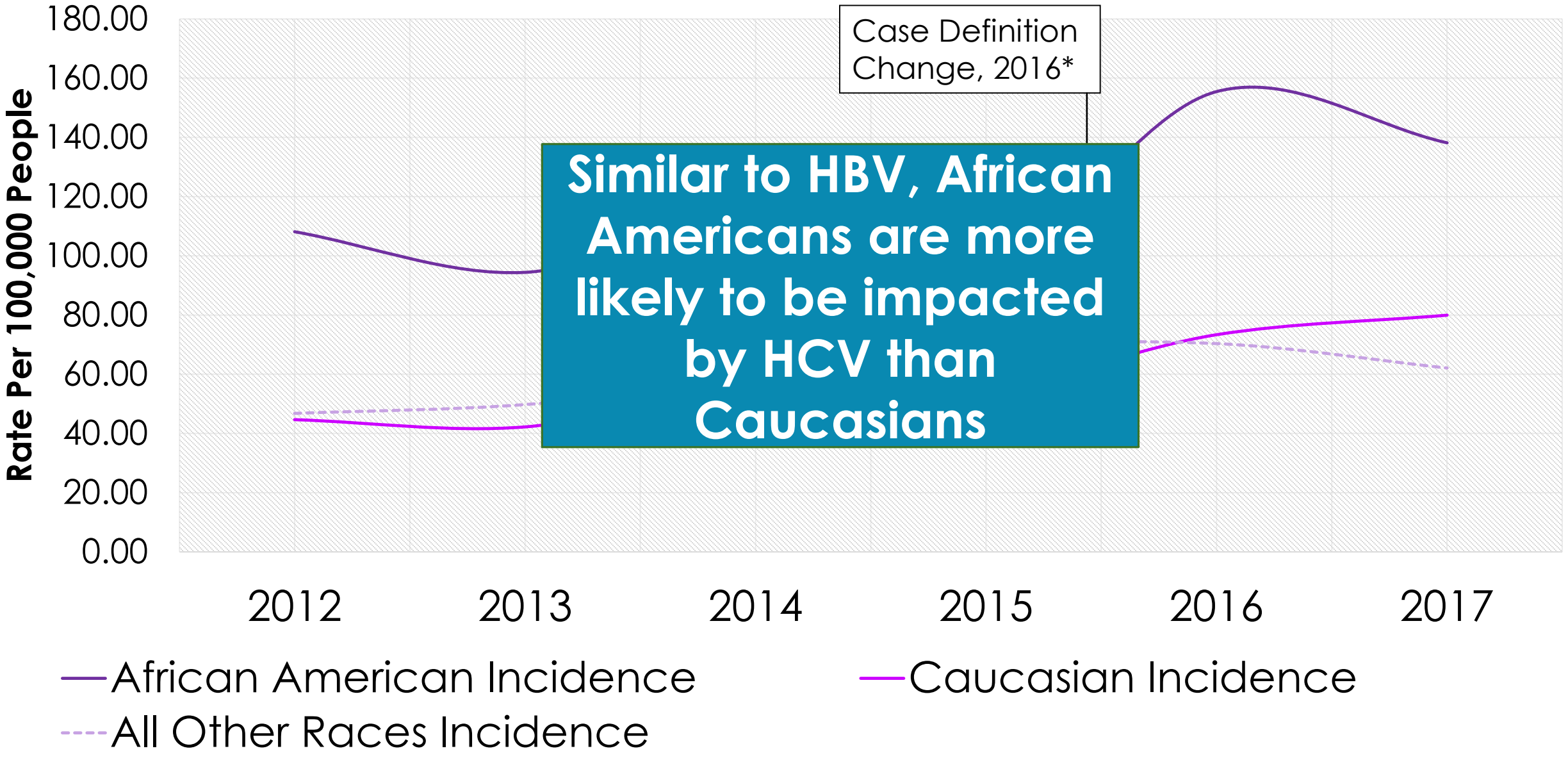
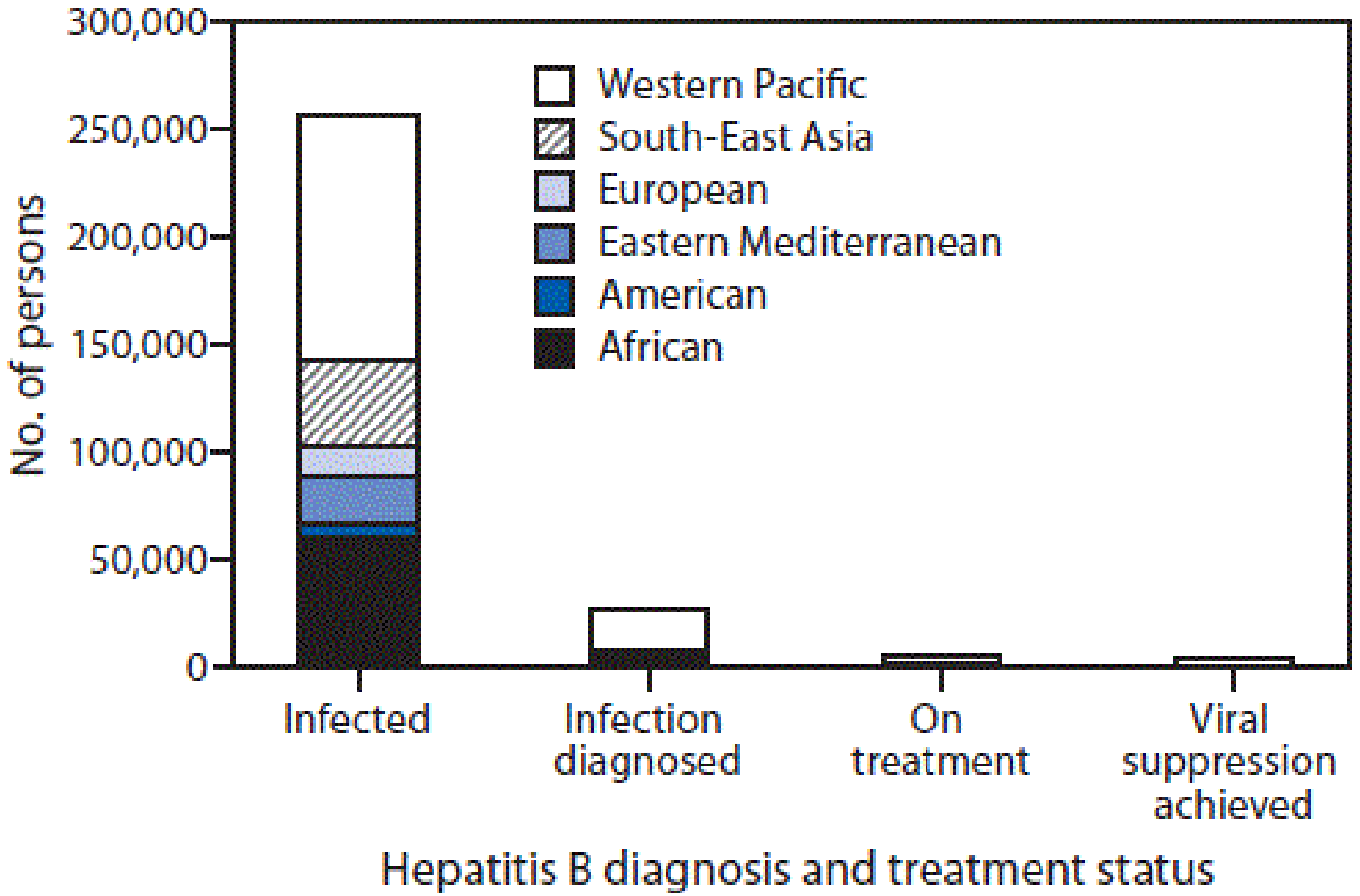


