

People With Hepatitis C Still Have Higher Mortality After Being Cured

Drug-related mortality, including overdose, was the leading cause of death.

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Despite successful treatment with direct-acting antiviral therapy, people with hepatitis C still have a substantially greater risk of death compared with the general population, according to study results [published in the British Medical Journal \(BMJ\)](#). Nearly one quarter died of overdoses and other drug-related causes, followed by liver failure and liver cancer.

“Our research shows that cured patients continue to face very high mortality rates after achieving a hepatitis C cure, driven by liver and drug-related causes. While antiviral therapies are crucial, it is clear they are not a panacea,” study principal investigator Hamish Innes, a senior research fellow at Glasgow Caledonian University, [said in a news release](#). “Hepatitis C treatment is an opportune time to address competing health problems, including alcohol and drug use, and to establish lifesaving screening for liver cancer. We should be doing much more to support patients after [a] cure. Otherwise, when we look back in years to come, we may see hepatitis C elimination not only as a great achievement but as a great missed opportunity too.”

Over years or decades, [chronic hepatitis C virus \(HCV\)](#) infection can lead to serious complications, including liver cirrhosis, hepatocellular carcinoma (the most common types of primary [liver cancer](#)) and liver failure.

[Direct-acting antivirals](#) (DAAs) can cure more than 95% of treated patients. Successful treatment can halt liver disease progression, and prior studies have shown that people who are cured have better health outcomes and decreased all-cause mortality. However, those who already have advanced liver disease when treated remain at risk for complications and death, underscoring the need for universal testing and prompt treatment.

“The high number of liver cancer deaths found in this study highlights the importance of diagnosing hepatitis C as early as possible to treat the virus before it causes irreversible damage to the liver,” Rachel Halford, CEO of The Hepatitis C Trust, said in the news release.

Innes and colleagues analyzed mortality rates for people successfully treated for hepatitis C in the modern treatment era. The first contemporary DAA regimens became available in 2014, replacing

interferon-based therapy, which was less effective, took much longer and could cause severe side effects.

The analysis included 21,790 people in England, Scotland and British Columbia, Canada, who were treated with DAAs from 2014 to 2019 and achieved a sustained virological response, which is considered a cure. About 70% were men. The mean age of people without cirrhosis was 44 in Scotland and 56 in British Columbia; people with cirrhosis were somewhat older.

The participants were divided into three liver disease severity groups: people without cirrhosis; those with compensated cirrhosis before treatment (the liver is damaged but can still carry out its vital functions); and those with end-stage liver disease, defined as decompensation or liver cancer. A majority of participants (74% in Scotland and 84% in British Columbia) did not have cirrhosis. The cohort from England, which included only people with cirrhosis, made up 10% of the total study population.

Follow-up started 12 weeks after treatment completion and ended on the date of death or at the end of 2019. A total of 1,572 participants (7%) died during follow-up. All-cause mortality rates, expressed as deaths per 1,000 person-years, were 22.7 for the Scotland cohort, 31.4 for the British Columbia cohort and 39.6 for the England cohort.

Overall, the leading causes of death were drug-related mortality, including overdoses (24%), liver failure (18%) and liver cancer (16%). Drug-related causes predominated among people without cirrhosis, but liver failure and liver cancer were the main causes among those with cirrhosis or end-stage liver disease.

After adjusting for age, all-cause mortality among people cured of hepatitis C was “considerably higher” than the rate for the general population across all disease severity groups and settings, the study authors reported. For example, in British Columbia, all-cause mortality was 3 times higher for people without cirrhosis and nearly 14 times higher for people with end-stage liver disease. In Scotland, the death rate was 4.5 times higher, and in England it was 5 times higher.

Older age, recent substance use or alcohol use disorder (based on hospitalization) and coexisting health conditions were associated with higher mortality rates. The excess risk of death among people cured of hepatitis C remained elevated even after adjusting for “area-based deprivation” (socioeconomic status), so the high mortality rates “cannot be explained by generic health inequalities,” according to the researchers. They noted that [a previous study](#) found that half the excess mortality among people with chronic hepatitis C in the United States could be attributed to health risk behaviors.

“Mortality rates among people successfully treated for hepatitis C in the era of interferon-free direct-acting antivirals are high compared with the general population. Drug- and liver-related causes of death were the main drivers of excess mortality,” the study authors concluded. “These findings highlight the need for continued support and follow-up after successful treatment for hepatitis C to maximize the impact of direct-acting antivirals.”

“Our findings bring into focus the importance of establishing robust care and harm reduction pathways after successful HCV treatment. As we move towards HCV elimination, treatment programs must strike the right balance between treating HCV and treating the patient,” they wrote. “[O]ur data suggest patients need more support to reduce drug and alcohol misuse after [an] HCV cure. Combining HCV treatment with wider intervention and wraparound services should be considered, especially because there is evidence that successful HCV treatment could be used as an opportunity to encourage changes in behavior....Population-level action—for example, prescribed safer supply of drugs and drug decriminalization policies recently implemented in British Columbia—will also be crucial to improve mortality in people successfully treated for HCV.”

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