



#OctoberIs4Livers

GlobalLiver.org/OctoberIs4Livers

Creating a Path of Equity in Liver Cancers

The State of Liver Cancer

2021 Inaugural Report

Executive Summary

Global Liver Institute (GLI) was built to solve the problems that matter to liver patients, equipping advocates to improve the lives of individuals and families impacted by liver disease. GLI promotes innovation, encourages collaboration, and supports the scaling of optimal approaches to help eradicate liver diseases. GLI believes liver health must take its place on the global public health agenda commensurate with the prevalence and impact of liver illness. GLI is the only patient-created, patient-driven nonprofit organization tackling liver health and all liver disease holistically, operating globally.

Liver cancer is a global public health threat and the third deadliest cancer in the world. To address the myriad and complex aspects of liver cancer, GLI developed the groundbreaking #OctoberIs4Livers program, spanning the globe to improve health outcomes for liver cancer patients.

The 2021 #OctoberIs4Livers Creating a Path of Equity in Liver Cancers program focuses on bringing to light the many disparities associated with this cancer that has continued to rise for decades. Liver cancer disparities reflect the interplay amongst many factors, including social determinants of health, behavior and genetics - all of which disproportionately impact people of color.

Liver cancer is the sixth most common and third deadliest cancer around the world, with 905,677 new cases and 830,180 deaths in 2020 alone. The American Cancer Society estimates that in 2021, there will be 30,230 deaths attributed to liver cancer and 45,230 new diagnoses.

Liver cancer is the
third deadliest
cancer in the world

According to the American Cancer Society, **up to 70% of new liver cancer cases could be prevented** by addressing underlying causes of liver damage, many of which are behavioral. As these conditions - such as hepatitis B and C, obesity, and alcohol abuse - continue to rise in prevalence in the United States, the medical community braces for an increase in new liver cancer cases.

Even with the reintroduction of the **LIVER Act**, and the introduction of the **Recognizing October 2021 as Liver Cancer Awareness Month Resolution**, individuals and organizations must work collaboratively to urge other Members of Congress to support and advance these pieces of legislation.

*We also encourage you to sign and share **GLI's Liver Cancer Call To Action** pledging support to double the five-year survival rate for liver cancer in your country.*

Table of Contents

Liver Cancer Overview	3
Global Burden of Liver Cancer	4
U.S. Burden of Liver Cancer	7
COVID-19 Impact on Liver Cancer	10
Call to Action	11
Cosponsor The Liver Illness, Visibility, Education and Research Act (LIVER Act) 116th Congress: H.R. 5675 and S. 3041)	11
Other available health policy actions that could protect all people impacted by liver disease:	12
Global Call to Action	13
Summary	14
References	15

Liver Cancer Overview

The liver is the largest internal organ in the body. It is located in the upper-right portion of the abdominal cavity and is composed mainly of cells called hepatocytes. There have been more than 500 functions identified with the liver including: production of proteins for blood plasma, production of special proteins to carry fats throughout the body, and secreting bile—including filtering out any toxic substances from the body.¹ At times, an individual can develop a condition that prevents the liver from functioning properly, which can put any patient at increased risk of developing liver cancer.²