Opportunities to Treat HBV and Cure HCV Infection

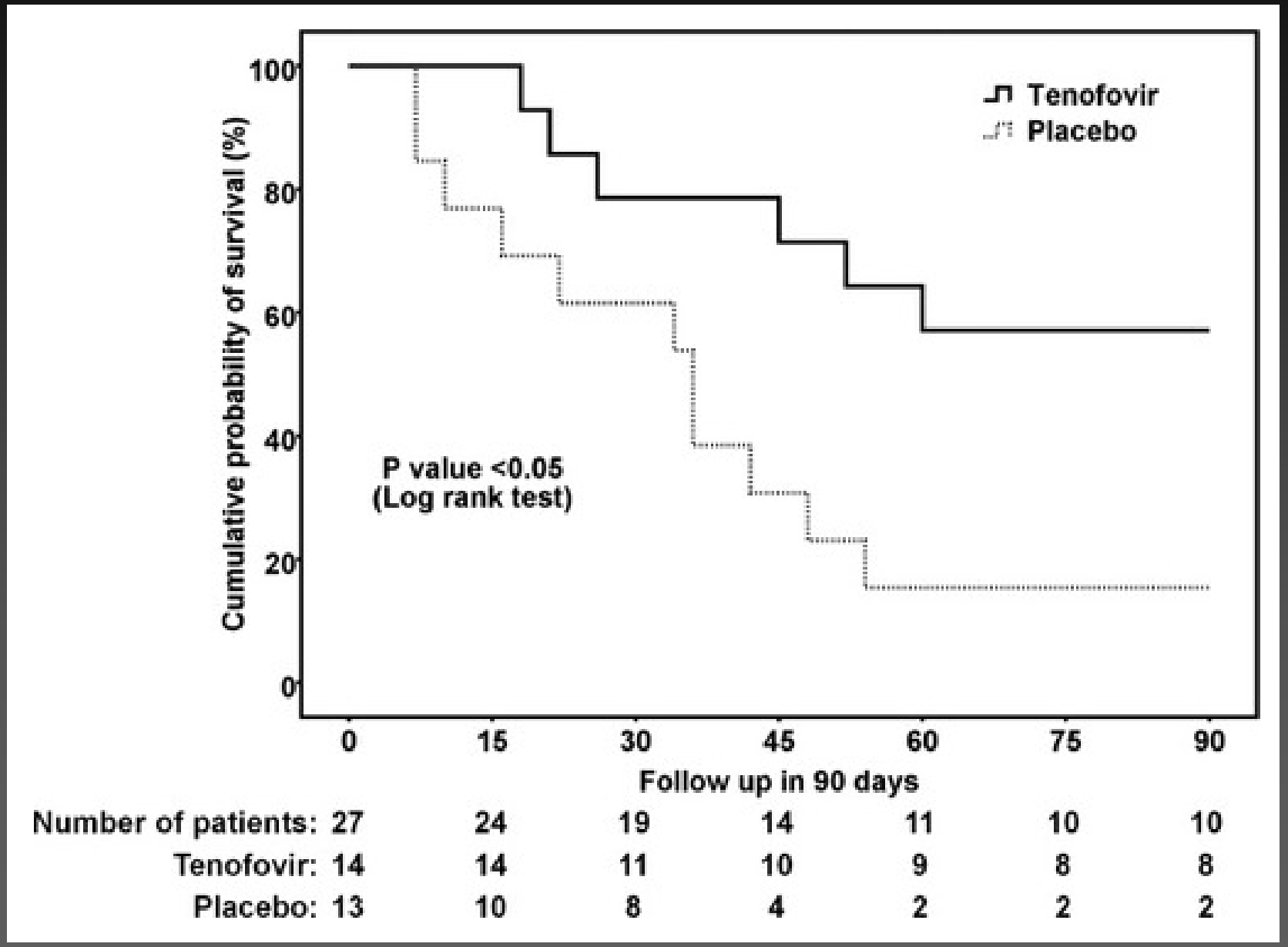
HBV Cure Cascade (Worldwide)

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

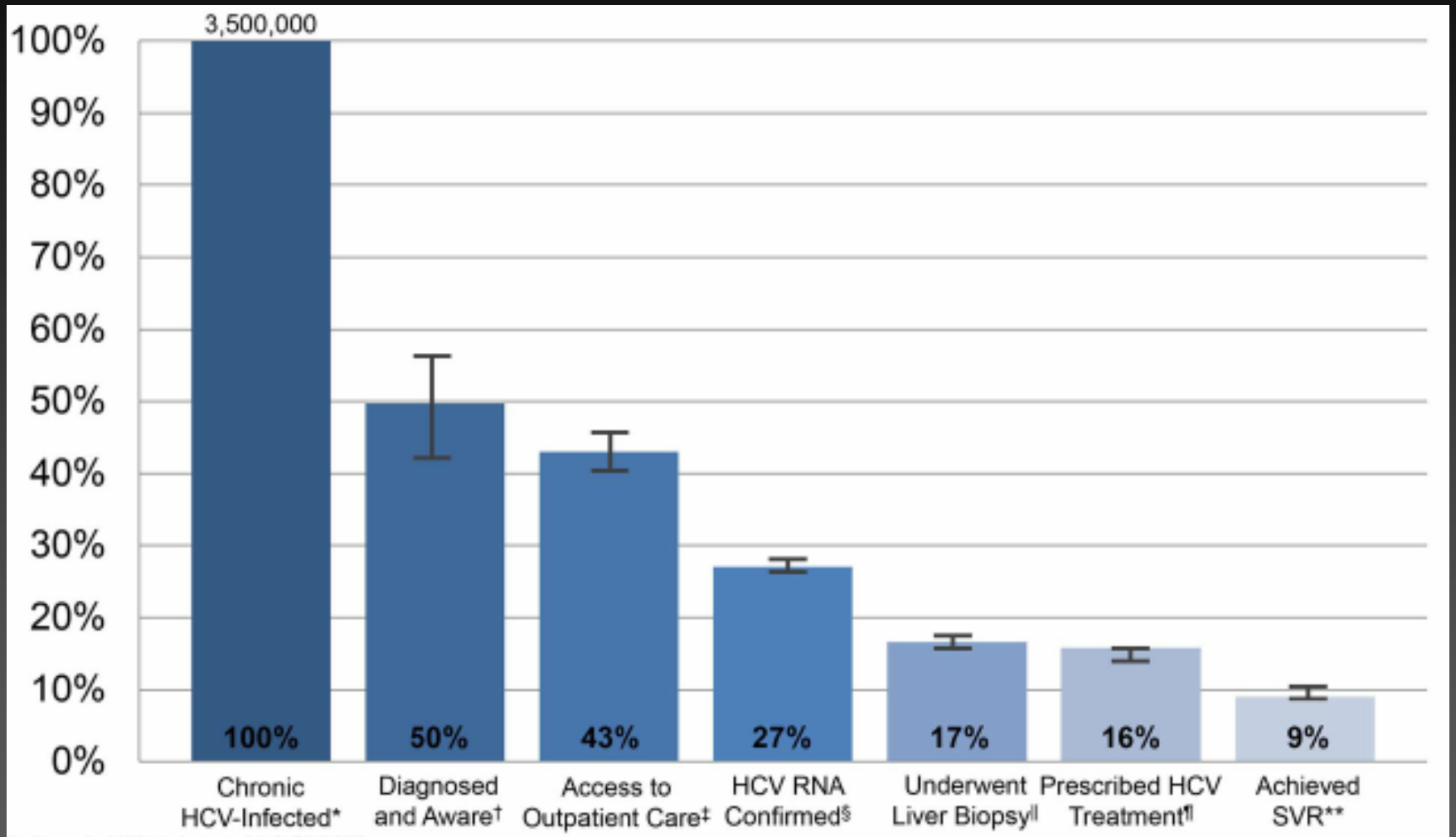


Hutin Y, Nasrullah M, Easterbrook P, et al. Access to Treatment for Hepatitis B Virus Infection — Worldwide, 2016. MMWR Morb Mortal Wkly Rep 2018;67:773–777. DOI: http://dx.doi.org/10.15585/mmwr.mm6728a2

