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The Increasing Burden of Liver Cancer in Wisconsin

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Introduction

The burden of primary liver cancer is increasing in Wisconsin, nationally, and worldwide[1,2]. While most cancers have declined in incidence and mortality in Wisconsin, liver cancer is a disturbing exception: incidence almost doubled over the past two decades, and the mortality rate increased faster for liver cancer than for any other cancer. The five-year survival rate for liver cancer in Wisconsin is 17 percent, among the lowest survival rates of all cancers.

Baby boomers, born between the years of 1945 and 1965, experienced the majority of the recent increase in liver cancer incidence and mortality. Men and certain ethnic and racial groups—including American Indians/Alaska Natives, African Americans, Asian/Pacific Islanders, and Hispanics/Latinos—are also significantly more likely to be diagnosed with and die from liver cancer due, in large part, to increased exposure to risk factors and inequities in access to health care.

The rising incidence of liver cancer has been attributed to increasing hepatitis B and C viruses and the prevalence of other modifiable risk factors, such as excessive alcohol consumption, tobacco use, and obesity. Fortunately, evidence-based practices and strategies proven to address many of these major risk factors provide critical opportunities to decrease the burden of liver cancer.

KEY POINTS

Liver cancer...

- is on the rise in Wisconsin.
- can be linked to hepatitis B and C; alcohol and tobacco use; and obesity.
- affects baby boomers, men, and certain racial and ethnic groups the most.
- can be prevented.

What you need to know:

The mortality rate for liver cancer is increasing faster than for any other cancer. Luckily, many risk factors for liver cancer can be prevented or reduced. When we understand *who* is at risk and *why*, we can implement evidence-based strategies to lower risk and save lives.

Data Sources and Methods

The incidence data in this report are from the Wisconsin Cancer Reporting System, originally reported by health care facilities in Wisconsin for primary invasive liver cancer and intrahepatic bile duct cancer (cholangiocarcinoma), commonly referred to together as liver cancer. Primary liver cancer refers to cancer originating in the liver, distinct from metastatic liver cancer that has spread to the liver from other cancer sites. Hepatocellular carcinoma (HCC) is the most common type of primary liver cancer, comprising approximately 80 percent of all primary liver cancer cases. Cancer of the intrahepatic bile duct (cholangiocarcinoma) is the second most common primary liver cancer, comprising about 15 percent of all cases.*

Mortality data are from the National Center for Health Statistics, based on the underlying cause of death. Incidence and mortality trend data are for years 1995 to 2015 (most recent year available).

To enhance racial/ethnic classification, the Hispanic/Latino and Asian/Pacific Islander Identification Algorithms from North American Association of Central Cancer Registries were applied to those cases with unknown or ambiguous race/ethnicity[3]. Additional American Indian/Alaska Native cases were identified by linkage with US Indian Health Service enrollment lists. The Hispanic/Latino classification in this report includes all races.

Statistical calculations were performed in SEER*Stat (Version 8.3.5) statistical software. All rates, expressed per 100,000 population, were directly age-adjusted to the 2000 US standard population, and confidence intervals (CI) are 95 percent for rates.

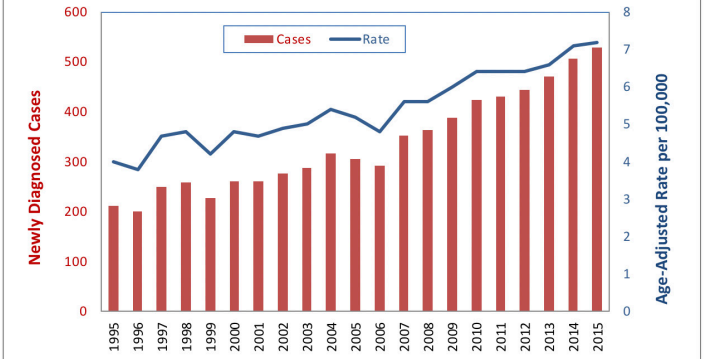
**All liver cancer data in this analysis includes both liver, including hepatocellular carcinoma (HCC), and intrahepatic bile duct cancer (cholangiocarcinoma), unless specified as exclusive to HCC.*

