Liver Cancer: Prevalence, Risk Factors and Strategies for Prevention and Treatment

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Physician Perspective:
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Good morning. My name is Allison Martin, I'm a cancer surgeon at Duke University and the Durham VA Medical Center in Durham, North Carolina. My primary role is to treat patients with liver, pancreas and bile duct cancers. First, I want to thank Representative Kelly for enabling us to be here today to discuss this very important topic and to the American Liver Foundation for inviting me to speak. I'm excited to be here to discuss liver disease prevalence and risk factors with you all.

I was born and raised in Greenville, Kentucky, a town of around 4,300 people located in western KY. If you've ever heard of the Everly Brothers or crooned along with Loretta Lynn to "Coal Miner's Daughter" then you understand a little bit about where I'm from. My dad was indeed a coal miner in his early career. I went to medical school at Vanderbilt and moved to Boston in 2011 for my master's degree—it was the first time I had lived more than a two-hour drive from my family in my adult life and it was the same year my aunt was diagnosed with a devastating and aggressive lung cancer. Her home in rural Kentucky was a long drive to the nearest oncologist. After her initial meeting with a medical team far from home, she elected to forgo chemotherapy and surgery and instead opted for palliative care close to home. Although she died with dignity, I suspect she may have chosen a different course had she had access to specialized doctors closer to home.

In America, no one should be unable to fight for their life because their access to specialized care is out of reach. Your zip code shouldn't be a death sentence. And for many rural Americans it can be. Rural Americans deserve a fighting chance just like their urban peers. You shouldn't need to live in the shadow of a large research hospital or major university to have high quality cancer care.

When I arrived in Durham, North Carolina in 2023 to start my faculty position at Duke and the Durham VA, I was not at all surprised to see that a patient from an affluent neighborhood in Chapel Hill and a patient from Lumberton, located in the coastal plains of North Carolina, were showing up to my clinic with similar cancers but in very different states of readiness to receive treatment for these cancers. According to data from the National Center for Health Statistics in Kentucky, where nearly 42% of the population is rural, a person diagnosed with cancer has a 36 percent higher risk of dying from a cancer-related cause than the same individual diagnosed in a non-rural setting. In both the United States and abroad, the burden of cancer-related morbidity and mortality is disproportionately laid on the shoulders of individuals living in resource-poor and often rural settings. My experiences growing up in a rural community gave me a first-hand view of how community and societal factors interact with the built environment and health systems to produce

health outcomes in far-reaching ways. It's pretty simple, if you are a patient with resources—wealth, family support, a car, health insurance—you are more likely to survive your cancer diagnosis. As health care providers, we treat every patient the same, but there are some patient circumstances that even the best available health care cannot change.

In North Carolina, where I currently work and see patients, the rural cancer burden is especially pronounced. Liver cancer is the 6th leading cause of death in North Carolina and the 13th most common type of cancer overall in the U.S., which translates to more than 40,000 Americans diagnosed with *new cases* of liver cancer annually. But where does liver cancer come from and who does it affect? Liver cancer begins as an excessive proliferation of tumor cells that eventually take over a portion of the liver's healthy cells to form a mass, a cancer. Though there are a multiple types of liver cancer, the most common primary liver cancer is hepatocellular carcinoma, which most commonly affects men in the U.S. at twice the rate of females. Sadly, liver cancer is considered to have one of the worst survival rates, with an average five-year survival rate of approximately 22%.

Liver cancer is often associated with a number of risk factors that increase the likelihood of its development, these include, but are not limited to, chronic hepatitis such as hepatitis B and C, alcohol-associated liver disease, metabolic dysfunction-associated steatotic liver disease (formerly nonalcoholic fatty liver disease), some rare liver diseases, obesity, and type II diabetes, among others.

There are several ways that we can link the experience of living in a rural area with higher rates of liver cancer. While there are many risk factors for liver cancer, patient-level barriers that many individuals face—limited health insurance, geographic access, and transportation—may be the most challenging. These factors are used by epidemiologists to calculate measures of inequality that define where a patient lives. We call these measures social vulnerability. How vulnerable is a patient to their physical or built environment and how does this affect their health outcomes, how long they live? These are factors largely beyond their control, such as the hospitals and doctors located nearby. Patients with high social vulnerability experience higher liver cancer-related death compared to patients with low social vulnerability. Yet, limited research exists on clinician- and center-level factors contributing to worse outcomes for rural patients. For example, rural patients with primary liver cancer face substantial challenges, being 10% more likely to be diagnosed at an advanced stage and 5% more likely to die from the disease compared to urban patients.

Additionally, rates of liver cancer are higher in Southwestern and Southeastern areas of the US, which have the highest populations of Black and Hispanic populations. As I said before, up to 25% of rural cancer patients are racial/ethnic minorities. On the other side of these statistics are the real-world results which tell us that Black and Hispanic patients who are diagnosed with liver cancers have worse outcomes compared to their white counterparts. These relationships with poor outcomes are persistent even when you control for all the other possible risks factors that make a person more likely to be diagnosed with a liver cancer. Beyond social circumstances, like personal finances or access to healthy foods, rural patients, particularly Black and Hispanic rural patients, are less likely to have easy access to specialist physicians who can manage and treat chronic liver disease and risks factors, like obesity and type 2 diabetes, which we strongly associated with higher risks of liver cancers. I see this in my practice over and over again. Patients who would otherwise be eligible for life-saving treatments, but who are so sick with diseases OTHER than cancer, they are no longer able to have their cancer treated. They are too sick at baseline for surgery, chemotherapy, or radiation. We have a responsibility to help these patients help themselves through policy shifts that support the most vulnerable patients at-risk for liver disease.

Rural communities are underserved by cancer clinicians and have a disproportionate share of socially vulnerable patients. Clinicians practicing specialized medicine are rare in rural communities; a recent survey found that only about 3% of 11,664 oncologists surveyed practiced in rural areas. These numbers tell a stark story about why the combination of social circumstances, racial and ethnic biologic differences (which are vastly under researched), gender (male), and access to primary care and specialists physicians come together to define the current experience of being poor, rural and at risk for liver cancer. I came here today to advocate for improved resources for diagnosis, treatment, prevention and research funding that will help us improve outcomes for patients with liver cancer. Specifically, as the American Liver Foundation is prioritizing the Treat and Reduce Obesity Act and the HELP Copays Act, amongst others for the 119th Congress, these are policy changes that could specifically impact the health and wellbeing of patients at risk for liver cancer, particularly rural patients for the reasons I have outlined today. I speak about rural patients the most because they are the most at risk with current budgetary shortages at both the state and federal levels. These are patients who my colleagues and I see and treat every day and I hope we can draw greater attention to the daily lived experiences that make them more likely to be diagnosed with and die from liver disease and liver cancer.