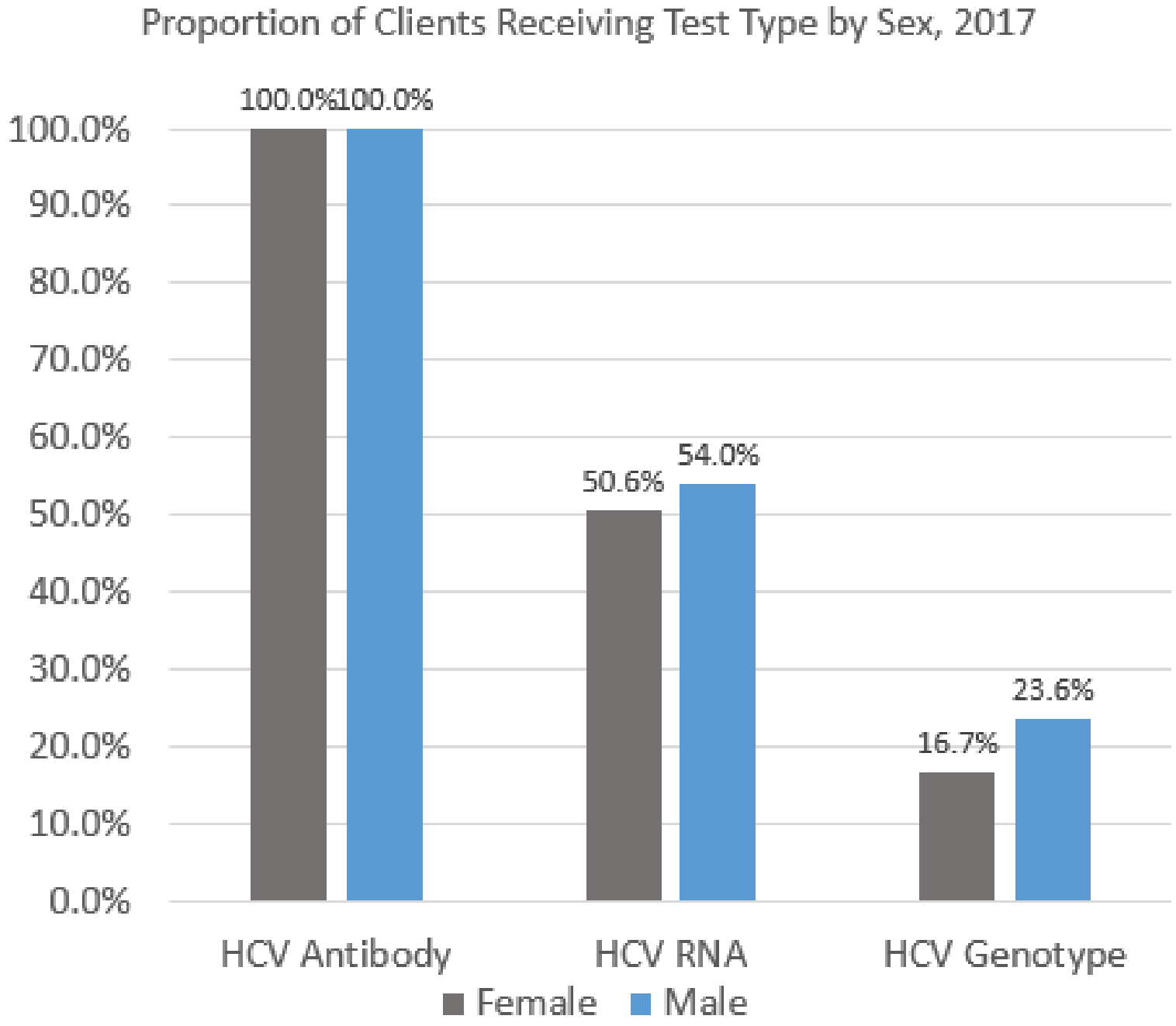
HBV Treatment Study



HCV Cure Cascade (U.S.)

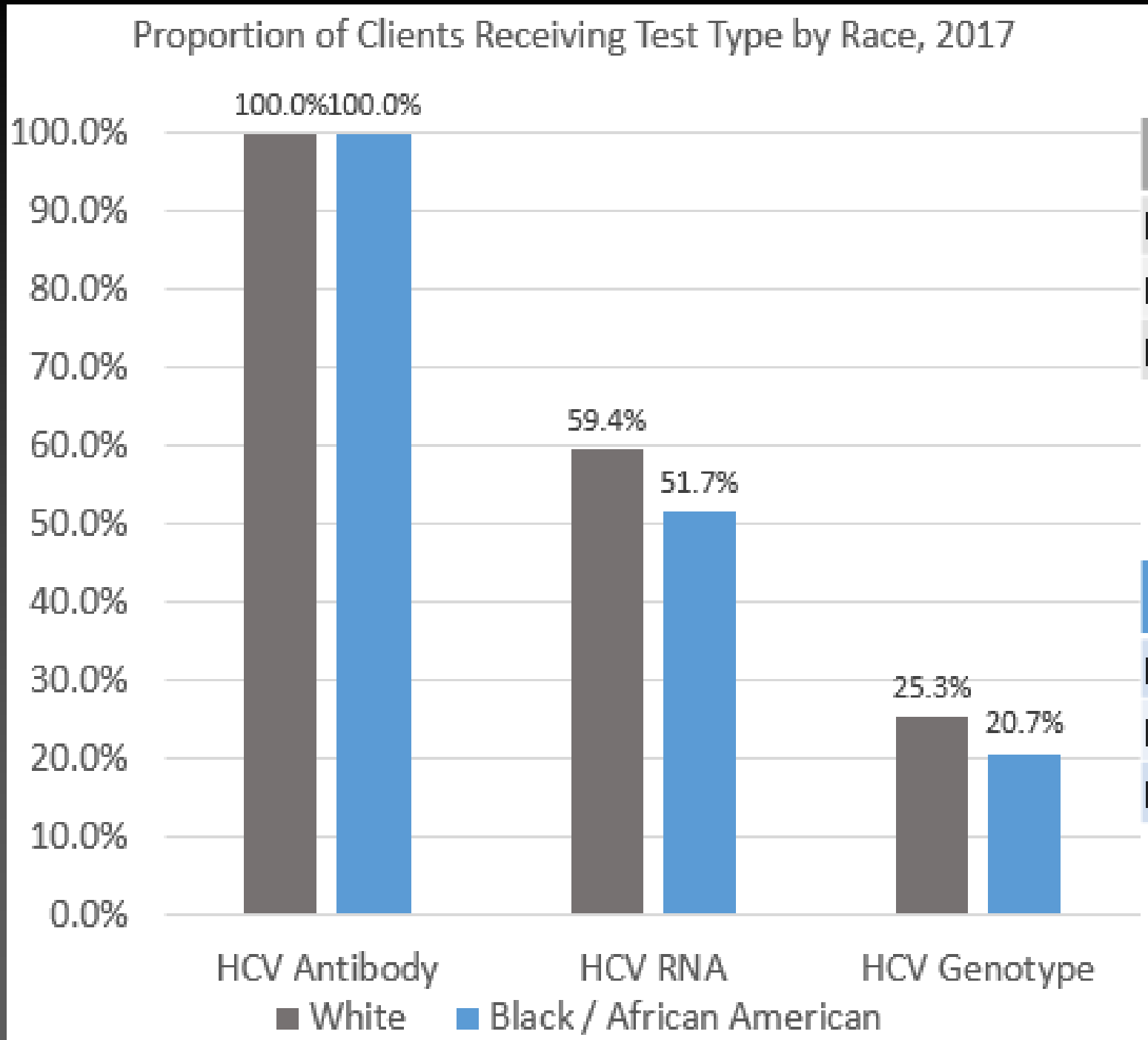


* Chronic HCV-Infected; N=3,500,000.
† Calculated as estimated number chronic HCV-infected (3,500,000) x estimated percentage diagnosed and aware of their infection (49.8%); n=1,743,000.
‡ Calculated as estimated number diagnosed and aware (1,743,000) x estimated percentage with access to outpatient 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.