Increasing Incidence and Mortality

From 1995 to 2015, more than 7,000 cases of liver cancer were diagnosed in Wisconsin. The annual number of liver cancer cases increased by 150 percent, from 211 cases to 529 cases during the past two decades (Figure 1). The age-adjusted incidence rate increased from 4.0 (CI, 3.5 - 4.6) in 1995 to 7.2 (CI, 6.5 - 7.8) in 2015, with an annual increase of 2.9 percent, and a total increase of 76.8 percent.

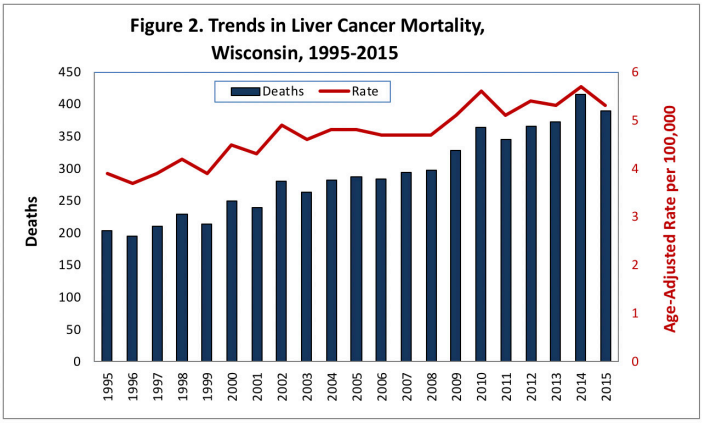
From 1995 to 2015, more than 6,000 liver cancer deaths occurred among Wisconsin residents. The annual number of deaths increased by 90 percent, from 204 to 390 deaths (Figure 2). The age-adjusted mortality rate increased from 3.9 (CI, 3.4 - 4.5) to 5.3 (CI, 4.8 - 5.9), based on an annual increase of 1.8 percent, for a total increase of 36.6 percent. Baby boomers disproportionately experience the burden of liver cancer in Wisconsin. In 2015, 96 percent of Wisconsin residents who were diagnosed with or who died from liver cancer were age 50 or older. Since 1995, the liver cancer incidence rate for Wisconsinites over age 50 increased by 85 percent (12.9 to 23.9), and the death rate increased by 42 percent (12.9 to 18.3). In contrast, the liver cancer incidence and mortality rates among the younger population in Wisconsin remain negligible and have not increased since 1995.

Figure 1. Trends in Liver Cancer Incidence, Wisconsin, 1995-2015



Source: Wisconsin Cancer Reporting System, Office of Health Informatics, Division of Public Health, Department of Health Services.

Figure 2. Trends in Liver Cancer Mortality, Wisconsin, 1995-2015



Source: National Center for Health Statistics.

Diagnosis and Survival

Liver cancer is being diagnosed at earlier stages. From 1995 to 2015, the proportion of liver cancers diagnosed early at the local stage increased from 26 percent to 41 percent. The proportion of liver cancers diagnosed at the regional stage increased to 30 percent, while distant stage diagnoses decreased to 20 percent. The percentage of unknown stage diagnoses decreased most dramatically from 41 percent to 9 percent, attributable to advances in diagnostic technology[4].