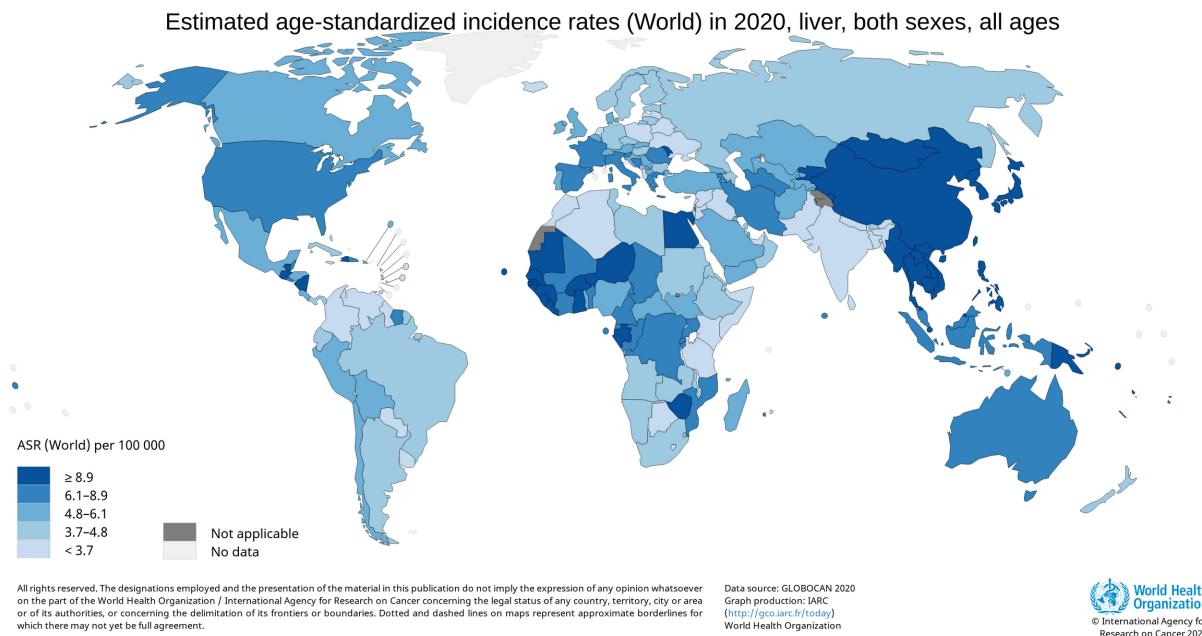
There are two primary types of liver cancer: Hepatocellular Carcinoma (HCC) and Intrahepatic Cholangiocarcinoma (iCCA). HCC is the most common form of liver cancer that makes up about 75-85% of cancer cases and is most common in men.³ This type of cancer has different growth patterns, some beginning as a single tumor that grows while others originate as several small cancerous nodules throughout the liver. One of HCC's subtypes is Fibrolamellar Hepatocellular Carcinoma, a very rare subtype that makes up less than 1% of HCC cases and is most common in women under the age of 35.³ iCCA is the second most common liver cancer, constituting about 10-20% of cancer cases, originating in the cells that surround the small bile ducts. Liver diseases such as cirrhosis, hepatitis B virus (HBV), hepatitis C virus (HCV), nonalcoholic fatty liver disease (NAFLD), nonalcoholic steatohepatitis (NASH), and primary biliary cirrhosis are risk factors that contribute to the manifestation of liver cancer. Forty four percent of all HCC cases are attributed to HBV, while 21% are caused by HCV.⁴ Other risk factors include lifestyle choices, metabolic factors, demographic factors, and environmental factors. Alcohol consumption contributes to 26% of HCC cases around the world, whereas 4.6-28.2% are attributed to aflatoxin. Additionally, it is expected that 4-27% of individuals with NASH will develop liver cancer.⁵



Global Burden of Liver Cancer

Throughout recent decades, rates of liver cancer have continued to rise, pushing it to now become one of the leading causes of death and illness worldwide.⁶ Liver cancer is the sixth most common and third deadliest cancer around the world, having 905,677 new cases and 830,180 deaths in 2020 alone.⁷ Within this one-year period, the occurrence of new cases in Asia amounted to 72.5% of all cases, especially in countries such as Mongolia and China where rates are 10-20 times higher than those in the United States.⁸

Figure 1. Global incidence rates



Globally, exposure to viral hepatitis and aflatoxin are the biggest risk factors to developing liver cancer. While this is true in Asia, some added risk factors that contributed to the increased incidence rate in the region could be attributed to tobacco smoking, alcohol consumption, and obesity.⁵ In 2020, trends showed that higher incidence rates were prevalent amongst low and lower-middle income areas across the globe.^{9,10} The primary cause of liver cancer in these areas was HBV. Yet, as lifestyles change—with increasing alcohol consumption, dietary changes, and sedentary routines—they are now becoming a larger cause of liver cancer prevalence around the world. Upon further review, males have been found to have a higher liver cancer incidence rate than females around the world.⁸ A study found this gender difference associating to males being more likely to acquire HBV and HCV, chronic hepatitis, and cirrhosis.¹¹

Less than half of new liver cancer cases are diagnosed when the disease is still confined to the liver, where curative treatment is the most successful.⁶ This late-stage diagnosis can be attributed to lack of inconsistent screening protocols, little health literacy and education on liver cancers, and absent symptoms that could lead to an early diagnosis.