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%



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…

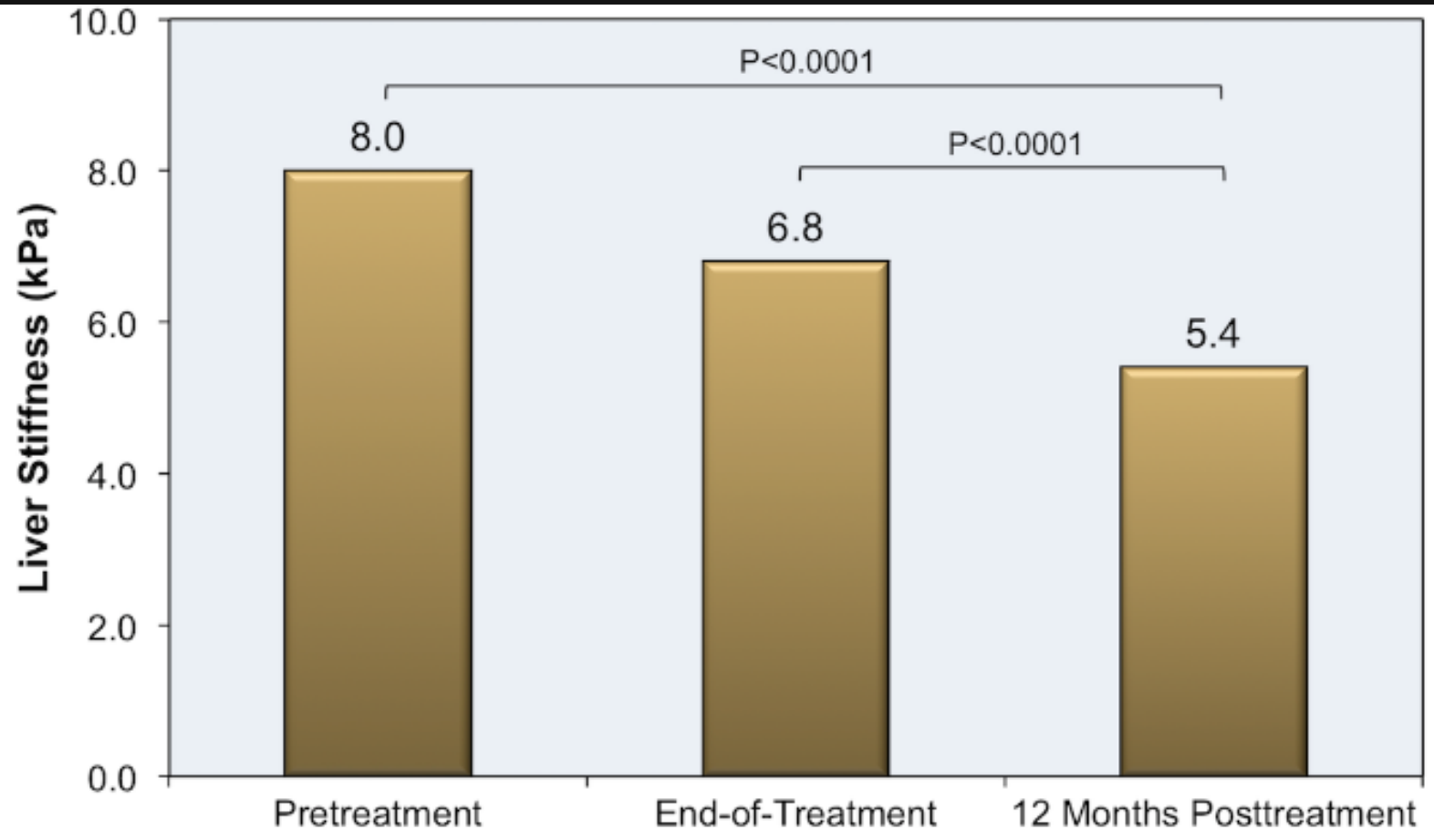


Figure 3 - Liver Stiffness Treatments in Patients Treated with Direct-Acting Antiviral Therapy
This study enrolled 70 patients who received direct-acting antiviral therapy for chronic HCV infection. This graphic shows liver stiffness measurement at baseline, end-of-treatment, and 12-month posttreatment. 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).

Source: Chan J, Gogela N, Zheng H, et al. Direct-Acting Antiviral Therapy for Chronic HCV Infection Results in Liver Stiffness Regression Over 12 Months Post-treatment. Dig Dis Sci. 2018;63:486-92.

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

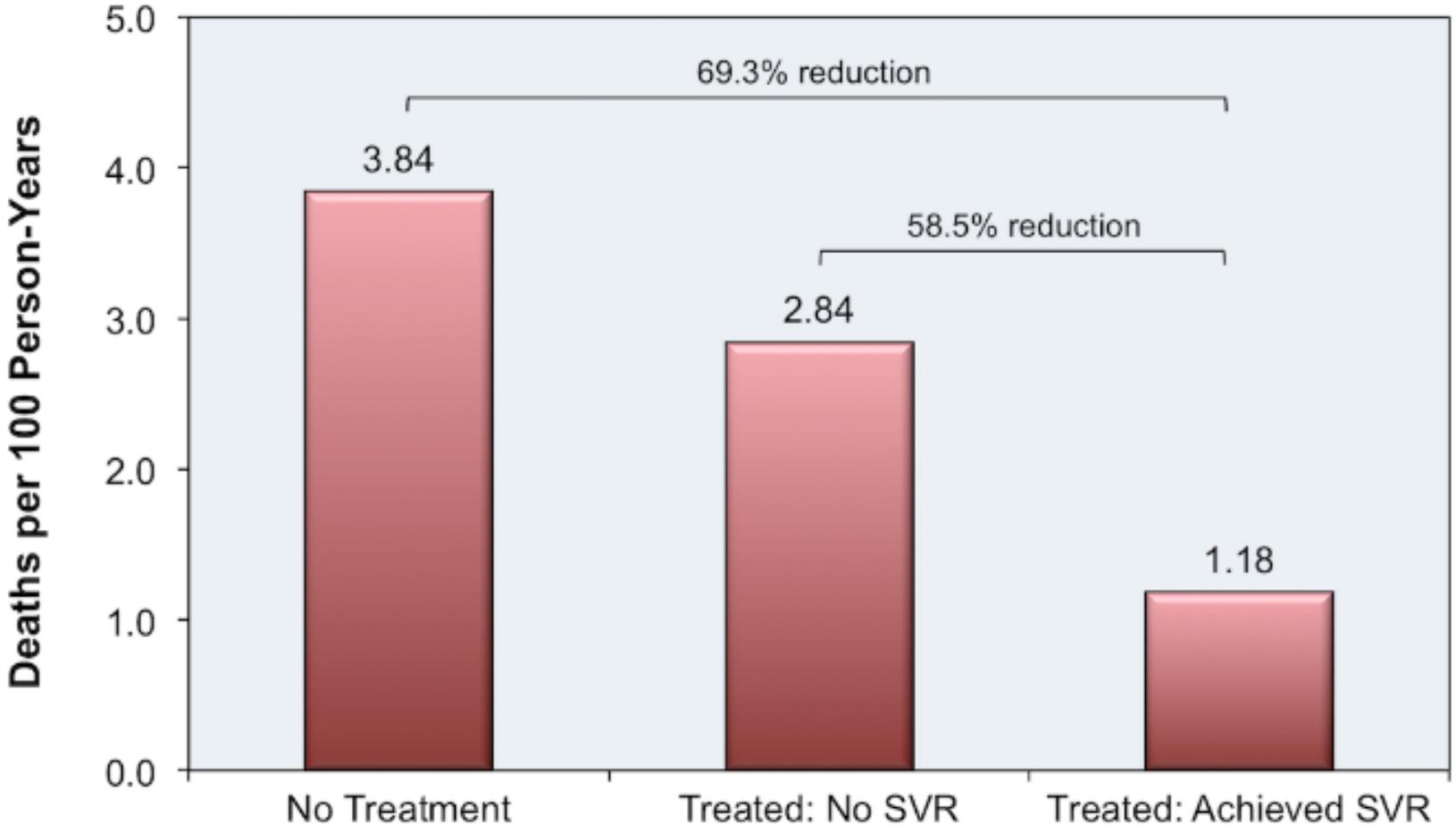
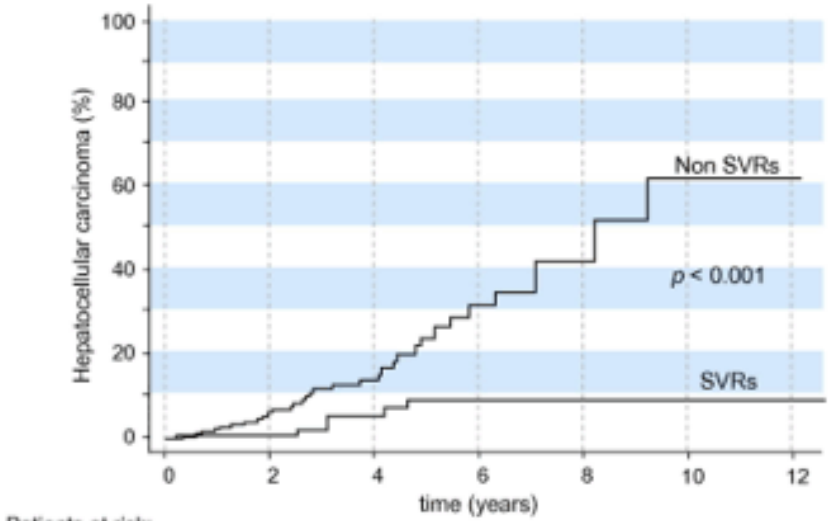