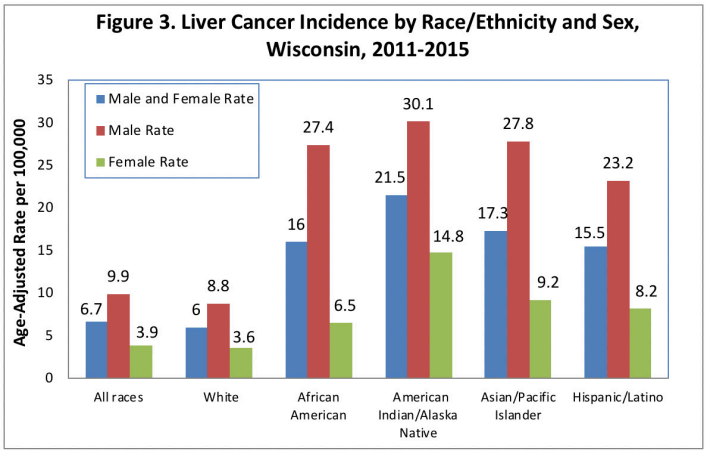
Based on survival data for liver cancers diagnosed from 2007 to 2013, the 5-year relative survival rate in Wisconsin is estimated at 16.7 percent[5]. Survival rates improve with earlier detection: The national five-year survival rate for liver cancer diagnosed at the local stage is 31 percent, compared to 11 percent diagnosed at the regional stage, and 2 percent for the distant stage[6].

Despite these gradual improvements and the promise of future advances in earlier detection of liver cancer, the overall survival rate remains low and the current prognosis is poor.

Disparities by Race/Ethnicity and Sex

Certain racial and ethnic populations are disproportionately burdened by liver cancer in Wisconsin. From 2011 to 2015, American Indian/Alaska Natives had the highest reported liver cancer incidence rate across all races and ethnicities in Wisconsin (Figure 3). Liver cancer was the fifth leading cancer site among American Indians/Alaska Natives and Asian/Pacific Islanders, the seventh leading cancer site among Hispanics, and the tenth leading cancer site among African Americans. In contrast, liver cancer incidence was ranked as 15th highest among whites.

Figure 3. Liver Cancer Incidence by Race/Ethnicity and Sex, Wisconsin, 2011-2015



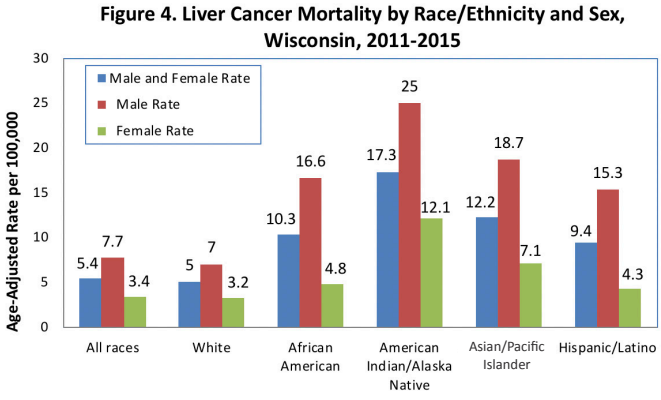
Source: Wisconsin Cancer Reporting System, Office of Health Informatics, Department of Health Services.

Parallel to the incidence rates, the liver cancer mortality rate is highest among American Indian/Alaska Natives, and significantly higher among racial/ethnic minority populations compared with whites (Figure 4).

Differences by sex are apparent across all population groups, with men being more likely to develop and die from the disease (Figures 3 and 4). Disparities by sex are greater within racial/ethnic populations with higher rates of liver cancer. Particularly striking, African American men are almost 4 times as likely as African American women to develop and die from liver cancer.

National studies of patients diagnosed with HCC reported that racial/ethnic differences in medical outcomes of HCC were associated with differences in stage of detection and receipt of treatment[7,8]. Differences in exposure to certain risk factors may also contribute to racial, ethnic, and sex disparities in HCC[9-11].

Figure 4. Liver Cancer Mortality by Race/Ethnicity and Sex, Wisconsin, 2011-2015



Source: National Center for Health Statistics.

Risk Factors

Any condition or disease that damages the liver increases the risk of liver cancer. Major risk factors for HCC include chronic hepatitis infection and excessive alcohol consumption, as well as other modifiable risk factors such as tobacco use and obesity.