Liver cancer disproportionately impacts most racial and ethnic groups globally on account of disparities such as lack of access to health insurance, lack of access to quality care, unconscious/conscious bias of providers, and a variety of other complex socioeconomic factors. Many of these inequities are reflected in death rates differentiating by sex, race/ethnicity, and location and through differences in risk factor prevalence.¹

Key disparities in liver cancer include:

- Asian Americans are four times more likely to have liver cancer than any other ethnic population;
- Excess liver cancer incidence and liver cancer mortality are highest among non-Hispanic Black males versus other races;
- U.S. Hispanics have a liver cancer incidence rate that is almost two times higher than non-Hispanic whites;
- Asian Americans comprise 60% of the U.S. population living with Hepatitis B, the leading risk factor for liver cancer;
- American Indian/Alaskan Natives have a liver cancer mortality rate almost two times higher than non-Hispanic whites

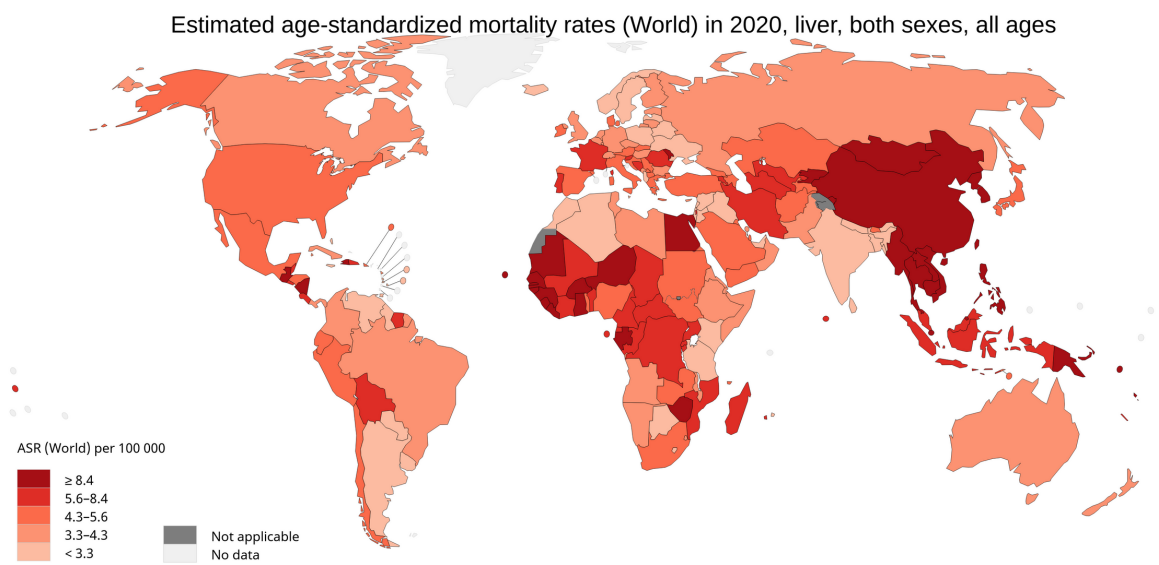
These differences in health outcomes are present in a countless number of diseases, many of which have established treatments. Around the world, minorities and people of color are often in a cycle of low education, poor working conditions and low income, resulting in these poor health outcomes. While liver cancer causes are unique to every region, many are exacerbated by rising barriers within vulnerable populations.

