New Reviews Support Broader Hepatitis B Treatment Criteria

Two large meta-analyses show that higher HBV DNA and ALT levels sharply raise liver cancer risk, identifying people who may benefit most from antiviral therapy.

June 12, 2026 By Sukanya Charuchandra

Two large meta-analyses published in The Lancet Gastroenterology & Hepatology offer new clarity on which people with hepatitis B are most at risk for liver complications. One analysis found that higher hepatitis B virus (HBV) viral load and elevated liver enzymes were strongly associated with worse outcomes, while the other found that antiviral therapy provided the greatest benefit for higher-risk groups.

Over time, chronic hepatitis B can lead to serious complications, including cirrhosis, liver cancer and the need for a liver transplant. Antiviral medications, such as tenofovir (Viread or Vemlidy) and entecavir (Baraclude), can suppress HBV replication indefinitely, but they seldom lead to a cure.

The 2015 World Health Organization (WHO) guidelines for chronic hepatitis B recommended antiviral treatment for people with cirrhosis, as well as those without cirrhosis who have persistently high levels of the liver enzyme alanine aminotransferase (ALT) and high viral load (HBV DNA above 20,000 IU/mL). Treatment was held off for patients with consistently normal liver enzymes and low viral levels (HBV DNA below 2,000 IU/mL). Yusuke Shimakawa, MD, of the Institut Pasteur in Paris, and colleagues conducted two systematic reviews and meta-analyses to help shape the updated 2024 WHO guidelines and determine whether to broaden criteria for treatment.

In the first analysis, the researchers assessed the incidence of clinical outcomes among untreated adults with chronic hepatitis B without cirrhosis. The second analysis examined the impact of antiviral therapy in a similar population. The team searched PubMed, Embase, Web of Science and the Cochrane Library for relevant studies published between January 2000 and February 2023 and went through reference lists to identify older trials. For both meta-analyses, the researchers selected studies in which HBV DNA and ALT measurements were available and used them to stratify outcomes.

Higher HBV DNA levels were clearly linked to worse outcomes. The higher the viral load, the greater the risk of cirrhosis, liver cancer and liver-related death. For example, liver cancer rates were nearly eight times higher among those with a viral load of 200,000 IU/mL or higher compared

to those with levels below 200 IU/mL. The same pattern held for cirrhosis and liver-related mortality, though no such relationship was found for overall mortality or liver decompensation.

Elevated ALT levels also had an independent effect. Levels 1.0 to 1.9 times the upper limit of normal (ULN) were associated with two- to threefold higher liver cancer rates across the different viral load groups. Importantly, people with persistently low viral load or persistently normal ALT across multiple tests fared slightly better than those assessed only once, suggesting that single measurements may overestimate risk. Overall, HBV DNA and ALT levels together provide a more complete picture of a patient's risk than either measure alone.

The second analysis showed that antiviral treatment offered clear benefits for hepatitis B patients with a high viral load (HBV DNA 20,000 IU/mL or higher) or elevated ALT, reducing liver cancer risk and improving multiple markers including liver scarring, inflammation and viral suppression. In practical terms, only 15 patients with a high viral load would need to be treated to prevent one case of liver cancer, compared to 149 patients with a low viral load.

However, for people with lower viral load (HBV DNA below 20,000 IU/mL), the evidence is far less clear. Antiviral therapy showed no statistically significant reduction in liver cancer risk in these groups, with limited data on other outcomes.

"These findings, alongside the linked systematic review and meta-analysis of antiviral treatment efficacy, supported the 2024 WHO guidelines expansion of treatment criteria to include individuals with HBV DNA concentrations >2000 IU/mL and ALT concentrations above the ULN," wrote the researchers. "For those with HBV DNA concentrations <2000 IU/mL and persistently normal ALT concentrations, treatment can be deferred."

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