Hepatitis B and C infection

In the United States, liver cancer risk has been largely attributed to chronic inflammation associated with hepatitis B virus (HBV) and hepatitis C virus (HCV)[11,12]. Chronic hepatitis can quietly attack the liver for years without causing symptoms before resulting in significant liver damage. The National Health and Nutrition Examination Survey found that 50 percent of people with chronic HCV infections are unaware of their condition[13].

HCV, most often spread through injection drug use, is the most common chronic blood infection in the United States and its incidence in Wisconsin is on the rise[12]. In 2017, 3,067 cases of HCV (past, present, chronic, or acute diagnoses) were reported to the Wisconsin Immunization Registry. The rate of HCV among Wisconsinites aged 15-29 has more than tripled since 2008, an increase attributed to increased injection drug use[12]. The rising HCV infection rate among adolescents and young adults indicates that liver cancer rates will progressively increase for the extended future[14, 15].

Heavy alcohol use

Heavy alcohol use is a well-established risk factor for liver cancer[16, 17]. Wisconsin has a high prevalence of alcohol consumption and excessive drinking—which includes both heavy and binge drinking. Heavy drinking is defined by the Centers for Disease Control and Prevention (CDC) as more than 14 drinks per week for men, and more than 7 drinks per week for women. Binge drinking is defined as five or more drinks for men and four or more drinks for women on one occasion. According to the 2018 County Health Rankings, 26 percent of Wisconsin adults reported either heavy or binge drinking in the past 30 days[18]. A major study of risk factor data collected by the CDC between 2002 and 2012 found Wisconsin to be the heaviest-drinking state in the nation[19].

Other modifiable risk factors

Other modifiable risk factors for liver cancer include tobacco use and obesity[9]. The 2016 Wisconsin Behavior Risk Factor Surveillance System (BRFSS) reported 17 percent of Wisconsin adults were current smokers and 26 percent were former smokers. Estimates of obesity from the Survey of the Health of Wisconsin, determined based on body mass index (BMI), found 39% of residents to be overweight, 33 percent were obese, and only 26 percent were of normal weight[20].

Implications for Cancer Control in WI

Liver cancer is among the few cancers on the rise in Wisconsin, including thyroid cancer, melanoma, and pancreatic cancer. Although thyroid cancer and melanoma are being diagnosed more frequently, the five-year survival rates are high, at 95 and 92 percent, respectively. In contrast, the pancreatic cancer survival rate remains among the lowest at 12 percent[5].

Because many of the risk factors for liver cancer are preventable or modifiable, Wisconsin has an opportunity to greatly reduce the liver cancer burden in our state through investments in evidence-based strategies.

Vaccination for HBV

The most effective way to reduce liver cancer risk from chronic HBV infection is to prevent the virus through vaccination. The HBV vaccine has been widely used since the early 1980s and has been effective in approximately 95 percent of cases.

The current CDC strategy to eliminate HBV transmission includes vaccination of all infants at birth and vaccination of adolescents and high-risk adults who have not yet received the vaccine[21]. The HBV vaccination is required for school attendance in Wisconsin, but exemptions are allowed for health, religious, and personal conviction reasons[22]. Strategies to reduce non-medical exemptions would include requiring a more rigorous process to apply for exemptions, as well as encouraging physician-patient conversations that include vaccination as the part of routine health care[23, 24].

To support vaccination of high-risk adults, universal HBV vaccination should be offered in outreach and other settings in which services are provided to persons at risk for HBV infection (e.g., needle-exchange programs, HIV testing sites, HIV prevention programs, and homeless shelters, correctional facilities)[21].

Testing & Treatment for HBV and HCV

Blood tests can detect and identify viral hepatitis B and C. Early detection of HBV and HCV, particularly among populations with more exposure to hepatitis viruses, has been identified as an effective strategy for reducing liver cancer incidence and mortality.