<50% of new liver cancer cases are diagnosed when a cure is possible

While many of these liver cancer cases could be prevented, there are no widely recommended routine tests for liver cancer—similar to those developed for cervical and prostate cancers. This has made it incredibly difficult to detect and treat liver cancer in a timely manner, making five-year survival rates devastatingly low around the globe with South Korea having the highest rate at 27%. Nonetheless, some preventative methods include limiting alcohol consumption, having a balanced diet, maintaining a healthy weight, getting the HBV and HCV vaccine, and screening those with liver disease who are at risk of developing liver cancer. At-risk individuals could be screened through an ultrasound with or without alpha-fetoprotein (AFP), and other options include CT, MRI, and hepatic angiography. Unfortunately, screening practices have a multitude of issues from lack of coordinated care and costs to unclear guidelines for patients and providers. Seeing as HCC is most prevalent in low and lower-middle communities, some of these screening methods might not be easily accessible or affordable. These disparities have driven global liver cancer cases to steadily rise by approximately 2% throughout the years.¹² Likewise, it is expected that the global burden of liver cancer will continue to grow.

Increasing alcohol consumption, dietary changes, and sedentary routines are becoming a larger cause of liver cancer worldwide

Figure 2. Global mortality rates



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Data source: GLOBOCAN 2020
 Graph production: IARC
<http://gco.iarc.fr/today>
 World Health Organization

World Health Organization
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U.S. Burden of Liver Cancer ¹

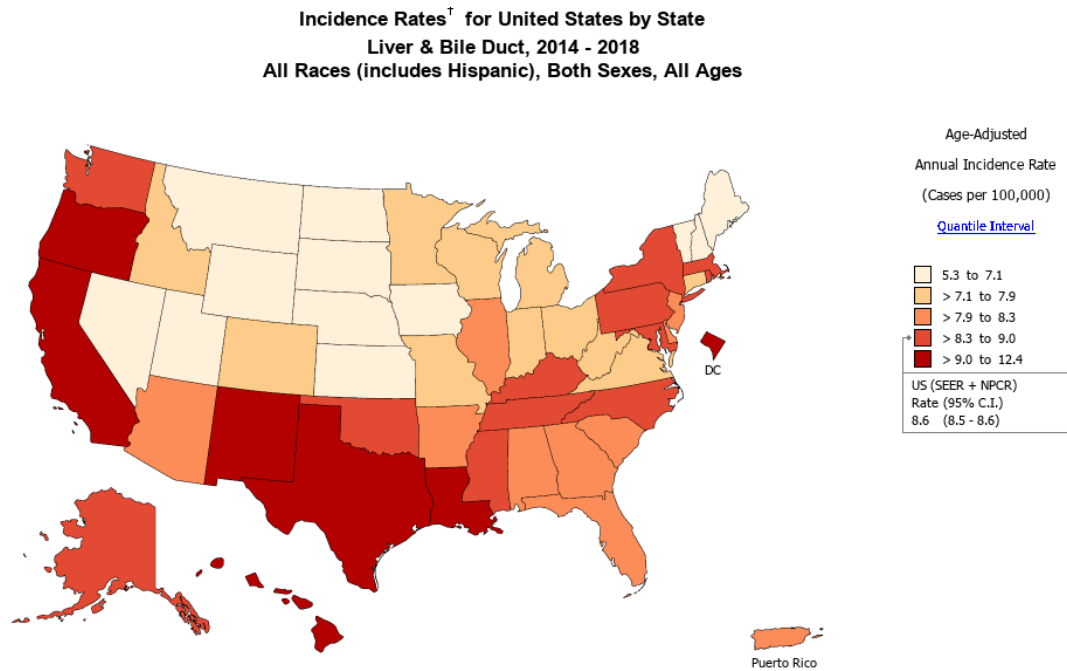
Since 1980, the incidence of liver cancer in the United States has nearly tripled, while death rates have more than doubled.⁶ It is estimated that in 2021, there will be 30,230 deaths attributed to liver cancer and 45,230 new diagnoses ⁶, making it the sixth deadliest cancer in the U.S.¹³

Despite the growing threat for liver cancer, the five-year survival rate has increased from 3% 40 years ago to 20% currently.¹⁴ Nonetheless, liver cancer has one of the lowest five-year survival rates in comparison to breast, thyroid, and prostate cancers which are at or greater than 90%.¹⁷

The 5-year survival rate for liver cancer is 20%.