Figure 7 - Impact of SVR on Mortality Rates with DAA Therapy

Source: Backus LI, Belperio PS, Shahoumian TA, Mole LA. Direct-Acting Antiviral Sustained Virologic Response: Impact on Mortality in Patients without Advanced Liver Disease. Hepatology. 2018 Jan 29. [Epub ahead of print]

… Decreases (but does not eliminate) incidence of hepatocellular carcinoma…

SVR Decreases But Does Not Eliminate Incidence of Hepatocellular Carcinoma



Patients at risk:

SVRs	103	86	49	28	12	5	3
Non SVRs	204	151	73	28	8	5	3

HCC risk after SVR to IFNa-based therapies (n=2266)

		Cirrhosis
•HCC risk after **10** years: 7%	(males 10%)	26%
•HCC risk after **20** years: 17%	(males 26%)	63%

Nagaoki et al., AASLD 2014; #1977

Source: Journal of Hepatology 2010; 52:652-652 (DOI:10.1016/j.jhep.2009.12.028)

… and reduces extrahepatic manifestations

Clinical Outcomes by HCV Treatment and Response

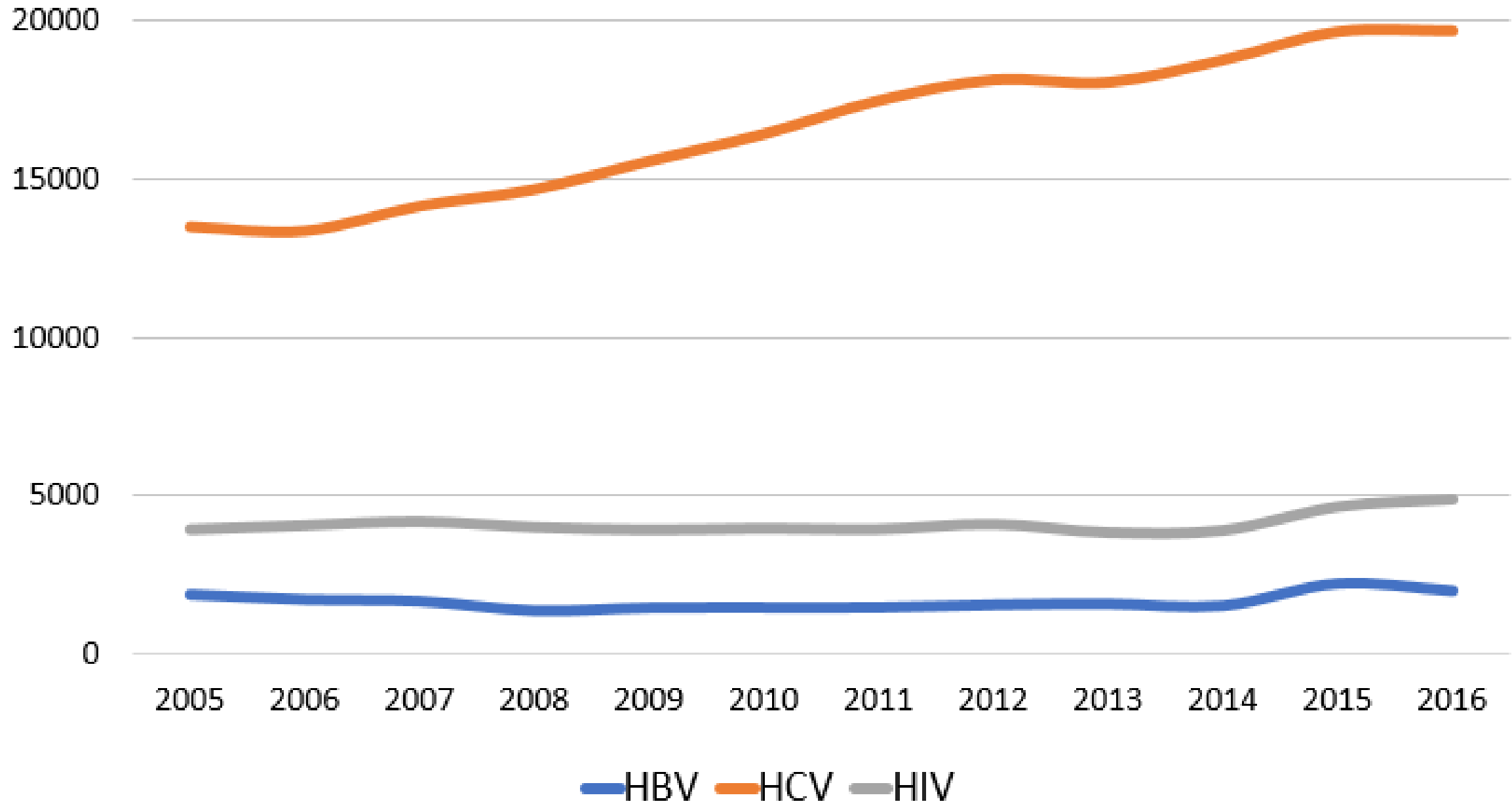
Outcomes	No Treatment	Treatment without SVR	Treatment with SVR
	Events per 1,000 Patient-Years		
Mixed cryoglobulinemia	0.72	0.52	0.33
Glomerulonephritis	2.83	1.62	1.09
Porphyria cutanea tarda	0.52	0.37	0.16
Lichen planus	0.68	0.71	0.56
Non-Hodgkin's lymphoma	0.91	0.55	0.43
Diabetes mellitus	21.6	17.0	13.9
Coronary heart disease	1.01	0.58	0.75
Stroke	9.14	4.64	5.10