Currently no vaccine exists for HCV, but recent advances in HCV treatment mean that more than 90 percent of people infected can be cured with treatment. For this reason, and to prevent the spread of the disease by individuals who may be unaware of their condition, the United States Preventive

Services Task Force (USPSTF) recommends HCV screening in persons at high risk for infection, as well as one-time screening for all adults born between 1945 and 1965[25].

A National Academies report offers suggestions for state and federal policymakers to address cost and other barriers to HCV treatment access. These include creative financing approaches like lump-sum purchase arrangements, increasing provider capacity to treat HCV in rural and underserved areas, and bringing hepatitis treatment to groups with the highest burden of infection, including individuals who are uninsured, experiencing substance use issues, or are incarcerated[26].

No cure currently exists for HBV; however, liver damage and cancer risk can be mitigated when chronic HBV infections are diagnosed, treated, and monitored by health care providers. Therefore, the USPSTF also recommends screening for all individuals at high-risk for HBV[27].

Reducing Excessive Drinking

Given the prevalence of excessive drinking in Wisconsin, public health strategies to reduce high-risk drinking represent a significant opportunity to reduce the liver cancer burden in our state.

Reducing high risk alcohol consumption is a priority of the WI Comprehensive Cancer Control Plan 2015-2020 (WI CCC Plan)[28]. Strategies include increasing awareness of the connection between alcohol and cancer, creating environments that discourage excessive alcohol use, and increasing screening and treatment for high-risk alcohol consumption.

Although alcohol use is a well-established risk factor for liver cancer and at least six other cancers, awareness of this connection is extremely low[29]. Evidence shows that increasing awareness not only can encourage individual behavior change, but also can increase support for policies and practices that reduce excessive drinking[30,31].

Policies and practices shown to discourage excessive drinking and support healthy decisions about alcohol include limiting the number of locations that sell alcohol, increasing the price of alcohol, and enhancing enforcement of laws that prohibit the use of alcohol by people under the age of 21[32].

Additionally, by screening for high risk consumption and providing interventions or referrals for treatment, health care and service providers can help individuals change their drinking habits and reduce their risk for liver cancer[33].

Opportunities to address other modifiable risk factors

Although Wisconsin's current overall adult smoking rate continues to decline, some groups have historically higher rates of tobacco use in Wisconsin, including African Americans, Native Americans, and individuals with low incomes or who identify as lesbian, gay, or bisexual[34] . The WI CCC Plan 2015-2020 supports preventing youth access to tobacco products, increasing access to and use of evidence-based tobacco cessation services for current tobacco users, and protecting and strengthening clean air laws to continue the overall trend and address higher smoking rates in certain populations[28].

To address Wisconsin's higher than average rates of obesity, the WI CCC Plan 2015-2020 supports policy and systems change to create environments supportive of physical activity and access to healthy foods, and increasing screening and treatment for obesity to support individuals in obtaining and maintaining a healthy weight[28].

Conclusion

Although death rates for all cancers combined has declined, a recent report from CDC emphasized that age-adjusted liver cancer death rates are increasing steadily for both adult men and women in the US [35]. Similarly, while there is predominantly positive news in overall declining cancer death rates in Wisconsin, liver cancer has maintained an upward rise during the past two decades. The liver cancer mortality burden increased 37 percent since 1995, and the rise is steepest among baby boomers aged 50 and older.

Although all populations are experiencing an increase in liver cancer, American Indians/Alaska Natives, African Americans, Asian/Pacific Islanders, and Hispanics/Latinos experience significantly higher rates of the disease, contributing to the current health inequities in our state. Men are most at risk, and the sex disparity is amplified among racial and ethnic minority populations.

Alarming increases in chronic HCV, along with continued high rates of excessive drinking and the high prevalence of obesity, suggest that liver cancer rates could continue to climb in Wisconsin. Fortunately, promising evidence-based strategies offer opportunities to reverse this trend.

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