As showcased in **Figure 3: Liver cancer incidence in the U.S.**, the age-adjusted annual incidence rate for liver cancer was 8.8 per 100,000 for the 2014 – 2018 reporting period. The highest rate of new cases are found in the District of Columbia at 12.4 per 100,000, Texas at 12.0 per 100,000, and Hawaii at 10.6 per 100,000. The lowest incidence rates were observed in North Dakota at 5.3 per 100,000, Vermont at 5.4 per 100,000, and Nebraska at 5.6 per 100,000.²⁰

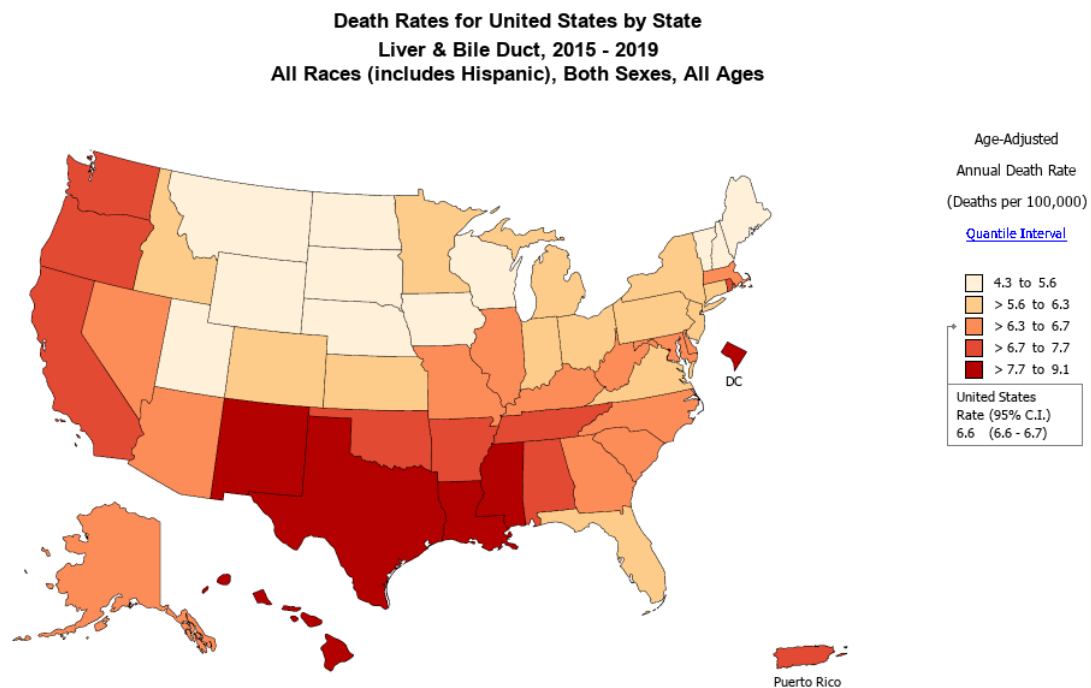
Figure 3. Incidence rates in the U.S. ²⁰



Notes:
 Note: Alaska, DC, Hawaii and Puerto Rico are not drawn to scale.
[State Cancer Registries](#) may provide more current or more local data.
 Data presented on the State Cancer Profiles Web Site may differ from statistics reported by the State Cancer Registries ([for more information](#)).
[†] Incidence rates (cases per 100,000 population per year) are age-adjusted to the 2000 US standard population (19 age groups: <1, 1-4, 5-9, ..., 80-84, 85+). Rates are for invasive cancer only (except for bladder which is invasive and in situ) or unless otherwise specified. Rates calculated using SEER*Stat. Population counts for denominators are based on Census populations as modified by NCI. The 1969-2018 US Population Data File is used for SEER and NPCR incidence rates.
 Rates are computed using cancers classified as malignant based on ICD-O-3. For more information see [malignant.html](#)
 ♦ [Data not available](#) for this combination of geography, statistic, age and race/ethnicity.
 Data for the United States does not include data from Puerto Rico