Figure 8 – HCV Treatment and Outcome of Extrahepatic Manifestations

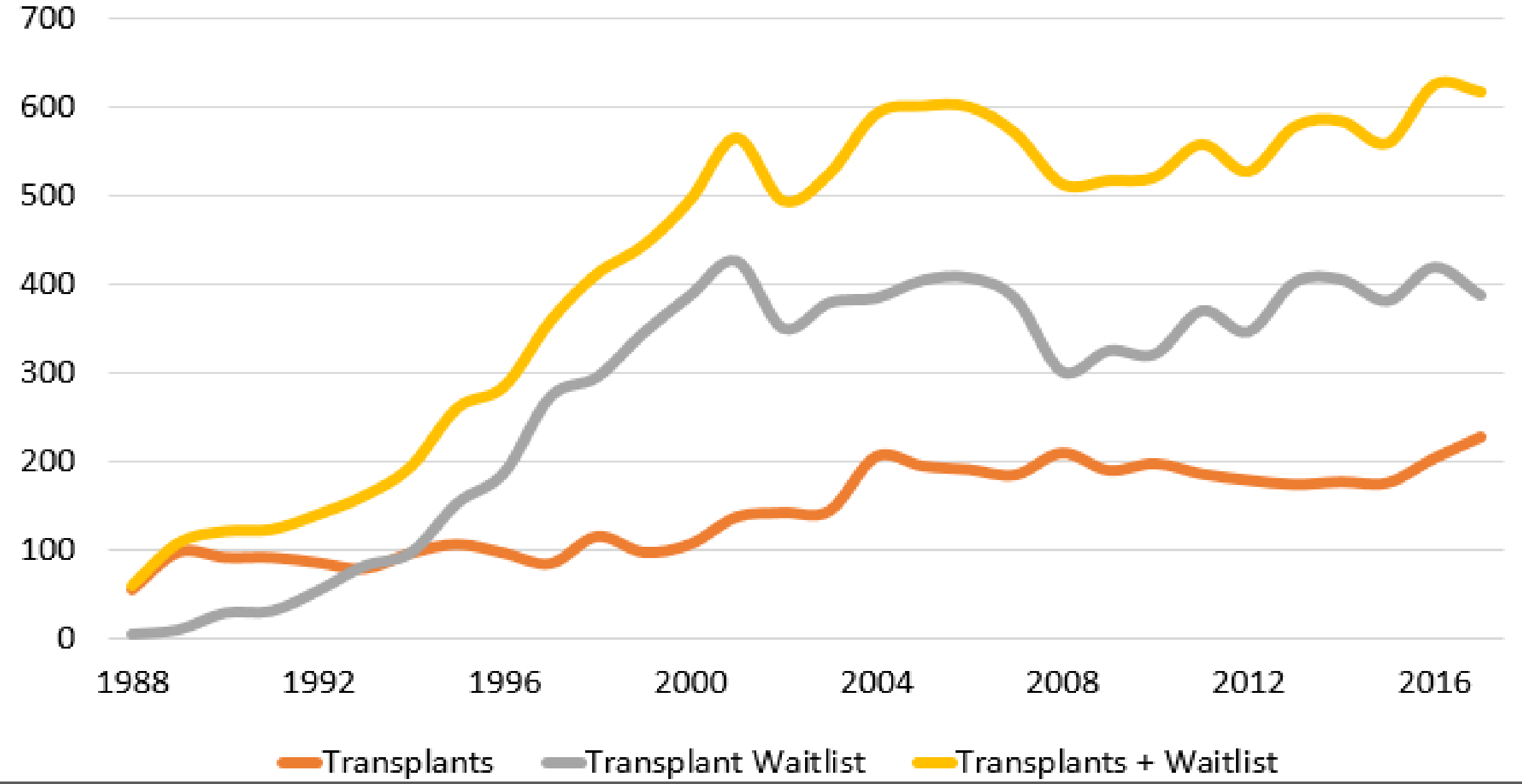
Source: Mahale P, Engels EA, Li R, et al. The effect of sustained virological response on the risk of extrahepatic manifestations of hepatitis C virus infection. Gut. 2018;67:553-61.

Viral Hepatitis Outcomes

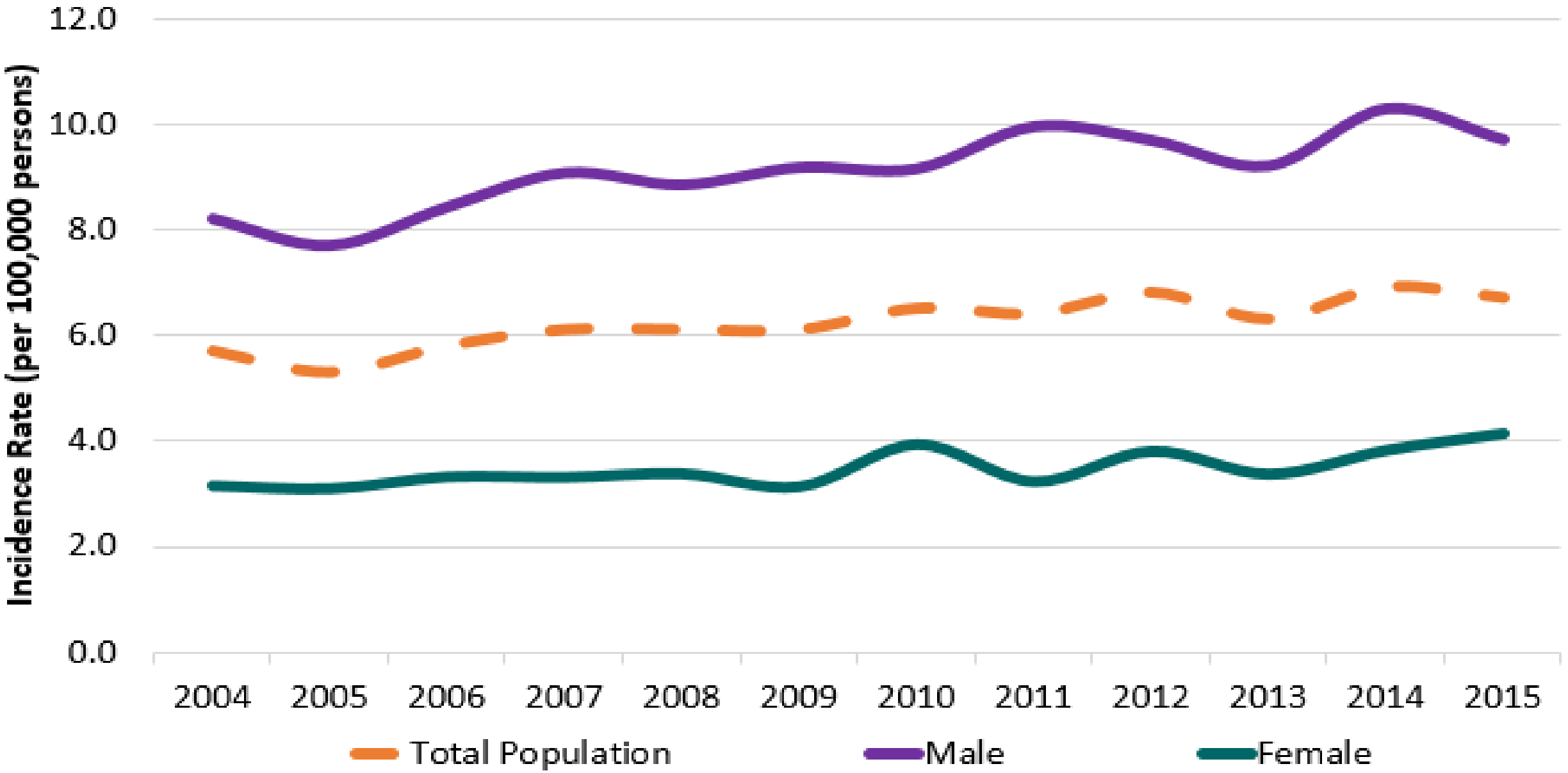
Hospitalizations Due to HBV, HCV and HIV, Michigan, 2005-2016