The age-adjusted annual death rate for liver cancer in the U.S. was 6.6 per 100,000 for the 2015 – 2019 reporting period. The highest rate of deaths are seen in the District of Columbia at 9.1 per 100,000, Louisiana at 8.8 per 100,000, and New Mexico at 8.4 per 100,000. States with the lowest death rates include Nebraska at 4.3 per 100,000, Utah at 4.8 per 100,000, and North Dakota at 5.0 per 100,000.²⁰ These data are shown in **Figure 4: Liver cancer mortality rates in the U.S.**

Figure 4. Liver cancer mortality rates in the U.S.²⁰



Notes:
 Note: Alaska, DC, Hawaii and Puerto Rico are not drawn to scale.
[State Cancer Registries](#) may provide more current or more local data.
 Data presented on the State Cancer Profiles Web Site may differ from statistics reported by the State Cancer Registries ([for more information](#)).
 Source: Death data provided by the [National Vital Statistics System](#) public use data file. Death rates calculated by the National Cancer Institute using [SEER*Stat](#). Death rates (deaths per 100,000 population per year) are age-adjusted to the [2000 US standard population](#) (19 age groups: <1, 1-4, 5-9, ... , 80-84, 85+). The Healthy People 2020 goals are based on rates adjusted using different methods but the differences should be minimal. Population counts for denominators are based on the Census [1969-2018 US Population Data](#) File as modified by NCI.
 Data for the United States does not include data from Puerto Rico

While survival rates depend on various risk factors, risk factors are disproportionately impacting different communities within the United States. There are many social structures that place burden, prejudices, and discriminations on various groups of people—in many cases causing detrimental health outcomes. Additionally, racial disparities that have manifested from decades of institutionalized racism alongside financial and structural inequities have had a significant and enduring impact on the delivery and quality of health care. This can be seen through elevated incidence, prevalence, and mortality rates of countless diseases.

Table 1. Incidence and mortality by race, all sexes²¹

	Incidence (per 100K)	Mortality (per 100K)
All Races	9.1	6.6
American Indian/ Native Alaskan	12.1	10.8
Asian/Pacific Islander	12.0	8.2
Black	10.4	8.2
Hispanic	13.9	9.4
Non-Hispanic White	7.4	5.9

In the U.S., Hispanics have an incidence rate that is almost two times higher than non-Hispanic whites, while American Indian/Alaskan Natives have a mortality rate almost two times higher than non-Hispanic whites.¹⁵ A study published by the United States Department of Health and Human Services found that while many disparities have decreased since 2000, many still persist amongst uninsured and low-income populations.²² This study particularly highlighted the difference in HCC successful transplantation measures - for instance, 40% of quality measures were worse for Black patients in comparison to non-Hispanic White patients.²² Similarly, Black and Hispanic patients, two ethnic groups with some of the highest incidence rates, have the lowest rates of curative HCC treatment.²² These disparities and rising risk factors have propelled liver cancer incidence rates to increase rapidly, growing two-three percent annually, in comparison to kidney, pancreas, and oral cavity and pharynx cancers.¹² Liver cancer disparities reflect the interplay amongst many factors, including social determinants of health, behavior, and genetics.

All of these factors have a profound effect on health, as shown by the increased liver cancer incidence and death rates in certain races and gender groups.