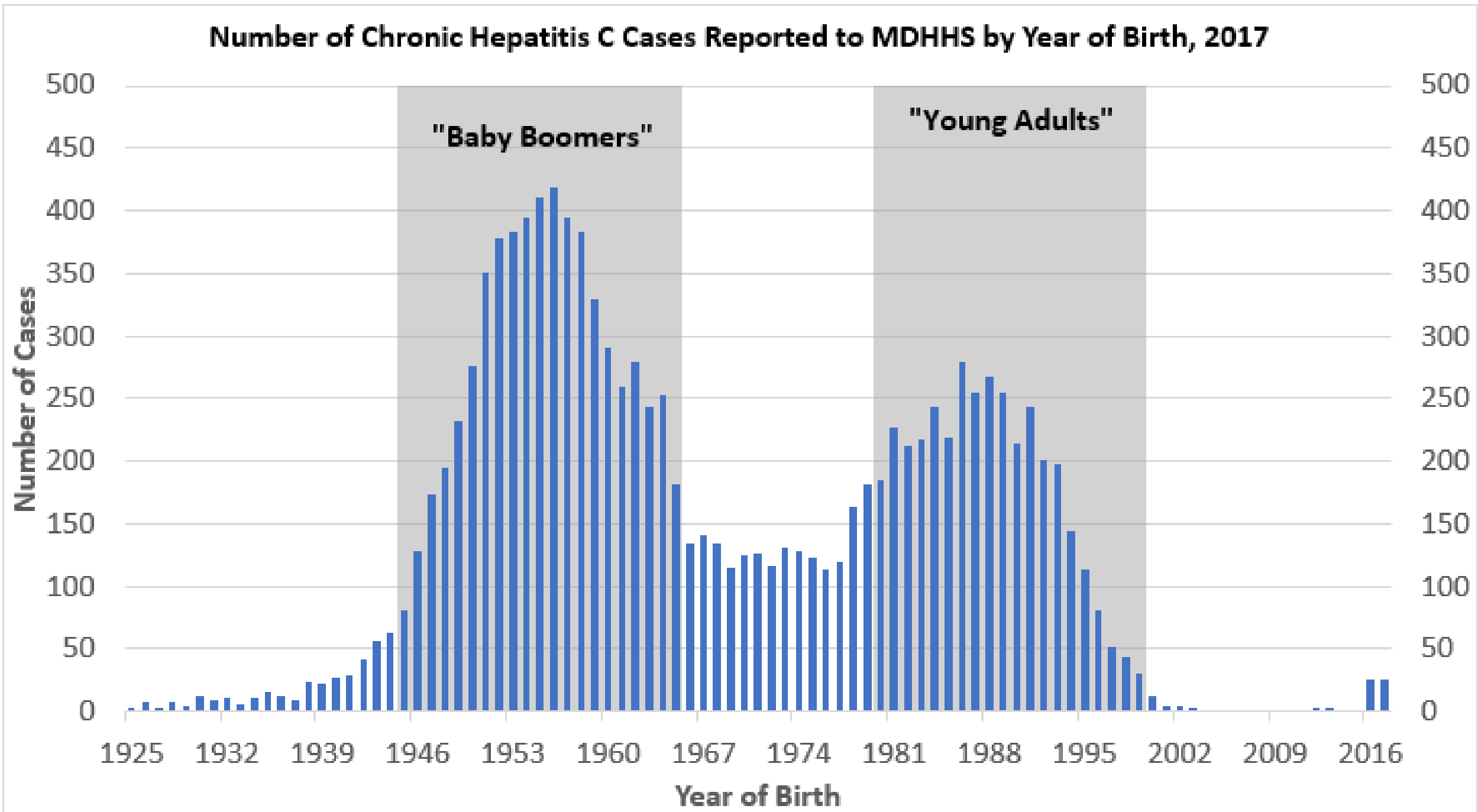


Liver Transplants and Transplant Waitlist, Michigan, 1988-2017



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




Number of Chronic Hepatitis C Cases Reported to MDHHS by Year of Birth, 2017
"Baby Boomers"
"Young Adults"
Number of Cases
Year of Birth
500
450
400
350
300
250
200
150
100
50
0
1925
1932
1939
1946
1953
1960
1967
1974
1981
1988
1995
2002
2009
2016

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

- 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.

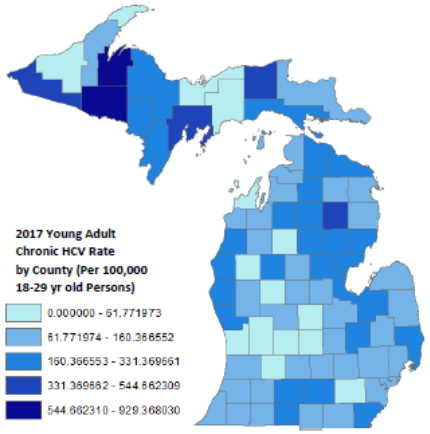
For more viral hepatitis surveillance data, visit: www.michigan.gov/hepatitis

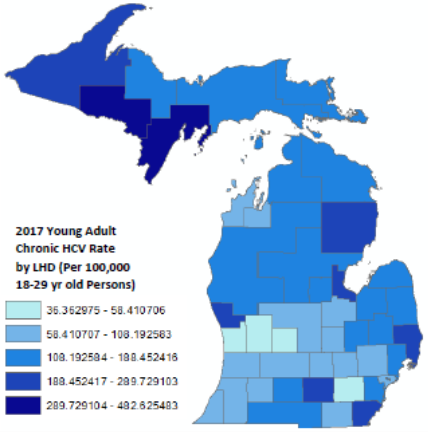
MDHHS
Michigan Department of Health & Human Services
RICK SNYDER, GOVERNOR | NICK LYON, DIRECTOR

2017 Hepatitis B and C Annual Surveillance Report

Viral Hepatitis Surveillance and Prevention Unit

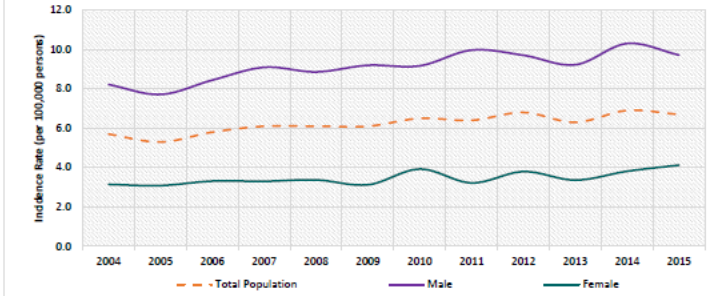
Young Adult (18-29 years old) HCV Case Rate Maps by County and Local Health Jurisdiction





Viral Hepatitis-Related Cancer & Mortality

Figure 16.3 Invasive Cancers of the Liver and Intrahepatic Bile Ducts in Michigan by Gender, 2004-2015



Viral hepatitis is a primary risk factor for the development of liver cancer. Figure 16.3 shows the age adjusted rate of liver and intrahepatic bile duct cancer by gender. The number of cases per year of liver and bile duct cancer have increased 46% between 2004 and 2015. African American males experience an incidence rate that is approximately 2.3 times higher, on average, than Caucasian males. The incidence rate for African American females tends to be similar to the state average, while Caucasian females have the lowest incidence rate of the specified race categories. Without improved efforts to test and treat persons with HBV and HCV infection, the rate of liver cancer may continue to rise, particularly as the population with greatest viral hepatitis prevalence ("Baby Boomers") ages.

Table 16.1 Incidence Rates of Invasive Cancers of the Liver and Intrahepatic Bile Ducts by Age-adjusted Rates of Race and Sex in Michigan, 2004-2015

Year of Diagnosis	Total		Caucasian Male		Caucasian Female		African American Male		African American Female	
	Incidence	Rate	Incidence	Rate	Incidence	Rate	Incidence	Rate	Incidence	Rate
2004	598	5.7	299	7.2	149	2.9	87	16.0	34	5.0
2005	572	5.3	290	6.9	142	2.8	80	13.5	36	5.2
2006	636	5.8	324	7.5	146	2.9	91	15.3	44	6.3
2007	679	6.1	346	8.0	161	3.1	103	16.8	34	4.8
2008	688	6.1	344	7.6	168	3.1	107	19.0	41	5.3
2009	706	6.1	361	7.9	154	2.9	116	18.8	36	4.7
2010	780	6.5	387	8.0	197	3.6	114	18.2	47	6.3
2011	767	6.4	419	8.8	156	2.9	122	18.3	42	5.5
2012	852	6.8	404	8.0	196	3.5	152	22.4	48	5.8
2013	797	6.3	404	7.9	173	3.0	133	18.8	48	6.0
2014	884	6.9	472	9.1	203	3.6	133	19.4	45	5.2
2015	874	6.7	448	8.5	206	3.6	130	19.2	66	7.6

Table 16.1 shows the rate of new cases of liver and intrahepatic bile duct cancer per year from 2004 to 2015 in Michigan per 100,000 people. The overall rate of liver and intrahepatic bile duct cancer in Michigan was 6.7 per 100,000 in 2015. African American males had an incidence rate of 19.2 per 100,000, which was 126% higher than that of Caucasian males (8.5 per 100,000). The incidence rate in African American females (7.6) was just over twice that of Caucasian females (3.6) in 2015.

Acknowledgements

- Joe Coyle, MPH
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- Contact the Viral Hepatitis Unit:
  MDHHS-Hepatitis@michigan.gov

MDHHS
Michigan Department of Health & Human Services

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

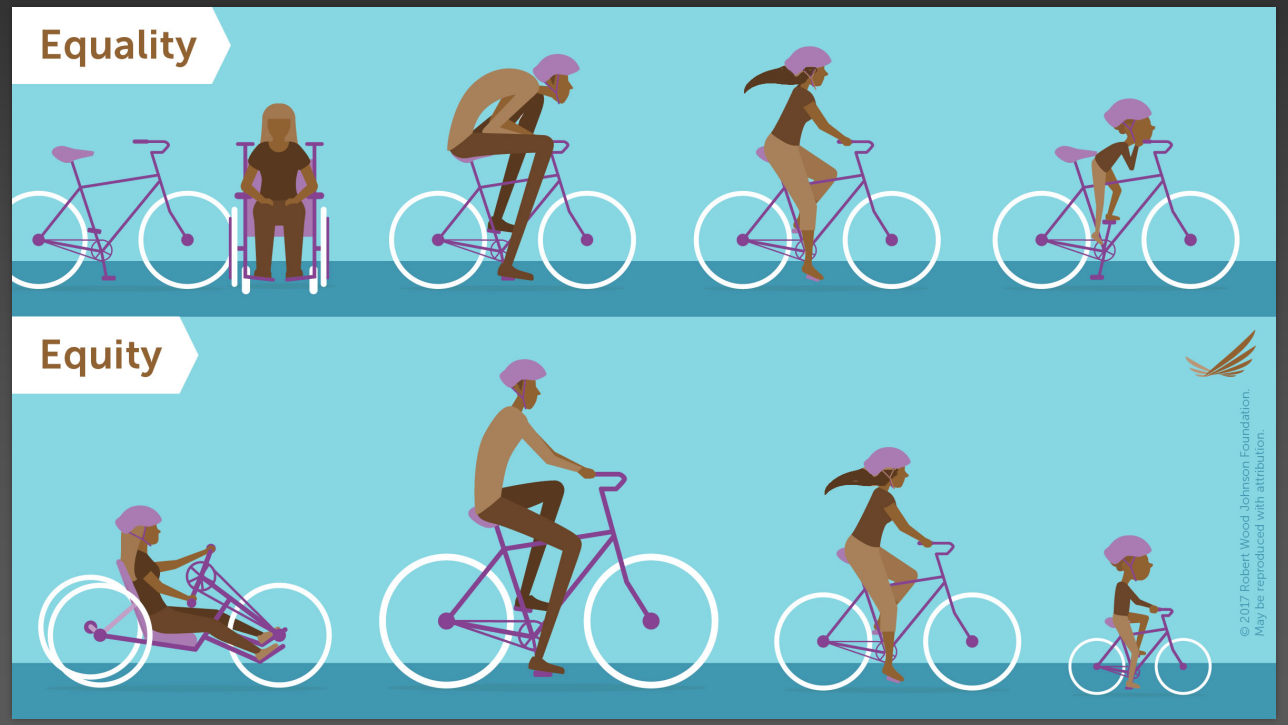
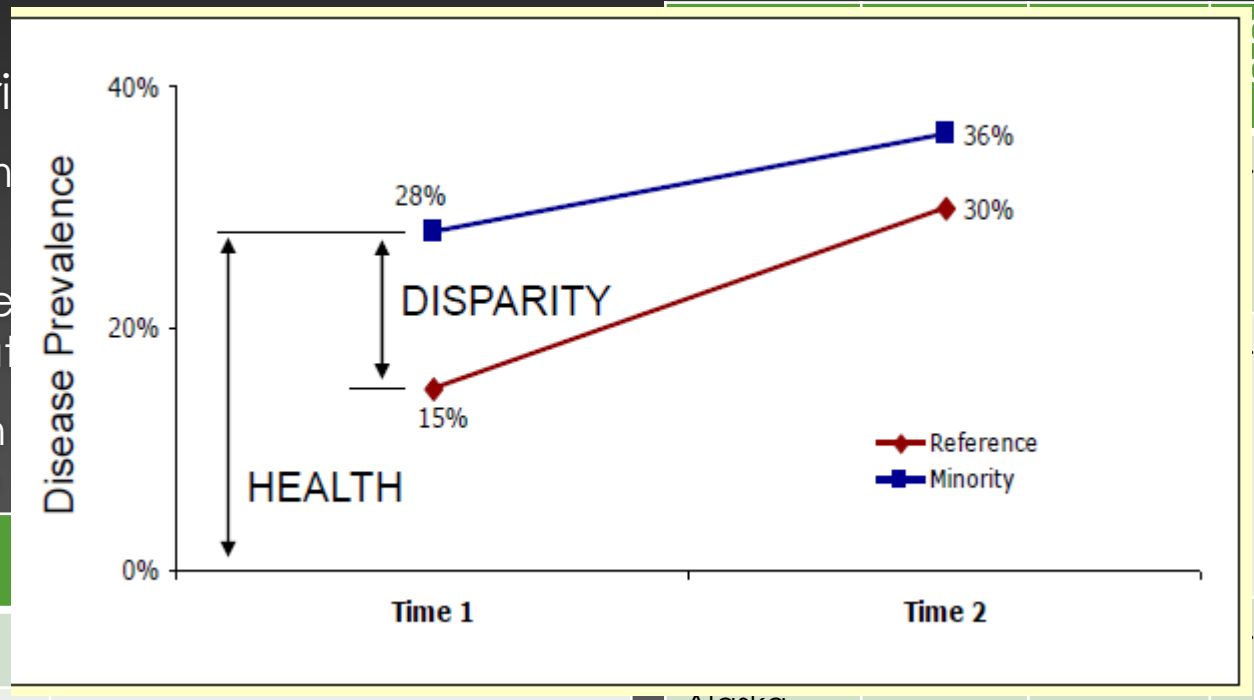


Image Source: Robert Wood Johnson Foundation

Monitoring Disparities

- Pairwise Dispari
  - Compares m group
  - Relative Diffe White Estimat
  - % Change in Time 1)/Time



Relative Difference % Change 2011-2013, 2014-2016	
Black, non-Hispanic	
Asian or Pacific Islander, non-Hispanic	19.98%
American Indian or Alaska Native	10.14%
Hispanic	21.82%

			005-007	2008-2010	2011-2013	2014-2016
			.07	1.79	1.90	1.71
			.77	2.04	1.43	1.15
			.84*	1.71*	2.98	2.13
Alaska Native						
Hispanic	2.00	2.16	1.63	1.58	2.00	1.56

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[5] = $(((\sum|r_n - R|) / N) / R)*100$

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

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

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