COVID-19 Impact on Liver Cancer

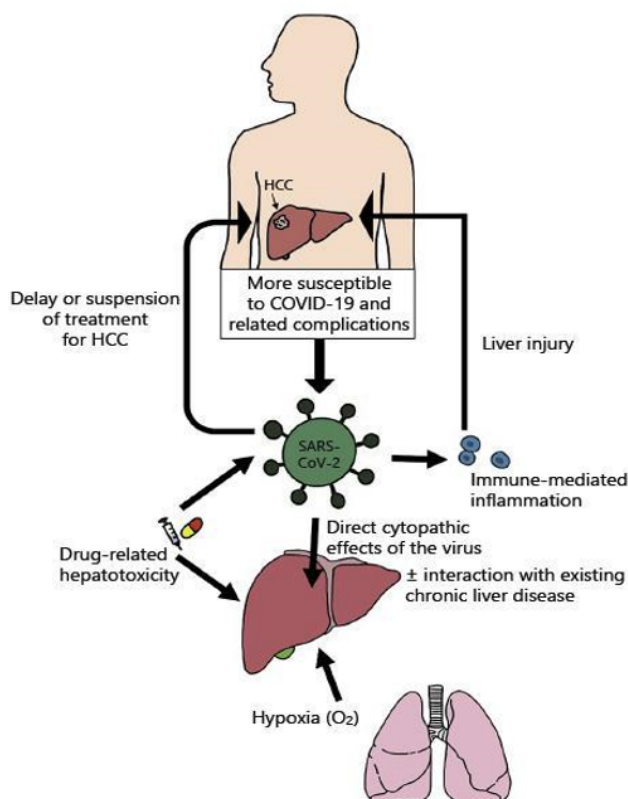
In 2020, there was an additional factor that contributed to the elevated global rates in liver cancer - the coronavirus pandemic (COVID-19). COVID-19 infections can cause organ dysfunction, thus complicating cancer treatments.¹⁷ A study found that 15-54% of patients infected with COVID-19 have hepatic injuries, characterized by elevated levels of bilirubin and transaminases.¹⁷ While these injuries could be transient, many have reported permanent damage to the liver for those with severe COVID-19 cases. Additionally, this viral disease has affected screening, treatment, and care for individuals diagnosed with liver cancers. Out of 76 centers studied around the world, 80.9% had to delay screening procedures, 50% cancelled

15-54% of patients infected with COVID-19 have hepatic injuries.

curative and/or palliative treatments, and 41.7% changed their transplantation programs due to the pandemic and rising risks of infection.¹⁸ Some patients experienced treatment delays of over two months, while others received an alternate treatment than originally planned. These changes in liver cancer management

raise the possibility of increased disease burden and complication, with more patients being diagnosed with late-stage cancer—ultimately making it harder to treat.

Figure 5. Impact of COVID-19 on HCC and the liver¹⁷



This highly dangerous cancer, liver cancer, has demonstrated increasing trends in prevalence, incidence, and mortality rates. It is estimated that the United States will have 42,230 new primary liver cancer cases and 30,230 deaths in 2021.¹⁴ There are many existing factors, such as health literacy, housing, environmental toxins, healthcare professional mistrust, and lack of insurance, that are directly affecting health and perpetuating health disparities. With the current COVID-19 crisis, these gaps are paving the way for poorer health outcomes, and liver cancer could steadily rise to startling proportions. It is crucial to review liver interventions currently deployed, and ensure they are effectively fighting against the rise of liver cancer and cancer disparities.

Call to Action

Co-sponsor the Liver Illness, Visibility, Education and Research Act (*LIVER Act*) 116th Congress: H.R. 5675 and S. 3041

The *LIVER Act* is a public health initiative that will help people of all ages, lifestyles, and ethnic backgrounds reduce their risk for liver cancer and related risk factors like viral hepatitis and NASH. At a high level, it will elevate the federal government's liver cancer research and surveillance initiatives while simultaneously empowering local entities to raise awareness, and prevent this deadly cancer.

The *LIVER Act* will:

- Authorize an additional \$45 million a year for five years for liver cancer and hepatitis B research at the National Institutes of Health (NIH)
- Raise the profile of liver disease at the NIH by adding Liver to the name of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) to make it the National Institute of Diabetes, Digestive, Kidney and Liver Disease
- Elevate the Liver Branch at NIDDK to a Division and require that the new Liver Division report directly to the Institute Director
- Direct the National Cancer Institute (NCI) to issue targeted calls for proposals, including a call for a new liver Specialized Program of Research Excellence for primary liver cancer, and have those proposals reviewed by a new Special Emphasis Panel
- Direct NIH to establish an inter-institute working group to coordinate hepatitis B and liver cancer research.
- Authorize an additional \$90 million a year for five years for prevention and awareness grants at the CDC, including grants for screening, vaccination, and treatment for liver cancer, hepatitis B, hepatitis C, nonalcoholic fatty liver disease, nonalcoholic steatohepatitis, and cirrhosis of the liver.

[Learn about the *LIVER Act*](#)

Other available health policy actions that could protect all people impacted by liver disease:

- Support the **October is Liver Cancer Awareness Month Resolution** to declare October as Liver Cancer Awareness month in order to raise awareness about the risk factors and health disparities connected to this deadly cancer.

October is Liver Cancer
Awareness Month Resolution

- Cosponsor the **Safe Step Act of 2021 (H.R. 2163/S. 464)** to improve step therapy protocols and amend the Employee Retirement Income Security Act (ERISA) to require a group health plan provide an exception process for any medication step therapy protocol to better ensure patients with liver cancer are able to safely and quickly access the best treatment for them.

Safe Step Act of 2021

- Cosponsor the **Seniors Prescription Drug Relief Act (S. 2911)** to strengthen Medicare Part D by making it easier for seniors to afford their medication through establishing a new out-of-pocket cap.

Seniors Prescription Drug
Relief Act

- Become an original cosponsor of the **NASH Care Act (116th Congress: H.R. 8658)**, which would implement the first federal response to survey, prevent, and address another serious chronic liver disease and risk factor of liver cancer, NASH.

NASH Care Act

- Urge the Administration and Congressional Leadership to act on the **Treat and Reduce Obesity Act (TROA) (H.R. 1577/S. 596)** to address a liver cancer risk factor, obesity, in older Americans by enhancing Medicare beneficiaries' access to lifestyle interventions and Food and Drug Administration-approved obesity drugs.

Treat and Reduce
Obesity Act

- Cosponsor the **CONNECT for Health Act (H.R. 2903/S. 1512)** to support the continuation of a number of telehealth flexibilities like eliminating geographic restrictions.

CONNECT for Health Act

Global Call to Action

Sign GLI's **2021 Global Liver Institute Liver Cancer Pledge** to join efforts to double the five-year survival rate by 2030 and create a path to equity in liver cancers around the world. Some actions to take to support the pledge:



- Raise awareness and prevention standards by acknowledging that October is Liver Cancer Awareness Month.
- Join the global powerhouse of supporters for reducing liver cancer by opting into being listed on our map, where patients and survivors can find how to reach your organization for more liver cancer information in their country.
- Sign up for **GLI's Liver Action Network** to get notified about policy initiatives and opportunities to advocate.
- Advocate for adequate awareness, prevention, and management standards for liver cancer across your country, targeting healthcare professionals, patients and families, risk groups, policy-makers and the general public.
- Encourage the adoption of liver cancer screening for patients with underlying risk factors.
- Ensure improved access to better disease management for all patients with liver cancer.
- Reduce existing inequities for patients with liver cancer by targeting under-served communities (e.g., organize culturally-appropriate information sessions and increase access to approved treatment).

Summary

As evidenced by the information in this report, liver cancer is a global public health threat. GLI and our partners are working tirelessly to raise awareness, provide education and support to the liver community, and change policy that ensures liver disease takes its proper place on the global public health agenda consistent with its prevalence and impact.

Visit [GlobalLiver.org](https://www.global-liver.org) for more information and resources about liver health, liver cancer, and our groundbreaking policy work in the liver community.

We deeply appreciate the following sponsors who have contributed so generously to support GLI's 2021 #OctoberIs4Livers program:

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